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Case Series

Glaucoma Surgery in Pregnancy: A Case Series and Literature Review

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Abstract

Glaucoma management in pregnant patients is a real challenge, especially when the glaucoma is not controlled with medications. We report the results of 6 incisional glaucoma surgeries for the management of medically uncontrolled glaucoma patients during pregnancy. This retrospective, case series was conducted on the 6 eyes of 3pregnant patients with uncontrolled glaucoma using maximum tolerable medications. Details of the glaucoma surgical management of these patients as well as their postoperative care and pregnancy and clinical outcomes on longitudinal follow-up are discussed. All 3 patients had juvenile open-angle glaucoma and were on various anti-glaucoma medications, including oral acetazolamide. The first case described underwent trabeculectomy without antimetabolites in both eyes because of uncontrolled intraocular pressure with topical medications. The surgery was done with topical lidocaine jelly and subconjunctival lidocaine during the second and third trimesters. The second patient had an Ahmed valve implantation in both eyes during the second and third trimesters because of uncontrolled IOP with topical medications and no response to selective laser trabeculoplasty. Surgery was done with topical tetracaine and subconjunctival and sub-Tenon's lidocaine. The third case had a Baerveldt valve implantation under general anesthesia in the second trimester. In selected pregnant glaucoma patients with medically uncontrolled intraocular pressure threatening vision, incisional surgery may lead to good outcomes for the patient with no risk for the fetus.

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What's Known

- There is a dearth of data on the safety and effectiveness of incisional glaucoma procedures in pregnant glaucoma patients.

What's New

- Pregnant patients with glaucoma and uncontrolled intraocular pressure my undergo glaucoma surgery (trabeculectomy or shunt surgery) to prevent irreversible optic nerve damage.
- Incisional glaucoma surgery in pregnancy may confer good outcomes for the patient with no risk to the fetus.

Introduction

The coincidence of glaucoma and pregnancy is thought to be rare, but about one-quarter of respondents to a survey of ophthalmologists in the United Kingdom were faced with this clinical situation.[1] The frequency of glaucoma during pregnancy seems to be increasing among women because some women wait longer to become pregnant. Therefore, we need to improve our understanding about glaucoma management in this very challenging population. There is a tendency for the intraocular pressure (IOP) to decrease during pregnancy, especially during the second and third trimesters.[2,3] Additionally, a reduced diurnal variation of the IOP and an increased retrobulbar blood flow have been reported in pregnancy.[2] Despite all the information

indicating that the IOP typically decreases during pregnancy, many glaucoma patients continue to require medical and surgical treatment and glaucoma may progress.[3]

Given the paucity of reports on glaucoma management in pregnant patients and the impossibility of conducting clinical trials in this group of patients, there are no guidelines for managing this clinical situation. There is a general level of uncertainty regarding management among ophthalmologists faced with a pregnant woman who has progression of her glaucoma.[1] Herein, we describe 6 glaucoma surgical procedures in 3 pregnant glaucoma patients with an uncontrolled IOP on maximum tolerable medication.

Cases Presentation

A retrospective case series was performed on 3 cases of uncontrolled glaucoma during pregnancies that were managed surgically at Wills Eye Institute, Philadelphia, USA, and Poostchi Eye Research Center, Shiraz, Iran. Relevant clinical and management details were extracted from the medical records.

Case 1

A 26-year-old asthmatic pregnant patient whose juvenile open-angle glaucoma had been controlled for 12 years with timolol, brimonidine, and latanoprost presented to the glaucoma service in her second trimester of pregnancy because of an uncontrolled IOP (44 mm Hg in both eyes) detected by her ophthalmologist. She used albuterol and ipratropium inhalers PRN for controlling her asthma. The best-corrected visual acuity (-6.00- 0.25×95 in the right eye and – 6.25 in the left eye) was 20/20, and the vertical cup/disc ratio was 0.7 in both eyes. The visual field in the right eye was normal, and the left eye showed a shallow inferior arcuate scotoma. The central corneal thickness was 550 µm and 557 µm in the right and left eyes, respectively. The patient underwent trabeculectomy in her left eye with 2% lidocaine jelly and subconjunctival 1% lidocaine with monitored anesthetic care at 24 weeks of gestation. Postoperatively, topical neomycin-polymyxin B- dexamethasone was started and tapered over 2 months.

Trabeculectomy was performed in the right eye while the IOP was 41 mm Hg at the 27th week of gestation. The IOP was 13 mm Hg 2 weeks after the second operation in both eyes and then was stable at low teens throughout pregnancy. She gave birth to a normal baby at the 38th week of gestation. The baby weighed 3050 grams and her Apgar score was 10. The course of glaucoma and the IOP (low teens) were stable during a second pregnancy 2 years later and a third pregnancy, 7 years after the first.

Case 2

A 24-year-old pregnant patient (16 weeks) was referred to the glaucoma service due to an uncontrolled IOP in her left eye on maximum tolerable topical anti-glaucoma medications (timolol, dorzolamide, latanoprost, and brimonidine) by her local ophthalmologist. Up to this point, the juvenile open-angle glaucoma had been controlled with timolol, dorzolamide, and latanoprost for the last 3 years. She had received all 3 medications during the first trimester due to an escalating IOP rise. Brimonidine had been added to her medications at the beginning of the second trimester. She had no history of prior glaucoma surgery.

On initial examination, the best-corrected visual acuity was 20/20 and 20/25 in right and left eyes respectively, wearing -5.25-1.75×170 OD and -6.5-2.75×170 OS. The IOP was 24 mm Hg in the right eye and 34 mm Hg in the left eye with timolol, dorzolamide, latanoprost, and brimonidine. The central corneal thickness in the right and left eyes was 550 µm and 560 µm, respectively. Heidelberg retinal tomography revealed a large optic disc (about 2.90 mm^2) with a 0.6 cup/disc ratio bilaterally. Stratus optical coherent tomography also revealed a normal nerve fiber layer thickness in both eyes. Visual field testing was normal in both eyes. She underwent selective laser trabeculoplasty in the left eye (16th week of pregnancy), although no beneficial effect was observed over 4 weeks (IOP=36 mm Hg). Visual field examination showed no significant change compared to her prior visual fields. Due to the possibility of an unfavorable outcome with trabeculectomy without mitomycin in young patients, an Ahmed valve (FP7, New World Medical, Rancho Cucamonga, California, USA) implantation was done on the left eye at 20 weeks of gestation. The surgery was accomplished by employing topical tetracaine and subconjunctival 2% lidocaine. The lidocaine (2%) was injected subconjunctivally in the superotemporal quadrant; and after opening the conjunctiva, additional lidocaine was administered in the sub-Tenon's space. No intravenous sedative was used. She tolerated the operation well and received topical chloramphenicol for 2 weeks and betamethasone for 8 weeks postoperatively. Topical chloramphenicol use in pregnancy is considered to be safe.[4] Nasolacrimal occlusion and eyelid closure were recommended after topical medication application. Four weeks after

surgery, the IOP in the left eye rose to 24 mm Hg and timolol/dorzolamide combination drop was started. The IOP in her right eye also rose to 44 mm Hg with topical medications. The same procedure was performed in right eye at 29 weeks of gestation. The operation was accomplished by placing the patient in the left down decubitus position to prevent systemic hypotension due to aortic and vena caval compression by the conceived uterus. The patient's hips, abdomen, and thighs were rotated to left while maintaining a normal head position for ophthalmic surgery. She and her fetus tolerated the procedure well, and similar postoperative medication and care were tailored. At the fifth postoperative week, the IOP was 25 and 14 in the right and left eyes. The patient was advised to start timolol/dorzolamide combination drop for the right eye as well. At the beginning of the ninth month of pregnancy, the IOP in both eyes was14 mm Hg with timolol/dorzolamide combination drop. Any possible side effect of timolol on the newborn's respiration and cardiovascular system was prevented by replacing the timolol/dorzolamide combination drop with dorzolamide in the ninth month. The IOP was 18 mm Hg in both eyes with dorzolamide over the last 2 weeks of pregnancy and 2 months after delivery. The mother gave birth to a healthy baby with a birth weight of 2750 grams and an Apgar score of 9.

Case 3

A 23-year-old healthy myope presented to her local ophthalmologist because of a decline in vision in both eyes. She was unaware that she might have juvenile glaucoma. She had a positive family history, as her father had juvenile glaucoma. Four days before referral to the glaucoma service, she presented with an IOP of 54 mm Hg and 60 mm Hg in the right and left eyes, respectively, and was started on medications. She smoked one pack of cigarettes per day and wore soft contact lens. The patient did not report to the treating physician or the staff that she was pregnant. She denied pregnancy when queried, and 2 pregnancy tests checked before eye operations at 20 and 24 weeks of her pregnancy with urine samples were negative. Later on, she admitted to switching urine samples with her mother in the ladies' room, as she was fearful that surgery would be denied to her due to her pregnant state.

On examination, the best-corrected visual acuity was 20/40 in the right eye and 20/100 in the left eye. The refraction in the right and left eyes was -10.00-1.5×005 and -9.75-1.5×015, respectively. The IOP was 14 mm Hg in both eyes with latanoprost, timolol/brimonidine combination drop, and acetazolamide (125 mg twice daily). The central corneal thickness was 565 µm in both eyes. Optic nerve examination showed a vertical cup/disc ratio of 0.85 in the right eye and 0.9 in the left eye with pallor and peripapillary atrophy. The visual filed defects in both eyes showed dense superior and inferior arcuate scotomas with dense nasal steps. The patient was advised to stop acetazolamide due to symptoms of nausea and fatigue. Two weeks later, the IOP in both eyes was17 mm Hg but the patient admitted to poor compliance with this medical regimen. One month later (24th week of pregnancy), the IOP in the left eye increased to 43 mm Hg and was not reduced after resuming acetazolamide. Given her age and contact lens wear, it was decided to proceed with a Baerveldt shunt under general anesthesia. At the time, it was not known that the patient was in her second trimester of pregnancy. Therefore, under general anesthesia, a Baerveldt 350-mm^2 (Advanced Medical Optics, Santa Ana, California, USA) was implanted augmented with mitomycin 0.4 mg/mL for 3 minutes in a pledget in the area of the plate. Postoperatively, topical moxifloxacin was given for 2 weeks and difluprednate for 6 weeks on a slow taper. One month after the left eye surgery, the IOP in the right eye increased to 40 mm Hg with all the aforementioned anti-glaucoma medications. Hence, the same procedure was done on the right eye at the 24th week of pregnancy. Again, the pregnancy urine test was negative. General anesthesia was used. One month later, the IOP was 14 mm Hg in the right eye and 16 mm Hg in the left eye. The IOP remained 14 mm Hg in both eyes with 0.5% timolol throughout the pregnancy and has continued to remain so over the following 2.5 years. The patient delivered a healthy baby girl with a birth weight of 2523 grams at term with an Apgar score of 10, three months after the second operation. The baby girl is completely healthy and at this point, has no known ocular disease or any other defects or pathology.

Discussion

In the present study, 6 eyes of 3 patients underwent surgical intervention to control their IOP. All the patients used various anti-glaucoma medications during their pregnancies, tolerated the operations very well, and gave birth to normal babies. There are limited reports on the surgical management of glaucoma in pregnancy. A successful case of trabeculectomy without adjunctive antimetabolites performed with retrobulbar anesthesia has been reported

in a pregnant patient. She had uncontrolled glaucoma with 3 medications without any response to argon laser trabeculoplasty.[5] Another study demonstrated IOP reduction after cyclophotocoagulation in a pregnant woman with uveitic aphakic glaucoma.[6] A search on the PubMed database reveled no report on shunt implantation in pregnant patients.

Although some studies indicate that the IOP decreases in pregnancy,[7-10] some patients may develop an elevated IOP during pregnancy. There are case reports describing pregnant women with glaucoma whose IOP has been difficult to control despite medical and surgical interventions.[6,11] In a retrospective study conducted on 28 eyes of 15 pregnant glaucoma patients with varying severity and types of glaucoma, Brauner et al.[12] reported that in 5 (17.9%) eyes, the IOP increased, but there was no progression of visual field loss. In 5 (17.9%) eyes, visual field loss progressed, while the IOP remained stable or increased. Two of our patients had a controlled glaucoma with medication before pregnancy and developed an uncontrolled IOP during gestation. Changes in the IOP should be monitored closely in pregnant patients with glaucoma due to the highly variable course of glaucoma during pregnancy.

In glaucomatous women of childbearing age, if possible, the treatment plan should be discussed before the woman plans to become pregnant, allowing for discussion of treatment options and possible risks. As we experienced in case 3, women do not always volunteer the possibility of pregnancy during ophthalmic consultation. In the third case, 2 urine pregnancy tests were negative because the woman switched her mother's urine for hers because of fears concerning the impact of pregnancy on her care. As the tests were negative, the patient was treated as a non-pregnant patient. She received a general anesthesia, and mitomycin was applied during shunt implantation. Another alternative would be to check serum beta-human chorionic gonadotropin (beta-HCG) in women of childbearing age.

Unfortunately, there is little definitive information concerning the medical management of glaucoma during pregnancy.[13] No topical anti-glaucoma agents have strong evidence of safety based on human studies.[3] The Food and Drug Administration (FDA) classification of drugs safety in pregnancy can be summarized as follows: Category A: safety established using human studies; Category B: presumed safety based on animal studies, but no human studies; Category C: uncertain safety, with no human studies and animal studies showing adverse effect; Category D: unsafe; evidence of risk that in certain clinical circumstances may be justifiable; and Category X: definitely unsafe, with the risk of use outweighing any possible benefit.

Table 1 lists the FDA's classification of selected anti-glaucoma medications as well as the reported teratogenic effects in animal and human studies. While no glaucoma medications are known to be human teratogens, none has been proven to be completely risk-free either. The majority of anti-glaucoma medications are in group C and the only medications in group B (animal studies show no harm to the fetus) are sympathomimetics.

As many pregnancies are unplanned, exposure to medication often occurs before women know that they are pregnant. During the first 12 weeks of gestation, organogenesis occurs and teratogenic drug effects are more severe when medicines are administered during thisperiod.[33] The last month of pregnancy is also important because the drugs pass through the placenta and reach the fetal circulation and may affect the newborn's cardiac, respiratory, and neurologic systems functions. Nasolacrimal occlusion, eyelid closure, or blotting the excess drops away during administration and punctual plugging should be discussed with pregnant women on topical anti-glaucoma medications.[13]

If maximum safe topical medications fail to control the IOP or a progressive visual field loss is noted, or a woman with severe glaucoma wishes to decrease the potential risk of medications to the fetus, surgical intervention should be considered.[3] A potential option before incisional surgeries is laser trabeculoplasty. The procedure would impose the least possible risk to the fetus and would not require the addition of preoperative and postoperative medications that invasive procedures would necessitate. Other advantages include it being an outpatient procedure, the use of topical anesthesia, sitting in an upright posture, faster rehabilitation, and very low risk to the patient. However, laser trabeculoplasty is less effective in patients younger than 50 years.[34] In this series, one of the patients who received laser trabeculoplasty had no IOP decrease, which was in line with Pickering's report.[5]

There are specific risks and considerations of glaucoma surgery in pregnant patients, including timing of surgery, position of the patient during surgery, risks of local and general anesthesia, and intra- and postoperative medications.[35] Agents like narcotics, paralyzing agents, inhaled anesthetic agents, and any of the central nervous system depressants which are used to anesthetize the patient can influence the

Table 1: Food and Drug Administration's classification of selected anti-glaucoma medications and potential side effects in pregnancy

	FDA's classification	Reported effect in animal studies	Reports of side effects in human studies
Preservative of medications, BAK	C*	Dose-related increase in fetal resorption and death and minor sternal defects[14]	
Beta-blockers	C		A case with cardiac conduction disorder. Arrhythmia and bradycardia (resolved after stopping the drug)[15] Systemic use: Intrauterine growth restriction and persistent beta-blockade in the newborn Impairment of respiratory control in the neonate, lethargy and confusion[16,17]
Carbonic anhydrase Inhibitors			
Oral	C	Forelimb anomalies[18]	Single case of sacrococcygeal teratoma (has not been substantiated by others)[19]
Topical	C	Fetal vertebral body malformations and decrease fetal weights (dose 31 times)[20,21]	
Prostaglandin analogs			
Latanoprost	C	Dead fetus (dose 80 times)[22]	A case of miscarriage in a 46- year-old woman that seems to be due to her reproductive risk related to her advance age, not the drug[23]
Travoprost	C	Teratogen (dose 250 times)[24]	
Bimatoprost	C	Reduced duration of gestation and increased incidence of dead fetus (dose 41 times)[25]	
Parasympathomimetics			
Pilocarpine	C	Teratogen[26]	Signs mimicking meningitis in the newborn[27]
Echothiophate iodide			Suppression of the infant's pseudocholinesterase
Sympathomimetic			
Non-selective	B**	Congenital cataract[2]	Systemic: Delays the second stage of labor or cause a prolonged period of uterine atony with hemorrhage Topical: Local side effects and a high rate of systemic side effects[28]
Brimonidine	B	No fetal damage[29]	In infants has central nervous system effects[30]
Fixed-combination Anti-glaucoma Medications	C		-
Fixed-Combination Timolol/dorzolamide	C[31]	As each component of the drug	
Fixed-Combination Timolol/brimonidine	C[32]	As each component of the drug	

*Uncertain safety, with no human studies and animal studies showing adverse effect; **Presumed safety based on animal studies

fetus. Nevertheless, there are no well-controlled human studies about the teratogenic effects of these agents. However, neither our patient who had 2 general anesthesia for both eyes surgeries nor a 22-year-old pregnant woman that had a sclerotomy operation at 32 weeks of gestation under general anesthesia experienced complications and both gave birth to normal babies.[36] Nonetheless, there are reports of increased incidence of low birth weight and an increased rate of neural tube defects with exposure to general anesthesia in the first trimester.[37]

Most local anesthetics have not been shown to be teratogen in humans and are considered relatively safe for use during pregnancy. In the FDA's classification, etidocaine, lidocaine, and prilocaine are categorized in group B and

bupivacaine and mepivacaine are placed in group C because of inducing fetal bradycardia.[38] Limiting the dose to the minimum required for effective pain control is obviously advisable.[39] Subconjunctival and anterior sub-Tenon's anesthesia combined with a topical anesthesia for glaucoma surgery may be well tolerated and may allow a less systemic absorption of the medication than a retrobulbar anesthesia.[39] The supine position in the second and third trimesters of gestation can induce profound systemic hypotension due to aortic and vena caval compression by the conceived uterus. Consideration should be given to rotating the patients' hips, abdomen, and thighs on their left side while maintaining a normal head position for ophthalmic surgery.[40]

Glaucoma filtration surgery in pregnant patients may be at relatively higher risk of failure because of young age, physiological changes during pregnancy, and contraindicated antimetabolite usage. Both mitomycin and 5-fluorouracil, which are used commonly as antimetabolite agents in glaucoma filtering surgeries, are in category X and contraindicated in pregnancy.[41,42] It is well known that in pregnancy, the serum levels of vascular endothelial growth factor (VEGF)[43] and placental growth factor (PGF),[44] which is a ligand for VEGF Receptor-1, are elevated. Because VEGF has a major role in angiogenesis and fibroblast and inflammatory cell migration and proliferation and synergistic effect of PGF with VEGF, it seems that wound healing at the trabeculectomy site during pregnancy is augmented.

The 5-year results of the Tube Versus Trabeculectomy (TVT)[45] study will probably encourage more surgeons to expand the indications for aqueous shunt surgery to include more primary surgical cases or at least encourage aqueous shunt surgery when both options are reasonable alternatives. Shunt surgery seems to be a reasonable alternative for some patients who need surgery in pregnancy.

For postoperative pain, acetaminophen may be the safest and it usually provides adequate pain relief. Because the pain may increase the possibility of premature labor, in the postoperative period the patient should receive adequate analgesia.[46]

Table 2 summarizes the risks of some post-glaucoma surgery medications in pregnancy.

Conclusion

It is now commonplace for women to choose to start families later in life; thus, the frequency of glaucoma during pregnancy may increase. It is logical not to defer the glaucoma surgery (trabeculectomy or shunt surgery) to the

Table 2: Food and Drug Administration's category and potential complications of medications used topically after glaucoma surgery

Drug	FDA's Classification	Reported Side Effects in Animal Studies	Reported Side Effects of Systemic Use during Pregnancy
Corticosteroid			
Dexamethasone	C*		Leukocytosis in infants with *in utero* exposure to systemic use[47]
Prednisolone	C	Developmental and teratogenic effect, cleft lip and palate, and sex organ abnormalities[47]	Increase in the risk of stillbirth, intrauterine growth retardation, and adrenal insufficiency[47]
Antibiotics			
Erythromycin	B**		
Polymyxin	C		
Aminoglycoside	D***	Hearing loss and nephrotoxicity[48]	
Sulfonamide	C	Cleft palate and other bony abnormalities[48]	Hyperbilirubinemia[48]
Fluoroquinolone	C	No teratogenic effects, decreased body weight, and delayed skeletal development[48]	Arthropathy[48]
Tetracycline	D		Discoloration of the primary teeth (after the third month of pregnancy)[48]
Chloramphenicol	C		Gray baby syndrome (Topical usage is safe.)[48]
Atropine	C		Probability of an effect on the fetal heart rate[49]

*Uncertain safety, with no human studies and animal studies showing adverse effect; **Presumed safety based on animal studies; ***Unsafe; Evidence of risk that in certain clinical circumstances may be justifiable

postpartum period in pregnant patients that have an uncontrolled IOP at a level that puts vision at risk in the short term as optic nerve damage is irreversible. Pregnant glaucoma patients present challenges, but with careful consideration regarding medication and surgery as discussed above, these patients may undergo incisional surgery with good outcomes for the patient with no risk to the fetus.

Conflict of Interest: None declared.

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