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Original Article

The Effects of Maternal Opium Abuse on Fetal Heart Rate using Non-Stress Test

CME Article

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Abstract

Background: Opium is one of the most commonly abused opiates in developing countries including Iran. Considering the importance of maternal health on the newborn, we aimed to assess the effect of opium abuse on fetal heart rate (FHR) characteristics in a sample of pregnant women in Zahedan, Southeast Iran.

Methods: This cross-sectional study was done on 100 pregnant women referring to Ali-Ibn-Abi Talib Hospital in Zahedan, during 2011-2013. The participants were divided into two groups comprising of opium abusers and healthy individuals. The participants received 500cc intravenous fluid containing dextrose and then non-stress test results were recorded for 20 minutes.

Results: We found no significant difference between the two groups with respect to their demographic characteristics. Fetal movements, variability, acceleration, and reactivity were significantly higher among addicted women ($P<0.0001$ for all). Periodic change was 9.8 times higher among opium abusers compared with the healthy women. Abnormal variability or oscillations of <15 beats/min, which indicates lack of beat-to-beat variability, was significantly higher in the fetuses of addicted mothers ($P<0.0001$).

Conclusion: Considering significant abnormal patterns in FHR characteristics among the opium abuser group, mothers addicted to opium need specific prenatal care.

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Keywords ● Opium ● Opioid-related disorders ● Fetal distress

What's Known

- Bishop score is used to assess successful vaginal delivery after the induction of labor.

What's New

- Transvaginal sonography can help predict successful vaginal delivery.

Introduction

The health of a community depends extensively on the health of mothers and children. In this regards, non-complicated pregnancies play an important role in the birth of a healthy infant. It has been shown that the number of women addicted to opiates is on the rise and this issue is increasingly alarming in pregnant women.[1] A national study in Iran showed that 7% of women were addicted.[2] The corresponding figures for Tehran and Zahedan were 15% and 19%, respectively.[3,4] Opiate addiction can severely damage maternal and fetal health and imposes high financial burden on the community due to the birth of infants with a wide range of abnormalities. Early diagnosis and treatment strategies to some extent can compensate infants' abnormalities. In this regard, it has been demonstrated that fetal growth restriction caused by maternal opiate addiction can be

recovered with proper treatment of addiction.[5] Identification of the early effects of opiate addiction on the fetus during routine visits helps to screen those mothers with high indication for therapy initiation. Among routine pregnancy examinations, assessment of fetal heart rate (FHR) is one the common examinations that are performed during pregnancy follow-up sessions. Therefore, initial change in FHR due to maternal opiate addiction is a warning signal that can be used to predict the need for intensive care. FHR is usually evaluated by non-stress test (NST) in which changes in FHR including acceleration, deceleration, and variability are examined.[6,7]

Opium is a major form of drug abuse in Iran, especially in Zahedan, and several neighboring regions.[8] It has been demonstrated that heroin abuse during pregnancy leads to the birth of infants with low birth weight (LBW).[9] Similarly, cocaine abuse has been shown to be associated with impaired fetal development and consequently infant malformations.[10] However, the effects of opium abuse among Iranian women have not yet been fully described. There are limited investigations demonstrating the effects of maternal opiate abuse on fetus. In this regard, reduced fetal heart rate has been observed by Schmid et al.[11] Studies evaluating the influences of opiate abuse on fetus are scarce. Here, we tried to determine whether FHR and non-stress test (NST) measures are different among the Iranian women addicted to opiates compared with healthy women.

Many studies have documented the negative effects of maternal opiate abuse (such as cocaine, morphine, and nicotine) on the fetus and neonate. In one study, reduced heart rate was observed in newborns exposed to cocaine, which was associated with increased risk of sudden death syndrome.[12] Other researchers have found a significant reduction in the FHR in women who had received intramuscular diamorphine for pain relief. Decreased fetal movement has also been observed after receiving diamorphine.[13] Other fetus complications such as neonatal abstinence syndrome (NAS) have also raised attention, especially during the treatment of maternal opiate addiction.[14] The existence of various ranges of fetus complications emphasizes the importance of investigating maternal opiate addiction, especially in developing countries. Opiate addiction not only can cause maternal and fetal complications itself, but it can also worsen coincidental comorbidities. For instance, it has been shown by Mauri et al.[15] that opiate addiction causes a further worsening of gestational and perinatal outcomes among women infected with human immunodeficiency virus (HIV) and it also increases susceptibility towards pathogens. All these evidences support the necessity of early diagnosis and treatment of opiate addiction among mothers to prevent maternal and fetal complications.

Opiate addicted individuals are more susceptible to be a cigarette smoker as well. In this regard, a significant negative correlation has been found between the number of cigarettes that a mother smokes during the first trimester and FHR.[16] Researchers have claimed that maternal smoking has significant effects on fetal reactivity and reduced FHR.[17]

By considering the clinical importance of the identification of opiate effects on fetus among the Iranian population, we aimed to assess the effect of opium on FHR characteristics in a sample of pregnant women in Zahedan.

Patients and Methods

Study Design

This study was performed on 100 pregnant women that referred to Ali-Ibn-Abi Talib Hospital (Zahedan, Iran) during 2011-2013. The participants were divided into two equal groups, comprising of opium abusers and healthy women. According to previous studies, the changes of fetal acceleration in addicted and non-addicted women were 75% and 95%, respectively (d=0.20). The sample size was calculated to be 50 women in each group (5% error, 80% power). Written consent was obtained from each individual upon entering the operating room. To meet ethical standards, no invasive procedure has been performed on the patients. Moreover, the patients were assured that their information would remain confidential and the questionnaires were coded without the patients' names. All procedures were initially explained to each patient. The study was approved by the Ethics Committee of Zahedan University of Medical Sciences.

Participants

We included 21-40 years old mothers with single live fetuses who were referred to terminate pregnancy with a gestational age of 37-42 weeks. Other inclusion criteria were cervical dilatation of 4-5 cm and 50% effacement upon pelvic examination. Opium abuse was defined as the consumption of opiates such that at least one month had passed since the first dose and 8 hours from the last dose. The time interval of 8 hours was selected based on inhaled opiate half-life. Synthetic opioid has a much shorter half-life about 2-3 hours, but inhaled opiate, which is the most dominant opiate used by addicted women have a half-life about 6-8 hours.[18]

The exclusion criteria were underlying disease such as diabetes mellitus or hypertension, specific complications during pregnancy (pre-eclampsia, preterm labor), consumption of other medications during pregnancy (such as benzodiazepines or anti-epileptics) except folic acid and iron and incorrect NST technique (unclear baseline, vague variability, lack of recording uterine and fetal movements).

Non-Stress Test (NST)

The non-stress test (NST) is one of the most important diagnostic fetal well-being tests, which is commonly used during the monitoring of labor and pregnancy. The diagnostic value of this test in determining maternal and fetal outcomes has been shown to be acceptable.[19] It has been demonstrated that NST has the capability to detect a spectrum of fetuses' compromises.[20] This test is a good indicator of fetal central nervous system oxygenation and has been widely used for fetal surveillance.[21] A reactive NST was defined as the presence of two or more fetal heart rate accelerations of 15 beats or more, within a 10-min window, lasting at least 15 seconds and associated with fetal movement.[22] FHR was assessed by recording NST for 20 minutes for each individual.

Periodic FHR changes included five defined FHR changes, namely accelerations, early decelerations, late decelerations, variable decelerations, and sinusoidal pattern.

Accelerations

Transient increases in the FHR and are associated with vaginal examinations, fetal movement, uterine contractions, umbilical vein compression, and fetal scalp stimulation.[23] Accelerations are considered indicative of fetal well-being. The presence of at least two accelerations, each lasting for 15 or more seconds above baseline and peaking at 15 or more bpm, in a 20-minute period is considered a reactive NST.

Early Decelerations

Caused by fetal head compression during uterine contraction that leads to slowing of the heart rate. Early decelerations have slow onset that coincides with the start of the contraction and a slow return to the baseline that coincides with the end of the contraction.

Late Decelerations

Indicative of uteroplacental insufficiency and provoked by uterine contractions. Late decelerations are associated with a decrease in uterine blood flow or placental dysfunction.

Variable Deceleration

Shown by an acute fall in the FHR with a rapid downslope and a variable recovery phase.[24] This type of periodic FHR change occurs frequently in patients with premature rupture of membranes.[25] Decreased amniotic fluid volume has also been shown to be associated with variable decelerations.[26]

Sinusoidal Pattern

This type of FHR change is associated with high rates of fetal morbidity and mortality. It is a regular typical sine wave that occurs with a frequency of 2-5 cycles per minute and an amplitude range of 5-15 bpm, which characterized by a stable baseline heart rate of 120 to 160 bpm and absent beat-to-beat variability. It indicates severe fetal anemia (e.g. in Rh disease) or severe hypoxia.[26]

Variability disorders were considered as any pattern of non-reactive NSTs, which are known to be associated with fetal morbidities. Beat-to-beat or short-term variability is the oscillation of the FHR around the baseline in amplitude of 5-10 bpm. Long-term variability has a frequency of 3-10 cycles per minute and amplitude of 10-25 bpm. Clinically, loss of beat-to-beat variability is more significant than loss of long-term variability. Fetal hypoxia, congenital heart anomalies, and fetal tachycardia also cause decreased variability.

Other Variables

In the operation room, the participants completed a demographic data questionnaire and received 500cc intravenous fluid containing dextrose in the presence of a nurse or midwife. NST results were recorded for 20 minutes. The questionnaires included patients' demographic data such as age, gestational age, ethnicity, number of children, and educational level, as well as a history of opium abuse, method of opium abuse, amount of consumption per day, method of delivery, and neonates' birth weight and Apgar score.

Fetal movements were defined as the number of perceived movements by mothers. The numbers of perceived fetal movements by mothers were indexed during NSTs recording.

Statistical Analysis

Data were analyzed using SPSS software version 18 (SPSS Inc., Chicago, IL, USA) and Strata software. Categorical data are presented with frequency number and percentage. Continuous variables are expressed by mean±SD (standard deviation). Chi-square and *t* tests were used as appropriate. P values <0.05 were considered statistically significant.

Results

Table 1 shows the comparison of baseline characteristics between the two groups. A total of 100 women (50 in opium abusers and 50 in healthy individuals) participated in this investigation. The most common mode of delivery in both groups was cesarean section (C/S) (62% and 72% among opium abusers and healthy individuals, respectively). Inadequate progression of labor and fetal distress were the most common indication of C/S. Maternal age, weight, ethnicity, gestational age, gravidity, parity, number of children, and the method of delivery were not different between the two groups (table 1). Only 9 (18%) neonates in the opium abuser group had good Apgar scores (score: 8-10) as compared with 37 (84%) neonates in the healthy women group (P<0.0001).

The most common method of opium abuse was inhalational (n=24). Fetal weight was significantly lower in the opium abuser group (P<0.0001). Furthermore, reactivity disorder was 3.61 times higher in the case group (P<0.0001). Abnormal variability or oscillations of <15 beats/min, which indicates lack of beat-to-beat variability, was significantly higher in the fetuses of addicted mothers (P<0.0001). We found that variability disorder was 3.4 times higher in the opium abuser group compared with the not addicted women.

The fetus of those women who used one grain of opium (0.125 ounce) each time and with more frequent daily manner had a 13.33 fold risk of abnormal variability of baseline FHR compared to the healthy women (P<0.0001). In fact, the risk of variability disorder was 10-13 times higher in opiate addicted mothers.

A significant reduction of FHR acceleration was observed among opium abusers (P<0.0001). No significant change in deceleration was observed in both groups. Periodic change was 9.8 times higher among opium abusers. Moreover, the risk of irregular recordings was 11.5 times higher in the opium abuser group.

The number of fetal movements was significantly lower among opiate addicted mothers compared to the control group (P<0.0001). Our findings revealed that the recording of irregular fetal movements by the mother was 5 times higher in the case group compared with the control group (table 2).

Discussion

This study demonstrates that non-reactive NST was more likely to be detected in the fetuses of opiate addicted mothers compared to healthy women. NST reactivity abnormalities occurred 3.61 times higher among addicted mothers. Consistent with our results, Oncken et al.[17] showed significant changes in reactivity in fetuses that were exposed to nicotine.

No significant effect of maternal opiate addiction on baseline FHR was detected in our study. Similarly, Graca et al.[27] reported

Table 1: Frequency (%) or mean±SD in baseline characteristics in the case and control groups

Variable	Case group (n=50)	Control group (n=50)	P value
Age (years)	29.36±6.70	27.28±7.54	0.11
Weight (kg)	69.38±8.04	66.86±8.83	0.32
Body mass index (kg/m^2)	27.85±5.5	27.01±4.2	0.88
Gestational age (weeks)	38.10±1.64	38.12±1.64	0.91
Gravidity	3.73±2.34	3.10±2.11	0.76
Parity	2.48±2.12	1.90±1.97	0.06
Number of children	2.22±2.07	1.70±1.87	0.07
Neonate's weight	2,984.00±265.43	3,191.00±302.31	0.12
Baseline FHR	141±10.10	138.30±10.08	0.27
Ethnicity			
Fars	16 (32%)	22 (44%)	0.33
Baloch	30 (60%)	25 (50%)	
Afghan	4 (8%)	3 (6%)	
Mode of delivery			
Cesarean section	31 (62%)	36 (72%)	0.08
Vaginal	19 (38%)	14 (28%)	
Neonatal apgar score			
7-8	18 (36%)	3 (6%)	<0.0001
8-9	23 (46%)	10 (20%)	
9-10	9 (18%)	37 (74%)	

Table 2: Comparison of the two groups with respect to fetal variables using chi-square test and *t* test as appropriate

Variable	Subgroup	Opiate addicted group (n=50)	Control group (n=50)	P value	Odds ratio	95% CI
NST reactivity	Reactive	3	37	P<0.0001	3.61	2.25-5.80
	Non-reactive	47	13			
NST variability	Normal	12	40	P<0.0001	3.4	2.0-5.7
	Abnormal	38	10			
FHR periodic change	Normal	4	32	P<0.0001	9.8	3.8-25.0
	Abnormal	46	8			
Fetal movement	Acceptable (normal)	7	38	P<0.0001	5.0	2.5-10.1
	Unacceptable (reduced)	43	12			

CI: Confidence of interval; FHR: Fetal heart rate; NST: Non-stress test

no noticeable changes in baseline FHR among fetuses of opiate addicted mothers. Nevertheless, the effect of nicotine on baseline FHR has been shown to be considerable. In this regard, Graca et al. found increased baseline FHRs by 10 beats/min in fetuses exposed to nicotine.[27] It can be concluded that changes in baseline FHR among addicted women resulted from coincidental smoking of cigarettes and is not merely due to opiate consumption.

Variability disorder was 3.4 times higher among addicted mothers. Moreover, our study shows that the frequency of opiate use plays a more important role in developing FHR abnormalities than the amount of used opiates. Until now, no investigation has revealed the effect of opiate daily use frequency on FHR. However, studies on synthetic opioids have shown similar outcomes. For instance, Ramirez-Cacho et al.[28] demonstrated that chronic maternal methadone therapy (which is a synthetic opioid) affects FHR patterns by reducing the variability and baseline accelerations. Studies of other drugs that are abused, especially in developed countries, have illustrated similar findings. Mehta et al.,[12] in a study on cocaine-exposed newborn infants, showed that newborns with intrauterine cocaine exposure had significantly reduced heart rate variability, which could be considered as a marker for increased risk of sudden infant death. Our results have shown that opioid abuse has the potential to affect FHR and NST similar to the abuse of other illegal drugs such as cocaine. These potential harmful effects of opioids on fetus must be considered when admitting addicted women.

In our study, periodic change was 9.8 times higher among opiate addicted women. The changes were only significant in acceleration phase and not in deceleration period. Our results are consistent with the previous study in which researchers found significant reduction of acceleration in fetuses exposed to diamorphine.[13]

With respect to the effects of opium on causing bradycardia and tachycardia, it can be concluded that although the maximum FHR was higher among opium abuser (170 beats/min); the difference was not statistically significant. Chazotte et al.[29] also found no significant effect of cocaine in causing tachycardia among exposed fetuses.

Previously, Finnegan[30] showed lower birth weight among infants born to opiate-dependent women. In the present investigation, neonates' weights were similar between the Iranian opiate-addicted women and healthy individuals, which contradict Finnegan's report.[26] One reason for this discrepancy can be the existence of multifactorial components including other maternal characteristics, which may affect birth weight. For proper assessment of the effect of opioid abuse on birth weight, the influence of other confounders should be considered.

Studies have not demonstrated a direct association between maternal age and FHR. However, Maisonneuve et al.[31] showed higher incidence of fetal acidosis among women older than 35 years of age. In our study, since the maternal age was not significantly different between the two groups, it was not considered as a confounder. Similarly, maternal age and BMI were similar between the groups and therefore they can be taken into consideration as confounders affecting FHR.

Our study showed that the dominant method of delivery in both groups of opiate addicted and non-addicted mothers was C/S. Recently, investigations have shown noticeable increase of cesarean section rate in Iran. Many factors have been identified that play an important role in such increasing rate and act as barriers in reducing the high rate of C/S in Iran. According to Yazdizadeh et al.,[32] these factors include too many interventions in the delivery process, shortage of human resources and facilities, and unpredictably and time-consuming process of vaginal delivery. Our study also confirms that the rate of C/S is noticeably high in Zahedan, which requires attention.

Our study had several limitations. Some mothers did not give complete information about

their addiction. In addition, the time interval between referral to the delivery room and labor was short for some mothers, thus it was not possible to complete the questionnaires and perform the NST. Moreover, considering that opium is mostly used in some Asian countries, we did not find any studies that assessed its effects on FHR and therefore we could not compare our results with those specific to opium abuse.

Conclusion

Considering the negative effects of maternal opium abuse on FHR characteristics, opiate addicted pregnant women are more susceptible to maternal and fetal complications. Therefore, NST should be repeated within shorter time intervals in case of observing any abnormal FHR in recorded NSTs. Moreover, it is necessary to increase the awareness of pregnant women about the negative effects of opium abuse during pregnancy, and encourage them to quit their addiction as soon as possible.

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Conflict of Interest: None declared.

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