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SUBJECTS

- Ovarian Rejuvenation
- Cell therapy in infertility
- Immunology & Psychology aspects of Infertility
- Novel sperm selection for ICSI
- Male & Female biomarkers for gamete morphology
- Ethical issues of infertility treatment
- Oxidative and reductive stress in infertility
- Timelapse in embryology

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Conservative Management of Endometrioma

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Abstract

Endometriosis is a common disease during fertility and affects about 10% of women. Endometriosis is defined as the existence of endometrial tissue outside the uterine cavity. Common clinical signs of endometriosis include dysmenorrhea, pelvic pain, and infertility. Heterogeneity is seen in clinical and anatomical manifestations of endometriosis. Among the various phenotypes of endometriosis, ovarian endometrioma has the greatest challenge in managing the treatment of infertility. The main surgical procedure for the treatment of endometrioma is laparoscopic cystectomy, although this procedure reduces ovarian reserve and has potentially negative effects on assisted reproduction technologies results. For this reason, in the treatment of endometrioma, there is a tendency to use less invasive methods. Drug therapy is used extensively in the management of endometrioma. A variety of progesterone compounds, oral contraceptive pills, and gonadotropin-releasing hormone agonists or antagonists are used for this purpose. Some studies reported aromatase inhibitors as an effective treatment for endometrioma. These drugs have been shown to be effective in relieving pain, reducing the size of endometrioma, and reducing recurrence after surgery. However, in these cases, the risk of recurrence of the disease after drug discontinuation is high. On the other hand, many studies conducted on the effect of sclerotherapy on the treatment of endometrioma. Sclerotherapy is performed under the guidance of vaginal ultrasound and ethanol is injected into the endometrioma after cyst aspiration. We evaluated two methods of sclerotherapy including ethanol washing and ethanol retention. The results showed that the recurrence rate after sclerotherapy using the ethanol retention method was lower than the ethanol washing method.

Keywords • Endometriosis • Sclerotherapy • Infertility

The Success of Various Endometrioma Treatments in Infertility: A Systematic Review and Meta-Analysis

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Abstract

Background: Endometriosis is seen in 0.5-5% of fertile and 25-40% of infertile women. Removing ovarian endometriomas is a matter of conflict before making any decision about pregnancy in infertile women between gynecologists. This systematic review and meta-analysis aimed to compare the effect of various endometrioma treatments on infertile women's pregnancy rate.

Methods: This review was conducted according to the PRISMA recommendations. An electronic search using PubMed, Scopus, Google Scholar, etc, from 2000 to 2018, in the English language, was conducted. Studies compare pregnancy rates based on four different treatment types of OMAs between infertile women: (surgery+assisted reproduction technologies (ART), surgery+spontaneous pregnancy, aspiration±sclerotherapy+ART, and ART alone) were included.

Results: At least eight prospective studies were included, in which 553 infertile women were compared in terms of treatment methods of OMAs before trying to become pregnant.

Conclusion: Treatment methods are usually chosen with the purpose of relieving pain, improving fertility, or both, based on the patient's clinical and individual condition. No significant differences between these four groups of the study were found; however, surgical procedures are more successful compared to other methods and the ART alone was the least successful of all.

Keywords • Endometriosis • Female • Infertility • Pregnancy rate • Reproduction

Cell Therapy Accompanied by Natural Biomaterials, A Novel Therapeutic Strategy for Primary Ovarian Insufficiency Treatment

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Abstract

Primary Ovarian Insufficiency (POI) is a complicated gynecological condition in more than 1% of women at age 35-45 years old. The disease causes follicle depletion and ovarian function cessation consequently, results in infertility. Besides, POI makes patients prone to cardiovascular diseases, sexual dysfunction, and osteoporosis. Hormone replacement therapy is the first-line therapeutic option for this disease. However, it is impotent to restore ovarian secretion and ovulation. In recent years, stem cell therapy has been proposed for the treatment of POI. In this review, we recapitulate the experimental findings of the application of cell therapy accompanied by natural biomaterials for treating POI. In summary, natural biomaterials including extracellular matrix (ECM), hyaluronic acid (HA), collagen, alginate, and fibrin have been combined with stem cells to treat POI. These biomaterials provide efficient mechanical support, restore ovarian function, and improve follicle growth. A xenogenic porcine decellularized scaffold containing ECM and rat ovarian cells was non-cytotoxic and showed only a minimal immunogenic response in the rat model. Moreover, the ECM-based scaffold supported penetration of rat granulosa cells, improved secretion of estradiol hormone, and delivered embryonic stem cell-derived mesenchymal progenitor cells using HA-based hydrogel to a mice model of POI. Transplantation of umbilical cord-derived mesenchymal stem cells on a collagen scaffold promoted ovarian function in both POI human patients and mice models. Encapsulation of human amniotic epithelial cells in a sodium alginate-bioglass composite hydrogel restored follicle development, repaired granulosa cell function, and enhanced ovarian angiogenesis in POI mice. Altogether, the combination of cell therapy with natural biomaterials has promising potential to treat premature ovarian insufficiency.

Keywords • Primary ovarian Insufficiency • Cell- and Tissue-based therapy • Transplants • Biocompatible materials

Isthmocele or Uterine Niche

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Abstract

Uterine niche is an iatrogenic pouchlike defect at the site of a previous caesarean scar due to defective tissue healing. Uterine niche occurs in 24-84% of women with previous caesarean of whom 30% are symptomatic. There are several symptoms for uterine niches including abnormal uterine bleeding, pain (such as dysmenorrhea), infertility, etc. However, during an ultrasound examination, isthmocele is found incidentally, because most of the women with isthmocele, remain asymptomatic. Potential risk factors for increasing the probability of isthmocele are including cervical dilation of >5 cm, >5 hour duration of labour, level of uterine incision, uterine closure techniques, adhesions, Retroflexed uterus, and patients' factors. Visualizing the niche using the hysteroscopy technique is the gold standard method to diagnose the isthmocele. Moreover, different techniques such as transvaginal ultrasound (TVUS), saline infusion sonohysterogram (SHG), 3D ultrasound, and magnetic resonance imaging (MRI) can be used. Several methods can be used to treat or manage isthmocele such as medical therapy, uterine sparing surgical treatment with hysteroscopy, and surgical repair including laparoscopy, laparotomy, and vaginal repair.

Keywords • Cesarean section • Pregnancy • Infertility

Ovarian Hyperstimulation Syndrome: A New Look at an Old Problem

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Abstract

Infertility affects approximately 12.1% of all women. Assisted reproductive technology is increasing and considered a safe procedure for women at risk of developing ovarian hyperstimulation syndrome (OHSS), but an important iatrogenic complication caused by an excessive response to controlled ovarian stimulation, with significant morbidity and mortality is expected. The pathogenesis of OHSS is complex and many of its aspects have not yet been elucidated. OHSS is considered a systemic aseptic of the inflammatory response of the vascular endothelium associated with high plasma concentrations of sex steroids (e.g. FSH), or human chorionic gonadotropin, accompanied by generalized endothelial damage and pronounced vascular permeability, leading to hypovolemia and hemoconcentration, large protein losses, thromboembolic events, Polyserositis, impaired renal perfusion, oliguria, abnormal liver function, Acute respiratory distress syndrome, and in severe cases multiple organ failure. Intense ascites with intra-abdominal hypertension (IAH) are the main factor for unfavorable outcomes in OHSS patients. A comparison of pathophysiology and clinical images indicates that symptoms of severe OHSS associated with organ dysfunction are almost identical to IAH syndrome. Therefore, the therapeutic principles should be consistent with the principles of therapy for IAH. The therapeutic course of OHSS remains insufficiently clarified, which needs further research and investigation.

Keywords • Ovarian hyperstimulation syndrome • Intra-abdominal hypertension • Infertility

Role of Doppler ultrasonography and 3D Ultrasound in Female Infertility

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Abstract

Medical ultrasound has made significant advancements in reproductive medicine, especially in infertility of female causes. It is a useful and very important tool in the diagnosis and management of various disorders. Transvaginal ultrasound, in particular, plays a vital role in infertility diagnosis, treatment, and follow-up, as it allows for the evaluation of normal and stimulated ovarian cycles, aspiration of follicles, and subsequent transfer of embryos. Color Doppler ultrasonography is emerging as a valuable diagnostic imaging modality in the field of medicine, primarily infertility, and is a high-throughput, sophisticated imaging technique for the assessment of uterine anomalies, intrauterine pathology, tubal patency, polycystic ovaries, ovarian follicular monitoring, endometrial receptivity, failed or an ectopic pregnancy, uterine, endometrial and ovarian vascularity. Assessments of the utero-ovarian pulsatility indices, resistance indices, and endometrial color signals are important determinants of *in vitro* fertilization cycles and pregnancy rates. Three dimensions (3D) ultrasound is a new imaging modality that is being introduced into clinical practice. With 3D ultrasound, a volume of a region of interest can be acquired and stored. 3D of the uterus is useful for mapping uterine fibroids and differentiation of adenomyosis of the uterus from fibroids and uterine Mullerian anomalies. Power Doppler ultrasound, in combination with 3D ultrasound, allows a whole assessment of relevant vessels and a quantitative assessment of vessel density and perfusion within a specified area for endometrial receptivity.

Keywords • Diagnostic imaging • Ultrasonography, dopplercolor • Fertilization *in vitro*

Clinical outcome of Artificial Oocyte Activation Following Intracytoplasmic Sperm Injection

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Abstract

The intracytoplasmic sperm injection (ICSI) is capable of improving male factor infertility significantly, but failed fertilization following ICSI still occurs in 1-5%, and about 40-70% of oocyte activation failure after ICSI, is associated with sperm factors. Artificial oocyte activation (AOA) is a procedure applied in couples with failed fertilization by using Ca²⁺-ionophores for the activation of oocytes. The literature background has demonstrated that the rate of fertilization increased from 25% to 48% after ICSI-AOA. Regarding the use of this technique to treat infertility, previous studies have shown the mean of the gestational week, birth weight, preterm birth rate, rate of birth defects, or gender ratio was similar between infertile couples treated with conventional ICSI and ICSI-AOA. While some publications have reported an increase in birth defects after ICSI-AOA. Due to the warnings and the unfamiliar safety problems, AOA is not considered a routine method and is only used for couples with low or zero fertilization in the previous cycles or couples with poor sperm quality such as globozoospermia and severe teratozoospermia. Therefore, in this review, the mechanism of oocyte activation, the main sperm factors involved in oocyte activation, and the latest therapeutic achievements of using ICSI-AOA will be discussed.

Keywords • Sperm injections, intracytoplasmic • Male • Fertilization

The Research Priorities in Infertility

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Abstract

The first test-tube baby born in 1978, is almost 44 years old now. Despite the dramatic advances in the field of *in vitro* fertilization (IVF), still, poor outcomes are challenging. The average live birth rate per embryo transfer is 37.8% in the United States. This poor outcome is the consequence of the knowledge gap in many aspects of infertility. Regarding our limited resources, what are the research priorities in infertility? By launching the top 10 infertility research priorities in 2020, the Human Fertilisation and Embryology Authority (HFEA), classified the research priorities into four categories including male infertility; female and unexplained infertility; medically assisted reproduction technologies (ART); ethics, access, and organization of care. Here I would like to add the following topics: Infertility prevalence and worldwide statistics by age, sex, race, and ethnicity; Using bioinformatics, gene expression, epigenetics, immunotherapy, transgenic/knockout models, and translational models; Using artificial intelligence and data science, new drug development, lipidomics, and proteomics; Evaluation of complementary medicine, psychotherapy, acupuncture, etc. For male infertility, major topics are the usefulness of sperm tests, environmental factors, modifiable risk factors, treatable co-morbidities, and the effectiveness of nutraceuticals. For female infertility, major topics are preventing age-related infertility, finding the best treatment strategies, the causes of unexplained infertility, the impact of uterine fibroids, and management of endometrial polyps and uterine septum. For ART major topics are the causes of implantation failure, the treatment of poor responders, the method of sperm/embryo selection, the usefulness of Intrauterine insemination and the optimal cycles to be done before shifting to IVF, emotional and psychological impact on the children born using donor gametes, and repeated implantation failures. For ethics major topics are public health interventions to prevent infertility, reducing the costs, providing accessibility/informational needs, regulations for social egg freezing, and long-term maternal and offspring outcomes after infertility treatments.

Keywords • Research priorities • Infertility, male • Infertility, female • Fertility preservation

How Old Is Too Old for Infertility Treatment?

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Abstract

The reproductive success of humans is highly dependent upon the age at which women attempt to conceive, which is progressively increasing worldwide. Fertility decreases as the woman ages, while the incidence of miscarriage and the prevalence of vital chromosomal abnormalities follow an opposite trend. The molecular and biochemical mechanisms involved in age-related infertility and their impact on oocyte and embryo quality remain to be clearly elucidated. Until now, several dysfunctions showed an association with impaired fertility in aged women. Together with a progressive reduction of the ovarian reserve, woman aging involves a compromised competence of the oocytes/embryos, because of defective physiological pathways, such as energy production and balance, metabolism, epigenetic regulation, cell cycle checkpoints, and increased meiotic missegregation. In *in vitro* fertilization (IVF), maternal age is among the strongest predictors of success. Specifically, advanced maternal age (AMA; defined as ≥ 35 years old) shows just a negligible impact on fertilization rate and a mild impact on embryo development to the blastocyst stage, but results in a dramatic impact on blastocyst aneuploidy rate. Evidence-based data should always guide the counseling and the patients should be scrupulously informed about their estimated chance to conceive, especially if they are older than 35 years old. Indeed, 35 years old should be the lowest age threshold to define AMA and 45 years old should be considered the highest age threshold to undergo IVF with their own eggs, at least according to the latest published report.

Keywords • Maternal age • Fertilization *in vitro* • Aging

The Role of Sexual Dysfunction in Men's Health

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Abstract

Male sexual dysfunction (MSD) generally includes an alteration in at least one of the basic sexual functions (desire, erection, orgasm, and ejaculation). The most common MSD-related complaints are erectile dysfunction (ED), hypoactive sexual desire disorder (HSDD), anorgasmia or difficulties in achieving orgasm, premature or delayed ejaculation, pain during sexual activities, and dissatisfaction with sexual life. As the most thoroughly studied sexual dysfunction in the context of epidemiologic research, ED is estimated to carry an overall adult male (older than 20 years old) prevalence rate of 10% to 20% worldwide, with the majority of studies reporting a rate closer to 20%. Sexual dysfunction affects all aspects of people's lives include: mental health (depression, anxiety), physical health, social problems, and family relationship (divorce, marital dissatisfaction). Therefore, to reduce the effects of sexual dysfunction on men's health and improve their quality of sexual life, actions have been taken in the health system. Current actions and interventions in the field of sexual health in the country are as follows: The National Men's Health document design of the Iranian men's basic health service package, holding various conferences, designing sexual health documents, and setting up sexual health clinics. Since sexual health is one of the most important aspects of reproductive rights, it should be considered in the macro policies of the country by health policymakers, medical societies, and experts.

Keywords • Erectile dysfunction • Sexual health • Male

Recombinant Follicle-Stimulating Hormone in Treatment of Sperm DNA Fragmentation

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Abstract

Sperm DNA abnormalities have significant and detrimental effects on sperm function and infertility. Sperm DNA integrity is often compromised in infertile men and sperm DNA fragmentation (sDF) represents the most common DNA abnormality. It is demonstrated that many types of insults provoke DNA breaks. They act through two main pathways: an apoptotic process, and a direct attack on DNA by free radicals. Possible therapies to prevent or decrease sDF are antioxidants and anti-apoptotic agents. Anti-apoptotic agents cannot be used because of the ubiquitous role of the apoptotic process in the body. Follicle-stimulating hormone (FSH) represents a notable exception. It regulates testis development and function and exerts anti-apoptotic actions on germ cells. The most probable mechanisms of action of FSH consist of anti-apoptotic and maturation-promoting effects at the tubular level. Few recent studies revealed a slight but significant decrease of sDF after FSH treatment for 3 months but not of other semen parameters. Although there is evidence for a beneficial effect of the hormone on sDF, further studies with clear and univocal patient inclusion criteria, including sDF cut-off levels for patients' selection are warranted to draw firm conclusions.

Keywords • DNA fragmentation • Spermatozoa • DNA • Follicle stimulating hormone

The Effect of Zinc on Tetrahydrocannabinol-Induced Sertoli Cells Apoptosis

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Abstract

Background: Consumption of exocannabinoids, such as Tetrahydrocannabinol (THC), affects spermatogenesis and induces the early apoptosis of sperm cells. Previous studies demonstrated the protective effects of zinc against toxicity induced by many drugs by regulating the apoptotic signaling pathway in different sexual organs. However, little is known about the effects of THC on Sertoli cells and the effects of zinc on THC-induced testicular injury. This study, therefore, aimed to investigate the effect of THC on apoptosis in Sertoli cells pretreated with zinc.

Methods: The mouse Sertoli cells (TM4) were cultured in the DMEM/F-12 medium. Then, TM4 cells were seeded in 96-well culture plates. The experimental groups were divided into THC (470 μ M), zinc (8 μ M), pretreatment (cells were pretreated with zinc before THC exposure), and control (untreated) groups. Cultured TM4 cells were exposed to the mentioned drugs, for 24 hours and then the number of apoptotic cells was assessed using the TUNEL staining method.

Results: Significant changes in the number of apoptotic and TUNEL-positive cells in the experimental groups ($P < 0.001$) were seen. The mean number of TUNEL-positive cells significantly increased from 20.18 ± 0.34 in the control group to 26.81 ± 0.88 in the THC group ($P < 0.001$). Moreover, the mean number of TUNEL-positive cells significantly decreased from 20.18 ± 0.34 in the control group to 15.87 ± 1.23 in the zinc group and from 26.81 ± 0.88 in the THC group to 18.56 ± 0.62 in the pretreatment group.

Conclusion: Evaluation of apoptosis via the TUNEL staining method demonstrated that THC decreases cell survival and exhibits a pro-apoptotic effect on isolated TM4 Sertoli cells. Zinc inhibits THC-induced apoptosis in Sertoli cells. Suppression of spontaneously or pathologically induced apoptosis of Sertoli cells by zinc indicates the medicinal effects of zinc on infertility associated with Exocannabinoids abuse in men. However, more studies are needed to clarify these findings.

Keywords • Apoptosis • Sertoli cells • Tetrahydrocannabinol • Zinc

Detection of SARS-CoV-2 in Follicular and Endocervical Fluid of *in Vitro* Fertilization Candidates with Positive Polymerase Chain Reaction Tests

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic was a unique global challenge with a wide range of severity extending from an asymptomatic form to a serious intense respiratory syndrome. This study aimed to detect SARS-CoV-2 in the follicular and endocervical fluid of *in vitro* fertilization (IVF) candidate patients with a positive polymerase chain reaction (PCR) test for SARS-CoV-2.

Methods: All participants and their partners, who were a candidate to start assisted reproductive technology (ART) from April 2020 to October 2020, completed a triage questionnaire two weeks before starting the ART cycle. According to Avicenna center protocol, a diagnostic test for COVID-19 using real-time PCR of nasopharyngeal swabs was performed on all ART candidates, 48 hours before the day of the oocyte trigger. In the operating room, sterile swabs were used to provide cervicovaginal specimens to determine SARS-CoV-2 in cervicovaginal fluid. Moreover, the first aspirated follicular fluid was referred to the lab to assess the presence of SARS-CoV-2.

Results: A positive PCR test for SARS-CoV-2 was verified in 32 participants. In this study, virus particles were not detected in the follicular and endocervical fluid of the women with positive PCR tests.

Conclusion: We are still at the beginning of the road and need reliable data on the safety of ART at the time of the pandemic. The risk of infection during all processes of ART including oocyte retrieval needs attention. The fluid from mature follicles is a potential site to be infected and the human cumulus cells could not be a deterrent factor to the entrance of the virus in the oocyte. This process may lead to gametes infection. We did not detect virus RNA in the follicular and endocervical fluid of the patients with a positive PCR test. Although, more studies with a larger sample size are mandatory in this field.

Keywords • COVID-19 • Real-time polymerase chain reaction • Pandemics • Infertility • SARS-CoV-2

The Role of Granulocyte Colony Stimulating Factor in Improvement of Implantation in Intrauterine insemination: A Randomized Control Study

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Abstract

Background: Subfertility is an issue of concern among couples. By increasing the implantation rate in *in vitro* fertilization (IVF) patients, the granulocyte colony-stimulating factor (GCSF) has been introduced as an immunomodulatory agent, aiming to improve the success rate of artificial reproductive techniques. Since intrauterine insemination (IUI) is a more reasonable non-invasive procedure compared to IVF, this study aimed to evaluate the possible effect of GCSF administration on the IUI success rate in order to decrease the need for IVF due to IUI failure.

Methods: In this double-blind, randomized control trial, 320 eligible patients who were referred to the referral infertility clinic of Shiraz University of Medical Sciences from February 2018 till the end of 2019, were enrolled. They were divided into two groups randomly. After collecting the demographic data, all patients received clomiphene citrate from the 5th day of the menstruation cycle for 5 days. 50-150 units of the recombinant purified follicle-stimulating hormone were started from the 8th day of the cycle. Follicle monitoring was done by transvaginal ultrasound till a mature follicle of 18 mm or more was developed. Human chorionic gonadotropin (HCG) injection was done in both groups with intrauterine administration of 300 µg GCSF in the case group and normal saline in the control group simultaneously. After 36 hours, IUI was performed. The clinical pregnancy, miscarriage, and ongoing pregnancy rates of both groups were measured.

Results: The present study showed improvement in clinical pregnancy rate (15.38% vs. 13.81%, OR=1.17 [0.62-2.21]), miscarriage rate (3.84% vs. 5.26%, OR=0.74 [0.25-2.20]) and ongoing pregnancy rate (11.53% vs. 8.55%, OR=1.37 [0.65-2.92]) in the GCSF group compared to the control group. However, these results were not statistically significant ($P>0.05$).

Conclusion: Although the results did not show any statistically significant differences, 300 µg intrauterine GCSF administration simultaneously with HCG injection in the standard IUI procedure, might increase the pregnancy outcomes. Further studies are needed.

Keywords • Embryo implantation • Granulocyte colony-stimulating factor • Insemination, artificial • Pregnancy rate

Prolonged Semen Incubation Alters the Biological Characteristics of Human Spermatozoa

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Abstract

Background: Semen incubation is a routine and crucial procedure in andrology laboratories. Therefore, paying attention to the incubation time in order to reduce possible damage to sperm parameters and other specific factors is noteworthy. The objective of this study was to assess the biological characteristics of human spermatozoa at different time intervals (0, 1, 1.5, and 2 hours) after incubation at 37 °C.

Methods: 25 raw normozoospermic semen samples were incubated at 37 °C. Incubation was performed in four-time intervals of 0 (after liquefaction), 1, 1.5, and 2 hours. Samples were evaluated for sperm parameters at each time interval. Sperm motility was reported as a percentage of non-motile, non-progressive, and progressive motility. Sperm viability and morphology were assessed using Eosin-Nigrosin and Diff-Quik staining, respectively. Reactive oxygen species production, sperm mitochondria, chromatin, and acrosome reaction were also assessed. DNA fragmentation rate was evaluated according to halo formation around the sperm head.

Results: The rate of progressive sperm motility decreased at 1.5 hours compared to 0 hour as well as 2 hours compared to the 1 hour and 0 hour. No significant changes were observed in sperm viability at any time intervals. Abnormal sperm morphology increased at 1.5 hours of incubation time. No significant changes were observed in DNA fragmentation at 1 hour compared to 0 hour, and 1.5 hours compared to 1 hour. However, a significant increase in DNA fragmentation was observed at 1.5 hours compared to 0 hour. Mitochondria membrane potential was decreased remarkably after 1 hour of incubation time. No significant differences were observed in acrosome reaction at 0, 1, 1.5, and 2 hours as well as malondialdehyde levels.

Conclusion: The normozoospermic samples incubation before using in assisted reproductive technology process should be less than 1.5 hours to minimize the destructive effects of prolonged incubation time on general and specific sperm parameters. It is, therefore, recommended to perform sperm processing within the time frame of 1 hour of incubation.

Keywords • Spermatozoa • DNA fragmentation • Acrosome reaction • Mitochondria • Membrane potentials

Correlation between Antral Follicle Diameters and Follicular Output Rate in Women under Controlled Ovarian Hyperstimulation for Assisted Reproductive Techniques

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Abstract

Background: Traditionally, the number of retrieved oocytes, is the main result of the ovarian response to gonadotropin stimulation. The diameter of antral follicles may be also important along with the number of antral follicles. The Follicular Output Rate (FORT) evaluates the ratio of FSH-responsive follicles. This ratio is known to be associated with *in vitro* fertilization (IVF) outcomes. This study determined the relationship between antral follicle diameters and ovarian response by FORT proportion in women undergoing IVF/intracytoplasmic sperm injection.

Methods: In this study, 100 women going through controlled ovarian hyperstimulation (COH) were selected. By using double-layered transvaginal ultrasound on days 1-3 of the cycle, the number of antral follicles (3-10 mm in diameter) was determined. Then, on the Human chorionic gonadotropin triggering day, the number of the follicles (16-22 mm in diameter) and the FORT was calculated. The correlation between FORT and age, antral follicle count (AFC), $AFC \leq 5$, $AFC > 5$, number of preovulatory follicles (16-20 mm in diameter), number of metaphase II (MII) oocytes, body mass index, infertility period, and anti-mullerian hormone (AMH) was evaluated.

Results: There were significant correlations between FORT and overall AFC, $AFC > 5$, number of preovulatory follicles (16-20 mm in diameter), and number of MII retrieved oocytes. Multiple linear regression analysis showed that there were no significant relationships between FORT and AMH and $AFC > 5$. There were significant correlations between MII retrieved oocytes and age, total AFC, $AFC \leq 5$, $AFC > 5$, number of preovulatory follicles (16-20 mm in diameter), and AMH. There was no correlation between $AFC \leq 5$ and $AFC > 5$, and positive correlations between the number of MII retrieved oocytes and $AFC \leq 5$ and $AFC > 5$ were found.

Conclusion: There was no significant relationship between FORT and $AFC > 5$. There were also significant correlations between the number of MII retrieved oocytes and age, total AFC, $AFC \leq 5$, $AFC > 5$, number of preovulatory follicles (16-20 mm in diameter), and AMH. Multiple linear regression analysis showed that $AFC \leq 5$ and $AFC > 5$ had an almost equal positive correlation with the number of retrieved MII oocytes.

Keywords • Infertility • Sperm injections, intracytoplasmic • Follicle stimulating hormone

The Correlation between Levels of MiR-34c, MiR-15b, and Sperm DNA Damage in oligoasthenoteratozoospermia Men

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Abstract

Background: One of the causes of sperm DNA damage is apoptosis. Due to the vital role of sperm microRNAs (miRNAs) in various pathophysiological processes, the possibility of controlling the process of apoptosis in sperm by miRNAs is raised. The present study was conducted to determine the correlation between levels of miR-34c, miR-15b, and sperm DNA damage in oligoasthenoteratozoospermia men.

Method: This study was performed on 30 men with oligoasthenoteratozoospermia referred to the fertility and infertility center, academic center for education, culture and research, Qom, Iran, for infertility treatment. A Semen sample was collected after 2-3 days of abstinence. The sperm concentration, total motility, progressive sperm motility, normal morphology, and DNA integrity were assessed according to the World Health Organization criteria (WHO) (2010). The expression of miRNAs in the patients' samples was measured by the real-time polymerase chain reaction method.

Results: In contrast to the oligoasthenoteratozoospermia samples, Sperm quality, and DNA integrity were significantly decreased ($P<0.05$). The level of miR-34c in the oligoasthenoteratozoospermia group was significantly lower compared to the control group ($P<0.05$). However, the level of miR-15b was significantly enhanced in the oligoasthenoteratozoospermia group in comparison to the control group ($P<0.05$). Significant correlations between DNA integrity damage, miR-34c, and miR-15b were observed ($P<0.05$).

Conclusion: Increased miR-34c expression, followed by decreased miR-15b expression, leads to increased sperm DNA integrity damage. In the future, miRNAs assessment could serve as a diagnostic tool to ensure the integration of sperm DNA in infertile couples with male factors.

Keywords • Spermatozoa • DNA damage • Asthenozoospermia

Is High-Risk Human Papillomavirus Infection Considered As A Risk Factor for Ovarian Endometriosis?

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Abstract

Background: Endometriosis is considered a chronic inflammation that affected 30% to 45% of women with infertility. Globally, sexually transmitted diseases (STDs) are the primary cause of infertility and papillomavirus (HPV) infection is the most common STDs, but few studies have investigated the effect of HPV infection on human reproduction. HPV infections are significantly associated with anogenital mucosa cancer. The aim of this study was to evaluate the possible correlation between endometriosis and high-risk HPV.

Methods: In this cross-sectional study, formalin-fixed and paraffin-embedded tissue sections from 50 and 49 ovaries with and without endometriosis, respectively, were evaluated for the presence of high-risk HPV using the polymerase chain reaction. The prevalence of HPV infection and other related characteristics of the studied population were compared.

Results: HPV infection was detected in 13 (26%) and five (10.2%) of the samples with and without endometriosis, respectively ($P=0.041$, $\chi^2=3.16$). Mean age and parity were not significantly different in subjects with and without HPV infection in the two studied groups ($P=0.70$ and $P=0.06$ for age in case and control groups, respectively; and $P=0.32$ and $P=0.09$ for parity in case and control groups, respectively).

Conclusion: The results of the study indicated a higher rate of high-risk HPV infection among ovarian endometriosis. Further studies with larger sample sizes are needed to clarify the role of high-risk HPV in causing endometriosis and infertility, and also the role of viral infection and their possible impact on cancer/endometriosis development in this group of patients.

Keywords • Papillomavirus infections • Endometriosis • Infertility

Association of Vitamin D level in Serum and Follicular Fluid with Follicular Response among Infertile Women Undergoing Intracytoplasmic Sperm Injection

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Abstract

Background: Some studies have shown the relation between vitamin D levels and the success rate of fertility in couples treated with assisted reproductive technology (ART). The aim of this study was to determine the association of vitamin D level in serum and follicular fluid with follicular response in infertile women undergoing an ART program.

Methods: 81 infertile women undergoing an ART program entered this cross-sectional study. Follicular fluids were extracted from follicles over 14 mm in diameter and blood samples were collected on the same day. Follicular fluid and blood samples were centrifuged and stored at -80°C . The level of 25-Hydroxyvitamin D was measured by the immunoassay method.

Results: The mean age of the subjects was 32.91 ± 4.83 years old. The average body mass index of the patients was 27.63 ± 3.97 Kg/m². There was no significant correlation between the vitamin D level in serum and follicular fluid and the number of oocytes as well as serum concentration of vitamin D and the number of oocytes ($P=0.57$ and $P=0.95$, respectively). There was also no relation between the number of ovarian follicles and vitamin D level in follicular fluid as well as the number of the ovarian follicles and vitamin D level in serum ($P=0.07$). Correlation analysis revealed a high relationship between vitamin D level in serum and follicular fluid ($P<0.001$).

Conclusion: Different concentrations of vitamin D in serum or follicular fluid have no significant correlation with the number of ovarian follicles and mature oocytes.

Keywords • 25-hydroxyvitamin D • Infertility • Oocytes • Follicular fluid

Advanced 3D Scaffold-Spermatogonial Stem Cells Seeded to Artificial Testis Generation

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Abstract

Background: Spermatogenesis is a process in which animals generate spermatozoa from spermatogonial stem cells (SSCs). Experimental evidence indicates that the companionship of spermatogonia with their associated somatic cells, set to be critical in normal spermatogenesis. Successful *in vitro* differentiation of SSCs towards spermatids holds a significant promise for regeneration of impaired spermatogenesis. The present study aimed to evaluate the efficiency of a 3D scaffold containing an antioxidant (naringenin) on proliferation and differentiation potentials of mouse SSCs.

Methods: By using electrospinning technique, a microfibrillar poly(lactide acid) (PLA) scaffold incorporated with multi-walled carbon nanotubes (MWCNTs) was fabricated. The microfibrillar PLA/MWCNTs were assessed using scanning electron microscopy (SEM), transmission electron microscope (TEM), fourier-transform infrared spectroscopy (FTIR), and water contact angle measurements. Then, the isolated SSCs were characterized using flow cytometry and seeded into the PLA/MWCNTs scaffolds and exhibited preferable survival and differentiation efficiency to subsequent cell lines using MTT assay, quantitative reverse transcription polymerase chain reaction (qRT-PCR) and immunocytochemistry tests.

Results: Morphological assessment of scaffold showed that PLA/MWCNTs randomly oriented as microfibrillar. Moreover, TEM images indicated presence CNT into PLA polymer. The characterize result of SSCs indicated that approximately 99% SSC were positive for PLZF. Then, SSC were seeded on the PLA/MWCNTs scaffolds and they had high survival rate and differentiated to subsequent cell lines. Moreover, qRT-PCR and immunocytochemistry results demonstrated that the SSCs on the 3D scaffold overexpressed the C-kit and SYCP3 genes whereas expression of the PLZF and ID4 had no significant differences between 2D and 3D groups. In addition, the reactive oxygen species (ROS) measurement data demonstrated that naringenin, an effective antioxidant, plays an important role in *in vitro* spermatogenesis.

Conclusion: This research showed that the engineered 3D scaffolds can support proliferation and differentiation of SSCs. Moreover, this 3D microenvironment could be useful as a new approach in 3D culture system especially for culture and differentiation of SSC.

Keywords • Naringenin • Stem cells • Spermatogenesis

Acceptance rate of Surrogacy in Iran

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Abstract

Background: Motherhood is considered as an enjoyable event, but some couples have difficulty conceiving. These people can use “assisted reproductive technologies”. One of the newest treatments is surrogacy. A surrogate mother is someone who carries a fetus for another. The surrogacy has its challenges and many factors are influential in choosing this method. The aim of this study is to evaluate the acceptance rate of surrogacy in Iran.

Methods: This systematic review was conducted according to the PRISMA recommendations. An electronic search using PubMed, Scopus, Google Scholar, etc, was conducted. The used keywords were surrogate mothers, mental health and surrogacy. Finally, after checking our inclusion and exclusion criteria, 8 articles were selected based on their title and abstract.

Results: The first successful pregnancy with this method was reported in 1985. Although it has many advantages, many problems and issues arise from legal, moral, psychological, biological, and sociological aspects. This method would ethically be acceptable if it won't get used commercially. From the aspect of religion in Shia rules, it is permitted if no illegal actions get done. Psychologically, a surrogate mother may experience mental problems such as depression and anxiety due to different reasons like Fear and worry about having an abnormal baby, problems in marital relationships, and relationships with family and relatives. Moreover, for parents, there are concerns regarding informing the relatives or even the child, of the pregnancy type, and resistance of surrogate mother to give away her baby. Biologically, it can harm the surrogate mother's body. Sociologically it has no obvious religious legitimation and social acceptability.

Conclusion: Rising infertility rates indicate that assisted reproductive methods, such as surrogacy, are an acceptable ethical approach to infertility treatment. However, this practice, in its commercial form, suffers from moral problems that are rooted in poverty and cannot be eliminated unless the socio-economic situation of these communities is improved.

Keywords • Surrogate mothers • Pregnancy • Mental health

Effects of Noise Pollution on Hormonal Parameters in Male Workers Working in Noisy Environments in Bushehr

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Abstract

Background: Noise is a factor that not only in the workplace, but also in the sleep and rest affects people. Due to the harmful effects noise pollution on fertility and changes in thyroid and sex hormones, we should try to minimize the effects of this type of stress. The aim of this study was to investigate the effect of noise pollution on fertility and changes in thyroid and sex hormones.

Methods: In this study, 30 workers of sexually active ages (20-40 years old) were selected. These workers were selected among who have worked in noisy environments, for at least five years, and being exposed to at least 100 decibels, five hours daily. The semen parameters were analyzed and compared. The results of the above parameters were compared between the case and the control groups.

Results: In the case group, compared to the control group, there was a significant decrease in male sex hormones, and also positive parameters of semen analysis, including sperm motility, and morphology. There was a significant decrease in thyroid hormones (TSH, T3, T4), especially with high intensity (119 dB). Examination of high frequency pituitary hormones (119 dB) increased prolactin and significantly decreased luteinizing hormone .

Conclusion: The results of this study showed that noise, especially at high intensities, can reduce infertility in men.

Keywords • Noise • Gonadal steroid hormones • Infertility

Comparison of Ethanol Sclerotherapy with Laparoscopic Surgery for the Management of Endometrioma: A Double-Blind Randomized Clinical Trial

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Abstract

Background: Endometriosis and infertility are two well-known associated pathologies that are found in approximately 25-40% of the cases. laparoscopic stripping of the cyst wall, is a method of treating endometrioma. It has many disadvantages which can affect ovarian reserve. It seems clear that another option needs to be found. Therefore, various studies have been performed in order to use safer and less invasive methods to manage this medical condition. One of the newest treatment modalities is sclerotherapy under an ultrasound guide. The authors compared the recurrence rate of endometrioma and ovarian reserve in patients with infertility undergoing sclerotherapy vs. laparoscopic ovarian cystectomy.

Methods: In this randomized clinical trial, a total of 70 infertile patients, with endometriomas were divided into two groups. The first group (n=35) had ethanol sclerotherapy (EST); the second group (n=35) underwent laparoscopic ovarian cystectomy. The authors measured the anti-mullerian hormone (AMH) levels, mean longest cyst diameter, and the recurrence rate of endometrioma at baseline, 3, and 12 months after each intervention and between the two groups.

Results: AMH concentrations were significantly increased 3 months after sclerotherapy but significantly decreased after laparoscopic cystectomy compared to the baseline. AMH concentrations were higher in the EST group than laparoscopy group, 3 months after interventions (P=0.009). Mean longest cyst diameter was significantly decreased 3 and 12 months after each intervention in both groups but cyst diameter was smaller in the laparoscopy group compared to the EST group 3 months after intervention. No differences were found when comparing recurrence rate before and after each procedure in both groups at 3 and 12 months after interventions (P=0.1 and P=0.6, respectively).

Conclusion: This study indicated that ethanol sclerotherapy can be a good alternative to surgery in the management of endometrioma in patients with infertility, with significant increases in serum AMH concentrations observed in the patients after sclerotherapy.

Keywords • Endometriosis • Surgery • Sclerotherapy

Comparison of Laparoscopic Ablation with Excision for Superficial Endometriosis-Associated Pain: A Randomized Clinical Trial

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Abstract

Background: The aim of this study was to compare the effectiveness of laparoscopic excision with ablation in patients with minimal to mild endometriosis.

Methods: This randomized clinical trial was performed during 2019-2021, in Isfahan, on 60 women with chronic pelvic pain, suspicious of endometriosis. Patients were randomized into two groups undergoing excision or ablation of endometriosis lesions. Patients underwent therapeutic procedures, and they were followed six months after surgery for evaluating their symptoms and their pain by visual analogue scale (VAS). Moreover, dysmenorrhea, non-cyclic pain, dyspareunia, and dyschezia among patients were measured and compared with each other.

Results: The intensity of dysmenorrhea, non-menstrual pain, dyspareunia and dyschezia decreased in all patients after the surgical procedures ($P < 0.001$). The intensity of dyspareunia was significantly lower in ablation group after the surgery compared to excision group ($P < 0.001$) but no other significant differences were observed between the two groups.

Conclusion: There were no significant differences between two surgical groups in terms of dysmenorrhea, non-menstrual pain, and dyschezia. All patients in the both groups reported significantly lower pain after the surgical procedures. However, the intensity of dyspareunia was significantly lower in patients in the ablation group, so careful patient counseling regarding expectations of surgical interventions is crucial in the management of endometriosis.

Keywords • Endometriosis • Dyspareunia • Dysmenorrhea

Comparison of the Impact of Flare-Up GnRH Agonist with Delayed Start GnRH Antagonist Protocols on the *in vitro* fertilization Outcome of Poor Responder Patients: A Randomized Controlled Trial

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Abstract

Background: Although, several studies have investigated the effect of controlled ovarian hyperstimulation on the *in vitro* fertilization (IVF) outcomes, but the optimal protocol for patients with poor ovarian response (POR) has still been a challenge. The current research was established to make a comparison between the delayed start gonadotropin-releasing hormone (GnRH) antagonist and flare-up GnRH agonist protocols in poor responder patients.

Methods: This randomized, prospective, controlled trial was performed on 150 women who referred to two distinct IVF centers in Iran. Patients were randomly assigned into two experimental groups, as one group was treated with the delayed start GnRH antagonist protocol (delayed start group), while another group was treated with the flare-up protocol (flare-up group).

Results: The serum concentrations of estradiol and progesterone, along with the thickness of endometrial tissue and the number of follicles (≥ 13 mm in diameter) were significantly increased in the delayed start group compared with the flare-up group. Moreover, the number of total oocytes, retrieved mature oocytes, total embryos, fertilized oocytes, as well as the quality of embryos were markedly higher in the delayed start group compared with the flare-up group. No statistically significant differences were found in the rates of fertilization, implantation, and pregnancy between the two experimental groups.

Conclusion: According to the above evidence, it seems that the effect of delayed start protocol on ovarian responsiveness was more pronounced during controlled ovarian stimulation in comparison with the flare-up protocol, and the delayed start protocol probably lead to better implantation and pregnancy rates in comparison with the flare up agonist protocol cycle in poor responders.

Keywords • Gonadotropin-releasing hormone • Ovarian hyperstimulation syndrome • Pregnancy

The Comparison of the Impact of Flare-up Gonadotropin-Releasing Hormone Agonist with Delayed-Start GnRH Antagonist Protocols on the *in Vitro* Fertilisation Outcome of Poor Responder Patients: A Randomized Controlled Trial

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Abstract

Background: Although, several studies have investigated the effect of controlled ovarian hyperstimulation on the *in vitro* fertilization (IVF) outcomes, the optimal protocol for patients with poor ovarian response (POR) has still been a challenge. The current research was established to make a comparison between the delayed-start *gonadotropin-releasing hormone* (GnRH) antagonist and flare-up GnRH agonist protocols in poor response patients.

Methods: The present study is a randomized, prospective, controlled trial that was performed on 150 women who referred to two distinct IVF centers in Iran. Patients were randomly assigned to two experimental groups, as one group was treated with the delayed-start GnRH antagonist protocol (delayed-start group), while another group was treated with the flare-up protocol (flare-up group).

Results: The serum concentrations of estradiol and progesterone, along with the thickness of endometrial tissue and the number of follicles ≥ 13 mm was significantly increased in the delayed-start group compared with the flare-up group. Also, the number of total oocytes, retrieved mature oocytes, total embryos, fertilized oocytes, as well as the quality of embryos were markedly higher in the delayed-start group when compared with the flare-up group. No statistically significant difference was found in the rates of fertilization, implantation, and pregnancy between the two experimental groups.

Conclusion: According to the above evidence, it seems that the effect of delayed-start protocol on ovarian responsiveness was more pronounced during controlled ovarian stimulation in comparison with the flare-up protocol and the delayed start protocol probably lead to better implantation and pregnancy rates in comparison with the flare up agonist protocol cycle in poor responders.

Keywords • Fertilization *in vitro* • Gonadotropin-releasing hormone • Ovulation induction

The Survey of Some Biochemical Parameters after Cryopreservation in Asthenozoospermic Patients after Using *Ceratonia Siliqua L* Extract

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Abstract

Background: Human sperm banking is an important procedure in assisted reproductive technology. Cryopreservation is a safe, easy, and inexpensive method for sperm cryopreservation. In spite of the many benefits of cryopreservation, this method may lead to deleterious changes in sperm structure and function. Cryopreservation causes lipid peroxidation in the membrane of sperm and, as a result, the formation of reactive oxygen species (ROS). ROS initiates lipid peroxidation that produces malondialdehyde (MDA), which leads to cell membrane destruction. Therefore, studies have shown that enriching media freezing with herbal extract antioxidants can reduce the harmful effects of sperm cryopreservation. It has been reported that the use of *Ceratonia siliqua L* fruit extract increased total antioxidant capacity (TAC), and decreased serum MDA levels. In this study, the effect of extract of *Ceratonia siliqua L* on some biochemical parameters after freezing in patients with asthenozoospermic is investigated.

Methods: Forty asthenozoospermic specimens were obtained in this study. Each sample was divided into six groups: fresh (group I), in groups II to VI, 0 (as the control group), 5, 10, 20, and 30 $\mu\text{g/mL}$ *Ceratonia siliqua L* extract were added to a freezing medium respectively. Then some biochemical parameters (MDA, ROS, TAC) were evaluated using related protocols after thawing. SPSS software was used to analyze the data.

Results: Supplementation of freezing media with *Ceratonia siliqua L* extract significantly decreased ROS and MDA levels after cryopreservation in asthenozoospermic patients. Also, the present study demonstrated that freezing medium supplemented with *Ceratonia siliqua L* extract increased TAC levels.

Conclusion: This study showed that supplementation of freezing media with *Ceratonia siliqua L* extract as an antioxidant significantly improved adverse effect of cryopreservation after freezing and thawing in asthenozoospermic patients.

Keywords • Asthenozoospermia • Fabaceae • Cryopreservation • Reactive oxygen species malondialdehyde

The Effect of *Ceratonia Siliqua L* extract on Semen Parameters, DNA Fragmentation after Cryopreservation in Asthenozoospermic Patients

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Abstract

Background: Sperm cryopreservation is useful for infertility treatment and fertility preservation. Freezing and thawing result in oxidative damage and physical and chemical changes in the sperm. Antioxidant supplements such as vitamin C, vitamin E, selenium, zinc and CoQ10, and ellagic acid can improve semen parameters (sperm motility, viability, and function) in infertile men and they have shown positive effects on sperm cryopreservation. Some studies have shown the effect of *Ceratonia siliqua L* extract on the improvement of sperm parameters and chromatin quality after sperm cryopreservation. *Ceratonia siliqua L* is a tree with fruits that have antioxidant properties. This study aimed to investigate the effect of different concentrations of *Ceratonia siliqua L* extract in a freezing medium on semen parameters and DNA fragmentation in asthenozoospermic patients.

Methods: Forty asthenozoospermic specimens were obtained in this study. Each sample was divided into six groups: fresh (group I), in groups II to VI, 0 (as the control group), 5, 10, 20, and 30 µg/mL *C. siliqua* extract were added to a freezing medium respectively. Then sperm parameters, Sperm DNA Fragmentation Assay (SDFA), were evaluated using related protocols after thawing in asthenozoospermic patients. SPSS software was used to analyze the data.

Results: Data analysis shows that *Ceratonia siliqua L* extract improves sperm parameters after freezing and thawing in asthenozoospermic patients. Also, the present study showed that the percentage of SDFA significantly reduced after freezing and thawing in asthenozoospermic patients.

Conclusion: This study showed the use of *Ceratonia siliqua L* extract in freezing media can improve the sperm parameters and chromatin quality in asthenozoospermic specimens.

Keywords • Fertility preservation • Infertility • Male • *Ceratonia siliqua L*

Comparison of Maternal and Neonatal Outcomes with and without Preimplantation Genetic Screening

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Abstract

Background: Aging is associated with a significant increase in aneuploidy and spontaneous abortion, which has led to the escalating usage of preimplantation genetic screening (PGS). The aim of this study was to compare maternal and neonatal outcomes in women undergoing assisted reproduction techniques with and without PGS.

Methods: This research was an analytical cross-sectional study, which included women who underwent assisted reproductive technology (ART) in Sarem Women's Hospital (Tehran, Iran) in 2020-2016. These women were divided into two groups including with PGS and without PGS. Both groups had at least one indication for PGS, such as a history of recurrent miscarriage, a history of assisted reproductive technology failure, a history of male factor infertility, and a chromosomal disorder. Patients' information was collected through hospital medical records and telephone calls in the checklist. Maternal and neonatal outcomes in the two groups compared.

Results: Among women underwent ART, 2123 women were without PGS and 80 women were with PGS. In the PGS group, 25 cases (31.25%) had been got pregnant whereas in the group without PGS, 375 cases (17.66%) had been got pregnant ($P < 0.05$). Indeed, PGS significantly increased the incidence of pregnancy by as much as 13.59%. In the parameters including, the number of previous pregnancies, the number of previous abortions, age, maternal outcomes (abortion, stillbirth, and live birth), hypertension, preterm labor, and neonatal birth weight, the significant statistical differences were seen between the two groups ($P < 0.05$). There were no significant difference between the two groups such for previous births, neonatal gender, diabetes, placenta abruption, and fetal abnormalities ($P > 0.05$).

Conclusion: The PGS has increased pregnancy rates, live births, and neonatal birth weight. It also has reduced abortions, preterm labor, and maternal hypertension. Therefore, the infertile women who are candidates for ART are recommended for PGS.

Keywords • Reproductive techniques, assisted • Aneuploidy • Pregnancy

The Relationship between PLCZ Gene Expression in Sperm and Intracytoplasmic Sperm Injections and Conventional *in Vitro* Fertilisation Outcome in Unexplained Infertile Couple?

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Abstract

Background: Over the last three decades, assisted reproductive technology (ART), particularly Intracytoplasmic Sperm Injections (ICSI) and *in vitro* Fertilisation (IVF), has been widely employed in infertility therapy. The association between PLCZ mRNA expression level and its success in IVF and ICSI patients, as well as the 3 and 5 days and entire embryos generated in each technique, were compared in this study.

Methods: In the ICSI and IVF groups, sperm motility and its connection with PLCZ mRNA expression levels were also assessed. The association between the expression of PLCZ and various risk factors such as age, Anti-Müllerian Hormone (AMH), and RL was also studied. In both groups of IVF and ICSI patients, the link between AMH and endometrium thickness, AMH and number of oocytes and entire embryos, and AMH and follicle number was analyzed and compared.

Results: In IVF and ICSI patients, there was no significant association between sperm morphology, count, and PLCZ mRNA expression level. We discovered that IVF patients with higher sperm motility had considerably higher PLCZ mRNA expression levels than ICSI patients. In contrast to the ICSI group, the IVF group also discovered a strong link between AMH and the quantity of oocytes and entire embryo. The endometrial thickness of IVF patients was also higher than that of ICSI patients. In the IVF group, there was also a significant association between age and the amount of oocytes and AMH.

Conclusion: We came to the conclusion that increased sperm motility in IVF patients is linked to PLC Z upregulation.

Keywords • Infertility • Reproductive techniques • Fertilization • Sperm injections, intracytoplasmic

The Effect of Myo-inositol on Fertility Rates in Poor Ovarian Responder in Women Undergoing Assisted Reproductive Technique: A Randomized Clinical Trial

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Abstract

Background: Poor ovarian response to gonadotropin is a significant challenge in assisted reproductive technique (ART) and affect 9–24% of ART cycles. This study aimed to evaluate the effect of Myo- inositol on fertility rates in poor ovarian responder women undergoing assisted reproductive technique.

Methods: This study was a double-blinded randomized controlled study that involved 60 poor ovarian responders included in an Intracytoplasmic Sperm Injection (ICSI) program and divided equally into two groups. The intervention group assumed Inofolic (4 g myo-inositol + 400 µg folic acid) before the enrollment day and control group assumed folic acid (400 µg) for the same period. Controlled ovarian stimulation was performed in the same manner in the two groups. The main outcomes were the assessment of oocytes retrieved number and quality, ovarian sensitivity index (OSI), required dose of Gonadotropins, fertilization rate, biochemical, and clinical pregnancy rate.

Results: There was no significant difference in clinical characteristics between the groups. The number of oocytes retrieved, number of MII oocytes, number of embryos transferred, chemical, and clinical pregnancy were higher in the intervention group. However, they are not statistically significant in comparison to the control group. The OSI and fertilization rate were significantly higher in the intervention group than the control group ($P>0.05$). The required dose of gonadotropin was significantly lower in the intervention group than the control group.

Conclusion: Our results suggest that the supplementation myo-inositol in poor ovarian responders significantly improved the ART outcomes such as fertilization rate gonadotropin, OSI and significantly reduced the required unities of gonadotropin. Additionally, more extensive randomized controlled studies are needed.

Keywords • Reproductive techniques, assisted • Sperm injections, intracytoplasmic • Folic acid • Fertilization

The Effect of Hydroalcoholic Extract of *Dracana Cinnabari* on Sex Hormones and Ovarian and Uterine Tissues of Rats

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Abstract

Background: Medicinal plants have a special value and importance in the health of communities due to treating and preventing the diseases. Iran has a unique place in the plant geography of the world. *Dracana cinnabari* is considered as a rich source of phytochemicals used widely in traditional medicine. It has several therapeutic properties. In the present study, the effect of *Dracana cinnabari* hydraulic extract on the reproductive system of female rats was investigated.

Methods: The samples were randomly divided into 4 groups (6 samples in each group), including three treatment groups and one control group, and all samples were kept at the same conditions. Progesterone was injected intraperitoneally for three consecutive days to co-cycle the rats. Hydraulic extract of *Dracana cinnabari* was prepared in different doses (50,100,150 mg/kg) and injected intraperitoneally daily for ten days, While physiological serum was used for injection in to the control group. After ten days of injection, the samples were placed at rest for one week and the samples were collected after one week. Estrogen and progesterone levels were measured by Enzyme Immunoassay *technique*. After dissection, the ovaries and uterine tissues were isolated for histological examination and tissue changes were carefully examined.

Results: The results revealed that the levels of estrogen and progesterone in Experimental Group 2 and Experimental Group 3 had a significant increase ($P < 0.001$). Regarding tissue changes, a significant increase was observed in epithelial thickness ($P < 0.001$), number of corpus luteum ($P < 0.01$), and graafian follicle ($P < 0.01$) in doses of 100 and 150 mg/kg.

Conclusion: Based on the results, it seems that *Dracana cinnabari* extract has an effect on the hypothalamic-pituitary axis and has increased the ovarian follicles by increasing the process of folliculogenesis. It also increases the uterine epithelium and endometrium thickness due to its estrogenic properties.

Keywords • Hormones • Herbal medicine • Rats • Genitalia

The Potential Role of Granulosa Cells in the Maturation Rate of Immature Human Oocytes and Embryo Development: A Co-culture Study

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Abstract

Background: In order to increase the number of mature oocytes usable for intracytoplasmic sperm injection (ICSI), we aimed to investigate the effect of co-culturing granulosa cells (GCs) on human oocyte maturation *in vitro*, the fertilization rate, and embryo development.

Methods: A total of 133 immature oocytes were retrieved and were randomly divided into two groups; oocytes that were cultured with GCs (group A) and oocytes that were cultured without GCs (group B). After *in vitro* maturation, only oocytes that displayed metaphase II (MII) underwent the ICSI procedure. The maturation and fertilization rates were analyzed, as well as the frequency of embryo development.

Results: The mean age of the patients, their basal levels of follicle-stimulating hormone, and the number of oocytes recovered from the patients were all comparable between the two study groups. The number of oocytes that reached MII (mature oocytes) was 59 out of 70 (84.28%) in group A, compared with 41 out of 63 (65.07%) in group B ($P=0.011$). No significant difference between fertilization rates was found between the two study groups ($P=0.702$). The embryo development rate was higher in group A (33/59, 75%) than in group B (12/41, 42.85%; $P=0.006$). The proportion of highest-quality embryos and the blastocyst formation rate were significantly lower in group B than in group A ($P=0.003$ and $P<0.001$, respectively).

Conclusion: The findings of the current study demonstrate that culturing immature human oocytes with GCs prior to ICSI improves the maturation rate and the likelihood of embryo development.

Keywords • Fertilization • Granulosa cells • *In vitro* oocyte maturation techniques • Sperm injections, intracytoplasmic • Oocytes

The Effects of Sirolimus and Cyclosporine Loaded Nano Lipid Carriers on T Cells Profile in Recurrent Pregnancy Loss Patients

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Abstract

Background: The use of nano lipid carriers (NLCs) can improve the therapeutic efficacy of immunosuppressive drugs, meanwhile decreasing side effects in recurrent pregnancy loss (RPL) women. In this in-vitro study, NLCs loaded with Sirolimus (SRL) and Cyclosporine A (CsA) were developed to investigate their effects on peripheral T cells profile in RPL women.

Methods: Solidified (S-NLCs), cationic (C-NLCs), and S-C-NLCs were designed and characterized. Then their effects on the function of peripheral T cells in RPL women as compared with healthy pregnant women were studied through Real-time polymerase chain reaction., Western blot analysis, and enzyme-linked immunosorbent assay.

Results: Optimal nanodrugs were validated with appropriate zeta potential, size, encapsulation efficiency, drug loading and cellular uptake. By co-delivering of SRL and CsA, the amount of them could be reduced to a large extent, whereas the rate of cell apoptosis was not significantly raised. The *in vitro* effects of NLCs on T cells profile in RPL women with a higher frequency of Th1, Th17 along with lower Th2, Treg cells revealed that the expression level of ROR γ t, T-bet reduced whereas the expression of Foxp3 raised. Furthermore, the level of tumor necrosis factor α (TNF-), interferon γ (IFN-), interleukin-21 (IL-21), and IL-17 decreased, and the level of transforming growth factor beta (TGF- and IL-10 increased. While there was no statistically difference in the responses of T helper 2 (Th2) cells. Following S-NLCs and C-NLCs intervention, significantly difference was observed in T cells profile of RPL women as compared with healthy group while following S-C-NLCs, no significant difference was found.

Conclusion: Co-delivery of SRL and CsA can be an effective method of balancing immune responses in RPL women in order to establish maternal immune tolerance. S-C-NLCs could provide higher therapeutic efficacy and minimal systemic toxicity for these patients.

Keywords • Sirolimus • Cyclosporine • T-Lymphocytes • Pregnancy

Evaluation of Chlamydia Infection Rate in Women with Abortion or Infertility Compared with Control Group by Real Time Polymerase Chain Reaction Method

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Abstract

Background: Chlamydia trachomatis is one of the most common sexually transmitted diseases around the world and there is widespread evidence of tubal obstruction following chlamydial infections. About 80% of women with this bacterial infection are asymptomatic, but ascending infections in the form of pelvic inflammatory disease and subsequently infertility are common in women with chlamydia. The aim of present study was screening based on diagnosing chlamydia trachomatis infection given its essential role in tubular infertility, chronic pelvic pain, and abortion.

Methods: Using a vaginal swab, samples were taken from eligible women after completing a questionnaire and obtaining their consent. DNA was extracted from clinical sample manually and Real time polymerase chain reaction (PCR) was performed using chlamydia specific primers.

Results: In the present study, among 789 women who were examined in terms of the presence of chlamydia, real time PCR results showed the presence of chlamydia at 5% in normal group, 12.7% in the infertile group, and 12.9% in the abortion group. No significant relationship was found between patients' demographic information including history of infertility, premature birth, abortion, history of vaginitis and symptomatic vaginitis. However, in terms of chlamydia, there was a significant difference between abortion and infertile groups and control group and there was no significant difference between abortion and infertile groups.

Conclusion: Owing to high sensitivity of real time PCR to diagnose chlamydia trachomatis infection, this method can be used as an effective screening for routine diagnosis of this infection and infertility and abortion associated with this infection can be prevented with timely treatment.

Keywords • Chlamydia trachomatis • Vaginitis • Real-time polymerase chain reaction

Next Generation Sequencing Platforms and Bioinformatics Pipelines for Variant Calling and Analysis

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Abstract

Next generation sequencing (NGS) is the latest diagnostic screening method with high accuracy for comprehensive testing of chromosomal abnormalities. Preimplantation genetic screening (PGS) in conjunction with NGS has revolutionized the world of infertility. PGS helps determine genetic disorders of embryos before being transferred to uterus. Couples with idiopathic inheritance disorders or women who have a history of recurrent miscarriage are good candidates for PGS-NGS. The aim of this review study is to provide an overview of NGS strategies to analyze genetic variants in mendelian and rare complex genetic diseases and also assessment bioinformatics pipelines for variant calling and analysis. We reviewed available NGS platforms including Roche 454, Illumina, SOLiD and Ion Torrent. The bioinformatic pipelines for variant calling workflow using whole genome sequencing and whole exome sequencing data including quality control of fastq files, alignment to reference genome, mark duplication, variant calling, filtration, annotation, and clinical report were also discussed. The quality of data achieved by NGS integrated with affordable costs, improved data handling capabilities, enhanced computational power and efficient bioinformatics analysis tools, revolutionized clinical genetic diagnostic testing and research approaches to identify associated mutation causing mendelian or complex genetic diseases. NGS-based methods could lead to representation de novo mutations with significant association or in the absence of association. In this review study, we highlighted NGS strategies combined with bioinformatic analysis programs to detect genetic variants involved in Mendelian and uncommon genetic diseases in research and clinical settings. This fast-progressing approach can help future studies to identify novel variants and genetic medicine.

Keywords • High-throughput nucleotide sequencing • Genetic testing, infertility • Genome

Correlation between Serum Transforming Growth Factor beta Levels and Recurrent Implantation Failure during Implantation Window in Women Undergoing *in Vitro* Fertilization

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Abstract

Background: Frequent implantation failure is a common problem among women who underwent *in Vitro* Fertilization (IVF) procedure. It is necessary to know the factors affecting recurrent implantation failure following (IVF. This study aimed to investigate the relationship between serum Transforming growth factor-beta (TGF- β) levels and recurrent implantation failure during the implantation window in women undergoing IVF.

Methods: This cross-sectional study was performed on 39 patients who referred to one infertility clinic during 2019 to 2020 in Mashhad, including 20 women with recurrent implantation failure (case group) and 19 women with successful pregnancies in the first IVF cycle (control group). Serum TGF- β levels were measured using enzyme-linked immunosorbent assay (ELISA) method. Age, Body Mass Index (BMI) and number of implantation failure in women were recorded.

Results: The mean serum levels of TGF- β in the individuals with recurrent implantation failure was significantly lower than the control group (663.48 pg/mL vs.1028.49 pg/mL). Moreover, the serum TGF- β levels was significantly different among case and control groups based on the age and BMI. However, there was no relationship between serum TGF- β levels in the case group and age, BMI and number of implantation failures.

Conclusion: TGF- β may play a crucial role in the pathophysiology of recurrent implantation failure. Measurement of this factor in the patients with recurrent implantation failure is recommended which may reduce the incidence of recurrent implantation failure following IVF treatment. However, further randomized clinical studies are required to clarify the definite correlation.

Keywords • Transforming growth factor beta • *In Vitro* fertilization • Infertility

The Role of Abdominal Obesity in the Pathogenesis of Polycystic Ovary Syndrome

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Abstract

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders that affects about 14-20% of women at reproductive ages and is associated with hyperandrogenism, hyperinsulinemia, ovarian dysfunction and obesity especially abdominal obesity (AO). Due to its complex manifestations, the full pathogenic mechanism of PCOS is not fully understood. Here in, we provide an in-depth discussion about PCOS pathogenesis especially the role of AO in the progression of PCOS. In the present review article, the published studies in PubMed, Science Direct, Google Scholar gateway and databases were assessed using the keywords Polycystic ovary syndrome, Pathogenesis, abdominal obesity, insulin resistance, and hyperinsulinemia using the “and” and “or” operators from January 2017 to December 2021.

The increasing prevalence of obesity in recent years has led to an increase in the prevalence of obesity-related diseases, including PCOS. Obesity, especially AO has important role in the pathogenesis of PCOS and its related complications including hyperinsulinemia, hyperandrogenism and insulin resistance (IR). It is estimated that AO observes in approximately 40- 80% of PCOS patients and is associated with IR, which counts as one of the main side effects of PCOS. It has been revealed that AO can significantly reduce the insulin sensitivity in normal weight PCOS patients with hyperandrogenism. In addition, IR, which is exacerbated by AO, can cause more accumulation of fat in the peritoneal region, creating a vicious feedback cycle between IR and obesity in patients with PCOS. Recent studies suggest that AO may play a more important role in the etiology of the PCOS than previously thought, Due to the underlying role of AO in causing and exacerbating other complications. It can improve the results of treatment ART cycles and be effective in controlling the complications caused by the PCOS.

Keywords • Polycystic ovary syndrome • Obesity, abdominal • Insulin resistance • Hyperinsulinemia

Comparing Four Different Methods for the Management of Ectopic Pregnancy: A Cross-sectional Study

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Abstract

Background: Ectopic pregnancy (EP) is one of the major causes of maternal mortality during the first trimester of pregnancy. Four treatment methods for EP including single-dose methotrexate (SD-MTX), double-dose methotrexate (DD-MTX), expectant and surgical management were considered

Methods: In this cross-sectional study, the clinical characteristics of 365 women aged 15-44 years who had been diagnosed with EP were reviewed from March 2017 to March 2019 in hospitals affiliated to Shiraz University of Medical Sciences, Shiraz, Iran. Receiver operating characteristics curves were plotted to determine the cut-off points for size of ectopic mass and beta-human chorionic gonadotropin (β -hCG) that suitably discriminated between DD-MTX and surgery management.

Results: The most common site of EP was adnexa. According to the receiver operating characteristics analysis, surgery was the best plan for the women with an ectopic mass >34.50 mm in diameter or with an initial β -hCG level >6419 mIU/mL. The β -hCG levels in the women successfully treated with SD-MTX were significantly lower than in those with failed treatment ($P=0.02$). The SD-MTX group had a higher success rate and significantly shorter duration of hospitalization, and so this was a more effective medical treatment in comparison with the DD protocol.

Conclusion: Surgery is proposed as the best option for the cases with large ectopic mass or high β -hCG level. SD-MTX had a higher success rate and shorter hospital stay than the DD protocol, and so was found to be an efficient and safe alternative. Further randomized clinical trials with larger sample sizes are recommended to validate the current results.

Keywords • Pregnancy, ectopic • Methotrexate • Chorionic gonadotropin • Therapeutics

Patients with Polycystic Ovary Syndrome Have Altered Blastocyst Endometrium Crosstalk before Embryo Implantation

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Abstract

Background: Embryo implantation is defined as the process by which blastocyst attaches to the endometrium and invades to endometrial stroma cells to form the placenta. Successful embryo implantation requires exchange of mediators between endometrium and blastocyst in the form of cross talk which alter the microenvironment of the oviduct and uterus and underly the homing of blastocyst. These factors mainly include interleukins, immunosuppressive and growth factors which facilitate implantation by increase the endometrial expression of integrins, leukaemia inhibitory factor, and Polycystic ovary syndrome (PCOS) is the most common endocrine disorder and major cause of anovulatory infertility. The reduced oocyte/embryo quality and decreased implantation rate has been reported as its common complications. Herein we aimed to provide a detailed discussion regarding endometrium-blastocyst cross talk in patients with PCOS to clarify the exact etiology of their low embryo implantation rate.

Methods: In the present article, the published studies in PubMed, ScienceDirect, Scopus and Google Scholar gateway and databases were assessed using the keywords: Polycystic Ovary Syndrome, Embryo Implantation, Endometrium, Blastocyst and Cytokine from January 2000 to February 2022.

Results: It was found that patients with PCOS have altered profile of embryo and endometrium secretome. It led to disrupted endometrium-embryo crosstalk.

Conclusion: It seems that the disrupted endometrium-embryo crosstalk in PCOS patients may be a main cause of low implantation rate among these patients.

Keywords • Polycystic ovary syndrome • Embryo implantation • Endometrium • Blastocyst • Cytokine

Effect of Melatonin on Sperm

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Abstract

Melatonin is an amino acid derivative synthesized in most vertebrates, including humans, mainly in the epiphyseal gland and regulated by the environment. Melatonin (N-acetyl-5-methoxytryptamin) can regulate some physiological phenomena and consequently plays an important role in regulating circadian and sleep rhythms. In addition, melatonin has an effect on cell proliferation and differentiation. This hormone is also known as a powerful antioxidant, which has a high potential to neutralize drug toxins, and removes and neutralizes large amounts of free and harmful radicals such as hydroxyl, peroxy and peroxy nitrate anions. In fact, melatonin reduces oxidative stress in a number of ways. In our study, keywords “Melatonin, Spermatogenesis, and infertility” were searched in gateway and database “PubMed and Google Scholar” without any time limitation, finally, the most relevant articles were selected and reviewed. Studies have shown that treating sperm with melatonin before or during fertilization improves the rate of single sperm fertilization and helps the early fetus. Melatonin directly detoxifies free radicals such as hydroxyl, nitric oxide, etc. and has the ability to scavenge and neutralize them. The anti-apoptotic and antioxidant effects of melatonin may reduce oxidative stress on sperm and increase fetal quality. Melatonin has anti-proliferative properties on both germ cells and other cells. Studies have also shown that the combination of melatonin and metformin can refine the atrophy of seminiferous tubules. The good quality of a sperm depends on various parameters such as number, motility and proper morphology, which are affected by numerous factors such as free radicals. Improved sperm quality is one of the first signs of the effects of melatonin on testicular function. Some studies have shown a significant increase in progressive motility when sperm were incubated with melatonin. As a whole, Melatonin is known as a powerful antioxidant that reacts with free radicals and enhances the effect of other antioxidants. In addition, melatonin improves sperm quality by affecting the expression of apoptosis-related genes. However, further studies are needed to elucidate its exact mechanism.

Keywords • Melatonin • Spermatogenesis • Infertility

Altered Methyltransferase Gene Expression, Mitochondrial Copy Number, and 4977-bp Common Deletion in Subfertile Men with Variable Sperm Parameters

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Abstract

Background: Semen parameters have been found to poorly predict reproductive success yet are the most prevalent diagnostic tool for male infertility. There are few but conflicting reports regarding the correlation of DNA methyltransferase (*DNMT*) genes expression, mitochondrial DNA copy number (mtDNA_{cn}), and deletion (mtDNA_{del}) with different sperm parameters. This study performed to investigate *DNMT* mRNA level, mtDNA_{cn}, and deletion in infertile men with different sperm parameters compared with fertile men.

Methods: Semen samples from 30 men with unknown male infertility and normal sperm parameters (experimental group I), 30 infertile patients with at least two abnormal sperm parameters (experimental group II), and 30 fertile normozoospermic men (control group) were collected. After semen analysis, total RNA and DNA were extracted. Isolated DNA was used for assessing the respective mtDNA_{cn} and the presence of 4977-bp common deletion in mtDNA by applying real-time quantitative polymerase chain reaction (PCR) and multiplex PCR, respectively. Synthesized cDNA from total RNAs was used to quantify *DNMT1*, *DNMT3A*, and *DNMT3B* transcripts in the study groups using real-time quantitative reverse-transcription PCR.

Results: Significantly higher proportions of mtDNA_{cn} were found in experimental group II. *DNMT1* was significantly down-regulated in both experimental groups. 4977-bp deletion was not detected. Progressive motility and normal morphology were significantly and negatively correlated with mtDNA_{cn}. A significant positive correlation was detected between sperm parameters and *DNMT1* mRNA levels.

Conclusion: Infertile men with different sperm parameter qualities showed elevated mtDNA content. mtDNA_{cn} could serve as a non-invasive biomarker in male infertility namely in unknown cases. Abnormal sperm parameters are associated with *DNMT1* gene expression, indicating the possibility of changes in some epigenetic aspects of spermatogenesis in subfertile men with different sperm parameters.

Keywords • Spermatozoa • Methyltransferases • Infertility • Gene expression

Ellagic Acid Administration Prevents Busulfan-Induced Testicular Damage, Oxidative Stress, and Sex Hormones Abnormality in the Relative Sterility Rat Model

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Abstract

Background: Male infertility can affect the life quality of men and women. Busulfan which is used for cancer treatment cause sterility in male patients. This study aimed to investigate the effects of ellagic acid on sexual hormones, testicular tissue, body antioxidant system, and apoptosis pathway in the busulfan-induced relative sterile rat model.

Methods: 65 male Sprague-Dawley rats were randomly divided into the following groups: control, Ellagic acid, busulfan, and busulfan plus ellagic acid. After 48-day of treatment, the rats were anesthetized with ketamine xylazine mixture and blood samples were collected by cardiac puncture. Then the animals were sacrificed and testicles were removed for stereological and gene expression analysis. Follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, catalase, total antioxidant capacity, malondialdehyde, and glutathione peroxidase activity were assessed. mRNA expression of Bcl-2 and caspase-9 was also assessed by real-time PCR. Testicular tissue changes were also examined by stereological methods.

Results: Busulfan group had significantly lower total antioxidant capacity, serum testosterone, Bcl2 mRNA expression, testicular volume, seminiferous tubule, germinal epithelium, and interstitial tissue volume, and the number of spermatogonia, spermatocyte, round spermatid, elongated spermatid, Leydig cells, and Sertoli cells than the control group. LH, FSH, caspase 9 expression, and malondialdehyde level were higher in the busulfan group. Ellagic acid administration significantly increased the testosterone, Bcl-2 expression, and antioxidant markers and also significantly decreased LH and FSH serum levels. Stereological parameters were improved after ellagic acid treatment.

Conclusion: Ellagic acid can prevent male infertility by improving antioxidant defense system. Busulfan induced testicular damage and sex hormone levels modulation.

Keywords • Ellagic acid • Oxidative stress • Busulfan • Rats

Evaluation of Pregnancy Outcomes in Women with Recurrent Implantation Failure after Intrauterine Receiving Peripheral Blood Mononuclear Cells: A Clinical Trial

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Abstract

Background: Some recurrent implantation failure (RIF) patients have no anatomical and serological problems but more accurate immunological tests show low Th-17/Treg ratio. We intended to investigate the effect of intrauterine administration of autologous human chorionic gonadotropin (hCG)-activated peripheral blood mononuclear cells (PBMCs) in RIF women with low helper T(Th)17/ regulatory T (Treg) cell ratio.

Methods: 100 women with at least three *in vitro* fertilization / embryo transfer (ET) failure and low Th-17/Treg ratio compared to healthy control were selected from 248 women who volunteered for PBMC-therapy. These 100 women were randomly divided into PBMC receiving (n=50) and control (n=50) groups. After the PBMCs were taken from the patients, they were treated with hCG for 48 hours. Then two days before ET and in the study group, PBMCs were administered into the uterine cavity. The inflammatory cytokines' concentration was investigated in the supernatant of cultured PBMCs after 2, 24, and 48 hours incubation by the enzyme-linked immunosorbent assay method.

Results: The Th-17, Treg frequency and the Th-17/Treg ratio was notably lower in RIF group than the healthy controls (P<0.0001). The inflammatory cytokines secretion was remarkably higher after 48 hours in comparison with 2 and 24 hours (P<0.0001). The pregnancy and live birth rate were considerably increased in PBMC-therapy group compared to phosphate buffer saline (PBS) -injecting (control) group (P=0.032 and P=0.047, respectively). The miscarriage rate was significantly lower in women undergoing PBMC- therapy (P=0.029).

Conclusion: According to our study, intrauterine injection of autologous hCG-activated PBMCs ameliorates pregnancy outcomes in patients with at least three IVF/ET failures.

Keywords • Fertilization in *Vitro* • Chorionic gonadotropin • Leukocytes • Mononuclear

A Comparative Study of Direct and Indirect Swim up Methods Efficacy on Pregnancy Rate of Intrauterine Insemination

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Abstract

Background: Swim-up is one of the techniques for sperm preparation which is commonly used to separate the functional motile spermatozoa from semen. This technique can be performed by two frequent methods: direct swim up and not direct (conventional) swim up. Intrauterine insemination (IUI) is the best first line and simple procedure for infertility treatment. There are scarcely studies comparing two methods of swim up simultaneously in IUI cycles. In the present study, we compared efficacy of two methods of swim up on pregnancy rate in infertile couples subjected to IUI.

Methods: A total of 177 infertile couples randomly included in this study were classified into two groups: direct swim up (n=92) and not direct swim up (n=85). Semen samples were collected and analyzed using conventional semen analysis according to the World Health Organization guidelines (2010). In method of direct swim up, liquefied semen sample is overlaid by culture medium in a conical tube without any centrifugation. While in conventional swim up, a pre-washed sperm pellet that obtained by centrifugation, is overlaid by culture medium. Fourteen days after IUI, positive or negative beta-human chorionic gonadotropin (β HCG) test were assessed and results compared between groups using independent T-test. P value less than 0.05 was considered significant value.

Results: There was no significant difference in positive β -HCG rate between groups (P=0.2). The mean percentages of positive β -HCG result in direct and not direct swim up groups were 15.2 vs 18.8, respectively. In addition, there were no significant difference in age and sperm quality (PH, volume, concentration, motility, morphology ...) between groups.

Conclusion: According to our study, both methods of direct and not direct swim up were effective in sperm preparation for IUI treatment, although not direct swim up method showed higher percentage of positive β -HCG result.

Keywords • Pregnancy rate • Chorionic gonadotropin • Insemination • Spermatozoa

Serum and Peritoneal Fluid Cytokine Profiles in Infertile Women with Endometriosis

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Abstract

Background: Endometriotic lesions are assumed to be the results of immune responses to retrograded endometrial cells and can cause infertility. Many immune cells including T helper subsets incorporate in immune responses. To achieve a good medical treatment, the main responsive cells and their cytokines should be determined. To unveil the pattern of T cell subsets and cytokines in endometriosis, cytokines related to T helper subsets (Th1/Th2/Th17/Treg) within both peripheral blood (PB) and peritoneal fluid (PF) samples from two groups of women were investigated and compared.

Methods: PB and PF samples were collected from 30 infertile endometriosis and 30 non-endometriosis fertile women during laparoscopy. Concentration of cytokines, including tumor necrosis factor alpha (TNF- α), Interferon gamma (IFN- γ), Transforming growth factor beta 1 (TGF- β 1), interleukin 4 (IL-4), IL-10, IL-17 and IL-23 were evaluated using Enzyme-linked immunosorbent assay method.

Results: Results indicated that the concentration of IFN- γ within serum was significantly reduced in endometriosis group (P=0.001). Regarding PF cytokines, TGF- β 1 was increased in endometriosis group (P=0.030). Furthermore, the ratios of IFN γ /TGF- β 1 and IL-17/IL-23 were significantly different between endometriosis and non-endometriosis women in serum samples (P<0.001 and P<0.01 respectively). The ratios of TNF- α /IL-10 and IL-17/IL-10 were also significantly different regarding PF samples between the two studied groups (P<0.04 and P<0.03 respectively). Finally, significant correlations were observed between the levels of IL-17 and IL-23, inflammatory and anti-inflammatory cytokines, in both samples and serum to PF inflammatory cytokines.

Conclusion: Based on the results of the present study, in women with endometriosis, the disturbance of cytokines network might gradually activate the inflammatory responses and tissue repair, resulting in endometriosis development after several years.

Keywords • Endometriosis • Infertility • T-lymphocyte subsets • Cytokines

The Potential Therapeutic Effects of Lactobacillus Plantarum and Inulin on Serum and Testicular Reproductive Markers in Diabetic Male Rats

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Abstract

Background: It is well established that diminished reproductive health is one of the notable long-term outcomes of type 2 diabetes mellitus (T2DM), especially among men. This negative outcome can be highly related to the oxidate phases in diabetes that impacts various organs and tissues, specifically testicular cells that are responsible for expression of several key proteins as well as testosterone production. It is suggested that 51 percent of cases with T2DM are facing subfertility and 40 percent of couples' fertility problems are due to male hypogonadism. On the other hand, recent studies suggested that administration of *L.plantarum* along with inulin promoted oxidative stress, serum markers, and neurological complications in diabetic male rats. Nevertheless, studies on the impacts of the supplementation on fertility problems are rare. The study investigated the impact of *Lactobacillus plantarum* (*L.plantarum*), inulin, and their combinatory supplementation on fertility markers and androgen receptor (AR)'s expression in diabetic male rats.

Methods: Thirty-five Male Wistar rats with Streptozotocin-induced T2DM were supplemented with *L.plantarum*, inulin, or their combination for 8 weeks. At the end-point, the animals were sacrificed and serum, testicular, and seminal parameters were studied using various methods.

Results: Administration of *L.plantarum* and inulin in diabetic male rats improved sperm motility and viability ($P<0.001$, both) as well as testicular tissue development via increasing leydig cell number, testicular spermatid count, and diameter of seminiferous tubules ($P<0.001$, all). *L.plantarum* administration increased testicular AR expression ($P=0.01$). In addition, we found that the study supplements could improve testicular function, possibly as a result of improved diabetic parameters and oxidative stress.

Conclusion: Supplementation with either *L.plantarum*, inulin, or their combination can prevent infertility caused by T2DM in male rats via improving AR expression, leydig cell count, and effectively increasing epididymal sperm motility and viability.

Keywords • *Lactobacillus plantarum* • Diabetes mellitus • Inulin • Rats

The Effects of Intra Ovarian Injection of Platelet-Rich Plasma on Ovarian Reserve and Clinical Outcomes in Infertile Women with Diminished Ovarian Reserve Undergoing *in Vitro* Fertilization

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Abstract

Background: Platelet-rich plasma (PRP) usage as intra-ovarian injection in women around menopause, increase antimullerian hormone (AMH) level but had no effects on this parameter in women with primary ovarian failure. There was limited evidence about this clinical practice in woman with diminished ovarian reserve. The aim of this study was to determine the effect of intra ovarian injection of PRP on ovarian reserve in infertile women with reduced ovarian reserve (DOR).

Methods: In this clinical trial, 15 infertile women, who had DOR were investigated. On the day of oocyte retrieval, platelet-rich plasma (PRP) autologous --calcium gluconate-activated 1 mL was injected into the ovaries.

Results: PRP injection increased AMH (0.54 ± 0.29 vs 0.64 ± 0.55), and although the levels of FSH, Estradiol and AFC were changed, this change was not statistically significant ($P>0.05$). One patient resulted in a miscarriage and another patient resulted in a live birth.

Conclusion: In infertile women with DOR, PRP injection is an alternative treatment option, especially at older ages and with tendency to use autologous eggs in the IVF cycle, but further studies are required on the benefits of using this method for ovarian reconstruction and its activation mechanism.

Keywords • Infertility • Platelet-rich plasma • Ovarian reserve • Fertilization *in vitro*

The Effect of Intrauterine Infusion of Platelet-Rich Plasma and Number of Infusion on Increasing Endometrial Thickness and Pregnancy Rate in Patients with Thin Endometrium: Before and After Clinical Trial

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Abstract

Methods: Intrauterine instillation of autologous PRP was done in 26 women between 20 and 40 years, with refractory thin endometrium (<7mm), and also patients with frozen embryo transfer (FET) cycle cancellations due to thin endometrium. In addition to estradiol valerate, hormone replacement therapy was administered for endometrial preparation in all participants. on the tenth day of the cycle, the thickness of the endometrium (ET) is determined, and if it was <7mm PRP intrauterine infusion was performed on day 11-12 and it was repeated on day 13-14 (after 48 hr) if ET<7mm. FET was performed when the endometrium reached an optimal pattern in terms of thickness.

Results: Endometrial thickness increased after the first intervention in all patients and All participants needed second intervention due to endometrial thickness is <7mm. The mean pre-PRP endometrial thickness (ET) was 5.64±0.79 mm (n=26) which significantly, increased to 7.20±1.27 mm (n=26) post-first PRP and increased to 7.65±1.29 mm (n=13) post-second PRP (P<0.001). There was a significant increase in second injection of PRP versus first injection in ET. Embryo transfer was done for all patients. The positive beta Human Chorionic Gonadotropin (HCG) rate was 23.1% and the clinical pregnancy rate was 19.2%. Six patients had chemical pregnancy; one patient had an ectopic pregnancy whereas the other five had healthy ongoing intrauterine pregnancies, and followed up till one of the patients had a twin spontaneous miscarriage due to rupture of membrane instead of normal cervical length in imaging in 23 week of gestational age.

Conclusion: According to the present study, it seems that injection of platelet-rich plasma (PRP) is an effective tool in increasing endometrial thickness and enhancing the results of IVF in women with refractory thin endometrium for embryo transfer and injecting twice between 24 till 72 hours is recommended in patients with thin refractory endometrium. PRP is made from autologous blood samples so it is a safe between method with minimal risk of transmission of infectious diseases and immune responses. However, as animal studies have been done before, more human studies are needed to further examine the benefits of platelet-rich plasma in the endometrium.

Keywords • Platelet-rich plasma • Endometrium • Infertility • Pregnancy rate

Evaluation of Quality and Quantity of Oocytes and Embryos in Patients with Unilateral Endometrioma and Its Comparison with the Opposite Side in Women Candidates for ICSI

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Abstract

Background: Endometriosis is one of the most common causes of infertility and implantation disorders. Ovarian endometrioma is a common form of endometriosis that may reduce the quality and quantity of oocytes and embryos. The aim of this study was to evaluate the quantity and quality of oocytes and embryos in women with infertility due to unilateral endometrioma and to compare these parameters with the opposite side.

Methods: This study included 98 women with unilateral endometrioma who were candidates for intracytoplasmic sperm injection (ICSI). Demographic characteristics including age, body mass index (BMI), spouse age, endometrioma size, and antimullerian hormone (AMH) level were recorded. Parameters such as total number of oocytes, number of germinal vesicle (GV), metaphase I (MI), and metaphase II (MII) oocytes, the total number of embryos, and quality of embryos were recorded and compared with opposite side.

Results: The mean age of the participants was 33.65 ± 3.92 years. There was no significant difference in the mean number of total oocytes ($P=0.100$) and MII oocyte ($P=0.060$) between the ovary with endometrioma and the opposite side, but the total number of embryos in the ovary with endometrioma (1.79 ± 1.78) was significantly lower than the opposite side (2.56 ± 2.49) ($P=0.002$). There was a statistically significant difference between the number of grade A and B embryos in the ovary with endometrioma and its opposite side ($P<0.05$).

Conclusion: Endometrioma may negatively affect the quality and quantity of oocytes, embryos, and consequently assisted reproductive technology outcomes.

Keywords • Anti-mullerian hormone • Oocytes • Embryonic structures • Infertility, female

Novel Non-Invasive Human Preimplantation Embryos Sex Determination Using STR-Based Fluorescent Multiplex Polymerase Chain Reaction on Days 3 and 5 Post-Fertilization

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Abstract

Background: Morphologically and genetically embryo selection prior to uterine transfer is a major aim of assisted reproductive techniques. To overcome the limitations of invasive embryo biopsy non-invasive methods such as the detection of cell-free DNA (CF-DNA) in biological fluids have been recently introduced. This study aimed to investigate the efficacy of CF-DNA in the spent cleavage and blastocyst media versus blastomere biopsy for sex identification using short tandem repeat (STR) markers for the first time.

Methods: 39 samples of spent culture media (SCM) from 6 couples were collected of which 28 samples were CF-DNA from blastocoel fluid (BF)+SCM (day 5) and 11 samples from SCM alone (day 3). The frequencies of allele drop-out (ADO), fail rate and informativity markers were considered. The relationship between the morphology of embryos and ADO and the amplification failure number of all markers was investigated. sex identification rate between CF-DNA isolated from culture media and Fluorescence in situ hybridization (FISH) was then compared with measurement of Agreement Kappa.

Results: The highest frequency of informative markers belonged to DXS6801 and hypoxanthine-guanine phospho ribosyl transferase. There was no relationship between the ADO number of all markers and embryo morphology. A significant difference was seen between embryo morphology and fail numbers. The Agreement Kappa value between CF-DNA isolated from culture media and FISH was 0.516 which is moderate. The ability of CF-DNA to detect the correct diagnosis of males and females showed that all values of specificity, sensitivity, positive predictive value, and negative predictive value were 100%.

Conclusion: The presence of embryonic CF-DNA in the SCM on day 3 as well as blastocyst media on day 5 using STR-based multiplex polymerase chain reaction is approximately consistent with FISH for sex identification. Advances in DNA extraction, amplification technique, and testing may allow for preimplantation genetic testing for aneuploidies (PGT-A) and preimplantation genetic testing for monogenic disorders (PGT-M) as non-invasive approach (NI-approach) without biopsy in the future either in sex determination or chromosomal abnormality.

Keywords • Sex determination analysis • Reproductive techniques, assisted • Genetic testing • Chromosome aberrations

Evaluation of the Effects of Fine Dust on Elliptical Tissues and Exocrine Glands in Male Rats in Asalouyeh, Iran

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Abstract

Background: Air pollution caused by fine dust can lead to diseases such as irritating asthma, bronchitis, heart and lung diseases, and respiratory allergies. Heavy metals such as cadmium, arsenic, mercury, nickel, lead, and zinc have recently demonstrated endocrine system inhibitory activity in laboratory animals. Therefore, considering the presence of heavy metals such as zinc, copper, iron, and nickel in the soil and dust of the Asalouyeh public area, and also the location of oil and gas facilities, this area is considered one of the most polluted areas in the world. This study aimed to investigate the effect of fine dust in Asalouyeh-infected areas on endocrine tissue changes as well as related hormones in adult rats.

Methods: Twenty-eight male rats were divided into three groups: control, negative control (exposed to dust in the Pak area of Gorgan), and treatment group (exposed to dust in the Asalouyeh infected area). At the end of the day, the animals were anesthetized, then blood samples and tissue biopsies were taken and the levels of thyroid, liver, prostate and testosterone hormones, and their tissue changes were evaluated. The levels of heavy metals, lead, cadmium, arsenic, and mercury in animal serum were also measured using atomic absorption. Descriptive statistics for the study quantitative variables were analyzed using mean and standard deviation and one-way ANOVA test to compare the mean of variables between groups.

Conclusion: Polluted air dust in Asalouyeh has toxic effects on testicular and exocrine tissues (prostate, meniscus) as well as the levels of related hormones (T3, T4, TSH, PSA, testosterone, AST, ALT, and ALP).

Keywords • Infertility • Exocrine glands • Dust • Rats • Iran

Schema Therapy on the Component of Being Guided by Others (Attracting Attention) of Infertile Women Under Treatment in Bushehr

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Abstract

Background: There has been scattered research on the effectiveness of schema therapy on other schemas in various fields domestically and internationally, but it is very difficult to gather information on the effectiveness of schema therapy on various psychological components. Schema therapy helps the therapist to more accurately define patients' chronic and profound problems and to organize them in a comprehensible way. Therefore, considering the importance of infertile women and the components affecting them, and the role of maladaptive schemas in the quality of treatment of infertile women in this study, this study aimed to investigate the effectiveness of schema therapy on the component of guidance by others (attracting attention) infertile women.

Methods: The research method was quasi-experimental using therapeutic schema and Young incompatibility schema. The statistical population included infertile women under treatment in Bushehr. Thirty people were selected by available methods (15 in the control group and 15 in the experimental group). Data analysis was performed in SPSS software.

Results: Schema therapy led by others (attracting attention) of infertile women treated in Bushehr has a significant effect. That is, the difference in the activity of being guided by others (attracting attention) of infertile women in the experimental and control groups is statistically significant.

Conclusion: Therapeutic schema has been able to reduce the activity of the schema of disturbed borders (entitlement and distrust).

Keywords • Schema therapy • Infertility, female • Attention • Iran

Schema Therapy on the Component of Disturbed Boundaries (Entitlement and Distrust) of Infertile Women Under Treatment in Bushehr

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Abstract

Background: Therapeutic schemas help the therapist to more accurately define patients' chronic and profound problems and organize them in a comprehensible way.

Therefore, considering the importance of infertile women and the components affecting them, and the role of maladaptive schemas in the quality of treatment of infertile women in this study, this study aimed to investigate the effectiveness of schema therapy on the component of disturbed boundaries (entitlement and distrust). Infertile women are being treated in Bushehr.

Methods: It was performed quasi-experimentally using therapeutic schema and Young incompatibility schema. The statistical population included infertile women under treatment in Bushehr. Thirty people were selected by available methods (15 in the control group and 15 in the experimental group. Data analysis was performed in SPSS software.

Results: Schema therapy has a significant effect on the component of disturbed boundaries (entitlement and distrust) of infertile women treated in Bushehr. That is, the difference in the activity of the disorder component of boundaries (entitlement and distrust) of infertile women in the experimental and control groups is statistically significant.

Conclusion: The treatment schema was able to reduce the activity of the schema of impaired boundaries (entitlement and distrust).

Keywords • Schema therapy • Infertility, female • Iran

The Effect of Eight Weeks of Aerobic Exercise in Water with Honey and Cinnamon Supplementation on Fertility Parameters in Inactive Men Aged 20-25 Years in Bushehr

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Abstract

Background: Research shows that one in six couples does not have children. Statistics show that there are more than three million infertile couples in Iran. Exercise and physical activity play an important role in vitality, improving blood circulation, and reducing stress. On the other hand, consuming hot and energetic spices such as honey and cinnamon combined with eight weeks of regular aerobic exercise can improve fertility parameters in men.

In this study, we compared fertility parameters in inactive men aged 20-25 years in Bushehr following aerobic exercise in water and simultaneous consumption of cinnamon and honey.

Methods: Sixty non-athlete men from Bushehr were included in the study. Water exercise training protocol was applied in the form of eight weeks of aerobic exercise, three sessions per week, and consumption of cinnamon 150 mg of water per day, a teaspoon of cinnamon powder, and a tablespoon of honey jam. A sampling of menu fluid was collected for cement analysis. We used an independent sample t test to compare quantitative variables between the case and control groups.

Results: Examination of semen analysis in non-athletes after a full period of different treatments showed that in inactive men, sperm motility increased relatively significantly, and this difference was significant. However, no morphological changes were observed in semen parameters. Also, the concentration and adhesion of cement fluid had a lower normal viscosity than after the treatment period.

Conclusion: Findings from this study showed that aerobic exercise in the water with natural energy supplements such as honey and cinnamon improves blood circulation and increases spermatozoon stimulation.

Keywords • Exercise • Fertility • Dietary supplements • Cinnamomum zeylanicum • Iran

The Relationship between Blood Group and Male Infertility in Infertility Centers in Urmia and Ardabil City

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Abstract

Background: Many studies have reported the association of blood types with several diseases. There are also reports that there may be similar links between blood types and infertility in humans, but few studies have been conducted in this area.

Methods: In the present cross-sectional study, 200 men registered as infertile in the Urmia and Ardabil infertility center systems were included, and their blood group information was collected and compared with the prevalence of blood groups in the normal population of Iran. The weight-by-count method and Chi-square test were used to compare the studied infertile population with the general population. Also, the relative risk of infertility for each blood group was calculated.

Results: The mean age of patients was 38.26 years (with a standard deviation of 7.74). 135 patients (67.5%) had blood group O, 10 patients (5%) had blood group A, 15 patients (7.5%) had blood group B, 40 patients (20%) had blood group AB, 185 patients (92.5%) had RH +, and 15 patients (7.5%) had RH -. The distribution of ABO blood groups in patients was statistically different in comparison with the normal population ($P < 0.001$), but there was no significant difference between these patients and the general population in terms of RH ($P = 0.142$). Men with blood groups O and AB had a significantly increased risk of infertility (OR=3.551 and $P < 0.001$ for blood group O and OR=3.031 and $P < 0.001$ for blood group AB), while men with blood groups A and B had a significantly decreased risk of infertility (OR=0.114 and $P < 0.001$ for blood group A and OR=0.259 and $P < 0.001$ for blood group B).

Conclusion: The results of the present study showed that there is a statistically significant relationship between blood groups and male infertility, so that the risk of infertility in men with blood group O or AB was significantly higher, while the risk in men with blood group A or B was significantly lower. However, these findings need to be considered and confirmed in other populations.

Keywords • Infertility, male • ABO blood-group system • Azoospermia • Iran

The Protective Effects of L-proline on Cryodamage of Normal Human Spermatozoa

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Abstract

Background:

Sperm cryopreservation as routine technique in Assisted Reproductive Technique (ART) labs has detrimental effects on spermatozoa. Various methods have been introduced to improve it. The aim of this study was to investigate the effects of L-proline supplementation in cryopreservation medium on human sperm during cryopreservation.

Methods: In this study, 30 semen samples were collected from normozoospermic men who referred to the IVF clinic of Kermanshah Motazedi Hospital. Cryopreservation media were supplemented with different concentrations of L-proline (0, 1, 2, and 4 mmol/L). The semen samples with the concentrations were cryopreserved. After thawing, sperm parameters (motility, morphology, and viability), sperm chromatin integrity (aniline blue (AB), toluidine blue (TB), sperm chromatin dispersion test (SCD) and Chromomycin A3 (CMA3)), reactive oxygen species (ROS), and total antioxidant capacity (TAC) and malondialdehyde (MDA) levels were evaluated.

Results: Cryopreservation significantly decreased all sperm parameters ($P<0.05$). 4 mmol/L L-proline significantly improved progressive motility and viability ($P<0.05$) and non-significantly normal morphology in treated sperm. MDA and ROS levels significantly diminished in samples that were cryopreserved by 4 mmol/L L-proline-supplemented cryopreservation media ($P<0.001$). Also, it significantly increased the TAC level. Also, the result showed that chromatin damages (AB, TB, CMA3) significantly improved in samples that were cryopreserved by 4 and 2 mmol/L L-proline supplemented cryopreservation media ($P<0.05$). In addition, these improvements were dose-dependent.

Conclusion: The results support the usage of L-proline-supplemented cryopreservation media to improve sperm parameters and chromatin integrity after cryopreservation. Also, it improved the oxidative stress of spermatozoa after cryopreservation.

Keywords • Cryopreservation • Spermatozoa • Oxidative stress • Proline • Chromatin

Functional Oocyte-like Cells Derived from Embryonic Stem Cells

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Abstract

Stem cell biology has grown rapidly recently, but there is considerable confusion about its function. Since their characterization of them is difficult, they are useful when provide a basis for understanding the physiology of differentiation. A multipotent stem cell can generate many differentiated cells with distinct functions and gene expression patterns. Due to their unlimited source and high differentiation potential, stem cells are considered for the treatment of infertility.

Stem cells could be stimulated *in vitro* to develop various numbers of specialized cells, including male and female gametes used in reproductive medicine. The continuation of mammalian species requires the formation and development of sexually dimorphic germ cells. This cell seems to be functional because of its physiological properties and embryo production. Totipotent embryonic stem (ES) cells are similar to primordial germ cells, and therefore they can differentiate toward gamete with the same functional behavior. ES cells may be ideal for creating a new embryo and its organs by new protocols.

The development of oogonia that enter meiosis, and recruit adjacent cells to form follicle-like structures, is a challenge of gamete creation which it needed more consideration.

Keywords • Embryonic stem cells • Oocytes • Infertility • Germ cells

The Effect of Maternal Age on the Outcome of *in Vitro* Fertilization Treatment

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Abstract

Infertility is the inability of a couple to become pregnant after one year of unprotected intercourse. Currently, there are several different types of infertility treatments, including ovulation induction, insemination with semen, and assisted reproductive technology (ART), such as *in vitro* fertilization (IVF). IVF is the process of fertilization outside the human body to treat infertility that involves ovarian hyper stimulation, oocyte and sperm retrieval, fertilization, and embryo formation in a laboratory. The characteristics of the couple such as parental age, reproductive history, and the cause of infertility can have a substantial effect on the IVF success rate. One of the main limiting factors to IVF outcomes is the female's age, especially in women over 40 years old. Advanced maternal age (AMA) as a social and clinical problem can be associated with career goals or medical reasons. AMA patients have the lowest number of retrieved oocytes, clinical pregnancy, and live birth. Also, maternal age shows adverse effects on embryo quality, blastocyst aneuploidy rate, and telomere length. This study aimed to determine the effect of maternal age on the outcome of IVF treatment.

Keywords • Infertility • Fertilization *in vitro* • Maternal age • Aneuploidy

Effect of Plasma-Rich Growth Factors on Sperm Parameters in Teratozoospermic Samples

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Abstract

Background: A direct correlation exists between teratozoospermia and oxidative stress, which causes poor assisted reproductive techniques (ART) outcomes.

This study aimed to investigate the effect of plasma-rich growth factors (PRGF) incubation on the quality of teratozoospermic samples.

Methods: Semen samples were collected from 25 teratozoospermic men attending clinics of Gandhi and Akbarabadi hospitals. After density gradient centrifugation, the spermatozoa culture medium was supplemented with different concentrations of PRGF (0%, 1%, 5%, and 10%). Sperm motility, viability (eosin-nigrosin), morphology (Papanicolaou), DNA fragmentation index (sperm chromatin dispersion test), mitochondrial membrane potential (JC-1 staining by flow cytometry), and lipid peroxidation (malondialdehyde) were measured and analyzed before and after one hour incubation.

Results: Our results showed that after one-hour incubation, the addition of 1% PRGF improved sperm progressive motility (47.72 ± 13.76) compared to the control group (17.36 ± 8.50) ($P < 0.001$). Also, 1% PRGF preserved the sperm's total motility and viability. A higher mitochondrial membrane potential and a lower DNA fragmentation were also observed in sperm supplemented with PRGF compared to controls, but the differences were not significant ($P > 0.05$). PRGF significantly reduced malondialdehyde levels in all doses compared to the control group ($P < 0.01$). The rate of normal sperm morphology was the same between different groups.

Conclusion: It seems PRGF improves the quality of the sperm and could be applied in ART to improve sperm parameters in teratozoospermic samples. Further studies assessing additional sperm parameters, including reactive oxygen species, and molecular mechanisms of PRGF effect on sperm quality and function, help clinicians to improve ART results.

Keywords • Teratozoospermia • Spermatozoa • Reproductive techniques, assisted • Plasma

Efficacy of Foeniculum Vulgare on Insulin Resistance and Anthropometric Indices in Women with Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is associated with metabolic syndromes such as insulin resistance and obesity. Foeniculum Vulgare (Fennel) is a traditional herbal safe remedy in many countries, especially in the Mediterranean region.

The study seeks to find the efficacy of fennel on the insulin resistance and anthropometrics of PCOS women.

Methods: This clinical trial study was carried out in an infertility center affiliated with Babol University of Medical Sciences in 2017- 2018. 28 PCOS women with insulin resistance received a hypocaloric diet for 3 months and then received essential oil of fennel (3 capsules 30 mg/day) and the diet was continued as well. Insulin resistance markers HOMA (IR), insulin sensitivity (QUICKI), and anthropometric indices before and after intervention were analyzed.

Results: The mean age of women was 26.7 ± 5.53 . A significant difference was found in the HOMA (IR) 29.67 ± 4.29 versus 30.57 ± 4.08 , $P=0.004$, QUICKI (0.38 ± 0.04 versus 0.14 ± 0.0 , $P=0.000$, and BMI (29.67 ± 4.29 versus 30.57 ± 4.08 , $P=0.000$) before and after the intervention on behalf of the fennel group. The waist-to-hip ratio was also compared before and after the intervention.

Conclusion: Fennel might potentially have certain antihyperglycemic properties and may act as a therapeutic option offered alongside other Insulin resistance treatments in women with polycystic ovary Syndrome.

Keywords • Foeniculum • Insulin resistance • Polycystic ovary syndrome • Anthropometry

Detection of SARS-CoV-2 RNA in the Seminal Fluid and its Impact on Male Fertility: A Systematic Review

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Abstract

Background: As there is an increase of infections in the male population, concerns have emerged about the potential impact of COVID-19 on male fertility. This study aimed to investigate systematically the presence of SARS-CoV-2 RNA in the semen and determine the contagiousness of sperm and its influence on male fertility after COVID-19 infection.

Methods: Electronic searches were performed in PubMed/MEDLINE, SCOPUS, and Web of Science up to December 2021 regarding the existence of SARS-CoV-2 RNA in seminal fluid, testis, and the effects of COVID-19 on male reproduction. A total of 24 original articles were included in the study.

Results: The presence of a virus in a semen sample is still a topic of discussion and research due to the small number of studies. Only two studies identified viral mRNA in the semen of infected men; others stated semen is not infectious with SARS-CoV-2 at one week or more after COVID-19 infection. However, couples with a desire for pregnancy should be warned that sperm quality after COVID-19 infection can be suboptimal. According to the existing clinical data, this virus could infect the testis and the male genital tract and cause damage to male fertility. It shows a negative impact on male reproductive health, inducing spermatogenic failure. However, the mechanism for testicular involvement remains doubtful.

Conclusion: SARS-CoV-2 RNA was undetectable in all semen samples, but it may cause testicular involvement and impact the male reproductive system inducing spermatogenic failure.

Keywords • Reproduction • Semen • SARS-CoV-2 • COVID-19
• Fertility

Application of Stem Cell Treatment for Infertility

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Abstract

Background: Infertility is now recognized as a global health problem, affecting about 15% of couples worldwide.

Hence, alternative therapies such as the use of stem cells have been considered. In this study, we discuss the effect of stem cells in the treatment of infertility.

Methods: In our study, the keywords “Stem Cell” and “Infertility” were searched in the Google scholar search engine and PubMed gateway without any time limitation. Finally, the most relevant articles were examined.

Results: Several factors contribute to the etiology of distrust, including genitourinary growth and functional defects, gametogenesis, gametogenesis, or erection defects. In this regard, stem cells show new hope in various experimental preclinical and clinical models to overcome infertility-related problems in the form of cell-based therapies. Stem cells are a subtype of cells that remain undifferentiated in embryonic and adult tissues and can self-renew and differentiate as needed.

According to their origin, stem cells are classified as follows: Embryonic stem cells (ESC), adult stem cells (includes mesenchymal stem cells MSC), induced pluripotent stem cells (iPSC), spermatogonial stem cells (SSCs), and ovarian stem cells.

Due to their unlimited origin and high differentiation potential, stem cells are considered as potential novel therapeutic agents for the treatment of infertility.

Conclusion: Stem cells are currently being increasingly studied as a promising alternative therapy in translational regenerative medicine research. To this end, stem cells have been extensively studied for their useful functions. Advances in this area have diminished the expectation that stem cell therapy can treat many diseases. However, increasingly large clinical trials are needed to demonstrate the safety and efficacy of stem cell-based therapies in the field of human reproduction.

Keywords • Stem cells • Infertility • Therapeutics

Gene Expression Profiles in Cumulus Cells in Poor Responders Undergoing Ovarian Stimulation

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Abstract

Background: Although several studies have investigated the effect of controlled ovarian hyperstimulation on oocytes gene expression, the optimal protocol for patients with a poor ovarian response (POR) has still been a challenge. This study aimed to compare the gene expression profile in human cumulus cells (CC) in terms of oocyte maturity in PORs to controlled ovarian hyperstimulation (COH) using delayed start (DS) Gonadotropin-releasing hormone (GnRH) antagonist versus Flare-up (FU) GnRH agonist.

Methods: This prospective randomized controlled study was conducted on 42 women, aged 34.5±3.64, who had POR according to bologna criteria. They were randomly divided into two groups, including the FU and the DS group. The growth differentiation factor 9 (*GDF9*), Bone morphogenetic protein 1 (*BMP15*), and leukemia inhibitory factor (*LIF*) gene expression levels in human CC and *in vitro* fertilization (IVF) outcomes were compared between groups.

Results: The mean number of immature, mature, and postmature oocytes was significantly different across the two groups. The gene expression level of *GDF9* in immature oocytes was significantly up-regulated in the FU group compared to the DS group (p=0.028). While, there was no significant difference in terms of the gene expression level of *LIF* and *BMP15* in both mature and immature oocytes between the two groups. A negative significant correlation between the *LIF* gene expression and AFC was observed in the FU group.

Conclusion: We concluded that the expression of the *GDF9* gene of CC is up-regulated in FU compared to the DS approach. Finally, there is no significant difference between the FU protocol versus DS protocol.

Keywords • Ovarian hyperstimulation syndrome • Growth differentiation factor 9 • Leukemia inhibitory factor • Cumulus cells • Ovulation induction • Female

Effects of Hypothermia and Pentoxifylline on the Adnexal Torsion/Detorsion Injuries in a Rat Testis Model

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Abstract

Background: The current surgical urogenital emergency in young adults and children is testicular torsion (TT) that has been regarded to be the second current surgical emergency in young males. Estimations indicated 1 of 4,000 young men aged over 25 years is affected by testicular torsion. Moreover, multiple results demonstrated variability of the pathophysiology of the injury concerning the grade and duration and ischaemia. The purpose of this study was to see how separate and combined administrations of hypothermia and pentoxifylline affected on the testicles in an experimental model of testicular torsion/detorsion injury in rats

Methods: Forty male adult Wistar rats were randomly divided into five groups, control, torsion/detorsion (TD), torsion/detorsion/hypothermia (TD+ICE), torsion/detorsion received of pentoxifylline (40 mg/kg, ip) (TD+PTX) and torsion/detorsion/hypothermia/PTX (TD+ICE+PTX). Left testicular torsion (TT) was performed for 4 and half hours, and ice fragments have been used at the beginning of the torsion. After the reperfusion period (a week), the oxidative marker's serum levels, testosterone hormone, sperm parameters, and histopathological and gene expression evaluations have been performed.

Results: Histological factors, sperm count, oxidative marker, testosterone hormone, Bax, BCL2, and caspase-3 expression all showed significant negative alterations in the TD group. The parameters investigated in the PTX group improved as compared to the TD group, although macroscopical parameters in the hypothermia and PTX+ICE groups did not vary from the TD group. The results showed that PTX, as an antioxidant ingredient, increased the activities of antioxidant enzymes, decreased the expression of Bax, and decreased the rate of apoptosis in rat testicular tissues following torsion detorsion, but hypothermia and hypothermia plus PTX did not.

Conclusion: The results revealed that PTX, as an antioxidant component, was protective against testicular torsion, while hypothermia and hypothermia plus PTX did not exhibit this property, which may have been due to the duration of hypothermia (4 hr) or reperfusion period.

Keywords • Pentoxifylline • Hypothermia • Testis • Ischaemia
• Reperfusion

MicroRNA-326 in CD4+ Lymphocytes Might be a Potential Suspect in Pre-Eclampsia

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Abstract

Background: Alongside the complex etiology of Pre-Eclampsia (PE), several determinants, such as the imbalance proportion of anti-angiogenic/proangiogenic factors and T-cell subsets, especially CD4+ (Th17/Treg), as well as the alteration in the expression profile of related cytokines, miRNAs, and transcription factors might have been implicated in PE pathogenesis. We assumed that miRNA-326 has a pivotal role in CD4+ lymphocytes, particularly Th17's development which can responsible for the release of many effector mediators such as IL-17 and IL-22. Furthermore, Th17 could be an extra source for the production of antiangiogenic factors.

Methods: CD4+ T-cells were collected from PE and non-PE pregnant women and cultured, subsequently. Therefore, several assessments by flow cytometry, real-time PCR, western blotting, and ELISA were performed to evaluate the level of targeted determinants related to PE symptoms, including sFlt-1, sEng, STAT-3, ROR γ t, SMAD-7, Foxp-3, IL-17, IL-22, Ets-1, and miRNA-326.

Results: Our results revealed that in women with preeclampsia, the miRNA-326 expression level increased in CD4+ T-cells and Th17s as a downregulation for Ets-1 expression to suppress Th17s development. Moreover, we showed that the number and expression level of Th17s and transcription factor ROR γ t escalated. However, Treg and its related transcription factor (Foxp3) demonstrate a decline. Flow cytometry evaluation illustrated that the Th17/Treg ratio increased in PE. Additionally, we claimed that expression and concentration levels of cytokines (IL-17 and IL-22) and anti-angiogenic molecules (sEng and sFlt-1) soared in isolated CD4+ cells from PE patients, which could be closely correlated with PE pathogenicity.

Conclusion: In conclusion, we comprehensively assessed immunological factors and molecules involved with PE manifestation. Interestingly, the CD4+ T-cell subset could be considered as an extra source for antiangiogenic factors throughout the maintenance of this hypertension disorder.

Keywords • Pre-eclampsia • Th17 cells • MicroRNAs • FLT1 protein, human • CD4-positive t-lymphocytes

Gallic Acid Improves the Quality of Post-Thaw Human Spermatozoa

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Abstract

Background: In the clinic, human sperm cryopreservation is the most effective treatment for male infertility. However, during cryopreservation, the generation of reactive oxygen species (ROS) has a deleterious impact on sperm quality and reproductive potential.

This study aimed to determine how post-thaw morphology, motility, viability, DNA structure, and plasma membrane lipid peroxidation are affected in sperm cryopreserved in medium supplemented with gallic acid.

Methods: The following four groups were considered for this study: 1) Fresh sperm before cryopreservation; 2) cryopreserved control sperm without supplementation; 3) cryopreserved sperm using freezing media supplied with 50 g/ml gallic acid; and 4) cryopreserved sperm using freezing media supplemented with 100 g/ml gallic acid.

Results: The results of this study showed that adding doses of 50 g/ml gallic acid to cryopreservation medium improved sperm morphology, motility, vitality, and DNA integrity, as well as reducing DNA fragmentation and lipid peroxidation when compared to the medium without any gallic acid supplementation ($P < 0.05$); however, adding 100 g/ml gallic acid had no significant effects on the mentioned sperm parameters ($P > 0.05$).

Conclusion: The findings of this study suggest that augmenting sperm freezing media with gallic acid as a natural antioxidant could improve sperm properties and reduce the negative effects of reactive oxygen species (ROS) on sperm DNA structure during cryopreservation. Gallic acid may thus aid in the improvement of the quality and, as a result, the fertilization potential of cryopreserved human sperm.

Keywords • Gallic acid • Spermatozoa • Infertility, male

Beneficial Effects of Quercetin on Ovariectomy-Induced Osteoporosis

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Abstract

Background: Male infertility can affect the life quality of men and women. Busulfan, which is used for cancer treatment, causes sterility in male patients. This study aimed to investigate the effects of Ellagic acid on sexual hormones, testicular tissue, the body's antioxidant system, and apoptosis pathway in the busulfan-induced relative sterile rat model.

Methods: Sixty-five male Sprague-Dawley rats were randomly divided into the following groups: control, Ellagic acid, busulfan, and busulfan plus Ellagic acid. After 48 days of treatment, the rats were anesthetized with a ketamine xylazine mixture, and blood samples were collected by cardiac puncture. Then the animals were sacrificed, and testicles were removed for stereological and gene expression analysis. FSH, LH, testosterone, catalase, total antioxidant capacity, malondialdehyde, and glutathione peroxidase activity were assessed. mRNA expression of Bcl-2 and caspase-9 was also assessed by real-time PCR. Testicular tissue changes were also examined by stereological methods.

Results: Busulfan group had significantly lower total antioxidant capacity, serum testosterone, Bcl2 mRNA expression, testicular volume, seminiferous tubule, germinal epithelium, and interstitial tissue volume, and the number of spermatogonia, spermatocyte, round spermatid, elongated spermatid, Leydig cells, and Sertoli cells than the control group. LH, FSH, caspase 9 expression, and malondialdehyde level were higher in the busulfan group. Ellagic acid administration significantly increased the testosterone, Bcl-2 expression, and antioxidant markers and also significantly decreased LH and FSH serum levels. Stereological parameters were improved after Ellagic acid treatment.

Conclusion: Ellagic acid can prevent male infertility by improving the antioxidant defense system, busulfan-induced testicular damage, and sex hormone level modulation.

Keywords • Quercetin • Osteoporosis • Ovariectomy • Female

Detection of SARS-CoV-2 in Follicular Fluid of COVID-19 Infected Women

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Abstract

Background: The coronavirus disease-2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is now spread all over the world. This study was designed to assess the possibility of SARS-CoV-2 presence in follicular fluid, which may have harmful effects on normal ovulation and fertility.

Methods: Five women who were candidates for Assisted Reproductive Technique (ART) and had a COVID-19 PCR-positive test on the day of oocyte retrieval participated in the study. SARS-CoV-2 tests were performed on the follicular fluid obtained from these women.

Results: SARS-CoV-2 RNA was detected only in one follicular fluid sample, and other follicular fluid samples were negative.

Conclusion: Because the COVID-19 effect on human reproduction is unknown, exact precautions should be taken during this pandemic, especially for women applying for ART.

Keywords • SARS-CoV-2 • Follicular fluid • Female • Reproductive techniques, assisted

Improving Effects of Vitamin E on Ovariectomy-Induced Osteoporosis

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Abstract

Background: Postmenopausal women complain of several menopause consequences. Osteoporosis is the most prevalent consequence of menopause, resulting in bone fragility and susceptibility to fracture due to loss of bone. This study aimed to assess the impacts of vitamin E on ovariectomy-induced osteoporosis.

Methods: Twenty-four adult female Sprague-Dawley rats were divided into 4 groups: sham operated, ovariectomized, vitamin E vehicle, and vitamin E. After 10 weeks of treatment, animals were sacrificed and tibias were removed for stereological investigation.

Results: Ovariectomy led to development of osteoporosis as demonstrated by decrease in bone and trabeculae volumes, bone weight, total number of osteoblasts and osteocytes, and increase in total number of osteoclasts. Vitamin E improved osteoporosis by reversing these changes.

Conclusion: Vitamin E has beneficial effects on ovariectomy-induced osteoporosis and can be considered a complementary treatment along with common anti-osteoporosis drugs.

Keywords • Vitamin E • Osteoporosis • Ovariectomy • Female

Treatment Effects of Selenium on Electromagnetic Field-Induced Apoptosis, Aromatase P450 Activity, Leptin Receptor Expression in Rat Testis

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Abstract

Background: The electromagnetic field (EMF) emitted by mobile may affect the male reproductive system. As an antioxidant, selenium may protect against the effect of electromagnetic field-induced tissue damage.

Methods: Twenty-four male Wistar rats were randomly divided into four groups, namely the EM group (2100 MHZ), EM/SE group (2100 MHZ + 0.2mg/kg), SE group (0.2mg/kg), and control group. Serum LH, FSH, testosterone, leptin and aromatase levels, testis weight and volume index, sperm parameters (count and abnormal percent), seminiferous tubule diameters, germinal epithelium thickness, and immunoreactivity of leptin receptor and caspase3 (for apoptotic cells in germinal epithelium) were investigated.

Results: Our results showed that serum LH, FSH, GnRH, testosterone level, sperm count, germinal epithelium thickness, and seminiferous diameters were significantly reduced compared to the control group ($P < 0.05$). However, serum leptin and aromatase level, sperm abnormality, apoptotic cells, and leptin receptors were significantly increased in the EM group compared to the control group ($P < 0.05$).

Furthermore, there was an increase in sperm count, germinal epithelium thickness, seminiferous diameters, serum LH, FSH, and GnRH, and testosterone levels, and a significant decrease in sperm abnormality, leptin receptor and apoptotic cell in EM/SE group compared to EM group ($P < 0.05$).

Conclusion: This study showed that EMF exposure may have detrimental impacts on the male reproductive system, which can be prevented by the use of selenium.

Keywords • Electromagnetic fields • Selenium • Apoptosis • Testis • Receptors, leptin

Recent Clinical Evidences on Traditional Persian Medicine Topical Suggestions for the Treatment of Sexual Dysfunction in Men: A Review Article

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Abstract

Background: Sexual dysfunction is one of the most prevalent complaints in men over age 50, which can negatively affect marital life and self-esteem. Consumption of oral drugs has various limitations, and they have adverse interactions with other oral agents.

Methods: In this review article, the Traditional Persian Medicine (TPM) resources were reviewed for topical suggestions on treating sexual dysfunction in men. The herbal medicines and their constituents were searched in modern medical search engines.

Results: In TPM resources, various agents in oil, decoction, dry powder, suppository, and enema preparations are suggested to treat decreased libido, premature ejaculation, and erectile dysfunction. These preparations often include volatile agents that enhance percutaneous absorption. Some of the known constituents of these preparations are known to enhance the regional blood flow to the genitalia, some of them induce venous smooth muscle relaxation, and others increase the tonicity of pelvic floor muscles.

Conclusion: TPM suggestions in treating sexual dysfunction in men can ignite new ideas for further research based on the proposed mechanisms of action.

Keywords • Medicine, Persian • Sexual dysfunction, physiological • Herbal medicine

Intrauterine Instillation of Human Chorionic Gonadotropin with Intrauterine Insemination Catheter Around the Golden Time of Embryo Transfer Does Not Improve *In Vitro* Fertilization/ Intracytoplasmic Sperm Injection Outcomes in Infertile Women: A Randomized Controlled Trial

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Abstract

Background: Instilled human chorionic gonadotropin (hCG) inside the uterine cavity before embryo transfer (ET) is believed to exert its effect via two principal mechanisms comprising instigation of immune cells immigration into the uterus, and induction of a variety of cytokines in endometrium within the implantation window by modulating cytokine signaling transduction pathways. Considering the results of the two last meta-analyses of randomized controlled trials, in infertile women undergoing assisted reproduction, the optimal *in vitro* fertilization (IVF)/ intracytoplasmic sperm injection (ICSI) outcomes including live birth rate (LBR), ongoing pregnancy rate (OPR), clinical pregnancy rate (CPR), and implantation rate (IR) can be obtained with local administration of 500 IU hCG via ET catheter during 15 minutes preceding ET, particularly at the cleavage stage. We set out to explore the effect of intrauterine hCG instillation by insemination (IUI) catheter before ET on assisted reproductive technologies (ART) outcomes of infertile women.

Methods: One hundred women with infertility who were scheduled for IVF/ICSI cycles were included in the study. They were randomly devoted to two groups: experimental (n=50) and control (n=50). In the experimental group, 500 IU hCG passed into the internal cervical orifice via an IUI catheter within 15 minutes before the transfer of fresh or vitrified cleavage-stage embryos. The control group underwent the same ET procedure without prior injection of hCG.

Results: None of the outcomes showed a statistically significant difference between the two groups. In the intervention and control groups, respectively, biochemical pregnancy rates were 26% and 18%, IR were 13.5% and 8.6%, CPR were 22% and 14%, OPR were 18% and 14%, and LBR were 14% and 12%.

Conclusion: Intrauterine injection of hCG via IUI catheter is not recommended in a clinical routine setting at this stage. Future efforts are warranted to further refine the applicability of this modality.

Keywords • Reproductive techniques, assisted • Embryo transfer • Chorionic gonadotropin • Infertility, female • Sperm injections, intracytoplasmic

Differentiation of Human Menstrual Blood Stem Cells into Female Germ Cells in Indirect Co-culture with Human Granulosa Cells

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Abstract

Background: Infertility is a genital disease that defines a couple's inability to conceive after twelve months of regular and unprotected sex. Infertility affects approximately 10 to 15 percent of couples worldwide. The evaluation of female factors has traditionally been the trigger for infertility studies. Causes of ovulation are the most common contributing factor to infertility. Despite advances in assisted reproductive technologies, infertility remains a serious problem. In recent years, significant advances in cell therapy have emerged as an emerging approach to infertility treatment.

This study aimed to differentiate human menstrual blood stem cells (MenSCs) from female germ cells in indirect co-culture with human granulosa cells (GCs), which is a type of human *in vitro* gametogenesis that can transform reproductive medicine.

Methods: In this study, MenSCs and GCs after isolation and culture were examined for expression of mesenchymal (CD105, CD29, CD44, CD73, CD90, CD10, and CD9) and hematopoietic (CD45, CD34, CD38, C and D133) markers by flow cytometry. Subsequently, the cells were divided into two groups, including the control group (culture of MenSCs without co-culture with GCs) and the co-culture group (culture of MenSCs in co-culture with GCs). After two weeks, the expression of specific markers of female gametes (Vasa, SCP3, and GDF9) at both molecular and protein levels were examined by Real time-PCR and immunocytochemistry techniques, respectively.

Results: Results from real-time PCR of the co-culture group showed the activation of germ cell-specific genes, including GDF9, Vasa, and SCP3, after two weeks, indicating cell differentiation. The expression of the above-mentioned genes was not observed in the control group. Immunocytochemical analysis used for the expression of oocyte markers showed that the mentioned genes were expressed in the co-culture group, while the control group did not express these genes.

Conclusion: Co-culture of GCs with MenSCs is an effective inducer for the differentiation of MenSCs into oocyte-like cells.

Keywords • Cell differentiation • Peripheral blood stem cells • Germ cells • Coculture techniques • Granulosa cells • Infertility, female

The Effect of Supplements on Spermatogenesis Quality: A Systematic Review

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Abstract

Background: One of the most controversial issues is male reproductive health and infertility. In the quality of male reproductive sperm, the quality of semen is important. Nutritional sperm concentration is important for reproductive function. Dietary supplements are essential for metabolism and various functions.

Methods: We systematically probed different databases and gateways including Scopus, PubMed, and Google Scholar following the PRISMA guidelines. The keywords used were “Spermatogenesis”, “Effect of supplement”, “Sperm quality”, and “Supplementation effect dietary”. Finally, 11 articles were selected based on their title and abstract.

Results: Cordyceps species, *C. militaris* (CM), and others are valuable traditional medicinal materials. CM has been traditionally used for the enhancement of sexual performance. Nutrition is important for reproductive performance; dietary supplementation with vitamin C causes a doubling of vitamin C levels in seminal fluid and reduced DNA damage. This would protect human sperm from endogenous oxidative DNA damage that affects sperm quality. Supplementation with selenium and vitamin E also improved sperm quality in boars and vitamin E increased the concentration of spermatozoa in semen. Sperm production is enhanced significantly in adult pigs with supplementation with CM. It is metabolized in the testis, where VDR-regulated proteins and enzymes mediate vitamin D in human spermatozoa and increase intracellular calcium concentrations, thus inducing sperm motility. Overall, Zn supplementation leads to successful outcomes in more than 50% of infertile cases. Following the supplementation of Zn with folate, an increase in sperm count was observed in oligospermic patients.

Conclusion: Spermatogenesis is a detailed and complex process. Evidence has shown that diet and supplements can affect spermatogenesis quality and quantity. In addition, there are herbal supplements such as Resveratrol and Maca that improve semen production. Evidence has shown that vitamin D and Zn supplementation is also an effective product in modulating testicular steroidogenesis.

Keywords • Dietary supplements • Spermatogenesis • Spermatozoa • Vitamins

Epithelial-Mesenchymal Transition Process During Embryo Implantation: Systematic Review

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Abstract

Background: A well-regulated epithelial-to-mesenchymal transition (EMT) within endometrial epithelial cells and trophoblast cells is required for successful embryo implantation, and abnormal EMT can cause implantation failure. Although the mechanisms involved in cancer cell EMT have been well studied, little is known about EMT during embryo implantation. Investigating the multiple factors in the EMT during embryo implantation will provide a strong impetus to clarify novel targets for the diagnosis and treatment of implantation failure. In this study, we comprehensively reviewed different factors that regulate the EMT during implantation, including hormones, growth factors, transcription factors, microRNAs, aquaporins, and ion channels.

Methods: The present review involved all published research articles investigating the pathways involved in type 1 EMT during embryo implantation. Combinations of the following terms were searched in Google Scholar, PubMed, and Science Direct databases with no limitation on the date of publication: “Embryo implantation”, “Endometrium”, “Trophoblast”, “Steroids”, “Growth factors”, “Transcription factors”, “MicroRNAs”, and “Aquaporins”.

Results: Although numerous factors and signaling pathways have been demonstrated to mediate EMT during physiological and pathological conditions, various types of EMT engage diverse mechanisms. Factors that can induce EMT in a cell may suppress EMT in another cell type. Moreover, abnormal EMT could cause pregnancy-related complications such as fetal growth restriction and preeclampsia.

Conclusion: Deficiency in each of the EMT-regulating factors during embryo implantation can cause implantation failure.

Keywords • Epithelial-mesenchymal transition • Embryo implantation

Assessment of Association Between Follicular Fluids Glycosaminoglycan and Hydroxyproline and Oocyte Quality in Polycystic Ovary Syndrome Patients in Comparison with Healthy Women

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Abstract

Background: Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in women of childbearing age. As a complex structure, the extracellular matrix and its components, including glycosaminoglycans and collagens, are highly affected by hormonal alterations.

In this study, the level of glycosaminoglycan and hydroxyproline present in the follicular fluid of women with the PCOS was measured.

Methods: Sixty-two women referred to the infertility center of Fatemeh Hospital in Hamadan were examined. Follicular fluid samples were taken from 31 women with PCOS during ovarian puncture. Follicular fluid samples were also taken from 31 healthy women who were treated with assisted reproductive techniques due to infertility related to their husbands. Special kits were used to measure the level of glycosaminoglycans and hydroxyproline.

Results: The results showed that there is no age difference between women with PCOS and healthy women. However, our results showed that the body mass index of women with PCOS was significantly higher than healthy women. Examination of oocyte counts showed that women with PCOS have higher oocyte counts than healthy women. Measurement of glycosaminoglycan and hydroxyproline indicated that their levels were meaningfully higher in the follicular fluid of women with PCOS.

Conclusion: Finally, the results of this study showed that weight gain and obesity, and increased oocyte production occur commonly in PCOS. Moreover, based on the study results, extracellular matrix changes in PCOS leads to an increase in the level of glycosaminoglycan and hydroxyproline in the follicular fluid. The evaluation of these markers may be a subject of further studies.

Keywords • Follicular fluid • Glycosaminoglycans • Hydroxyproline • Oocytes • Polycystic ovary syndrome

COVID-19 Vaccination and Menstrual Cycle Changes: A Review Study

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Abstract

Background: There has been increasing public concern that COVID-19 vaccines cause menstrual cycle disturbances. There are concerns that vaccination against Coronavirus disease 2019 (COVID-19) may be associated with abnormal menstrual cycles. Unfortunately, clinical trials of the current COVID-19 vaccines did not collect menstrual cycle outcomes post-vaccine. According to social media reports, menstrual disturbances are much more common, but these disturbances are temporary. Menstrual cyclicity is an overt sign of health and fertility. This normal variability may be perceived as concerning, especially in conjunction with a new exposure such as COVID-19 vaccination. This study evaluates the menstrual changes after COVID-19 vaccination in three studies.

Methods: We analyzed three retrospective cohort studies of menstrual cycle data that were collected prospectively from October 2020 to March 2021 in the UK and US and Oslo.

Results: The first study in the UK found that among premenopausal vaccinated individuals who menstruated in the 12 months preceding the survey, 20% reported any changes to their menstrual cycles up to 4 months after receiving their first injection. In the second study that was done in the US (2019), individuals had been evaluated to determine whether COVID-19 vaccination was associated with menstrual cycle disturbances during cycles when vaccination occurs. They found that individuals with normal menstrual cycles experienced small variations in cycle length. The third study that was done in Oslo (2021) showed the prevalence of unusually heavy and prolonged bleeding, short intermenstrual intervals, and increased pain during periods was higher after the first vaccine dose compared to the prior vaccination.

Conclusion: There is currently limited data to evaluate the impact of vaccination on menstrual health, and it limits our ability to sufficiently address these concerns.

Keywords • COVID-19 vaccines • Menstrual cycle • Menstruation disturbances • Female

Chlorella Vulgaris Supplementation Mitigates Sperm DNA Fragmentation Induced by Oxidative Stress

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Abstract

Background: Antioxidants have shown a favorable effect on sperm parameters by mitigating oxidative damage to sperm lipids and DNA. Chlorella Vulgaris extract (CVE) as a natural antioxidant may have a protective effect on testis oxidative stress, sperm DNA fragmentation, and parameters in Carbon tetrachloride (CCl₄) treated rats.

This study aimed to evaluate the protective effects of CVE on sperm DNA fragmentation and testis oxidative stress in CCl₄-exposed rats.

Methods: Thirty healthy male Wistar rats were divided into 5 groups (n=6): Control; CCl₄; CVE; CCl₄+CVE50; CCl₄+CVE100. At the end of the experiment, epididymal sperms were used to evaluate the sperm parameters. The testicular oxidative stress parameters were also estimated. The Chromomycin A3 (CMA3) and Acridine orange (AO) staining were performed to examine the sperm DNA fragmentation status.

Results: Our findings showed a significant decrease in sperm count, viability, normal morphology, and motility in CCl₄-treated rats (P<0.05). However, CVE in a dosed manner has shown an elevated sperm with forward movement, viability, and normal morphology (P<0.05). CCl₄ treatment significantly reduced total antioxidant capacity (TAC), glutathione (GSH) levels, and superoxide dismutase (SOD) levels. Normal rats treated with CCl₄ also showed significantly higher concentrations of testicular malondialdehyde (MDA) and total oxidant status (TOS) level (P<0.05), as well as CMA3 (P<0.05) and AO (P<0.001) positive sperm. However, CVE supplementation has revealed a significant decrease in the percentage of CMA3 (P<0.05) and AO (P<0.001) positive sperms. Moreover, CVE significantly decreased testicular MDA and TOS levels (P<0.05) and considerably increased the TAC, GSH levels, and SOD activity in comparison with CCl₄-treated rats (P<0.05).

Conclusion: In conclusion, our analyses suggest that CVE may play a critical role in attenuating the CCl₄-induced oxidative stress in the testis, thereby protecting the sperm membrane and DNA against oxidative damage.

Keywords • Chlorella vulgaris • Spermatozoa • DNA fragmentation • Oxidative stress

Effect of Vitamin A and Vitamin E on Attenuation of Titanium Dioxide Nanoparticles-Induced Toxicity in Testicular Tissue of Wistar Male Rats

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Abstract

Background: Titanium dioxide (TiO₂) could impair the testis function and sperm parameters. TiO₂ nanoparticles (TiO₂ NPs) induced Toxicity on the sperm, including damage to its membrane integrity, protein instability and oxidation, and nucleic acid damage. The protective effects of fat-soluble vitamins A and E against TiO₂ NPs-induced oxidative in rat testis were studied.

This report aimed to examine the validity of vitamins A and E on spermatogenesis disorders caused by TiO₂ NPs.

Methods: Thirty-six male Wistar rats were randomly divided into 6 groups. Groups intoxicated with TiO₂ NPs received 300 mg/kg TiO₂ NPs (20nm, 80% anatase) for two weeks by gavage. Treated groups with vitamin E (100 IU/kg), vitamin A (100 IU/kg), and a mixture of these vitamins were orally administered for 3 weeks (started 7 days before TiO₂ NPs administration). The effects of TiO₂ NPs on the rat's testis tissue were determined through total antioxidant capacity (TAC), total oxidant status (TOS), lipid peroxidation, the activity of Catalase, activity and genes expression of superoxide dismutase (SOD), glutathione peroxidase (GPx), genes expression of NF-κB (mRNA) and TNF-α.

Results: Sperm count, motility, and viability significantly decreased in TiO₂ NPs intoxicated rats (P<0.05). Sperm chromatin staining also showed that spermatozoa with impaired chromatin were upper in the nanoparticle receiving group matched to the controls (P<0.05). Histopathological lesions like inflammation were found in the group treated by TiO₂ NPs compared to the controls (P<0.05). Accordingly, vitamins E and A could significantly prevent these changes (P<0.05).

Conclusion: Vitamins A and E have antioxidant and anti-inflammatory properties as effective agents against the toxicity of TiO₂ NPs in the testis. The combination of the two vitamins showed a better performance than the separate administration of each one.

Keywords • Vitamin A • Vitamin E • Titanium dioxide • Rats, Wistar • Male

The Critical Role of Vitamin C on Ameliorating Age-Related Testicular Damages: Promises of Antioxidant Substances

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Abstract

Background: Aging is an irreversible process associated with declined biological functions that can lead to the reduction of reproductive organ capacities in males and females. Paternal age is a significant predictor of offspring health and development.

This study aimed to evaluate the effects of vitamin C on histopathological and biochemical testicular changes following the aging process with a focus on stereological methods.

Methods: For this study, adult male NMRI mice were divided into two control and experimental groups. Mice in the experimental group were supplemented with vitamin C (150 mg/kg), including 24-hour intervals by oral gavage for 33 weeks. The same regime was performed for animals in the control group, except that vitamin C was replaced by water. Then, right testes were extracted for stereological, and left testes were used for molecular analyses on weeks 8, 12, and 33.

Results: Our findings showed low semen quality, decreased level of serum Luteinizing hormone (LH), Follicle-stimulating hormone (FSH), and testosterone, along with increased reactive oxygen species (ROS) production and higher apoptotic gene expression following aging. Stereological studies showed that the volume of testes, the length of seminiferous tubules, and the number of spermatogenic and non-spermatogenic cells decreased significantly during aging. Also, vitamin C consumption for 33 weeks significantly improved biochemical and histological indices. The impact of aging on male reproduction seems to be inevitable worldwide.

Conclusion: It can be concluded that the use of protective and preventive remedies conserving male fecundity is very important, and based on our results, vitamin C is a beneficial candidate for improving age-related testicular changes due to the aging process.

Keywords • Ascorbic acid • Testis • Antioxidants • Paternal age

Treatment of Ovarian Hyperstimulation Syndrome in a Rat Model by Cannabidiol: An Angiogenesis Pathway Inhibitor

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Abstract

Background: Previous research suggested that lowering VEGF levels could help avoid OHSS syndrome. However, commercially available VEGF-lowering pharmaceuticals now have side effects that can be ruled out as a treatment for OHSS in young women, which is why researchers are investigating new medications to treat OHSS. We aimed to investigate the role of CBD in the pathophysiology of OHSS, and its use to modulate the pathway of angiogenesis and the VEGF gene.

Methods: Thirty-two female immature NMRI rats were randomly assigned to four groups (n=8 in each group). The control group (n=8), Group 2 (n=8) was the induction of OHSS, Group 3 (n=8) received 32 nmol DMSO after induction of OHSS, Group 4 (n=8) received 30 mg/Kg CBD after induction of OHSS, respectively. Both the body and ovaries' weight were measured. Then, the vascular permeability (VP), and the number of ovarian follicles were counted, and levels of the *VEGF* gene and protein in the blood serum were examined in all animals.

Results: CBD reduced the body weight, ovary weight, and VP compared to that of the OHSS group (P<0.05). VEGF expression in ovaries and peritoneal VEGF levels were decreased significantly in the CBD group compared to that of the OHSS group (P<0.05).

Conclusion: CBD was active in the alleviation of OHSS through suppression of VEGF and VP. Overall, we concluded that CBD was effective in the downregulation of VEGF and improvement in vascular permeability in OHSS.

Keywords • Models, animal • Cannabidiol • Ovarian hyperstimulation syndrome • Vascular endothelial growth factor A

Time-lapse Parameters and Embryo Grading

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Abstract

Background: Advancements in embryo selection methods for transmission are directly related to increased pregnancy rates. Therefore, research in this field is of great importance. This study aimed to investigate the use of time-lapse morphokinetic parameters to achieve a more accurate and non-invasive method in embryo evaluation.

Methods: 149 embryos from 20 female oocyte donors were examined based on morphokinetic characteristics using time-lapse. Parameters T5 (time to reach five cells), S2 (time from three to four cells), and CC2 (time from two to three cells) were recorded for embryos of all groups. Embryos were divided into high-quality, moderate, and bad-quality groups based on these parameters. Then, a comparison was made between time-lapse parameters in the high-quality group and other groups (moderate and bad groups) in healthy women who donated oocytes.

Results: According to the findings of the study, T5 had a statistically significant decrease between the moderate group compared to the high-quality group. Furthermore, when comparing the low-quality group to the high-quality group, T5 and S2 showed a statistically significant decrease and a statistically significant increase, respectively.

Conclusion: Embryos that were graded with a time-lapse system in different groups had time differences in some morphokinetic parameters. It seems that embryo selection using embryo cytokinetic parameters can improve embryo selection and pregnancy rate.

Keywords • Embryonic structures • Pregnancy • Oocytes • Pregnancy rate • Time-lapse imaging

Resveratrol Protected Mice Spermatogenesis against Bisphenol A Induced Toxicity

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Abstract

Background: Bisphenol A (BPA) is a xenoestrogen and is associated with male reproductive toxicity. Research indicated that BPA performs this process by altering the pattern of expression of genes involved in apoptosis as well as increasing oxidative stress. Previous studies highlighted that the use of antioxidants can reduce the effects of BPA on the genital system. Therefore, This study aimed to investigate the effect of resveratrol on reproductive toxicity induced by BPA in male mice.

Methods: Forty mice were randomly classified into five groups, including Control; Bisphenol A; Bisphenol+Resveratrol; Resveratrol; and vehicle. Then, variables such as histological alterations, oxidative stress markers, and sperm parameters were examined.

Results: BPA caused an evident decrease in sperm motility, count, viability, and oxidative stress markers ($P<0.05$). Furthermore, an increase in malondialdehyde, tissue damage, and abnormal sperm was observed in the BPA group ($P<0.05$). However, the treatment with resveratrol significantly increased these disarrays ($P<0.05$).

Conclusion: The results of this study showed that the administration of resveratrol prevents fertility damage caused by BPA.

Keywords • Bisphenol A • Malondialdehyde • Fertility • Oxidative stress

Effect of Oral Consumption of Vitamin D on Uterine Fibroids: A Randomized Clinical Trial

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Abstract

Background: Uterine fibroids are common tumors of the female reproductive system. Symptomatic uterine fibroids require surgical or medical therapy depending on the severity of the symptoms. This study was conducted to investigate the effect of vitamin D on uterine fibroids.

Methods: A randomized clinical trial was conducted from June to November 2018. Eligible women were randomly assigned to receive vitamin D or a placebo for 12 weeks. The change in the volume of fibroids was considered to be the main variable in the efficacy evaluation.

Results: There were no statistically significant changes in the size of the fibroids in the experimental group ($P=0.085$). Besides, a significant increase was observed in the size of fibroids in the control group ($P=0.001$).

Conclusion: Vitamin D consumption might inhibit the growth of uterine fibroids. However, its long-term effects are still unknown.

Keywords • Vitamin D • Leiomyoma • Female • Genitalia, female

The Effectiveness of Inositol and Metformin on Infertile Polycystic Ovary Syndrome Women with Resistance to Letrozole

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Abstract

Background: The purpose of this randomized single-blind controlled clinical trial is to compare the effectiveness of myo-inositol and metformin in infertile women with polycystic ovary syndrome (PCOS) treated with letrozole.

Methods: This is a randomized single-blind controlled clinical experiment including 150 PCOS infertile women. Letrozole is prescribed to all patients at a dose of 7.5 mg per day for 5 days beginning on the third day of menstruation. This study included patients who had not ovulated. They were then separated into three pretreatment groups: group I (control) with 200 g of folic acid (as a placebo), group II with 1500 mg of metformin daily with 200 g of folic acid, and group III with inositol 2 g plus 200 g of folic acid twice daily for three months. In the last cycle, 7.5 mg of letrozole was prescribed for the induction of ovulation. The primary outcomes were ovary function and pregnancy.

Results: The ovarian function was not significantly different in the studied groups. However, the ovarian function of the inositol+folic acid group with normal BMI was found significantly higher than other BMI spectra. In addition, the ovarian function was significantly higher in the inositol+folic acid group through increasing the infertility duration. The incidence of pregnancy was lower in the letrozole+folic acid+inositol group than the other studied groups; however, this finding was not statistically significant.

Conclusion: The addition of inositol and metformin to the treatment of infertile PCOS women with letrozole resistance improved their ovarian function; however, it was not significant.

Keywords • Pregnancy • Letrozole • Polycystic ovary syndrome • Infertility, female

Effect of Herbal Medicine on the Process of Spermatogenesis

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Abstract

Background: Medicinal herbs can be used as therapeutic alternatives, safer alternatives, or as the only viable treatment in some cases. Plants are used to make several well-stabilized medications. Herbal medications have a wide range of effects on the body's functions. Among these activities are hormonal ones. As a sex hormone in men, testosterone plays an important part in the process of spermatogenesis, which can be altered by herbal medications. Spermatogenesis is the process of producing haploid spermatozoa from germ cells in the testicular tubule. Male fertility requires that this procedure be carried out appropriately.

Methods: A comprehensive literature search was conducted using electronic databases and gateways such as PubMed (PMC Central, MEDLINE) and Google Scholar. All articles published up to 2022 were included in the study. The search was performed using the keywords ("male infertility" OR "herbal medicine", OR "spermatogenesis").

Results: The results reported by some researchers reveal the effects of herbal medicine on the process of spermatogenesis, such as consumption of *Nigella* and *O.basilicum*, and administration owing to an increase in sperm motility and density, as well as an increase in preputial gland weight. Herbal medicine causes a reduction in ROS. The reduction of ROS is a crucial factor in the production of sperm. In conclusion, *Nigella sativa* consumption has a positive influence on the reproductive system and fertility. Long-term use of herbal supplements increases the chance of fertility and improves sperm parameters, sperm quality parameters, total serum testosterone, and CAT. It seems isoflavone, Catharines, and polyphenol components of safflower increase spermatogenesis, and its extract may have an effect on spermatogenesis.

Conclusion: Herbal medication affects male fertility in a variety of ways. We can highlight the rise in testicular weight and sperm production tube, which helps the spermatogenesis process and treats sperm weakness. Herbal medicine also has the impact of activating the hypothalamus, pituitary, and testes, which accelerates testosterone biosynthesis and, as a result, increases testosterone concentrations and sexual potency. With testosterone in the testicles, male fertility and spermatogenesis are feasible. Herbal medicine can help in the spermatogenesis process.

Keywords • Plant extracts • Infertility, male • Plants, medicinal • Spermatozoa • Testosterone

Consumption of Ganoderma during Pregnancy and Development of Alopecia Areata in Treated Pregnant Mice

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Abstract

Background: Alopecia is a common condition that 2% of people around the world have experienced at least once. The main cause of this disease is still unknown and is probably due to the wrong attack of the immune system on the hair follicles. With the administration of immunosuppressive drugs, the symptoms disappear faster and the recovery occurs sooner. There are three different types of alopecia, including alopecia areata which occurs in pieces, alopecia totalis which affects the whole head, and alopecia Universalis which affects the whole body. Unfortunately, hair regrowth is rare in severe alopecia, which is why patients are more likely to take corticosteroids and rapid treatment, both of which have life-threatening adverse effects. Ganoderma lucidum is a helpful medicinal fungus that has been used to treat incurable ailments for over 5,000 years and is still highly respected today. Polysaccharides and triterpenoids are abundant in this fungus. The benefits of using this fungus are numerous, but according to the study, its usage before and during pregnancy is not advised. This study aimed to investigate the pathogenicity of Ganoderma lucidum extract during pregnancy in mice.

Methods: In this study, NMRI mice were used as an alternative model for human studies. Mice were divided into seven different groups and received 25, 50, 75, 150, and 300 mg/Kg of water-soluble Ganoderma lucidum extract daily for 12 days from the first day of their pregnancy.

Results: The results showed that all the mice in the highest dose group had different degrees of alopecia. These results were evaluated clinically and comparatively with the control group. With Ganoderma discontinuation, mothers returned to normal condition after eight weeks.

Conclusion: As a result, Ganoderma should not be used during pregnancy because it can cause autoimmune illnesses such as alopecia.

Keywords • Pregnancy • Alopecia universalis • Alopecia areata • Autoimmune diseases

Consumption of Ganoderma Lucidum during Pregnancy and the Formation of Albino Offspring from Completely Healthy Parents: A Mouse Model

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Abstract

Background: Albinism is the world's first hereditary disorder in which melanocyte pigments are improperly distributed or produced. There is no effective treatment for this condition. Albinism is not fatal, but because of the increased sensitivity of the skin to even mild sunlight, brittleness, and social incomprehensibility, increasing the risk of various skin and eye diseases, and the high daily costs for various care, actions must be taken to prevent its transmission to future generations. Ganoderma lucidum is a helpful medicinal fungus that has been used to treat incurable ailments for over 5,000 years and is still highly respected today. Polysaccharides and triterpenoids are abundant in this fungus. The benefits of using this fungus are numerous, but according to the study, its usage before and during pregnancy is not advised. This study aimed to investigate the pathogenicity of Ganoderma lucidum extract during pregnancy in mice.

Methods: In this study, NMRI mice were used as an alternative model for human studies. Mice were divided into seven different groups and received 25, 50, 75, 150, and 300 mg/Kg of water-soluble Ganoderma lucidum extract daily for 12 days from the first day of pregnancy.

Results: The results showed that all infants in the highest dose group had ocular-albinism from non-sick parents. These results were evaluated clinically and comparatively with the control group. From birth, the infants had completely whiter skin, ears, and tails, as well as redder eyes than infants in the control group.

Conclusion: As a result, Ganoderma lucidum, despite its high medicinal value, should not be used before or during pregnancy.

Keywords • Mice • Albinism • Pregnancy • Polysaccharides

Cell Therapy as a Recent Advanced Approach in Female Infertility

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Abstract

Background: Infertility is one of the most common problems in the world, with negative consequences for society and infertile couples. Female infertility, among the several causes of infertility, has an impact on the quality of life and well-being of affected individuals and couples. Infertility can be caused by female reproductive illnesses such as primary ovarian insufficiency, polycystic ovary syndrome, fallopian tube obstruction, and Asherman syndrome. Despite breakthroughs in Assisted Reproductive Technologies, infertility remains a significant issue. Significant progress has recently been made in cell therapy as an emerging strategy for the treatment of infertility. The present review evaluated the role of cell therapy in female infertility.

Methods: In this Review study, a comprehensive literature search was conducted using electronic databases and gateways such as PubMed (PMC Central, MEDLINE), Scopus, and Web of Sciences, and national databases including Scientific Information Database, MagIran, IranMedex, and IranDoc. Thereafter, articles in both English and Persian referring to “Cell therapy” and “female infertility” were included.

Results: Cell therapy involves utilizing lymphocytes, platelet-rich plasma, PBMCs, and different types of stem cells as therapeutic agents. Stem cells are usually multipotent cells that existed in embryos, fetuses, and adults that proliferate and differentiate into different cell types under certain circumstances. The main types of stem cells are embryonic stem cells, decidual stromal cells, MSCs, human amniotic epithelial cells, and induced pluripotent- stem cells each functioning in a different way. Generally, cell therapy mechanisms of action are inducing the production of cytokines, blocking antibodies and growth factors, the proliferation of B10 cells, reducing the activity of NK cells, increasing Th₂ and Treg cells, and decreasing Th₁ and Th₁₇ cells.

Conclusion: In general, cell therapy can be an effective strategy as it provides an interactive, dynamic, specific, and individualized treatment. Although cell therapy is a promising approach, it still needs more investigation in order to improve and make it safer.

Keywords • Cell therapy • Infertility, female • Reproductive techniques, assisted

Oxidative Stress: A Possible Cause of Male Infertility

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Abstract

Background: Numerous research has recently been conducted on the impact of reactive oxygen species (ROS) and antioxidants on the male reproductive system. Evidence suggests that disrupting the balance between reactive oxygen species levels and antioxidant contents in seminal plasma causes oxidative stress; excessive levels of sperm ROS can then induce sperm malfunction, sperm DNA damage, and diminished male reproductive potential or male infertility. The present review evaluated the role of oxidative stress in male infertility.

Methods: In this Review study, a comprehensive literature search was conducted using electronic databases and gateways such as PubMed (PMC Central, MEDLINE), Scopus, and Web of Sciences, and national databases including Scientific Information Database, MagIran, IranMedex, and IranDoc. from 2005 to 2021. Thereafter, articles from 2005 to 2021 in both English and Persian referring to “oxidative stress” and “male infertility” were included.

Results: The membrane of mammalian spermatozoa is extremely sensitive to ROS attack because it is rich in polyunsaturated fatty acids (PUFA), and ROS targets the fluidity of the sperm membrane and damages mitochondria. ROS appears to have an important part in gamete interaction as well as effective fertilization. ROS levels in culture media may have an effect on post-fertilization development, such as cleavage rate, blastocyst yield, and quality (indicators of assisted reproduction outcomes). OS has been linked to both natural and assisted fertility. Both external and intracellular ROS should be intercepted by antioxidant methods. Antioxidants like vitamins E and C, carotenoids like carnitine, and herbal items have been shown to help restore the equilibrium between ROS formation and scavenging.

Conclusion: In conclusion, a good lifestyle, regular exercise, avoidance of stress, and observing safety rules at work are habits that can reverse male infertility.

Keywords • Oxidative stress • Infertility, male • Antioxidants • Spermatozoa • Fertility

Preserving Effect of Loboob, a Traditional Multi-herbal Formulation, on Sperm Parameters of Male Rats with Busulfan-induced Subfertility

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Abstract

Background: Male infertility caused by genotoxic substances during reproductive age is a serious concern. The purpose of this experimental study was to see how loboob affects sperm parameters.

Methods: 55 healthy rats were selected, weighed, and divided into five groups (n=11 for each group). The control group received no treatment. The first experimental group received 10mg/Kg busulfan, and the rest of the experimental groups received 10mg/Kg busulfan and 35, 70, and 140 mg/Kg loboob, respectively. Finally, sperm parameters and weights of the rats were compared using Kolmogorov–Smirnov, non-parametric Kruskal-Wallis, and Dunn-Bonferroni tests.

Results: All sperm parameters and weights were significantly decreased among rats receiving Busulfan. All loboob dosages were beneficial in increasing slow sperm motility, but only 70 and 140 mg/Kg of loboob could increase progressive sperm percentages (0.024 and 0.01, respectively). Loboob at a dose of 140 mg/Kg has the potential to improve sperm viability. It did not improve normal morphology or count, nor did it reduce immotile sperm. Loboob had no effect on mean rat weights.

Conclusion: Loboob has dose-dependent protective effects on several sperm parameters in busulfan-induced subfertile rats.

Keywords • Busulfan • Infertility • Infertility, Male • Rats • Spermatozoa • Medicine, traditional

TGF- β 1 Role in Uterine Leiomyoma and Endometrial Polyp: an Insight into Drug-based Treatment instead of Surgical Techniques

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Abstract

Background: Considering the high prevalence of leiomyoma and endometrial polyps, investigating the contributed factors and determining the pathophysiology of these lesions is essential. Target therapy is now an acceptable method in the treatment of some diseases. We aimed to determine the expression of TGF- β 1 in endometrial polyps and leiomyoma to discover a drug-based method to overcome surgical treatments.

Methods: In this cross-sectional study, 55 patients with leiomyoma and 55 patients with polyp were included. Prepared slides from leiomyoma and adjacent myometrium or polyp lesions and adjacent endometrium were obtained and investigated for TGF- β 1. Then, the obtained data were analyzed using SPSS version 22.

Results: The mean age of the participants was 40.6 ± 5.8 years. Based on the reports, 88.2% (N=97) of patients in the study population had abnormal uterine bleeding with similar distribution among both groups. About 63.5% of the leiomyoma group did not express TGF- β 1. However, in normal myometrium, 23.6% had the highest degree of TGF- β 1 expression. Polyp tissue did not stain for TGF- β 1 in any of the patients. Besides, 89.1% of non-polypoid endometrium did not express TGF- β 1. Normal tissue has a significantly greater amount of TGF- β 1 than the leiomyoma and endometrial polyp.

Conclusion: TGF- β 1 is expressed more prominently in normal myometrium with mostly high-intensity features compared to leiomyoma. Moreover, polyps showed no staining for TGF- β 1, while normal endometrium showed a low-density staining pattern.

Keywords • Cytokines • Polyps • Leiomyoma • Uterus

Correlation between ADA and MPO Activity in Follicular Fluid and Oocyte Quality in Polycystic Ovary Syndrome Patients and Healthy Women

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Abstract

Background: Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in women of reproductive age. Inflammation and oxidative stress caused by the activity of immune enzymes such as Adenosine D-Aminase (ADA) and Myeloperoxidase (MPO) can play a key role in the pathogenesis of the disease. This study aimed to evaluate the activity of ADA and MPO enzymes in the follicular fluid of women with PCOS and compare them with healthy women.

Methods: In this study, 62 women who were referred to the Infertility Center of Fatemeh Hospital in Hamadan entered the study. Follicular fluid samples were taken from 31 women during ovarian puncture. Follicular fluid samples were also taken from 31 healthy women of the same age and sex who were being treated for their husbands' infertility problems. The colorimetric method was used to measure the ADA enzyme, and a special kit was used to test MPO.

Results: The results showed that the body mass index in women with PCOS was significantly higher than the healthy women group ($P=0.021$). Moreover, they had higher oocyte counts than healthy women ($P=0.04$). The activity of MPO and ADA enzymes in the follicular fluid of women with polycystic ovary syndrome was significantly increased compared to the healthy group ($P<0.05$).

Conclusion: In conclusion, our analyses suggest that increased activity of ADA and MPO as inflammatory enzymes, might be correlated with polycystic ovary syndrome. Further investigations are needed to clarify the precise mechanism of MPO and ADA enzymes related to inflammation's role in polycystic ovary syndrome pathogenesis.

Keywords • Polycystic ovary syndrome • Follicular fluid • Oxidative stress • Inflammation • Body mass index

The Effect of Electromagnetic Fields (EMFs) on Male Infertility

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Abstract

Background: The question that electromagnetic fields (EMFs) cause adverse effects on human fertilization potential has raised significant concerns. EMFs are known to be the largest pollutants in the Earth's environment. In today's world, with the advancement of technology, people are often exposed to EMFs. People are exposed to EMFs from a variety of sources, and the conditions in people's daily lives are different. EMFs can induce biological and genetic effects. One of the major physiological systems of the human body, which is involved with EMFs, is the reproductive system. In the following, we will examine this issue.

Methods: A systematic search of publications up to 20202 in Medline (via PubMed) database and Google Scholar gateway by using keywords such as electromagnetic fields (EMFs), reproductive system, and male infertility was performed.

Results: EMFs are highly permeable and can displace charged particles in macromolecules and big polymers such as electrons and ions. As a result, EMFs with high electron and ion concentrations can be harmful to tissues. EMFs alter biological components in a variety of ways, including anomalies in cell proliferation and differentiation, chromosomal abnormalities, and mutations. According to the research findings, similar changes can also be seen in the male reproductive system. Sperm count and motility, as well as viability and morphology, are all altered. These factors damage the male reproductive system, resulting in infertility.

Conclusion: In general, many studies show that there is a negative correlation between EMFs and male fertility. EMFs can have destructive effects on the gonads, sex hormones, and fertility. Therefore, people need to be aware of the negative effects of EMFs. Although the effect of EMFs at different frequencies is different, it is recommended to stay out of reach of these waves as much as possible.

Keywords • Infertility, male • Chromosome aberrations • Polymers • Sperm count • Cell proliferation • Fertilization

The Effect of *Taraxacum Officinale* (Dandelion) Flower Extract on Infertility Induced by Cadmium Chloride on Testicular Tissue of Adult Male Wistar Rats

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Abstract

Background: *Taraxacum officinale* extract (TOE) has bioactive phytochemical effects which can protect the DNA against damage of reactive oxygen species (ROS). Cadmium acts as a toxin Reproductive system and destroys the process of spermatogenesis. The destructive function of cadmium metal increases the level of free radicals and induces oxidative stress. This study was carried out to examine the protective effect of hydroalcoholic extract of TOE on infertility induced by cadmium chloride on testicular tissue of adult male Wistar rats.

Methods: 40 male Wistar rats were randomly allocated into eight groups: the control, Cd, TOE extract (100,200 and 400 mg/Kg/body weight), and chloride cadmium-TOE (100,200 and 400 mg/Kg/body weight). Rats were intraperitoneally injected with TOE extract once daily for 28 days. Serum levels of MDA and SOD were measured. Motility, viability, and total count of sperm were measured. In order to investigate the Johnson score, a testis histopathology was done.

Results: The number of spermatogonia, spermatocytes, and spermatids was substantially lower in the Chloride Cadmium group compared to the control group ($P<0.05$). However, when compared to the Chloride Cadmium group, the Chloride Cadmium-TOE extract group had more cell types. The dandelion treatment group had higher motility ($P<0.05$) and lower dead sperm rate ($P<0.001$) as compared to the chloride cadmium group. Serum levels of SOD and MDA were increased and lowered in the chloride cadmium and TOE at 400 mg/Kg groups, respectively, when compared to the other groups ($P<0.01$).

Conclusion: The findings indicated that *T.officinale* extract had a protective effect on the testis probably by scavenging free radicals and reducing toxicity caused due to oxidative stress.

Keywords • Rats, wistar • Cadmium chloride • Testis • Reactive oxygen species • Spermatozoa • Oxidative stress

The Effect of *Salvia Officinalis* (sage) Extract on Infertility Induced by Cadmium Chloride on Testicular Tissue of Adult Male Wistar Rats

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Abstract

Background: There is relatively little information pertaining to the effect of the hydroalcoholic extract of *salvia officinalis* on the reproductive system of animals. *Salvia officinalis* is an aromatic and medicinal plant well known for its antioxidant properties. Toward the increment level of free radicals and inducing oxidative stress, as chloridecadmium roles a toxic agent, it affected the Reproductive system and destructs the process of spermatogenesis. This study aimed to investigate the effect of the hydroalcoholic extract of *salvia* on infertility induced by cadmium chloride in testicular tissues of adult male Wistar rats.

Methods: 40 male Wistar rats were randomly allocated into eight groups: the control, chloride cadmium, *salvia officinalis* extract (100, 200, and 400 mg/Kg/body weight), chloridecadmium-*S.officinalis* extract (100, 200, and 400 mg/Kg/body weight). Rats were intraperitoneally injected with *S.officinalis* extract once daily for 28 days. The blood samples were collected by using a cardiac puncture method. Furthermore, the serum levels of MDA and SOD were measured. Testes were removed and then became fixed, and sections were cut and stained for histological studies. The sperm parameters (motility, viability, and total count) were also determined.

Results: *Salvia officinalis* extract (200 and 400 mg/Kg) enhanced the number of spermatogonia, spermatocytes, and spermatids, according to the findings. When chloride cadmium-*salvia Officinalis* 400 was compared to the 100 and 200 groups, serum levels of SOD and MDA were increased and lowered, respectively ($P<0.01$). Sperm motility ($P<0.05$) and dead sperm rate ($P<0.001$) were enhanced and decreased in *S.officinalis* treated groups compared to the chloride cadmium group, respectively.

Conclusion: Toxicity reduced based on *S.officinalis* extract minimizes chloride cadmium tissue damage on testes by scavenging free radicals.

Keywords • Antioxidants • Rats, wistar • Cadmium chloride • Testis • Plants, medicinal • Spermatozoa

Effects of Conditioned Media of Human Umbilical Cord Wharton's jelly-Derived Mesenchymal Stem Cells on the Expression of Granulosa Cells Steroidogenic Enzymes in Healthy Women and Patients with PCOS

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Abstract

Background: Polycystic ovary syndrome (PCOS) is characterized by various hormonal imbalances. Previous research reported that conditioned media-derived mesenchymal stem cells play an important role in proper steroidogenesis and follicular development. Therefore, we investigated how conditioned media of human umbilical cord Wharton's jelly-derived mesenchymal stem cells (hWJMSCs-CM) affected the expression of steroidogenic enzymes in human normal granulosa cells (N-GCs) and polycystic ovaries (PCO-GCs).

Methods: Ovarian GCs were obtained during the oocyte retrieval procedure from 10 women with PCOS and from 10 healthy women who were referred to Ghadir Mother and Child Hospital (Shiraz, Iran). To assess aromatase and 3 β -hydroxysteroid dehydrogenase (3 β -HSD) gene expression, total cellular RNA was extracted from GCs using a total RNA Purification Mini kit. Extracted mRNAs were reversely transcribed into first-strand cDNA using a cDNA synthesis kit. The qRT-PCR was accomplished using SYBR Green PCR Master Mix. Then, the samples were quantified by the comparative $\Delta\Delta C_t$ method with β -actin as an internal control. All the experiments were performed in triplicate.

Results: Basal aromatase and 3 β -HSD gene expression by N-GCs was significantly higher than PCO-GCs. The hWJMSCs-CM significantly increased aromatase and β -HSD gene expression in N-GCs and PCO-GCs. In the presence of hWJMSCs-CM, 3 β -HSD gene expression in the PCO-GCs was not significantly different from N-GCs.

Conclusion: The hWJMSCs-CM had positive impacts on luteinized GCs through its effect on the expression of steroidogenic enzymes. It can improve PCO-GCs to normal conditions by affecting the main aspects of GCs' function, such as hormonal biosynthesis.

Keywords • Granulosa cells • Culture media, conditioned • Mesenchymal stem cells • Aromatase, hydroxysteroid dehydrogenases

Distinguishing Obstructive from Non-obstructive Azoospermia and Necessity of Diagnostic Testis Biopsy

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Abstract

Background: Accurate etiology of azoospermia is required for optimal management of patients. This study aimed to determine serum hormonal level and testicular long-axis cut-off points to distinguish obstructive azoospermia (OA) from non-obstructive azoospermia (NOA) in Iranian patients. Moreover, the necessity of diagnostic testis biopsy in azoospermic patients was evaluated.

Methods: In this retrospective study, data from 471 azoospermic patients such as history and physical examination, serum hormonal level, semen fluid parameter, and testicular long axis based on ultrasound were evaluated from 2016 to 2020. All patients were examined by a single urologist and underwent a diagnostic testis biopsy for a definite diagnosis. The diagnostic parameters were analyzed using SPSS software version: 26. Statistical tests such as *t* test and Chi square tests and receiver operating characteristic (ROC) curves were used to distinguish NOA from OA.

Results: A total of 127 patients with OA and 284 with NOA were included in the study. The mean serum testosterone level was significantly higher in OA than NOA (4.2 vs. 3.4 ng/mL), whereas the mean serum follicular stimulating hormone (FSH) (5.3 vs. 19.1 mIU/mL) and Luteinizing hormone (LH) (5.3 vs. 11 mIU/mL) were lower in OA group. The ROC curve analysis indicated that FSH and the testicular long axis were the best diagnostic predictors. Using a combination of serum FSH (8.9 mIU/mL) and testicular long axis (39mm), the positive predictive value for NOA and OA was 97.02% and 78.8%, respectively.

Conclusion: A combination of serum FSH higher than 8.9 mIU/mL and testicular long axis lower than 39 mm were strong predictors to distinguish NOA from OA in our Iranian patients. In addition, diagnostic testicular biopsy seems to be necessary for patients with OA and NOA characteristics.

Keywords • Azoospermia • Follicle stimulating hormone • Luteinizing hormone • Testosterone • Biopsy

Premature Ovarian Failure and Oxidative Stress Biomarkers

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Abstract

Background: Premature ovarian Failure (POF) is one of the clinical manifestations of ovarian damage and is defined as the cessation of ovarian function under the age of 40 years. POF is characterized by amenorrhoea, hypoestrogenism, and elevated serum gonadotropin levels. A wide spectrum of pathogenic mechanisms may lead to the development of POF. Therefore, This study aimed to review the involvement of oxidative stress biomarkers in POF cases.

Methods: In order to find relevant studies to the research question, a comprehensive electronic search with time (recent five years, up to 2022) and language (English) restrictions was conducted using the PubMed database. The search was performed using keywords such as “Premature ovarian Failure” AND “Oxidative stress”. Then, the most recent studies including original research and review articles were selected.

Results: Previous research found that superoxide dismutase and glutathione peroxidase activities were significantly decreased in POF women, but MDA levels were greater. Another study found that higher ROS generation contributes to oophoritis associated with early ovarian insufficiency. High ROS levels induce mitochondrial DNA, resulting in mitochondrial malfunction. This could result in reduced ATP synthesis due to decreased oxidative phosphorylation, resulting in poor oogenesis, low oocyte quantity, and POF.

Conclusion: The function of oxidative stress in the development of POF has received little attention. One of the first stages in addressing POF patients is determining the pathophysiology. Further clinical research on these patients is required.

Keywords • Primary ovarian insufficiency, oxidative stress, DNA, mitochondrial • Oxidative phosphorylation • Superoxide dismutase • Oocytes

The Effects of Platelet-Rich Plasma on Pregnancy Outcomes in Recurrent Implantation Failure Infertile Women: A Randomized Controlled Trial

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Abstract

Background: Recurrent implantation failure is a significant problem in assisted reproduction, and despite several therapies that have been reported previously, there is no consensus on which is the best approach. The purpose of this study was to determine the efficacy of autologous platelet-rich plasma (PRP) on pregnancy rate in recurrent implantation failure.

Methods: Between 2016 and 2019, a total of 98 women who were unable to conceive after three or more high-quality embryo transfers underwent frozen-thawed embryo transfer with or without an intrauterine infusion of platelet-rich plasma. Thus, 0.5 mL of platelet-rich plasma at a concentration 4-6 times greater than peripheral blood was administered intrauterine 48 hours before embryo transfer. A control group followed the normal protocol.

Results: There were no significant differences between the two groups in terms of age, body mass index (BMI), duration and cause of infertility as well as total transferred embryos, and kind of treatment protocol. However, secondary infertility and endometrial thickness 96 hours before embryo transfer, were more prevalent in the intervention group. The clinical pregnancy (48.3% versus 23.26; P=0.001) and ongoing pregnancy (46.7% versus 11.7%; P=0.001) and implantation rate (58.3% versus 25%; P=0.001) were more significant in the intervention group than the control group.

Conclusion: In recurrent implantation failure, intrauterine injection of platelet-rich plasma 48 hours before freeze-thawed embryo transfer may improve *in vitro* fertilization (IVF) outcomes.

Keywords • Platelet-rich plasma • Fertilization *in vitro* • Pregnancy rate • Embryo transfer

Infertility and Periodontitis

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Abstract

Background: Periodontal Medicine (the concept of inflammatory conditions) acts as a reservoir of pathogens and toxins that may enter the circulatory and lymphatic systems, causing damage in sites outside than the mouth has been the focus of periodontics studies in recent decades. Recently, the relationship between periodontal diseases and female infertility has been investigated. This study aimed to explore the association between periodontal diseases and female infertility.

Methods: A comprehensive literature search was carried out to assess if there is an association between periodontal diseases and female infertility. An extensive search was conducted in PubMed and Cochrane Library databases. Epidemiological studies, experimental studies, inquiries, and editorials on the subject of periodontitis and infertility published until March 2022 were included in this review study. Specific keywords including “female infertility”, “periodontal disease” AND “periodontitis” were used.

Results: The findings from previous epidemiological studies revealed that periodontal disease might be a factor that increases the time to conception, on average by two months more, which is as negative as obesity. The experimental studies pointed out that the infertility problem is a secondary outcome in rodents challenged with periodontitis. The possible biological explanation is that periodontitis causes a systemic inflammation, which could prevent ovulation, implantation of the embryo, or not sustain its implantation.

Conclusion: It is known that oral health incorporates into the general health agenda and is crucial for optimal health and general well-being. Therefore, women trying to conceive should be in the best possible health, which will be achievable through effective multidisciplinary teamwork including dental care.

Keywords • Infertility, female • Periodontal disease • Periodontitis

Vitamin D and Infertility Treatment

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Abstract

Background: The significance of vitamin D in reproductive physiology has recently sparked an interest. Despite multiple articles, its impact on reproductive health is unclear. This paper reviews the literature on the role of vitamin D in reproduction processes and its importance in infertility therapy.

Methods: This review was conducted based on an analysis of available literature indexed in MEDLINE, Cochrane, and PubMed databases between 2015 and 2021. Specific keywords including “infertility” AND “vitamin D” were used. Epidemiological studies, experimental research, inquiries, and editorials on the mentioned subject were all included.

Results: Evidence from animal and human studies suggests that vitamin D is involved in several reproductive system activities in both sexes. Serum vitamin D concentrations in healthy women were found to be greater than in PCOS patients. Vitamin D supplements should be included in PCOS treatment plans due to improved insulin resistance and the outcomes of infertility treatment. Vitamin D has a direct effect on AMH synthesis, resulting in extended ovarian reserve maintenance in patients with higher vitamin D concentrations. In male infertility, both low (20 ng/mL) and high (>50 ng/mL) vitamin D concentrations in serum have a deleterious effect on the number of spermatozoa per mL of sperm, their progressive motility, and morphology.

Conclusion: The explanation of the vitamin D activity mechanism in patients with infertility with different pathophysiological aspects requires further research and studies with superior methodological characteristics are needed to establish a role for vitamin D in the treatment of both female and male infertility.

Keywords • Fertility • Infertility • Vitamin D

Altered Methyltransferase Gene Expression, Mitochondrial Copy Number, and 4977-bp Common Deletion in Subfertile Men with Variable Sperm Parameters

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Abstract

Background: Although semen parameters were found to poorly predict reproductive success, they are the most prevalent diagnostic tool for male infertility. There are few but conflicting reports regarding the correlation of *DNMT* gene expression, mitochondrial DNA copy number (mtDNAcn), and deletion (mtDNA_{del}) with different sperm parameters. Therefore, this study aimed to investigate *DNMT* mRNA level, mtDNAcn, and deletion in infertile men with different sperm parameters and compare them with fertile men.

Methods: Semen samples from 30 men with unknown male infertility and normal sperm parameters (experimental group I), 30 infertile men with at least two abnormal sperm parameters (experimental group II), and 30 fertile normozoospermic men (control group) were collected. After semen analysis, total RNA and DNA were extracted. Isolated DNA was used for assessing the respective mtDNAcn and the presence of 4977bp common deletion in mtDNA applying real-time quantitative PCR and multiplex PCR, respectively. Synthesized cDNA from total RNAs was used to quantify *DNMT1*, *DNMT3A*, and *DNMT3B* transcripts in study groups using real-time quantitative reverse-transcription PCR.

Results: Experimental group II had significantly higher proportions of mtDNAcn than the other groups. *DNMT1* was significantly down-regulated in both experimental groups. 4977bp deletion was not detected. Progressive motility and normal morphology were significantly and negatively correlated with mtDNAcn. A significant positive correlation was found between sperm parameters and *DNMT1* mRNA levels.

Conclusion: Infertile men with different sperm parameter qualities showed elevated mtDNA content in comparison with the other studied groups. It was found that abnormal sperm parameters are associated with *DNMT1* gene expression, indicating the possibility of changes in some epigenetic aspects of spermatogenesis in subfertile men with different sperm parameters.

Keywords • Infertility, male • Semen analysis • Spermatozoa • DNA, mitochondrial

Predicting Factors Affecting Clinical Pregnancy Rate in Assisted Reproductive Technology

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Abstract

Background: The cryopreserved embryo transfer cycle is regarded as the final critical stage in assisted reproductive technology (ART), with a direct impact on clinical pregnancy rates. Predicting the components in freeze transfer cycles that can improve such results would thus be useful. This study aims to assess the factors that influence pregnancy outcomes by comparing the greatest and lowest rates across a year.

Methods: This study was conducted in December 2020 (Group 1; with 77 patients) and February 2021 (group 2; with 100 patients) at the Novin Infertility Treatment Center. All the statistical analysis was performed by applying the Student *t* test and Chi square tests by using SPSS software.

Results: Our results show that the clinical pregnancy rate was highest in February (56.4%) and lowest in December (42.9%) ($P=0.07$). The percentage of embryos with good quality (A+AB grades) was greater in February, at 85.8%, compared to 66.6% in December ($P=0.05$). Furthermore, patients who underwent embryo transfer in the most successful month had fewer extended cycles (30.4%) than those who had it in the other month (42.4%) ($P=0.2$). Severe male factor cases were also observed to be higher in group 1 than group 2 (54.9% vs. 45.1%) ($P=0.47$). There was no statistically significant difference in preparation methods (letrozole or estradiol), RIF and RAB history, frozen-thawed cycle type (cleavage, dual, or blast), or mean maternal age.

Conclusion: An increase in the rate of patients with severe male infertility can result in reducing the rate of good-quality embryos, which acts as an underlying factor of a lower clinical pregnancy rate within a month. Moreover, extending FET cycles would seem to be a second parameter affecting outcomes.

Keywords • Embryo transfer • Reproductive techniques, assisted • Pregnancy rate • Infertility, male, female

The Effect of Seminal Plasma Exosomes on Sperm Function in Asthenoteratozoospermia Patients

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Abstract

Background: The human semen contains a heterogeneous population of extracellular vehicles (EVs) that are consistently involved in the promotion of sperm motility, regulation of sperm capacitation, induction of acrosome reaction, or antibacterial and antiviral mechanisms. The purpose of this study was to investigate the role of seminal plasma exosomes on sperm function.

Methods: Normozoospermic and severe asthenoteratozoospermia men in the age range of 25–40 years were considered for the study. Seminal plasma was collected and processed to separate spermatozoa and exosomes. Seminal plasma exosomes had typical nano-structure morphology as measured by scanning electron microscopy (SEM). The effect of exosomes on spermatozoa was determined by evaluating sperm parameters according to the World Health Organization criteria (WHO, 2010).

Results: Exosomes were identified and described from the seminal plasma of normozoospermic and severe asthenoteratozoospermic patients. They have distinct characteristics in terms of count, form, and size. Exosomes from normozoospermic persons, but not asthenozoospermic individuals, increased spermatozoa motility, capacitation, and acrosome reaction (P0.05). The lower total antioxidant capacity (TAC) and higher DNA damage in asthenoteratozoospermic people were determined (P0.05) due to the lack of exosomes in the plasma seminal fluid.

Conclusion: These findings provide evidence that exosomes in seminal plasma can affect the quality of the sperm. Thus, it is recommended, in the future, exosome assessment served as a diagnostic tool to ensure the sperm parameters of infertile couples with male factors.

Keywords • Exosomes • Asthenoteratozoospermia • Sperm motility

Hyperketonemia and Serum Levels of Estrogen and Progesterone at First Insemination in Holstein Cows

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Abstract

Background: Negative energy balance in dairy cows is caused by a variety of factors, including metabolic stress, a lower body condition score, lower blood glucose levels, and hormonal changes, particularly increased glucagon levels. Increased glucagon levels cause glycogenolysis, lipolysis, beta-oxidation of fats, gluconeogenesis, and ketogenesis in the liver (which produces acetic acid, acetone, and beta-hydroxybutyrate [BHBA]). Furthermore, negative energy balance is associated with a decrease in LH surge concentration and a lower chance of pregnancy at first insemination. This study aimed to evaluate hyperketonemia on the serum levels of estrogen, progesterone, and pregnancy rate at first insemination.

Methods: This study included a total of 70 Holstein average of three multiparous cows from one of the industrial dairy farms in Isfahan province, Iran. 10 mL of jugular vein blood was collected at each sampling time twice: once at 7–14 days of postpartum to measure the BHBA, and once at first insemination, to measure estrogen and progesterone hormone levels. All the statistical analyses were carried out by IBM SPSS Statistical Software version 20, and statistically significant differences were represented by $P < 0.05$.

Results: This research indicated that cows with BHBA level greater than 600 $\mu\text{mol/L}$ had lower estrogen levels ($P=0.03$) and higher progesterone levels ($P=0.07$) during the first insemination. At first insemination, pregnant cows had significantly lower serum BHBA ($P=0.03$) and higher estrogen levels ($P=0.009$) than nonpregnant cows.

Conclusion: The present study confirms the negative effects of the higher ketone bodies on estrogen levels and pregnancy rates at the first insemination in hypertonic cows.

Keywords • Cattle • Pregnancy • Estrogens • Stress, physiological • Glucagon • Blood glucose

An Ultrastructural Study of the Antioxidant Effects of Vitamin E and Fennel Extract on Zona Pellucida Cell Changes of Rats' Ovaries under Non-Ionizing 50Hz Electromagnetic Fields

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Abstract

Background: Everyday use of various electronic tools and appliances has caused a large number of people to constantly be under the influence of electromagnetic fields (EMFs).

Methods: For this study, 40 female rats were randomly selected from the animals' laboratory. The rats chosen for the study were three months old and weighed 200 ± 20 g. The animals were then randomly divided into four groups; Control (n=10), Experiment 1 (n=10), Experiment 2 (n=10), and Experiment 3 (n=10). During the experiment, all four groups were maintained in the same conditions and received the same feeding procedure. The experimental groups 1, 2, and 3 were under the influence of a 50 Hz EMF for eight weeks. Subsequently, the second and third groups were kept away from the effects of EMF for another eight weeks. At the end of the study, after removing the ovarian using glutaraldehyde, they were prepared for electron microscopy study. The rats in experimental group 2 were not sacrificed and were maintained for another eight weeks in a normal laboratory environment away from the impacts of EMF. Then, the rats were fed vitamin E (100 mg/Kg) and fennel extract (1.5 gr/Kg/body weight) was added to their daily diet. Samples were taken from this group at the end of the second eight weeks. At the end of the second eight weeks, samples from experimental group 3 were collected under normal conditions without the use of vitamin E or fennel extract. The control group (n=10) rats were biopsied at the same time as the experimental group 1 sample.

Results: The findings of this study showed that in the groups that were exposed to electromagnetic radiation, zona pellucida cells had lost their microvilli and mitochondrial crystal structure. In the groups that were exposed to vitamin E and fennel extract, these changes were reduced.

Conclusion: The use of vitamin E in combination with fennel extract can reduce the damaging effects of non-ionizing radiation with 50 Hz frequency on the zona pellucida cells of rat ovaries.

Keywords • Electromagnetic fields • Foeniculum • Ovary • Vitamin E

The Efficacy of Hydroalcoholic Extract of Ashrasi Date Palm on Viability and Motility of Sperm in Diabetic Male Rats

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Abstract

Background: Oxidative stress and high levels of ROS have an adverse effect on sperm parameters and fertility in men. It was shown that Ashrasi date palm (ADP) has antioxidant and protective properties. This study evaluated the antioxidant effects of the hydroalcoholic extract of ADP on the viability and motility of sperm in diabetic male rats.

Methods: 40 male Wistar rats were purchased from an animal house, at Razi University, Kermanshah, and were randomly divided into five groups. Groups 1-5 were control, diabetic, and diabetic+ADP (30, 90, and 270 mg/Kg of ADP hydroalcoholic extract), respectively. ADP extract was administered, and after its phytochemical screening, it was orally administered to animals of groups 3-5, once a day for five weeks. Finally, the viability and motility of the sperm in all studied groups were evaluated.

Results: The doses of 90 and 270 of ADP hydroalcoholic extract significantly increased sperm viability as well as decreased the immotile sperm ($P<0.05$). Moreover, the dose of 270 of ADP hydroalcoholic extract leads to a considerable enhancement in forward sperm motility ($P<0.05$).

Conclusion: The findings of this study demonstrated that ADP hydroalcoholic extract has antioxidant effects against oxidative stress due to diabetes, and this extract can enhance the viability and motility of sperm. Thus, substances that have antioxidant and protective properties can be considered a significant approach to the reduction of oxidative stress and stress-induced complications.

Keywords • Oxidative stress, antioxidant • Viability • Infertility

Cell Therapy: A Significant Strategy in the Treatment of Infertility

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Abstract

Today, cell therapy as the new phase of the biotechnology revolution is one of the important strategies and promising in the treatment of damaged tissues and various diseases including infertility. It is a type of treatment based on groundbreaking scientific advancements and uses stem cells or stem cell-derived products through successful transplantation. The purpose of cell-based therapies is to substitute, repair, or improve the biological function of damaged cells or tissues. It can be performed via the transplantation of taken cells and corrected an individual to a target tissue with suitable quality for them to restore function to survive for a long time. Recent studies represent the majority of cell-based therapies are still at an early phase of experimental. Infertility is one of the significant health issues which affects nearly 15% of all couples worldwide. Assisted reproductive techniques (ARTs) are effective ways to therapy human infertility, however, these methods have some limitations. For instance, they cannot be used for patients with no sperm. Recently the evaluation of stem cell transplantation or the derivation of germ-like cells from stem cells, as powerful as new therapeutic approaches in infertility treatment, has high importance. In this regard, embryonic stem cells, induced pluripotent stem cells (iPSC), mesenchymal stem cells, and spermatogonial stem cells are used in the treatment of infertility. It was shown that normal spermatogenesis can restore in busulfan-induced azoospermic guinea pigs by the transplantation of bone marrow-derived mesenchymal stem cells (BM-MSCs) into seminiferous tubules. Generally, to achieve a great result in cell-based treatments, integration in the sciences of molecular biology, cell biology, immunology, materials science and transplantation biology, tissue engineering, and clinical expertise related to various diseases including infertility are required. Thus, increasing the knowledge about new technologies of medicine can help in the early and new treatment of infertility in both women and men.

Keywords • Cell- and tissue-based therapy • Stem cells • Infertility • Male • Female

A study of the Protective Effects of Vitamin E and Fennel Extract on Mitochondria Changes in Mice Ovary due to Electromagnetic Field Exposure

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Abstract

Background: Everyday use of different types of electrical instruments and appliances has caused a large number of people to constantly be under the influence of electromagnetic fields.

Methods: For this study, 40 female rats weighing 200 ± 20 g were randomly chosen from a group of three-month-old rats in the animals' laboratory. Then, they were randomly divided into four groups; control (n=10), experiment 1 (Ex1) (n=10), experiment 2 (Ex2) (n=10), and experiment 3 (Ex3) (n=10). During the experiment, all four groups were maintained in the same conditions and received the same types of feeding. Experiment groups 1, 2, and 3 were under the influence of a 50 Hz electromagnetic field (EMF) for eight weeks. Subsequently, the second and third groups were kept away from the EMF effect for another eight weeks. At the end of the study, after the removal of the ovaries by glutaraldehyde, they were prepared for examination using an electron microscope. Group Ex2 rats were not sacrificed and were maintained in the normal laboratory environment for another eight weeks away from the impacts of EMF. The rats were fed vitamin E (100 mg/Kg) and fennel extract (1.5 g per body weight) every day orally and at the end of the second eight weeks, samples were taken. During the second eight weeks, group Ex3 was kept in normal conditions without the use of vitamin E and fed fennel extract, and then, samples were taken. Samples were taken simultaneously from 10 rats of the control group and Ex1 group.

Results: The results from the mitochondria in the ovary in the groups exposed to electromagnetic waves revealed that this intracellular organ was deformed and the majority of the organs were vacuolated when compared to samples from the control group. The values for mitochondrial vacuolization in the first through fourth groups were 1 ± 0.55 , 9 ± 0.55 , 6 ± 0.55 , and 11 ± 0.55 , respectively.

Conclusion: Vitamin E and fennel extract can reduce the damaging effects of non-ionizing radiation at 50 Hz frequency on the ovarian follicles.

Keywords • Electromagnetic fields • Foeniculum • Mitochondria • Ovary • Rats

Association of CGB5 Gene Polymorphism and its Maternal Serum β -hCG Level on *In Vitro* Fertilization and Embryo Transfer Outcome

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Abstract

Background: Successful pregnancy depends on the ability of the embryo to achieve the appropriate extent of trophoblastic proliferation and human chorionic gonadotropin level, once implanted into the maternal endometrium. Some studies indicated that maternal genetic factors could affect pregnancy success rates after *in vitro* fertilization (IVF). This study aimed to evaluate a possible association between CGB5-155G/C polymorphism as well as human serum chorionic gonadotropin level and the clinical pregnancy outcome of women undergoing embryo transfer.

Methods: A total of 200 infertile women were included in this study. The DNA fragment containing the target single nucleotide polymorphism site was amplified by polymerase chain reaction followed by restriction fragment length polymorphism and the serum level of chorionic gonadotropin was measured using the ELISA technique.

Results: The genotype frequencies of CC, GC, and GG in the IVF⁺ (controls) group were 17%, 30%, and 53%, and in the IVF⁻ group were 5%, 42%, and 53%, respectively. The results showed that women carrying the CC genotype had a higher chance to have successful pregnancies following embryo transfer. Predictably, ELISA results showed that serum β -hCG levels in the IVF⁺ group (15.16 ± 4.95 ng/mL) were significantly ($P=0.005$) higher than that of the IVF⁻ group (12.14 ± 3.73 ng/mL) at the third week after embryo transfer.

Conclusion: The findings of this study showed a significant association between CGB5 polymorphism as well as maternal β -hCG serum level with IVF-ET outcomes. It can be suggested that the CGB5 (-155G/C) CC genotype could have a supportive effect on embryo transfer outcomes.

Keywords • Fertilization *in vitro* • Chorionic gonadotropin, embryo transfer

Oxidative Stress and Male Infertility

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Abstract

Background: Infertility affects approximately 15% of couples worldwide, and male factors contributed to about half of all cases. Male infertility is a complex and multifactorial condition. The etiology of the disease is still unknown in many patients and is classified as idiopathic male infertility. Oxidative stress (OS) is defined as an imbalance between reactive oxygen species (ROS) and antioxidants. In 30%-80% of male infertility cases, the level of OS in seminal plasma is more than fertile men. Many factors are associated with OS in ejaculation such as leukocytes or abnormal spermatozoa in the seminal sample, alcohol consumption, opiates, smoking, obesity, insulin resistance, psychological stress, and infections. This study aimed to investigate the association between oxidative stress and male infertility.

Methods: The present study was performed by exploring a comprehensive literature search in English review publications of the last five years in PubMed, Google Scholar, and Scopus databases. Keywords, such as “male infertility”, “oxidative stress”, “reactive oxygen species”, AND “sperm” were used.

Results: ROS plays critical roles in spermatogenesis and sperm maturation, capacitation, hyperactivation, acrosome reaction, and sperm-oocyte fusion as well as embryonic morphogenesis. However, supraphysiological ROS levels lead to an increase in lipid peroxidation and abortive apoptosis, dysregulation of male reproduction endocrine axes, disrupted testicular functions, impede sperm membrane fluidity and permeability, decreased sperm count, quality, and function, and mitochondrial dysfunction. OS impacts genetic and epigenetic modifications of sperm. Besides, it increases DNA fragmentation in both nuclei and mitochondria. High levels of sperm DNA fragmentation result in decrease conception rate with natural pregnancy, increased recurrent pregnancy loss, poor pregnancy outcomes, and may also affect offspring. Moreover, OS is related to poor outcomes of assisted reproductive technology like arrest embryonic development, implantation failure, pregnancy loss, and lower live birth rates.

Conclusion: According to the findings, there is strong evidence that OS negatively impacts sperm quality and male fertility. Hence, its early detection and management merit more attention.

Keywords • Infertility • Oxidative stress • Spermatozoa

Microfluidics Technology and Sperm Selection

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Abstract

Background: In a natural pregnancy, only competent sperm could pass the female reproductive tract and fertilize an oocyte, but artificial reproductive technologies (ART) particularly ICSI bypass regular sperm selection. Microfluidics systems could be used to isolate the most potent sperm for ART. In this technology, seminal samples located in a microfluidic chip contain a definite flow rate and motile spermatozoa which could swim against a laminar flow and will be separated from non-viable spermatozoa. Systemic motivators include chemical factors, mechanical forces, and thermal gradients. It may be used for the evaluation of sperm characteristics, sperm isolation and manipulation, embryo culture, cryopreservation, studying the effects of different stimuli on gametes and embryos, and metabolite analysis. Sperm sorting could be conducted by passive or active methods. Passive sorting strategies include geometry, rheotaxis, and fluid flow, and active strategies include acoustic waves, chemotaxis, and both chemotaxis and thermotaxis. Hence, this study aimed to explore the efficacy of microfluidic systems for sperm selection.

Methods: The study was conducted by searching keywords such as “microfluidic”, “sperm selection”, AND “assisted reproductive technology” in databases of PubMed, Scopus, and Google scholar. Then, all English review articles from 2017 to 2022 were investigated.

Results: Studies revealed microfluidic techniques are effective to obtain viable high-quality sperms. They decrease the time of male infertility diagnosis and treatment and improve the ICSI success rate, ongoing pregnancy rate, and euploid embryos in ART. Disadvantages of these techniques include being costly and having a low sperm retrieval rate. Active methods in comparison with passive methods are more complicated and expensive. Passive methods are simpler; however, they have lower proficiency. The Microfluidic system is appearing as an economical and fast test to assess male fertility in clinics as well as at home. However, it needs to be optimized.

Conclusion: Although the microfluidic technique is an effective method for sperm selection, there is still so much to investigate.

Keywords • Spermatozoa • Microfluidics • Reproductive techniques

Antioxidant Therapy in Male Infertility Management

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Abstract

Background: Male oxidative stress infertility is considered the main mechanism in many cases of idiopathic male infertility. Antioxidants are chemicals with the power to combat oxidative stress by decreasing reactive oxygen species (ROS) concentrations or resolving oxidative damage. They play an essential role in the male reproductive system. Semen contains antioxidants such as superoxide dismutase, glutathione peroxidase, catalase, and peroxiredoxins. Antioxidant supplementation is known as an appealing strategy to manage male factor infertility. Antioxidant micronutrients include vitamin A, vitamin C, vitamin E, L-carnitine, coenzyme Q10, N-acetylcysteine, and trace elements such as selenium and zinc. Although antioxidant therapy has both benefits and side effects, its administration remains controversial. Therefore, this study aimed to examine the possible effects of antioxidants on sperm and male infertility.

Methods: The study was performed by exploring English review articles concerning oxidative stress, male infertility, sperm, reductive stress, and antioxidants, which were published in PubMed, Scopus, and Google Scholar databases in the past five years.

Results: Several studies demonstrated that antioxidants play protective roles against OS-induced injuries, and they could improve sperm concentration, morphology, motility, vitality, sperm DNA fragmentation, increase rates of fertilization, pregnancy, and live birth, and also decrease miscarriage rates. In contrast, some studies reported that antioxidants failed to improve semen parameters and male fertility. Moreover, studies that reported the beneficial effects of antioxidants on pregnancy and live birth rates are heterogeneous. For antioxidant usage, the maintenance of balance between physiological levels of ROS and antioxidants is necessary. Antioxidant overuse may result in “reductive stress” or “antioxidant paradox” phenomena, which could be harmful to general health, sperm quality, and male fertility, and even maybe harmful to embryos.

Conclusion: Antioxidant supplementations may not be a good choice in ROS-independent male infertility. Target therapies and the development of diagnostic tools for personalized medicine are necessary for male infertility management.

Keywords • Oxidative stress • Spermatozoa • Infertility • Antioxidants

Formation of Testicular Organoids on Porous Three-Dimensional Scaffolds Obtained from Fibroin Silk-Alginate-Laminin

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Abstract

Background: As a valuable resource for cell therapy, spermatogonial stem cells (SSCs) have raised hopes for the treatment of male infertility. Various three-dimensional methods have been developed to produce cellular aggregates and mimic the organization and function of the testis. In order to improve *in vitro* spermatogenesis, the present study was performed to form testicular organoid (TO) from mouse testicular cells in porous three-dimensional macro scaffolds obtained from fibroin silk-alginate-laminin.

Methods: The silk cocoons were placed in a solution of sodium carbonate to remove sericin. The purified silk fibers were then dissolved in lithium bromide solution and dialyzed. After characterizing the purified silk fibroin, 8% silk fibrin, 8% alginate, 8% fibroin silk -8% alginate (1:1), and 8% fibroin silk -8% alginate (1:1), -5% laminate solutions were dehydrated. The morphology, porosity, FTIR, swelling, degradability, non-toxicity, and *in vivo* biocompatibility of scaffolds for SSCs were examined. Then, the differentiation of mouse testicular cells on porous structures was investigated using Real Time-PCR, ICC, flow cytometry techniques, and H&E staining. The functionality of Leydig and Sertoli cells was determined by their ability for hormone secretion.

Results: The findings indicated that scaffolds obtained from fibroin silk-alginate-laminin could increase the hydrophilicity and subsequently enhance the swelling properties, proper surface properties, and good biocompatibility in comparison to the other studied groups. Furthermore, inoculation of neonatal mouse testicular cells onto composite structures resulted in the generation of multicellular TOs in which the differentiation of SSCs to post-meiotic cells was confirmed. Hormonal analysis of composite scaffolds revealed the functionality of TOs in the secretion of testosterone.

Conclusion: In general, our study suggested that a porous composite scaffold can be used to design a functional bioartificial testis *in vitro* that would offer a new fertility restoration option.

Keywords • Stem cells • Laminin • Sertoli cells • Adult germline stem cells

Three-Dimensional Co-culture of Mouse Spermatogonial Stem Cells with Sertoli Cell on the Engineered Scaffold by Three-Dimensional Printing of Extracellular Matrix

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Abstract

Background: Male infertility accounts for about 50% of all infertility cases, and 25% of infertile men are azoospermic. Due to the very small number of spermatogonia stem cells (SSCs) in testicular tissue biopsy specimens, SSCs culture for infertile patients could be essential. Thus, this study aimed to evaluate the proliferation of SSCs co-cultured with Sertoli cells on a printed scaffold derived from the extracellular matrix (ECM) of testicular tissues.

Methods: Rat testicular tissue was decellularized using a hypertonic solution -Triton X-100 for 30 minutes. The extracted ECM (5% ratio) was used as a bio-ink for the fabrication of artificial testis along with alginate and gelatin. SSCs were then isolated from the testes of neonate mice after enzymatic digestion. Finally, cell viability was evaluated using the MTT Assay tests. Then, the proliferation of SSCs co-cultured with Sertoli cells on alginate-gelatin scaffolds (group I) and ECM-alginate-gelatin scaffolds (group II) was assessed using immunocytochemistry, flow cytometry, and real-time PCR techniques.

Results: The MTT test indicated that the cell viability on the composite scaffold was significantly higher than on the hybrid scaffolds ($P > 0.05$). The results of two weeks of proliferation on the printed system showed that the expression of the *Plzf*, *Id4*, *Gfra1* gene using real-time PCR in group II was significantly higher than group I ($P > 0.05$). Flow cytometry analysis also showed that the number of *Plzf*-positive cells in group II was significantly higher than group I ($P > 0.05$). Besides, the immunocytochemistry results confirmed that *Plzf*, *Id4*, and *Gfra1* markers were expressed in both groups. However, their expression in group II was significantly higher than in group I ($P > 0.05$).

Conclusion: We concluded that the proliferation of SSCs on ECM-derived scaffolds increases the viability, colonization, and proliferation of SSCs and achieves a higher number of cells for differentiation of the *in vitro* studies. Therefore, 3D printing using an extracellular matrix of the testis can be an ideal strategy for the regeneration of seminiferous tubules.

Keywords • Stem cells • Sertoli cells • Extracellular matrix • Printing, three-dimensional

Comparison of Oocyte and Embryo Quality in Women with Polycystic Ovary Syndrome and the Control Group Candidate for *In Vitro* Fertilization and Intracytoplasmic Sperm Injection

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most prevalent endocrinopathy and one of the most common causes of female infertility. The primary oocyte quality has an utmost important effect on the survival of the embryo, as well as in the establishment and maintenance of pregnancy, fetus growth, and even in possible adulthood illnesses. Therefore, This study aimed to compare the oocyte and embryo quality between the PCOS women with the control group candidate for *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI).

Methods: The current study was designed in the prospective cohort format at the Milad Infertility Research Center and was conducted on 100 cases of infertile women with confirmed PCOS (case group) and the male factor (control group) as first IVF cycle candidates. Both groups underwent the ovary stimulation cycle and ICSI under the standard antagonist protocol. The collected data were then processed and analyzed using the SPSS software, version 16.

Results: The mean age of study cases was 35±3, and oocyte necrosis was the underlying pathological factor in both groups (28% and 26% in the PCOS and control groups, respectively). In addition, most embryos belonged to either grade 1 or 2 or were 8-cell embryos. Furthermore, the highest number of transferred embryos among the patients was related to the 8-cell and grade 1. The occurrences of biochemical pregnancy in the PCOS and control groups were up to 31.91% and 22%, respectively, leading to 72.73% and 60% childbirth in cases of both groups. Finally, there were no significant differences concerning the quality and the quantity of the embryos, the oocyte, the transferred embryo, the germinal vesicle oocytes, and the rate of pregnancy among the two groups ($P>0.05$).

Conclusion: According to the results of the present study, no differences were found concerning the oocyte quality, embryo, and pregnancy rate between PCOS cases and any other patients requiring ICSI. Therefore, such cases can similarly benefit from ICSI methods as well.

Keywords • Polycystic ovary syndrome • Intracytoplasmic • Sperm injections • Infertility, female • Pregnancy rate • Oocyte • Fertilization

Subcutaneous Administration of Granulocyte-c Colony-Stimulating Factor versus Local Infusion on IUI Outcomes in Women with Unexplained Infertility

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Abstract

Background: Despite important advances in assisted reproductive techniques, implantation rates remain relatively low. Previous studies indicated that intrauterine infusion of granulocyte colony-stimulating factor (G-CSF) can improve embryo implantation and continuation of pregnancy. Thus, This study was designed to evaluate the effect of single-dose subcutaneous G-CSF administration versus intrauterine infusion on IUI outcomes in patients with unexplained infertility.

Methods: This was a randomized clinical trial in a tertiary setting at the Infertility Clinic affiliated with Hormozgan University of Medical Sciences between June 2020 and December 2020. One hundred and thirty-nine eligible patients, on the day of human chorionic gonadotrophin (HCG) administration, were randomly divided into three groups:(A) patients received 300µg G-CSF subcutaneously, (B) 300µg G-CSF was infused intrauterine, and (C) patients received no G-CSF treatment. Biochemical pregnancy and clinical pregnancy were measured and compared between groups.

Results: The pregnancy outcomes in women who received G-CSF increased significantly in comparison to the control group ($P<0.05$). Moreover, the findings of the study showed that the chemical pregnancy and clinical pregnancy were higher in women who received intrauterine G-CSF infusion than those who received subcutaneous administration (24.4% vs 20% and 24.4% vs 15.55%, respectively). However, these differences were not statistically significant($P>0.05$).

Conclusion: G-CSF can conceivably improve pregnancy outcomes. The intrauterine route appears to be more effective than the subcutaneous. However, Further studies with a higher sample size are needed to establish the best route of G- CSF administration in particular with regard to women with unexplained infertility undergoing IUI.

Keywords • Granulocyte colony-stimulating factor • Embryo implantation • Infertility

The Effectiveness of Inositol and Metformin on Infertile Polycystic Ovary Syndrome Women with Resistance to Letrozole

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Abstract

Background: Recently, inositol has been introduced as a new insulin sensitizer that improves reproductive function in patients with PCOS by reducing the hyperinsulinemia state. Moreover, in contrast to metformin, no side effects have been reported following treatment with myo-inositol. The purpose of this study is to assess the effectiveness of myo-inositol and metformin in infertile women with polycystic ovary syndrome (PCOS) treated with letrozole.

Methods: This study is a randomized single-blind controlled clinical trial undertaken in 150 infertile PCOS women. For all patients, letrozole is prescribed at a dose of 7.5 mg per day from the third day of menstruation for five days. Patients who did not ovulate were included and divided into three groups: group I (control group), 200 µg of folic acid (as a placebo); group II, 1500 mg of metformin daily plus 200 µg of folic acid, and group III, inositol 2 g plus 200 µg of folic acid received for three months. In the last cycle, 7.5 mg of letrozole was prescribed for the induction of ovulation.

Results: The ovarian function was not significantly different in the control group and the first experimental group, whereas the ovarian function of the inositol+folic acid group with normal BMI was found significantly higher than other BMI spectra. In addition, the ovarian function was significantly higher in the inositol+folic acid group through increasing the infertility duration. The incidence of pregnancy was lower in the letrozole+folic acid+inositol group than in the other groups. However, it was not significant.

Conclusion: The addition of inositol and metformin to the treatment of infertile PCOS women with letrozole resistance improves ovarian function; however, it was not significant. It is worth mentioning that, inositol was more effective than metformin in patients with normal BMI.

Keywords • Metformin • Polycystic ovary syndrome • Inositol • Infertility • Letrozole

Preventative Effects of Vitamin E on Testicular Damage and Sperm Parameters in the First-generation Mice Pups Due to Pre- and Postnatal Mancozeb Exposure

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Abstract

Background: Exposure to toxins, fungicides, and oxidants can lead to testicular dysfunction and spermatogenesis. The present study aimed to evaluate the effects of vitamin E on mancozeb-induced testis damage in first-generation pups during intrauterine and lactating periods.

Methods: Two groups of pregnant NMRI mice received 500 mg/Kg mancozeb (MNZ) as the MNZ group and 200 mg/Kg vitamin E as the MNZ+vitamin E group before receiving MNZ. In addition, a vehicle and a control group were designed every other day in gestation and lactation periods. The male pups from each group were maintained until adulthood (8-10 weeks). The left testes and epididymides were removed following the sacrifice of the pups. Then, they were weighed, and sperm parameters including number, viability, motility, morphology, as well as testis structure were evaluated.

Results: A significant decrease occurred in sperm parameters of the mancozeb-treated pups compared to the control and vehicle groups. Treatment with vitamin E reversed the deleterious effects of MNZ to a nearly normal condition. Testis parameters including the weight, gonadosomatic index, seminiferous tubule diameters, and Johnsen's score, as well as the number of germ cells such as spermatogonia, spermatocyte, spermatid, and Sertoli, decreased significantly in the MNZ group, compared to those of the control and vehicle groups.

Conclusion: Based on the results, the exposure of pups to mancozeb during pregnancy and lactating periods negatively affected the reproductive system of male pups. However, concomitant use of vitamin E could prevent the harmful effects of mancozeb on most sperm and testicular parameters.

Keywords • Vitamin E • Mancozeb, germ cells • Lactation • Mice

Studying the Predictive Effects of Bacterial Carotenoids in the Treatment of Endometriosis Using Virtual Screening Methods

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Abstract

Background: Endometriosis is a chronic inflammatory disease defined as the presence of endometrial tissue outside the uterus, which causes pelvic pain and infertility. Cytokines appear to play vital roles in the development and progression of endometriosis and associated infertility. Tumor necrosis factor- α (TNF- α) is a multifunctional pro-inflammatory cytokine, responsible for autoimmune and inflammatory disorders. TNF- α plays an important role in endometrial physiology as well as during early implantation. In addition, this cytokine has a considerable pathophysiological function in diseases such as menorrhagia, endometriosis, or infertility due to its regulatory impact on proliferation, differentiation, and angiogenesis in the human endometrium. In women with endometriosis, TNF- α levels increase in peritoneal fluid and serum significantly. In the present study, we focused on finding novel small molecules that can directly block TNF- α -hTNFR1 (human TNF receptor 1) interaction.

Methods: In this regard, TNF- α inhibiting capacity of natural carotenoids was investigated in terms of blocking TNF- α -hTNFR1 interaction with the help of a combination of *in silico* approaches, based on virtual screening, molecular docking, and molecular dynamics (MD) simulation.

Results: A total of 125 carotenoids were selected out of 1204 natural molecules, based on their pharmacokinetics properties, and they all met Lipinski's rule of five. Among them, sorgomol, strigol, and orobanchol had the most favorable ΔG with the best pharmacokinetics properties and were selected for MD simulation studies, which explored the complex stability and the impact of ligands on protein conformation. It was shown that sorgomol formed the most hydrogen bonds, resulting in the highest binding energy with the lowest RMSD and RMSF.

Conclusion: Our results showed that sorgomol was the most appropriate candidate as a TNF- α inhibitor. In conclusion, the present study could serve to expand possibilities to develop new therapeutic small molecules against TNF- α which plays an important role in the inflammation of endometriosis.

Keywords • COVID-19 • Tumor necrosis factor-alpha • Carotenoids • Molecular docking simulation

The Effect of COVID-19 on the Human Reproductive System: A Review Study

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Abstract

Background: Evidence reveals that COVID-19, in addition to impacting the respiratory system, affects other organs, including the male and female reproductive systems. The purpose of this study was to examine the impact of COVID-19 on the human reproductive system.

Methods: Data were collected in SID, Science Direct, PubMed, and Google Scholar databases. The keywords including COVID-19, reproductive system, fertility, and factors related to mesh term utilization and Boolean strategy were used. Papers from 2019 to 2022 were extracted. Finally, out of 58 searched articles, 20 articles related to the purpose of the study were reviewed.

Results: The results were organized into two categories. The first category deals with the effect of COVID-19 on the female reproductive system including Sleep disorders following quarantine on gonadotropin release and its effect on the ovaries and menstrual cycle, preterm delivery, increased cesarean delivery, the possibility of intrauterine infection of the fetus and dysfunction of the reproductive glands. The second category concerns the effect of COVID-19 on the male reproductive system including abnormal semen quality, possible effect on gonocyte differentiation in the early stages of spermatogenesis, negative effect on spermatogenesis, testicular dysfunction, and changes in testosterone concentration by increasing serum LH, testicular inflammation, decreased sperm concentration in semen, impaired sperm motility, dysfunction of the reproductive glands, significant damage to the seminiferous tube, swelling of Sertoli cells, decreased Leydig cells, significant disorder on semen volume and impaired sperm morphology.

Conclusion: The findings revealed that COVID-19 has an impact on various aspects of the human reproductive system. Midwives and gynecologists should alleviate couples' fears about infertility by recognizing these cases and offering suitable counseling to couples infected with COVID-19.

Keywords • COVID-19 • Genitalia • Fertility

Mental Disorders and Infertility

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Abstract

Background: 8–12% of the world’s population is thought to be affected by infertility, which is associated with things like the timing of unintended pregnancy loss, the age of the female spouse, and the prevalence of disorders that affect fertility. High amounts of psychological discomfort may make it harder to get pregnant. In this study, stress, depression, addictions, eating disorders, and sleep disorders—which are frequently reasons to contribute to idiopathic infertility—were examined in relation to both female and male fertility.

Methods: This review has been conducted based on an analysis of available literature indexed in MEDLINE, Cochrane, and PubMed databases between 2015 and 2021. Specific keywords including “infertility”, “psychological disease” AND “mental disorder” were used. Epidemiological studies, experimental studies, inquiries, or editorials on the mentioned topic were included.

Results: An examination of the literature during the current review reveals that mental problems such as stress, depression, sleep disorders, eating disorders, and addictions have a negative impact on female and male fertility. These illnesses alter the functioning of endocrine glands and the immune system at both the tissue and cellular level, all of which may result in diminished fertility. Tubal spasms, anovulation, and vaginismus are symptoms of emotional stress in women. Impotence with erection and ejaculation, on the other hand, can be the main cause of psychological disorders that lead to infertility in men.

Conclusion: Mental disorders may negatively impact female and male fertility. Further studies are required to explain the exact role and contribution of mental disorders to fertility.

Keywords • Mental disorders • Depression • Infertility

The Role of Melatonin on amelioration of the Detrimental Effects Induced by Methamphetamine Consumption during Pregnancy and Breastfeeding in the Reproductive System of Male Neonates

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Abstract

Background: Methamphetamine (Meth) is a psychostimulant that has detrimental effects on organs such as the nervous system, and reproductive system. Since many meth users are at reproductive age, it is a threat to the next generation of meth consumers. Meth can pass through the placenta and also secretes in breast milk. Melatonin (MLT) is the main hormone of the pineal gland that regulates the circadian cycle, and it is also an antioxidant agent which can ameliorate the effects of toxic agents. This study aims to investigate the protective effects of melatonin against the detrimental effects which were induced by Meth in the reproductive system of male neonates, whose mothers consumed Meth during pregnancy and breastfeeding period.

Methods: Thirty female adult balb/c mice were divided into three groups; the control, the vehicle which receives normal saline, and the experimental group which received 10mg/Kg Meth intraperitoneal during pregnancy and breastfeeding period. After the breastfeeding period, the male offspring of the experimental group was divided into two subgroups. One of them received 5mg/Kg melatonin intragastrically for 21 days, as equal to the breastfeeding period (Meth-MLT), and the other one didn't receive Meth-D.W. After treatment, mice were sacrificed, and testes tissues and epididymis were obtained. Then, the testes' weight, seminiferous tubule diameter, apoptotic cells, biochemical factors, sperm parameters, and expression of PCNA and CCND genes were investigated.

Results: According to the findings of the study, seminiferous tubule diameter, SOD activity, total Thiol groups concentration, catalase activity, sperm count, and expression of PCNA and CCND genes were decreased in the Meth-D.W group compared to the control and vehicle groups. Apoptotic cells, MDA level, abnormal sperms, and DFI were increased. All the mentioned changes were ameliorated in the Meth-MLT group compared with Meth-D.W and the testes' weight had no significant change.

Conclusion: The current study represents that Meth consumption during the pregnancy and breastfeeding period can induce detrimental effects in the reproductive system of male neonates which can ameliorate by melatonin consumption.

Keywords • Methamphetamine • Melatonin • Spermatozoa

Injectable Platelet-rich Fibrin (i-PRF) Optimizes the Hormonal Function of Mouse Ovarian Tissue after Transplantation

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Abstract

Background: Ovarian transplantation is a successful method of maintaining fertility in young women; however, the occurrence of ischemic reperfusion can affect the endocrine activity of Transplanted tissue. Injectable platelet-rich fibrin (i-PRF) is a liquid formulation of platelet-rich fibrin (PRF) without the use of anticoagulants. The i-PRF is a bioscaffold that contains leukocytes, circulating stem cells, platelets, and growth factors. All of these factors can affect the growth and proliferation of granulosa cells and corpus luteum, and thus cause the resumption of ovarian hormonal activity after transplantation. This study aimed to investigate the effect of i-PRF bioscaffold on the serum level of progesterone and estradiol following mouse ovarian tissue transplantation.

Methods: 18 female mice were divided into three groups: control, autograft+saline (whole ovarian tissue transplanted in the gluteus superficialis muscle, saline directly injected into it), and autograft+i-PRF (whole ovarian tissue transplanted in the gluteus superficialis muscle, i-PRF was directly injected into it). Then, 28 days after ovary transplantation, serum concentrations of progesterone and estradiol were assessed. Statistical analysis was done with One-way ANOVA and Tuckey's *Post hoc* tests. and $P < 0.05$ was considered statistically significant.

Results: The serum level of progesterone and estradiol in the control group increased significantly compared to the other groups, while it showed a significant increase in the autograft+i-PRF group compared to the autograft group ($P < 0.05$).

Conclusion: For the first time, our findings showed that the Injection of i-PRF into the graft site could reduce ischemic-reperfusion injury and improve ovarian tissue hormonal activity.

Keywords • Ovary • Transplantation • Platelet-rich fibrin

The Freezing Medium Containing Melatonin improves Spermatogonial Stem Cell Survival after Transplantation in an Azoospermia Mouse Model due to Testicular Torsion

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Abstract

Background: Spermatogonial stem cells (SSCs) are essential to the initiation of spermatogenesis. Cryopreservation, long-term maintenance, and auto-transplantation of SSCs could be new infertility treatments. This study aimed to add melatonin to the basic freezing medium and to evaluate its effect on the efficiency of the thawed SSCs after transplantation into the testicles of azoospermic mice.

Methods: SSCs were isolated from newborn NMRI mice, and the cells were enriched to assess morphological features. The thawed SSCs were evaluated for survival, apoptosis, ROS level before transplantation, and proliferation (MVH and ID4). Besides, differentiation markers such as c-Kit, SCP3, TP1, TP2, and Prm1 of SSCs were examined using immunofluorescence, western blot, and quantitative real-time polymerase chain reaction (PCR) after transplantation.

Results: The result showed that the survival rate of SSCs after thawing was significantly higher in the melatonin group than in the cryopreservation group containing a basic freezing medium. In addition, the rate of apoptosis and level of ROS production also decreased significantly in the cryopreservation group with melatonin ($P < 0.05$). The expression of proliferation and differentiation markers after transplantation was significantly higher in the cryopreservation group with melatonin than in the cryopreservation group ($P < 0.05$).

Conclusion: The results suggest that adding melatonin to the basic freezing medium can effectively protect the SSCs by increasing the viability and reducing the ROS production and apoptosis and improving the transplantation efficiency of SSCs after cryopreservation, which will provide a significant suggestion for fertility protection in the clinical studies.

Keywords • Melatonin, cryopreservation • Transplantation • Stem cells

Three-dimensional Co-culture of Human Spermatogonial Stem Cells with Sertoli Cells in a Soft Agar Culture System Supplemented by Growth Factors and Laminin

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Abstract

Background: Three-dimensional (3-D) culture system for *in vitro* proliferation of human spermatogonial stem cells (SSCs) is a useful tool for the investigation of the spermatogenesis process and the management of male infertility, particularly in prepubertal cancer patients. The purpose of this study was to investigate the proliferation of human SSCs co-cultured with Sertoli cells in a soft agar culture system (SACS) supplemented by Laminin and growth factors.

Methods: Testicular cells were isolated from the testes of brain-dead patients and cultured in a two-dimensional (2-D) culture system for three weeks. After three weeks, functional SSCs were evaluated by xenotransplantation and also identification of cells was assessed by immunocytochemistry, flow cytometry, and RT-PCR. SSCs and Sertoli cells were transferred to the upper layer of SACS for three weeks. The number of colonies and expression of specific SSCs and Sertoli cell markers and apoptotic genes was evaluated.

Results: Transplanted SSCs migrated into the basement membrane of seminiferous tubules of recipient mice. Expression of PLZF, $\alpha 6$ -Integrin, and Vimentin proteins in SSCs and Sertoli cells were observed in 2-D and 3-D culture systems. The expression rate of PLZF, $\alpha 6$ -Integrin, Bcl₂, and colony number in SACS supplemented by Laminin and growth factors group were significantly higher than non-supplemented groups ($P \leq 0.01$). The expression rate of c-kit and Bax in supplemented group were significantly lower than non-supplemented groups ($P \leq 0.05$). The three-D co-culture system decreased apoptosis and increased the propagation of human SSCs.

Conclusion: This designed system can be utilized to increase the proliferation of human SSCs in prepubertal male cancer and azoospermia patients.

Keywords • Coculture techniques • Adult germline stem cells • Laminin • Stem cells • Cell proliferation

In Vitro Proliferation of Human Spermatogonial Stem Cells in Two-dimensional and Three-dimensional Culture Systems of PRP

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Abstract

Background: The microenvironment of SSCs has critical roles in self-renewing and differentiation ability. Platelet growth factors stimulated cell proliferation, cryoprotection, chemotaxis, and differentiation. Activation of PRP by CaCl₂ solidified plasma and forming fibrin network. Fibronectin and fibrin in PRP act as adhesion molecules that can promote cell migration and the fibrin network structure within PRP can hold cells in a 3-D organization. Here, in this study, we evaluated the effect of PRP on the self-renewing of adult human SSCs in two-dimensional and three-dimensional culture systems.

Methods: Testicular cells of four brain-dead patients were cultivated, characterization of SSCs was performed and their functionality was assessed by xenotransplantation to azoospermia mice. After the preparation of the PRP scaffold, cytotoxic and histological evaluation was performed. Then, the SSCs were cultivated into three groups: control, 2-D culture by an optimized dose of PRP, and PRP scaffold. The expression of GFRa1 and c-KIT were evaluated by performing real-time PCR.

Results: The expression of PLZF and GFRa1 was identified through immunocytochemistry. Labeled cells were transplanted on the seminiferous tubules basement membrane in azoospermic recipient testes as an individual cells and didn't create a cluster. This proved the existence of SSCs after 2-D pre-culture and evaluate the homing and colonization of SSCs in the recipient testis. The proliferation rate and viability of SSCs on PRP scaffolds showed a striking time-dependent increase. Histological evaluations revealed cross-linked fibrin in pink, these randomly oriented fibril organizations appeared to present an efficient microstructure for human SSCs. Expression of c-KIT showed a significant increase (P<0.05) in the PRP-2-D group, and expression of GFRa1 and c-KIT revealed a significant increase in the PRP scaffold group (P<0.001).

Conclusion: The potential of platelet-rich preparation was mainly due to the cytokines, growth factors obtained from platelets, and 3-D microstructure of the PRP scaffold that mimicked the niche of SSCs.

Keywords • Stem cells • Cell proliferation • Azoospermia • Receptor protein-tyrosine kinases • Fibrin

Overview of Varicocele and Oxidative Stress Biomarkers

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Abstract

Background: Varicocele is one of the most important causes of male infertility. Several pathophysiological mechanisms have been reported for varicocele. Current evidence suggests that oxidative stress is the fundamental element contributing to infertility in men with varicocele. The present study aimed to review the association between oxidative stress biomarkers and varicocele.

Methods: In order to find relevant articles to the research question, an electronic search with time (recent five years, up to 2022) and language (English) restrictions was conducted using PubMed including keywords such as “Varicocele” AND “Oxidative stress”. Most recent studies including original research and review articles were selected. Analysis was done and data were synthesized and compiled in a sequential and presentable paradigm.

Results: Higher levels of oxidative stress biomarkers in varicocele patients along with lower total antioxidant capacity (TAC) in comparison with healthy controls were reported. Higher lipid peroxidation including malondialdehyde (MDA) in the semen and plasma of infertile males with varicocele was the most reported one. Moreover, a decreased expression of antioxidant enzymes like superoxide dismutase and glutathione peroxidase activities were reported in varicocele patients.

Conclusion: As the findings from previous studies revealed, varicocele was closely mediated by oxidative stress, and also significant interest in antioxidants-based treatment could be considered. Notably, further clinical investigations examining the impact of varicocele repair and/or the use of antioxidants on seminal oxidative stress in these patients are required.

Keywords • Varicocele • Oxidative stress • Antioxidant function

Ameliorative Effects of Hydro-Alcoholic Extract of *Nigella Sativa* on Follicular Atresia and the Gonadal Steroid Hormones Level in a Rat Model of Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a complex endocrine disorder with an unknown basis. The most reasonable indication of the existence of PCOS is the increase of blood androgen (Hyperandrogenism). *Nigella sativa* (*NS*) belongs to the *Ranunculaceae* family and is an annual herb that is used in different curative cases and contains pharmacological properties including anti-infertility, anti-apoptotic, anti-oxidant, anti-inflammatory, etc. The present study was conducted to investigate the ameliorative effects of the hydroalcoholic extract of *Nigella sativa* on follicular atresia, the level of gonadal steroid hormones in a rat model of PCOS.

Methods: In this research, 32 mature female rats were divided into four groups: Control, PCOS- induced (4mg estradiol valerate, IM), PCOS+NS (200mg/Kg/day), and PCOS+NS (600mg/Kg/day). The rats received *NS* extract by gavage for 63 days. After treatment, the animals were weighed and sacrificed and their blood serum samples were taken to measure steroid hormones level. On the other hand, the ovaries were collected and weighed and the tissue incisions from obtained ovaries to study follicular atresia were prepared. Statistical analysis was performed using one-way ANOVA and Tukey's post hoc tests. $P < 0.05$ was considered statistically significant.

Results: A significant increase in body weight, ovary weight, follicular atresia, testosterone level, and a significant decrease in the level of estrogen, and progesterone was observed in the PCOS group compared to the control group ($P < 0.05$). However, a significant reduction in the ovary weight, follicular atresia, the testosterone level, and a significant increase in progesterone was found in *NS* groups compared to the PCOS group ($P < 0.05$).

Conclusion: The findings demonstrated that *NS*, especially at a dose of 600mg/Kg decreased the complications of PCOS by balancing the level of gonadal steroid hormones and improving follicular growth.

Keywords • Rats • *Nigella sativa* • Polycystic ovary syndrome • Gonadal steroid hormones • Follicular atresia

Effect of Black Seed Hydro-Alcoholic Extract on Malondialdehyde (MDA) Enzyme Level and Total Antioxidant Capacity in Ovarian Tissue of PCOS Model Rats

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common disease that affects 5-10% of women of childbearing age and is associated with ovulation reduction, androgen enhancement, and insulin resistance. Black seed has a rich medical and religious history and consists of powerful chemical compounds that can have many effects on human health. In this study, the effect of the hydro-alcoholic extract of black seed on the antioxidant properties of ovarian tissue in PCOS model rats was examined.

Methods: 32 adult female rats were randomly divided into four groups: the control group, PCOS induced (4 mg estradiol valerate intramuscular injection), PCOS+black seed group (200 mg/Kg body weight), and the group treated with PCOS+black seed (600 mg/Kg body weight). The animals received black seed extract orally by gavage for 63 days. After treatment, all animals in the estrous phase were sacrificed and the MDA and TAC levels in ovarian tissue were measured.

Results: The findings revealed an increase in the MDA concentration and a decrease in the total antioxidant capacity in the PCOS-induced group compared to the control group ($P<0.05$). However, in the black seed-treated groups, the TAC level was increased as well as MDA concentration was decreased compared to the PCOS-induced group. Besides, among the applied doses, 600 mg/Kg had the most positive effect ($P<0.05$).

Conclusion: Black seed had antioxidant activity and reduced oxidative stress in the rats.

Keywords • Rats • Nigella sativa • Polycystic ovary syndrome • Ovary

The Effect of Sildenafil Citrate and Alpha-Lipoic Acid on the Sperm Biochemical Parameters during Cryopreservation in the Asthenozoospermic Infertile Men

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Abstract

Background: Cryopreservation is a common method for assisted reproductive technology that causes oxidative stress on sperm, which is the main reason for sperm disruption. Cryoprotective media are commonly supplemented with antioxidants that improve sperm quality post-thawing. This study investigated to assess the effects of Sildenafil Citrate (SC) and Alpha-Lipoic Acid (ALA) supplementation on oxidative stress during cryopreservation in asthenozoospermic infertile men.

Methods: 30 semen samples were collected from the asthenozoospermic patients. Each semen sample was divided into five groups: Control (fresh), Freeze (treated with cryo-protectant alone), Freeze+SC (treated with cryo-protectant+0.67 μ M SC), Freeze+ALA (treated with cryo-protectant+0.5mM ALA), and Freeze+SC+ALA. In each sample, sperm Tumor necrosis factor alpha (TNF- α), Malondialdehyde (MDA) level, and antioxidant enzymes, including Catalase (CAT), Glutathione (GSH), and Superoxide dismutase (SOD) levels were evaluated by Enzyme-linked immunosorbent assay (ELISA).

Results: Our results showed that the freeze group had a significant reduction in antioxidant enzyme levels and a significant increase in sperm TNF- α , and MDA levels compared to the control group ($P<0.05$). The Freeze+SC, Freeze+SC+ALA, and Freeze+ALA groups compared to the freeze group had a significant increase in antioxidant enzyme levels, and a significant decrease in TNF- α and MDA levels ($P<0.05$). Antioxidant enzyme levels were significantly higher, but TNF- α and MDA level was significantly lower in the Freeze+ALA group compared to Freeze+SC and Freeze+SC+ALA groups ($P<0.05$). Antioxidant enzyme levels in the Freeze+SC+ALA group had significantly increased compared to the Freeze+SC group ($P<0.05$).

Conclusion: Our findings revealed that the utilization of ALA and SC along with a cryoprotective medium caused improvement in the biochemical parameters of sperm against cryodamage.

Keywords • Asthenozoospermia • Cryopreservation • Biochemical parameters • Oxidative stress • Sildenafil citrate • Thioctic acid

The Effect of COVID-19 Vaccine on Women's Menstrual Cycle

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Abstract

Background: COVID-19 has had a huge impact on women's health. Physical, mental, and psychological effects are a small part of the effects of COVID-19 on women. Menstrual disorders are also a significant complication of COVID-19 in women and girls. This study was performed as a review to investigate the effects of Covid-19 on the menstrual cycle in women.

Methods: In this study, by using the keywords "COVID-19", "women", AND "menstruation", databases such as Google Scholar, SID, PubMed, and Science Direct were searched and several studies were reviewed.

Results: Heavy, light menstruation, irregular periods, and missed periods are some of the COVID-19 effects on women. However, the side effects are short-term and go away about one to two months after getting infected. The effects of the COVID-19 vaccine are almost the same as those gotten infected by COVID-19. Astra-Zeneca and Pfizer vaccines had the most symptoms and caused menstrual disorders compared to other types of vaccines.

Conclusion: Women and girls make up a large portion of society. Hence, it is recommended that health planners and policymakers make efforts to improve their physical and mental health by focusing on women's health and solving their problems. Menstrual disorders were short-term, but in women who had many problems for more than two months, it is recommended to see a specialist and a doctor.

Keywords • COVID-19 • Menstruation • Vaccine • Woman

Antioxidant Function and Male Infertility Treatment

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Abstract

Background: Oxidative stress (OS) has been recognized as one of the most important causes of male infertility. Since antioxidants suppress the activity of reactive oxygen species, these compounds have been used in the medical treatment of male infertility or have been added to the culture medium during sperm separation techniques. Treatments have varied over the years involving the use of many different compounds, such as carnitines, glutathione, and vitamins A, E, and C. This review considers the effects of the main antioxidant compounds used in clinical practice on male infertility treatments.

Methods: An electronic search with time (recent five years, up to 2022) and language (English) restrictions was conducted using PubMed. In order to find relevant studies to the research question, specific keywords including “male infertility”, “antioxidant treatments” AND “oxidative stress” were used. Then, the most recent studies including original research, *in vivo* trials, and review articles were selected.

Results: Previous studies reported an elevation of sperm count and a decrease in the percentage of abnormal spermatozoa with the co-administration of vitamins E and C. Moreover, vitamin E and selenium supplementation produced an improvement in sperm motility. One study evaluated the impact of glutathione therapy on sperm parameters and found an increase in sperm concentration and an improvement in sperm kinetic parameters and sperm morphology. However, some *in vivo* studies did not find such an impact.

Conclusion: Although many clinical trials demonstrated the beneficial effects of antioxidants in male infertility, some studies failed to demonstrate the same benefit. Multicentre, double-blind studies are still needed to provide conclusive evidence on the benefit of antioxidants as a treatment modality for male infertility.

Keywords • Infertility, male • Oxidative stress, antioxidant activity

The Association between Serum Vitamin D level and Sperm Parameters/Sperm DNA Damage

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Abstract

Background: Semen parameters and sperm DNA damage are used in clinical settings to assess male reproductive potential. Micronutrients affect spermatogenesis and sperm cell maturation, which affect the quality of the sperm. Given the extensive range of vitamin D's functions and its regulatory impact, it is possible to hypothesize that vitamin D may have an impact on the quality of male infertility and semen. However, based on the literature, there is a controversy about the correlation between vitamin D and semen quality. Regarding insufficient evidence showing whether serum vitamin D is related to semen quality, we investigated the association between serum levels of vitamin D and sperm parameters among a number of Iranian infertile men. Moreover, the association between sperm DNA damage and vitamin D was assessed for the first time.

Methods: This pilot cross-sectional study was carried out among infertile males. A researcher-made checklist was designed to collect data on the basic characteristics of patients. Serum vitamin D levels as well as sperm parameters including sperm concentration, volume, vitality, total motility, progressive motility, abnormal morphology, DNA fragmentation, and chromatin maturity were assessed according to standard protocols. Subjects with a serum vitamin D level of ≥ 30 ng/mL and 20-29 ng/mL were categorized as vitamin D sufficient and insufficient groups, respectively.

Results: According to our results, sperm parameters except for sperm volume were significantly different between the two groups ($P < 0.05$). There was a positive significant correlation between sperm concentration, vitality, progressive motility, and total motility with serum levels of vitamin D ($P < 0.05$). A negative significant correlation was observed between sperm abnormal morphology, DNA fragmentation, and chromatin immaturity with serum levels of vitamin D ($P < 0.05$).

Conclusion: Results of the current study showed that low vitamin D levels can be considered a potential risk factor for male infertility among the Iranian population.

Keywords • Spermatozoa • Infertility, male • Micronutrients • Vitamin D • DNA fragmentation • Semen analysis

Early Onset and Atypical Severe Preeclampsia in a Woman Undergone IVF

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Abstract

Background: Assisted reproduction technology (ART) is used worldwide, at increasing rates, and data show that some adverse outcomes occur more frequently than following spontaneous conception. To report a rare case of severe and atypical preeclampsia at the gestational age of 18 weeks in a woman undergone IVF due to sex selection, not infertility.

Methods: A 35-year-old woman G3P2L2 with a gestational age of 18 weeks was referred to Al-Zahra Hospital with blood pressure (BP) of 220/120 mm Hg, headache, and 3100 g protein in 24-hour urine collection. Her pregnancy had achieved via IVF due to sex selection (male selection) by the frozen embryo. Thus, she did not have infertility. She had a history of hypothyroidism. She did not have any chronic HTN or other diseases. Sonography of her pregnancy showed normal nuchal translucency (NT) in 13 weeks. The risk of the down syndrome was 1.75 in a double test. Therefore, she had done cell-free DNA, and it was low risk for aneuploidies. Lab data including CBC, LFT, and serum creatinine were normal. Antiphospholipid, lupus, anti-GBM, and complement tests were within normal ranges.

Results: Due to severe preeclampsia and uncontrolled blood pressure regardless of the 300 mg labetalol prescription, termination of pregnancy was scheduled for her by vaginal route. The male fetus with 300 g weight was born. The placenta was normal. Following delivery, she had a BP of 160/100 for one week which was controlled by valsartan. After that, her BP became normal without any medication. Four weeks later, the quantitation of proteinuria was 80 g.

Conclusion: Although infertility may play a role in adverse pregnancy outcomes such as pregnancy-induced hypertension (PIH) in IVF, factors related to hormone stimulation or IVF methods in general also play a role, and a woman should be informed about these adverse maternal outcomes before undergoing IVF, even if she has no history of infertility.

Keywords • Pre-eclampsia • Fertilization *in vitro* • Proteinuria

A Comparison of Ethanol Sclerotherapy with Laparoscopic Surgery for the Management of Endometrioma: A Randomized Double-blind Clinical Trial

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Abstract

Background: Endometriosis and infertility are two well-known associated pathologies that are found in approximately 25–40 % of cases. For the treatment of endometrioma, there is laparoscopic stripping of the cyst wall. The mentioned method for treating it has many disadvantages which can affect ovarian reserve. It seems clear that another alternative needs to be introduced. Therefore, various studies were performed in order to use safer and less invasive methods to manage this medical condition. One of the newest treatment modalities is sclerotherapy under an ultrasound guide. Thus, this study aimed to compare the recurrence rate of endometrioma and ovarian reserve in patients with infertility undergoing sclerotherapy vs laparoscopic ovarian cystectomy.

Methods: In this randomized clinical trial, a total of 70 infertile patients, with endometriomas were divided into two groups. The first group (n=35) had ethanol sclerotherapy (EST) and the second group (n=35) underwent laparoscopic ovarian cystectomy. The authors measured the AMH levels, the mean longest cyst diameter, and the recurrence rate of endometrioma baseline three and 12 months after each intervention and between the two groups.

Results: AMH concentration was significantly increased three months after sclerotherapy, however significantly decreased after laparoscopic cystectomy compared to the baseline. The AMH concentrations were higher in the EST group than the laparoscopy group, three months after the interventions (P=0.009). The mean longest cyst diameter was significantly decreased between three and 12 months after each intervention in both groups, but the cyst diameter was smaller in the laparoscopy group compared to the EST group three months after the intervention. No differences were found when comparing the recurrence rate before and after each procedure in both groups, three and 12 months after interventions (P=0.1 and 0.6).

Conclusion: This study indicated that alcohol sclerotherapy can be a good alternative to surgery in the management of endometrioma in patients with infertility better than surgery, with significant increases in serum AMH concentrations observed in the patients after sclerotherapy.

Keywords • Endometriosis • Surgery • Sclerotherapy

Co-treatment of Melatonin and Platelet-rich Fibrin Bioscaffolds Improves the Endocrine Function of Mice Auto-transplanted Ovaries through Reduction of Oxidative Stress and Inflammation

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Abstract

Background: Young cancer patients who receive chemotherapy and radiation therapy may benefit from ovary transplantation as a good technique for maintaining ovarian function and fertility. The purpose of this study was to look at the interaction between melatonin and Platelet Rich Fibrin (PRF) on inflammation, oxidative stress, and mouse ovarian function after autotransplantation.

Methods: 60 female NMRI mice, (4-5 weeks of age), were divided into five groups (n=12). The name of the groups was the control, autografted+saline (20mg/Kg/day), autografted+PRF (Ovaries are embedded in PRF), autografted+melatonin (20mg/Kg/day i.p. injection for one day until seven days after transplantation) and autografted +PRF+melatonin. Each group was divided again into two subgroups, based on days 7 and 28 post-transplantation (n=6). Serum samples were collected on days 7 and 28 to evaluate the inflammation rate, concentrations of MDA, total antioxidant capacity, and progesterone and estradiol levels. Data were analyzed using One-way ANOVA and Tukey's *post hoc* tests, and $P < 0.05$ was considered statistically significant.

Results: The levels of TNF- α ($P < 0.001$), IL-6 ($P < 0.001$), and MDA ($p < 0.001$) increased significantly in the autografted+saline group compared to the control group. These parameters decreased significantly in the experimental groups compared to the autografted+saline group ($P < 0.001$). Meanwhile, the MDA level in the treated groups received to the level of the control group ($P > 0.05$). The level of IL-10 ($P < 0.001$), Progesterone, and Estrogen ($P < 0.001$), and the total antioxidant capacity ($P < 0.01$) decreased significantly in the autografted+saline group compared to the control group. These parameters increased significantly in the experimental groups and compensated for the level of the control group ($P > 0.05$).

Conclusion: The findings indicated that co-administration of melatonin and PRF reduces oxidative stress and inflammation in the grafted ovaries leading to improved ovary endocrine function in mice models.

Keywords • Melatonin • Platelet-rich fibrin • Oxidative stress • Inflammation

Overview of Varicocele and Oxidative Stress Biomarkers

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Abstract

Background: Varicocele is one of the most important causes of male infertility. Several pathophysiological mechanisms have been reported for varicocele. Current evidence suggests that oxidative stress is the essential constituent contributing to infertility in men with varicocele. The present study aimed to review the association between oxidative stress biomarkers and varicocele.

Methods: In order to find relevant studies to the research question, an electronic search with time (recent five years, up to 2022) and language (English) restrictions was conducted using PubMed including keywords such as “Varicocele” AND “Oxidative stress”. Then, the most recent studies including original research and review articles were selected. The analysis was done and the obtained data were synthesized and compiled in a sequential and presentable paradigm.

Results: In contrast to healthy controls, varicocele patients had higher levels of oxidative stress biomarkers and decreased total antioxidant capacity (TAC). The most prevalent lipid peroxidation found in the semen and plasma of infertile males with varicocele was malondialdehyde (MDA). Additionally, patients with varicocele were shown to have lower expression levels of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase.

Conclusion: As the findings of the previous studies revealed, the varicocele is closely mediated by oxidative stress, and also significant interest in antioxidants-based treatment could be considered. It is worth mentioning that, further clinical investigations which examine the impact of varicocele repair and/or the use of antioxidants on seminal oxidative stress in these patients are required.

Keywords • Varicocele • Oxidative stress • Antioxidant activity

Comparison of Domestic Violence in Fertile and Infertile Women

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Abstract

Background: Infertility in women has socio-psychological consequences. One of them is violence against infertile women. However, the fact that the rate of violence against infertile women is higher than fertile women is still debated. Therefore, this study aimed to investigate domestic violence in fertile and infertile women.

Methods: The current study, a case-control study, was conducted in 2021 on fertile and infertile women who were referred to Al-Zahra Educational, Research, and Medical Hospital in two groups and at one stage. Data collection was carried out utilizing available and convenient sampling methods. 172 infertile women and 172 fertile women, who were sent to our hospital's infertility, gynecology, and ultrasound clinics, made up the 344 samples used in this research. Demographic data and a psychometric domestic abuse questionnaire are utilized as data-gathering tools. The mann-whitney test was used to assess the levels of domestic violence between fertile and infertile women. Data were analyzed using SPSS 22.0. $P < 0.05$ was considered statistically significant.

Results: The mean age of fertile women was 35.43 ± 6.20 years and infertile women were 34.47 ± 5.88 years. With regard to the educational level of the participants, the majority of them had a diploma (46.5% fertile and 39.5% infertile) and were housewives (86% fertile and 82% infertile). The duration of their infertility was 5.98 ± 4.98 . The total score of domestic violence in infertile women was (6.38 ± 9.69) , which was significantly lower than the fertile women (11.96 ± 13.84) ($P < 0.001$). Moreover, the scores of domestic violence in psychological, physical, and sexual domains in infertile women were significantly lower than in fertile women ($P < 0.001$, $P < 0.001$, and $P = 0.013$), respectively.

Conclusion: Based on the findings of the present study, domestic violence of fertile women was higher than infertile women. Due to the study gap in violence against infertile women, further studies are recommended to investigate the extent of violence against infertile women.

Keywords • Domestic violence • Fertility • Infertility

The Relationship between the Levels of Lead and Cadmium in Semen and Serum with Different Semen Parameters of Men Referred to Bushehr Infertility Center

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Abstract

Background: A few research have been done in Iran to precisely evaluate how environmental contamination affects infertility. Pollutant exposure, such as lead and cadmium exposure, may have an impact on male reproductive potential. Globally, Men's sperm counts and sperm quality are deteriorating. In this study, we investigated the relationship between Lead and Cadmium levels in semen and serum with different semen parameters.

Methods: In this cross-sectional study, the case group consisted of 50 infertile men, and the control group consisted of 50 fertile men who were referred to Bushehr Infertility Center. ICP-MS was used to measure Lead and Cadmium in the semen and serum samples of the patients. The obtained data were analyzed by using SPSS software version 24.

Results: It was shown that the variable distribution, type of infertility, sperm count, and total motility were significantly different between the two groups ($P < 0.05$). Lead and Cadmium levels in serum samples were significant between the patient and control groups ($P < 0.05$). However, there was no significant relationship between Lead and Cadmium metal levels and the studied parameters. Logistic regression test showed that as the level of serum Cadmium increases, their chances of infertility increase either ($P = 0.041$ and $OR = 5.86$).

Conclusion: The result of this study showed that the increase in the serum Lead and Cadmium in the semen of infertile men within the normal range had no significant relationship with the semen parameters. However, the increase in the serum Cadmium was associated with an increased chance of infertility.

Keywords • Infertility • Cadmium • Lead • Infertility, male

The Effect of Melatonin on Female Offspring Ovarian Reserve and Quality in Balb/C Mice after Exposure Their Mother to Methamphetamine during Pregnancy and Lactation

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Abstract

Background: Nowadays, Methamphetamine (METH) abuse as a psychotropic drug is increasing. There is insufficient information on the adverse effects of METH on the ovarian reserve of the next generation. Herein, this study aimed to investigate the effect of METH and subsequently, the treatment effect of Melatonin on ovarian reserve in offspring whose mothers abused methamphetamine during pregnancy and lactation.

Methods: In the present study, 24 female pregnant Balb/C mice were divided into three groups: Control, Saline, and METH (5mg/Kg). METH was injected during pregnancy and lactation. Then, the female offspring of each group was divided into two subgroups; the first one received 10 mg/kg Melatonin daily until puberty (six weeks) and the second group received water. The mice were sacrificed after six weeks of age, and blood samples were collected for hormonal assessments. Therefore, their right ovaries were removed and fixed for TUNEL and Hematoxylin & Eosin staining, and their left ovaries were removed and stored for gene expression and oxidative stress evaluation.

Results: In the METH group two indicators of ovarian reserve, including anti-Müllerian hormone (AMH) and primordial follicles and Cyclin D1 (CCND-1) and Proliferating Cell Nuclear Antigen (PCNA) genes expression were significantly decreased, and the oxidative stress and apoptosis were significantly increased in comparison to other studied groups. Melatonin treatment after lactation in the METH group significantly improved the ovarian reserve, and gene expression, and declined apoptosis and oxidative stress.

Conclusion: METH abuse during pregnancy and lactation decreased ovarian reserve in the next generation. The administration of Melatonin as an antioxidant agent after lactation could protect against the adverse effect of METH on the ovaries of the offspring.

Keywords • Melatonin • Ovary • Methamphetamine • Pregnancy • Lactation

Concentration-Dependent Effects of 2-Arachidonyl Glycerol in Cultured Mouse Sertoli Cells: A Hint for Male Fertility

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Abstract

Background: The endocannabinoid system (ECS) is deeply involved in regulating male reproduction through the endogenous release of endocannabinoids such as the 2-arachidonyl glycerol (2-AG). Disturbing the delicate balance of the ECS can negatively impact reproductive potential. Some previous studies have reported that ECS plays an empirical role in the hypothalamus-pituitary-gonadal axis, spermatogenesis, and sperm function such as motility and capacitation. However, no identified investigation has been conducted so far on the effects of 2-AG on Sertoli cells (SC), which may be involved in fertility. Therefore, in this study, the role of 2-AG administration on cultured SC was investigated and the role of different concentrations of 2-AG on cell viability after 24 or 48 hours of exposure in SC was illustrated.

Methods: The mouse SCs were cultured in a DMEM-F12 medium. SCs cells (10000/per well) were incubated in 100 μ L of the medium on a 96-well plate. To determine the effect of 2-AG, SCs were exposed to 0, 10⁻⁶, 10⁻⁷, 10⁻⁸, 10⁻⁹, and 10⁻¹⁰ M 2-AG for 24 or 48 hours. The cellular viability was then assessed using the MTT method.

Results: Cellular viability increased in the 2-AG-exposed cells compared to cells of the control group. The cellular viability in control cells was 100 \pm 6%, which was significantly increased to 191 \pm 13% in cells exposed to 10⁻⁶ M 2-AG (P<0.05). The 24 and 48 hours exposure period increased cell viability compared to the control in a concentration-dependent manner, but the results did not differ significantly depending on exposure duration.

Conclusion: The 2-AG promoted cell proliferation was based on a concentration-dependent manner in SCs. This research sheds new light on the impact of 2-AG on SC viability via the modulation of testis hemostasis. However, more information about the potential effects of 2-AG on testicular function and cell signaling is needed to assure this finding.

Keywords • Cell survival • Endocannabinoids • Fertility • Male • Sertoli cells

Molecular Detection of Sexually Transmitted Viruses in Cervical Cytobrush Specimens of Infertile and Fertile Females Referred to Infertility Clinics in Kerman, Iran

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Abstract

Background: Infertility is a prevalent problem affecting almost 15% of couples worldwide. Among several causes of infertility, urogenital infections seem to be more important. Reproductive alternations may be related to some viral sexually transmitted infections (STIs) such as human herpes virus (HSV), human papillomavirus (HPV), human cytomegalovirus (HCMV), and human immunodeficiency virus (HIV). The effect of viral STIs on human fertility is not still well understood. This study aimed to determine the frequency of the HPV, HSV, and Epstein-Barr virus (EBV) in cervical samples of infertile and fertile women.

Methods: From March to August 2020, a total of 190 infertile and fertile females who were referred to the Research and Clinical Centers for infertility in Kerman (Iran) were included in this cross-sectional study. Sampling was performed by a gynecologist using a sterile cervical cytobrush from the cervical mouth of each woman under sterile conditions. Real-time-polymerase chain reaction (RT-PCR) was used to determine the presence of viruses.

Results: The HPV, EBV, HSV-1, and HSV-2 were detected in 14 (14.7%), 3(3.2%), 2 (2.1%), and 5(5.3%) infertile females, respectively. Only 3(3.2%) and 1(1.1%) of fertile women were infected with HPV and HSV-2, respectively. 25.3% (n=24) of infertile females versus 4.2% (n=4) of fertile females were positive for only one tested organism. There was a significant difference in the presence of HPV between infertile and fertile females (P=0.005).

Conclusion: Since urogenital viruses may play a role in female infertility, screening particularly for asymptomatic women and treatment of infected individuals seems to be indispensable.

Keywords • Alphapapillomavirus • Cytomegalovirus • Cervix uteri • Sexually transmitted diseases

Polycystic Ovary Syndrome and Periodontal Disease

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age, which has been associated with impaired fertility and negatively affects various health systems. Previous studies indicated that PCOS might increase susceptibility to periodontal disease and increase levels of pro-inflammatory cytokines. The mechanisms that link both conditions are not still entirely understood. Therefore, the aim of this study was to explore the association between periodontal diseases and female infertility.

Methods: A comprehensive literature search was carried out to assess if there is an association between periodontal diseases and female infertility. An extensive search was conducted in PubMed and Cochrane Library databases. Specific keywords including “female infertility”, “periodontal disease” AND “periodontitis” were used. Then, Epidemiological studies, experimental studies, inquiries, or editorials on the theme of periodontitis and infertility published until March 2022 were selected and included in this study.

Results: The findings from previous epidemiological studies revealed that periodontal disease might be a factor that increases the time to conception, overall, by two months more, which is as negative as obesity. The experimental studies pointed out that the infertility problem is a secondary outcome in rodents challenged with periodontitis. The possible biological explanation is that periodontitis causes a systemic inflammation, which could prevent ovulation, implantation of the embryo, or not sustain its implantation.

Conclusion: It is known that oral health incorporation into the general health agenda is crucial for optimal health and general well-being. Therefore, women trying to conceive should be in the best possible health, which will be achievable through effective multidisciplinary teamwork including dental care.

Keywords • Infertility, female • Periodontal diseases • Periodontitis

Ameliorative Effects of Hydro-alcoholic Extract of *Nigella Sativa* on Follicular Atresia and the Gonadal Steroid Hormones levels in a Rat Model of Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a complex endocrine disorder with unidentified reasons. The most reasonable indication of the existence of PCOS is the increase of blood androgen (Hyperandrogenism). *Nigella sativa* (NS) belongs to the *Ranunculaceae* family and is an annual herb that is used in different curative cases and contains pharmacological properties including anti-infertility, anti-apoptotic, anti-oxidant, anti-inflammatory, etc. The present study was done to investigate the ameliorative effects of the hydroalcoholic extract of *Nigella sativa* on follicular atresia, the level of gonadal steroid hormones in a rat model of PCOS.

Methods: In this research 32 mature female rats were divided into four groups: Control, PCOS-induced (4mg estradiol valerate, IM), PCOS+NS (200mg/Kg/day), and PCOS+NS (600mg/Kg/day). The rats received NS extract by gavage for 63 days. After treatment, the animals were weighed and sacrificed. Then, the blood serum samples were obtained to measure steroid hormones level. On the other hand, the ovaries were collected and weighed and the tissue incisions from obtained ovaries to study follicular atresia were prepared. Statistical analysis was performed using One-way ANOVA and Tukey's Post hoc tests. $P < 0.05$ was considered statistically significant.

Results: A significant increase in body weight, ovary weight, follicular atresia, testosterone level, and a significant decrease in the level of estrogen, and progesterone, was observed in the PCOS group compared to the control group ($P < 0.05$). However, a significant reduction in the ovary weight, follicular atresia, and testosterone level, and a significant increase in progesterone was found in the NS groups compared to the PCOS group ($P < 0.05$).

Conclusion: The results of the present study demonstrated that NS, especially at a dose of 600mg/Kg decreases the complications of PCOS by balancing the level of gonadal steroid hormones and improving follicular growth.

Keywords • Rats • *Nigella sativa* • Polycystic ovary syndrome • Gonadal steroid hormones • Follicular atresia

The Effect of Hydro-alcoholic Extract of Black Seeds on Malondialdehyde Enzyme Level and Total Antioxidant Capacity in Ovarian Tissue of PCOS in a Rat Model

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a frequent condition that affects 5-10% of women of childbearing age and is related to ovulation reduction, androgen augmentation, and insulin resistance. The potent chemical compounds found in black seed have a long history in medicine and religion and can have a variety of effects on human health. This study aimed to investigate the effect of the hydro-alcoholic extract of black seed on the antioxidant properties of ovarian tissue in rats with PCOS.

Methods: In this experimental study, 32 adult female rats were randomly divided into four groups: the control group, PCOS induced (4 mg estradiol valerate intramuscular injection), PCOS+black seed group (200 mg/Kg body weight), and the group treated with PCOS+black seed (600 mg /Kg body weight). The black seed extract was administered to the rats, orally by gavage for 63 days. At the end of the treatment procedure, all animals in the estrous phase were sacrificed, and MDA and TAC levels in ovarian tissue were measured.

Results: The results of this study showed that the PCOS-induced group had higher levels of MDA and lower levels of total antioxidant capacity when compared to the control group (P 0.05), whereas the black seed-treated groups had higher levels of TAC and lower levels of MDA when compared to the PCOS-induced group (P 0.05), with 600 mg/Kg having the most beneficial effects among the doses used.

Conclusion: According to the findings of the study, black seeds had antioxidant activity and decreased oxidative stress in the rats.

Keywords • Rats • Nigella sativa • Polycystic ovary syndrome • Ovary • Antioxidants

Saponin-Ferritin Nanoparticles Effects on Uterine Changes in Female NMRI Mice Infected with *Streptococcus pneumoniae*

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Abstract

Background: Saponin's anti-inflammatory characteristics can show how bacterial infection-related uterine problems are positively impacted. In order to assess the impact of *Streptococcus pneumoniae* infection on the number of fetuses and histological changes to the uterus in pregnant mice, this study established an infectious model in female NMRI mice.

Methods: In the present study 50 NMRI mice were divided into three groups: Control, *Streptococcus pneumoniae* as the inoculated group, and the treatment group receiving saponin-ferritin nanoparticles. Real-time PCR and hematoxylin-eosin staining were used to assess Heparin-binding EGF-like growth factor gene expression and changes in uterine tissue, respectively.

Results: When compared to the pneumonia group, HB-EGF gene expression increased significantly in the nano saponin group ($P < 0.001$). Based on histopathological evaluations of uterine tissue in the two study groups, it was discovered that the thickness of the endometrial layer of uterine tissue increased in the nanosaponin group compared to the pneumonia group, resulting in thickness stratified cuboidal epithelium with an increase in the number of cells. On the other hand, endometrial layer vascularization increased in this group compared to the pneumonia group. The scans showed that the thickness of the uterine myometrium rose more than the pneumonia group. The thickness of the endometrial layer and myometrial layer was twice as thick in the nanosaponin group as it was in the pneumonia group.

Conclusion: In addition to enhancing uterine conception for fertility by increasing endometrial thickness and embryo count, saponin encapsulated with ferritin nanoparticles can also be used as an effective combination in setting up the ideal circumstances for a successful pregnancy brought on by bacterial infection.

Keywords • Models, animal • Ferritins • Nanoparticles • Saponins, pneumonia • Pulmonary inflammation

Evaluation of Saponin Encapsulated by Ferritin Nanoparticles on Pulmonary Changes Induced by *Streptococcus Pneumoniae* in Pregnant NMRI Mice

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Abstract

Background: Pneumonia can cause pregnancy problems and inflammation of the cervix due to inflammation and increased oxidative stress. This study aimed to evaluate the therapeutic role of ferritin nanoparticles containing saponins to achieve an enhanced effect with low toxicity, high biocompatibility, and antibacterial effects on lung changes in NMRI mice.

Methods: After fabrication and characterization of saponin-loaded ferritin nanoparticles through a scanning electron microscope and dynamic light scattering, 50 NMRI mice were divided into five groups: control, pneumonia (receiving *Streptococcus pneumoniae*), treatment group receiving ferritin nanoparticles, saponin nanoparticles, and saponin. Then, the real-time PCR and hematoxylin-eosin staining were used to assess tumor necrosis factor-alpha (TNF α), interferon-gamma (IFN- γ) genes expression, and the changes in lung tissue, respectively.

Results: The saponin-loaded ferritin nanoparticle group did not indicate statistically significant changes in TNF α and IFN- γ compared to the control group ($P > 0.05$). At the same time, they reported a statistically significant decrease compared to the pneumonia group. Based on the histopathological findings, the rate of inflammation, secretion of mucus, and inflammatory cells pulmonary hemorrhage, as well as the thickening of the air sac wall were higher in the pneumonia group than in the other groups. In pneumonia treated via saponin-loaded ferritin nanoparticles group, histopathological findings indicated that the bronchioles had a normal appearance, the pulmonary hemorrhage was significantly reduced among the cells compared to the pneumonia group, and the thickness of the air sacs (alveoli) and bronchi wall was trivial.

Conclusion: Saponin-loaded ferritin nanoparticles, with their antibacterial, anti-inflammatory, and antioxidant potential had protective effects against pneumonia.

Keywords • Pregnant • Ferritins • Nanoparticles • Saponins • Pneumonia • Pulmonary inflammation

The Effect of Injectable Platelet-rich Fibrin (i-PRF) on the Structure and Survival of Transplanted Mouse Ovarian Tissue

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Abstract

Background: Ovarian transplantation can be an effective technique to restore fertility in women with cancer who undergo radio/chemotherapy. However, this technique also faces limitations such as ischemic-reperfusion injury and decreased blood supply after transplantation. Ovarian dysfunction and destruction of follicles lead to loss of reproductive and endocrine activities. Injectable platelet-rich fibrin (i-PRF) is a liquid formulation of platelet-rich fibrin (PRF) without the use of anti-coagulants, which also has anti-inflammatory properties. The i-PRF is a bioscaffold that contains leukocytes, circulating stem cells, platelets, and growth factors. Therefore, we investigated the effect of i-PRF bioscaffold on the total volume of the ovary, the volume of the cortex and medulla, and the number of types of follicles following mouse ovarian tissue transplantation.

Methods: 18 Mice were randomly divided into three groups; namely control, autograft+saline (whole ovarian tissue transplanted in the gluteus superficialis muscle, saline directly injected into it), autograft+i-PRF (whole ovarian tissue transplanted in the gluteus superficialis muscle, i-PRF was directly injected into it). Afterward, the total volume of the ovary, the volume of the cortex and medulla, and the number of types of follicles were estimated 28 days after ovary transplantation. Statistical analysis was done with one-way ANOVA and Tuckey's *Post hoc* tests.

P values less than 0.05 were considered statistically significant.

Results: In the autograft group, the total volume of the ovary, the volume of the cortex and medulla, and the number of types of follicles decreased significantly compared to the control, while all these parameters showed a significant increase in the autograft+i-PRF group compared to the autograft group ($P < 0.05$).

Conclusion: The findings of the study indicated that the use of an i-PRF bioscaffold improved ovarian function after transplantation by reducing ischemic reperfusion injury.

Keywords • Ovary • Transplantation • Platelet-rich fibrin • Ischemia • Reperfusion injury • Ovaray dysfunction

Oocyte Donor's Emotions towards the Potential Offspring: Development and Psychometric Properties

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Abstract

Background: Childbearing is one of the basic desires of human beings, which is founded on the human desire for immortality and interest in children. Infertile couples' needs have been met successfully through the use of assisted reproductive procedures (ART). However, in certain ART variants, in which a third party is used, the plurality of the individuals involved in the treatment process can bring up major complications. The present study aimed to develop a questionnaire for assessing the emotional feelings of female donors toward the potential offspring resulting from assisted reproductive techniques.

Methods: A 12-item questionnaire that measures three factors were developed. Then, its construct validity was evaluated through a cross-sectional study of 150 Iranian oocyte-donating women who undergoing donor egg programs in Isfahan, Iran. The self-report questionnaire was completed within one to ten days after the oocyte donation. The reliability of the questionnaire was determined using internal consistency and stability.

Results: The results of the factor analysis were extracted with three factors with a predictive power of 89.57% in 12 items. The internal reliability of the questionnaire was calculated based on Cronbach's alpha coefficient of 0.792. The stability of the questionnaire was confirmed based on intra class correlation index (0.71).

Conclusion: A 12-item questionnaire was a valid tool for assessing the emotions of oocyte donors shortly after taking part in the donor egg programs.

Keywords • Oocyte donation • Emotions • Reproductive techniques, assisted

The Role of Pro-inflammatory Cytokines in Human Embryo Implantation

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Abstract

Background: Successful embryo implantation is required for human pregnancy. It arises from coordination between the mother's endometrium and the embryo's blastomeres as well as cellular and molecular events which leads to growth, uterine differentiation, adhesion of the blastocyst, and placenta formation. Inflammatory and anti-inflammatory molecules including cytokines, chemokines, growth factors, and adhesion molecules are involved in preparing the uterus and generating a receptive endometrium for successful implantation. In this regard, some pro-inflammatory cytokines, known as TNF- α , IL-6, IL-1, and IL-8 are involved in blastocyst adhesion to the endometrial luminal epithelium, facilitating the physical contact between embryo and uterus and promoting placental development. This study aims to clarify the profile of pro-inflammatory cytokines involved in successful embryo-endometrium crosstalk.

Methods: In the present review article, we studied both original and review articles published in Gateways and databases such as PubMed, Science Direct, Scopus, and Google Scholar via searching the keywords including "Human", "embryo implantation", "pro-inflammatory cytokines", "crosstalk", AND "endometrium" from July 2005 to December 2021.

Results: Recent study indicated that chronic inflammatory mediators including TNF- α , and IL-6, played an important role in embryo-endometrium dynamics, which might help embryo implantation to be improved.

Conclusion: Implantation can be described as an inflammatory response in which pro-inflammatory cytokines are primarily responsible for this process. It seems that the development of low-level inflammation at the time of embryo-endometrium interaction could contribute to successful human embryo implantation.

Keywords • Embryo implantation • Uterine diseases • Placentation • Interleukin-8 • Interleukin-6

Destructive Effects of Formaldehyde on Blood Factors and Oxidative Status in Genes Expression Related to the Development of Ovarian Follicles: An Experimental Study

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Abstract

Background: Formaldehyde (FA) is a ubiquitous environmental pollutant. It also has genotoxic and cytotoxic properties and causes DNA damage and apoptosis of the oocyte. This study aimed to investigate the destructive effects of Formaldehyde on blood factors, oxidation status, and follicular development-related gene expression in rats.

Methods: 24 female Wistar rats were randomly divided into three groups: FA, control, and sham. FA was intraperitoneally injected in rats (10 mg/Kg) every day for 14 days. Gene expression related to folliculogenesis and development was assessed in exposed ovarian tissue samples using real-time reverse transcription polymerase chain reaction. The blood factors and oxidant status were measured in rats' serum as well.

Results: The mRNA expression of *klotho* and *factor in germ line alpha* genes significantly increased in the FA group compared to the control group ($P=0.03$, 0.01 , respectively). A significant decrease was observed in the FA group regarding the *BCL-2* mRNA levels compared to the controls ($P=0.02$). There was no change regarding the *FSHR*, *BAX*, and *GDF-9* transcripts. *BAX* to *BCL-2* ratio was more than 1 in the FA group compared to the other studied groups. Red blood cells, Hemoglobin, Mean Corpuscular Hemoglobin Concentration, and Hematocrit were significantly lower in the FA group than those in the control group ($P=0.03$, 0.02 , 0.04 , and 0.04 , respectively). A glutathione peroxidase activity was observed significantly higher in FA in the control group ($P=0.005$).

Conclusion: FA could damage the ovaries through oxidative stress and apoptosis induction as well as dysregulation of gene expression in the ovary. The increase of *klotho* might be an important mechanism of ovarian toxicity induced by FA in female rats. FA could change some of the blood's biochemical factors to which it was exposed and also the oxidant index.

Keywords • Formaldehyde • Ovarian follicle • Rats, wistar • Proto-oncogene proteins c-bcl-2 • Environmental pollutants

Toxic Effect of Light on Oocyte and Pre-Implantation Embryo: A Systematic Review

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Abstract

Background: In the female reproductive tract, oocytes and embryos are in a dark environment, while during *in vitro* fertilization (IVF), they are exposed to various visible and invisible lights such as daylight, microscope, and laminar hood fluorescent lights. Studies have shown that light could damage the cellular compartments of oocytes and embryos and consequently decrease the rates of fertilization, development, and blastocyst formation. However, due to the lack of consensus about the effects of light on the embryos, and subsequently the inability to make definitive decisions regarding the light exposure management to improve IVF results, in the present study, we systematically reviewed the effect of light with different wavelengths and intensities on pre-implantation embryos.

Methods: A comprehensive literature search was conducted in the PubMed, Science Direct, Google Scholar, and Cochrane library databases for published original articles in English.

Results: Conditions in the female reproductive tract can protect oocytes and embryos from possible environmental damages such as visible and invisible light irritations. However, in IVF labs, the side effects of lights are sometimes inevitable. The toxic biological impact of light depends on the wavelength, intensity, and duration of light exposure. Therefore, it is rational to assume that the usage of filters may alleviate the detrimental effect of light in IVF labs

Conclusion: it can be suggested that using the red filter can significantly prevent the adverse effects of microscope light on the oocytes and embryo.

Keywords • Light • Embryo implantation • Oocytes • Fertilization *in vitro*

The Effect of Co-administration of Quercetin and Vitamin E on the Improvement of Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders in women of reproductive age. The pathophysiology of PCOS is complex. The etiology of PCO syndrome is still unknown. However, evidence proposes that PCOS might be a complex multigenic disorder with strong epigenetic and environmental influences, including diet and lifestyle factors. In the present study, we simultaneously investigated quercetin as an antioxidant as well as vitamin E in the mice with PCOS that found the effect of both antioxidants and vitamins on PCOS improvement.

Methods: In this experimental work, adult female mice were used as the PCOS model for eight weeks. The 30 mice were placed into five groups: control, PCO (estradiol valorite or EV at 40 mg/Kg), quercetin (50 mg/Kg intraperitoneally), vitamin E (60 mg/Kg/day, orally), and quercetin+vitamin E. After the mice were sacrificed, their ovarian tissue was collected and histological and morphometric examinations were done. Following tissue examination, total antioxidant capacity and oxidative stress were assessed using the FRAP technique and flow cytometry, respectively.

Results: The findings of tissue sections indicated that EV administration caused cyst formation in the study groups. Cyst formation and the percentage of preantral and antral follicles in the group that received quercetin and vitamin E together were significantly lower ($P \leq 0.001$) than in the groups that received each separately. In comparison to the other studied groups, in the group that received a combination of both antioxidants and vitamins, the level of oxidative stress and total antioxidant capacity were the lowest and the highest, respectively.

Conclusion: The results showed that co-administration of quercetin and vitamin E in PCOS mice reduced the amount of oxidative stress by increasing the antioxidant properties and also reduced the number of cysts and enhanced the symptoms of this syndrome.

Keywords • Polycystic ovary syndrome • Quercetin • Vitamin E

Comparison of Follicular-Phase versus Luteal-Phase Endometrial Scratching on the Success of Intrauterine Insemination (IUI): A Randomized Controlled Trial

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Abstract

Background: Endometrial scratching can lead to a dramatic rise in blastocyst implantation success rate. However, the appropriate time for performing endometrial scratching during the menstrual cycle is a controversial unresolved matter. In this study, the effect of endometrial scratching on IUI success was compared in two follicular and luteal phases in infertile women who have been treated with IUI.

Methods: A total of 75 infertile women were included in the study. Patients were randomly divided into three groups (n=25 per group). Group I consisted of patients who underwent endometrial scratching between days 19-24 of the menstrual cycle in the luteal phase. Group II included women who received the same treatment on the 8th day of the menstrual cycle in the follicular phase. The patients in group III did not receive any endometrial scratching treatment before IUI.

Results: No significant difference was found between the three groups in terms of age, BMI, duration of infertility, infertility type, and baseline hormone levels ($P>0.05$). The clinical pregnancy rate, concept moreover, there were statistically significant differences among the three groups based on the Chi-square test results ($P<0.05$). In addition, Fisher's exact test did not show any differences between the three groups in terms of abortion and EP ($P>0.05$).

Conclusion: We concluded that the follicular phase was the most appropriate time to perform endometrial scratching, and it could improve the pregnancy rate in IUI.

Keywords • Endometrium • Insemination, artificial • Body mass index • Follicular phase

The Effect of Oral Dydrogesterone with Vaginal Progesterone on the Success of Intrauterine Sperm Injection (IUI) in Patients with Inexplicable Infertility: A Randomized Clinical Trial

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Abstract

Background: Some studies have shown that taking some of the drugs following intrauterine injections (IUI) of sperm might enhance the chances of fertility. This study aimed to determine the effect of Dydrogesterone and vaginal progesterone on the success of pregnancy in patients undergoing.

Methods: In this randomized clinical trial, 210 infertile women under Intrauterine Sperm Injection were randomly divided into three groups of 70. The first group received 400 mg vaginal progesterone suppository, once at night. The second group received 10 mg of oral Dydrogesterone once a day, and the third group received placebo at the same time and dose. After 16 days, their level of BhcG was evaluated for the occurrence of pregnancy. If the test result was positive, the treatment was continued with one of the medications for up to 12 weeks. Consecutive ultrasounds were performed to assess the fetal status and the outcomes of the treatments were compared in three groups.

Results: According to the results, overall success fertility among patients under IUI was 14.3%. The success rate of fertility in the control, vaginal progesterone, and oral Dydrogesterone was 10%, 14.3%, and 18.6%, respectively (P=0.35). The chance of successful fertility in the oral dydrogesterone group was 3.79 times more than the control group (P=0.024)

Conclusion: According to the results of the study, it was found that prescribing oral Dydrogesterone had a positive effect on enhancing the chance of successful fertility in patients under Intrauterine Sperm Injection. However, according to our study limitations, such as the small sample size, further studies are required.

Keywords • Semen • Spermatozoa • Dydrogesterone • Pregnancy • Female • Male

Early Onset and Atypical Severe Preeclampsia Diagnosis in a Pregnancy Managed with IVF: A Case Report

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Abstract

Assisted reproduction technology (ART) is used worldwide, at increasing rates, and the statistics indicated that some adverse outcomes might occur more frequently than following spontaneous conception. Here, we report a rare case of severe and atypical preeclampsia at the gestational age of 18 weeks in a woman undergone IVF due to sex selection, not infertility. A 35-year-old woman with a gestational age of 18 weeks was referred to Al-Zahra Hospital with indications such as blood pressure of 220/120 mm Hg, headache, and 3100 g protein in 24-h urine collection. Her pregnancy had achieved via IVF due to sex selection (male selection) by the frozen embryo. Therefore, she did not have infertility. She had a history of hypothyroidism. She did not have any chronic HTN or other diseases. The ultrasound findings of her pregnancy showed normal nuchal translucency (NT) in 13 weeks. The risk of the down syndrome was 1/75 in a double test. Thus, she had done cell-free DNA, and it was low risk for aneuploidies. Lab data including CBC, LFT, and serum creatinine levels were normal. Antiphospholipid, lupus, anti-GBM, and complement tests were within normal ranges. Due to severe preeclampsia and uncontrolled blood pressure, and regardless of the 300 mg labetalol prescription, the termination of pregnancy was scheduled for her by vaginal route. The male fetus with 300 g weight was born. The placenta was normal. Following delivery, she had a BP of 160/100 for one week which was controlled by valsartan. After that, her BP became normal without any medication. Four weeks later, her level of proteinuria was 80 g. Although infertility may contribute to the adverse outcomes of pregnancy such as pregnancy-induced HTN (PIH) in IVF, factors related to hormone stimulation, and or IVF methods per se, also as part, a woman should be informed about these adverse maternal outcomes before undergoing IVF, even without a history of infertility.

Keywords • Ultrasonography • Gestational age • Pregnancy • Infertility, fertilization *in vitro*

Physiotherapy Techniques for Infertility: A Brief Systematic Review

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Abstract

Background: Physiotherapy techniques including manual therapy, electrotherapy, and electro-acupuncture could be used to improve pregnancy success rates in patients with occluded fallopian tubes, endometriosis, premature ovarian failure, polycystic ovary syndrome, elevated follicle-stimulating hormone, and higher pregnancy rate when compared to IVF alone. This article aimed to introduce physiotherapy techniques according to Evidence-based medicine for infertility using a brief systematic review.

Methods: After defining PICO clinical question, keywords including Medical Subject Headings (MeSH) Terms and Free text keywords were selected by conducting a preliminary search in the PubMed database. Then, the following bibliographic databases were searched for retrieving related citations: MEDLINE (via PubMed), The Cochrane Library, EMBASE, Scopus, and Web of Science. In addition, hand searching, tracking similar articles, reference checking, and searching for gray literature were performed.

Results: Three main subjects in extracted data were discussed: Manual Therapy, Electrotherapy, and electro-acupuncture.

Conclusion: Physiotherapy could be a helpful conservative supportive treatment along with other treatments.

Keywords • Rehabilitation • Infertility • Musculoskeletal manipulations • Electric stimulation therapy • Acupuncture therapy

The Protective Effect of Kombucha against Silver Nanoparticles Induced Toxicity on Testicular Tissue in NMRI mice

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Abstract

Background: Silver nanoparticles (SNPs) can pass from the cell membrane and testicular blood barrier due to their small size, and by increasing oxidative stress they cause disorder in the male reproductive system. Kombucha is a traditional fermented drink with detoxification and potent antioxidant properties. We aimed to examine the protective effect of Kombucha against the damages due to SNPs on the testis tissue.

Methods: In this experimental study, NMRI mice were randomly separated into four groups (n=6), namely control (distilled water), SNPs (500 mg/Kg), Kombucha extract (9 mL/Kg), and SNPs+Kombucha. All the mice were treated with gavage for 35 days.

Results: A significant decrease in testosterone level and total antioxidant capacity, and a significant increase in malondialdehyde concentration was observed in the SNPs group in comparison with the control group. Histological studies on the testis of mice treated with SNPs showed vacuolation, a decrease in generational epithelium thickness, seminiferous tubules diameter, testis volume, and the number of spermatozoa in the lumen of the seminiferous tubule, as well as an increase in the volume of interstitial space. However, the mentioned parameters were improved in the SNPs+Kombucha group compared to the SNPs group.

Conclusion: Kombucha reduced the adverse effects of SNPs on testis tissue and improved the function of the male reproductive system.

Keywords • Testosterone • Cell membrane • Oxidative stress • Seminiferous epithelium • Metal nanoparticles • Silver • Oxidative stress • Testis

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