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Original Article

Comparison of the Effect of Vaginal Misoprostol and Intravenous Oxytocin on Fetal-Neonatal Complications in Primigravid as Who Referred to Shahid Sadoughi Hospital, Isfahan, Iran in 2017

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ABSTRACT

Background: Oxytocin and misoprostol are used to initiate labor which can sometimes cause complications to the fetus and neonate. The purpose of this study was to determine the combined effect of vaginal misoprostol and intravenous oxytocin on fetal/neonatal outcomes in primigravidas whoreferred to Shahid Sadoughi Hospital, Isfahan, Iran.

Methods: This clinical trial study was performed on 102 pregnant mothers in Isfahan Shahid Sadoughi Hospital. The participants were randomly divided into two groups of oxytocin induction with vaginal misoprostol (n=51) and oxytocin alone (n=51). Finally, fetal heart rate decline during labor and delivery, Apgar scoresat1and 5min, presence of meconium, and admission to neonatal intensive care unit (NICU)were evaluated. The data were then analyzed in SPSS software (version 22).

Results: The results revealed that the meconium excretion was significantly higher in the intervention group than the control group (P<0.05). The frequency of early deceleration was significantly lower in the intervention group than in the control group (P<0.05). There was no significant difference between the two groups regarding the frequency of late deceleration and variable deceleration in the fetal heart (P>0.05). Frequency of late deceleration and beat-to-beat changes were quite similar in both groups. There was no significant difference in mean Apgar scoresat1 and 5 min between two groups (P<0.05). Frequency of neonatal hospitalization in the intervention group was significantly higher than the control group (P<0.05). Frequency of neonatal need for resuscitation was similar in both groups.

Conclusion: According to the results of this study, concurrent use of misoprostol and oxytocin increased neonatal meconium excretion and NICU admission.

Keywords: Fetal monitoring, Fetus, Misoprostol, Neonate, Oxytocin

Introduction

Childbirth is a physiological process that most women go through without complications. Occasionally, complications during pregnancy and childbirth can occur very quickly and unexpectedly, leading to early admission to the delivery unit, especially if it is found during prenatal care that it poses a threat to the mother, fetus, or both (1). Therefore, the induction of labor is a selective measure based on medical indications. The purpose of induction is to stimulate uterine contractions for natural vaginal delivery (2). Induction of labor in developed countries is a common midwifery practice so that more than 25% of all deliveries are induced at

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term (3). Pharmacological approaches include using oxytocin and prostaglandins (misoprostol and dinoprostol)(1).

Misoprostol is currently widely used in gynecology and midwifery. In fact, in some cases, it is the best treatment and in some cases an important alternative to the main treatment. The effective dose of the drug varies from 25 to 600 micrograms depending on the use and pregnancy conditions. The important point in taking this drug is to choose the appropriate therapeutic dose to achieve the desired effects with the minimum side effects (1).

According to the American College of Gynecology and Midwifery, vaginal misoprostol is more easily absorbed and its blood level remains higher, compared to the oral form. It is effective in cervical softening and induction of labor and its vaginal use is more effective than oral use. Misoprostol can induce labor effectively, reduce the need for oxytocin ,increase the rate of normal vaginal delivery within 24 h after induction, and reduce the distance between induction and delivery (4). Vaginal misoprostol is currently used in cases of need for induction and cases of the undesirable cervix. Risks and side effects of misoprostol include uterine hyper stimulation, increased uterine contractions, meconium excretion, and meconium aspiration. Moreover, if it is taken at high doses, it will cause excessive uterine stimulation and increase the chance of cesarean delivery(5,1). According to the results of a study carried out by Chen (2015), misoprostol consumption was associated with more complications than dinoprostone, such as uterine tachycystol, abnormal fetal heart rate, and fetal distress (6).

Another method is the induction of oxytocin which is one of the most commonly used drugs in the United States. Oxytocin is the first polypeptide hormone synthetically synthesized (1).Although the effect of oxytocin on labor induction and induction is well known, this method has potential maternal and fetal risks (7).High-dose diets can cause severe and prolonged contractions, uterine rupture, hypertension, decreased pulse rate, headache, water intoxication, seizures, and even death (1). For this reason, Oxytocin was added to the list of high-risk drugs in 2007 by the Institute of Safe Medicines. Oxytocin has an antidiuretic effect and in the case of an infusion of 20 milliliters per minute or more, it will result in water intoxication which can cause coma attacks and death. In cases of usage of high doses of oxytocin, uterine tachycystol was discontinued. The purpose of induction or enhancement of therapy is to achieve a level of uterine activity (less than 200 Montevideo units) and at the same time avoid the uncertain conditions of the fetal heart, causing cervical and fetal decline (1). The half-life of oxytocin is 5 min and the response to oxytocin occurs within 3-5 minutes of initiation. Within 40 minutes of starting a constant level of it, it develops in the blood. The dominant method for the induction of labor in Iran is using oxytocin (8,9).In one study Ghanbarzadeh quoted the Sheriff's Office (2013) as suggesting that oxytocin should be used to induce sufficient uterine activity to modify cervix and fetal descent so as not to cause uterine stimulation or risk for the fetus. She also noted that there is no physiological difference between oxytocin-induced vaginal delivery and normal vaginal delivery and it is difficult to predict the amount of oxytocin required for childbirth. This amount varies for different individuals, causing a different and unpredictable level of sensitivity in people. Consequences of induction include abnormal fetal heart rate pattern , meconium excretion, Apgar's low scores, need for neonatal intensive care, need for cesarean section, uterine tachysystole, changes in vital signs, and even gastrointestinal problems. However, oxytocin can be used in lower doses and if it is combined with misoprostol, it may reduce the usage of low doses of oxytocin in the induction of labor (10).

Usage of labor stimulants is associated with maternal and fetal complications, such as uterine fatigue, euthanasia, uterine tachysystole, increased postpartum hemorrhage, uterine rupture, fetal distress, increased rate of cesarean delivery and non-cesarean delivery (11,12). Therefore, the consequences of such inductions should be evaluated so that the least threatening ones can be recognized and recommended. Therefore, the present study was conducted to compare the effect of vaginal misoprostol and intravenous oxytocin on fetal/neonatal outcomes in primi gravidas who referred to Isfahan Shahid Sadoughi Hospital, Iran in 2017.

Methods

This clinical trial study was performed on 102 pregnant mothers who referred to Shahid Sadoughi Hospital in Isfahan for their delivery in 2017. At first, eligible mothers were selected using the convenient sampling method. The inclusion criteria were1) Iranian nationality, 2) written informed consent for participation in the study, 3) age range of 18-40, 4) single-fetus term

pregnancy over 37 (37-41) full weeks based on mp, and first trimester ultrasound, 5) cephalic position of the fetus, the head of the fetus fits with the mother's pelvis , 6) lack of uterine contractions, 7) dilatation of ≤3 cm, or scurvy of<4 (1), 8) lack of any fetal heart rate abnormalities and sinusoidal pattern (variability, increase and decrease in heart rate) prior to the study, 8) normal non-stress test (reactive NST), 9) estimated infant weight of<4000 g (according to Sun Johnson's law), 9) lack of placenta grading ≥3, 10) sever intrauterine growth restriction with respect to pregnancy care records and if uterine height is less than three-weeks normal,11) lack of asthma and glaucoma, cycle tuberculosis, adrenal in sufficiency, and hepatitis, (misoprostol contraindication), 12)lack of any specific diseases in the mother and genital herpes (by taking prenatal care records since they are low), 13) absence of inducements, such as classical or uterine incision and head and neck placenta with diagnosis of ultrasound, lack of myoma or uterine abnormalities, or fetal abnormalities, rupture of the membranes for more than 12 h, unknown vaginal bleeding, and previous cervical surgery, 14) lack of cephalopelvic disproportion(overall assessment of pelvic and fetal size and their matching by the researcher) (Johnson's Law), and 15) non-usage of herbal stimulants 24 h prior to the study (such as saffron and cumin). On the other hand, the exclusion criteria consisted of1) unwillingness to continue the study, 2) unknown vaginal bleeding in the course of the study, 3) fetal heart rate disorder and long-term fetal distress, and 4) any problems that could interfere with normal delivery. The used questionnaire consisted of two parts, namely demographic and fertility characteristics and fetal neonatal outcomes (i.e., abnormal fetal heart rate pattern, preterm and late fetal heart rate abnormalities, fetal heart rate abnormalities, prolonged fetal heart rate decline, neonatal Apgar score at1 and 5 min, meconium excretion, infant hospitalization in neonatal intensive care unit[NICU]).The questionnaire was approved by 10 midwifery faculty members. The intervention group (A) received misoprostol with oxytocin, while the control group (B) received oxytocin. The participants were randomly assigned to two groups using a random number table.

For the intervention group (A), 25 µg misoprostol tablets were placed in the posterior fornix.

After the misoprostol administration, the pattern of contractions was examined. If the pattern of at least 3 contractions within 10 min was achieved, induction with oxytocin was not initiated. Otherwise, after 3 h of misoprostol administration, 10 units of oxytocin was administered in 1000 cc (1 liter) ringer and infused 1mL/min (13). Due to the continuous attachment of fetal heart rate monitoring and tachometer probe to the mother since the beginning of induction, the fetal heart rate pattern and uterine contractions were evaluated. The initial regimen of oxytocin and its incremental dose was one milliliter per minute. The dose of oxytocin was increased to a maximum of 40 mM until the effective contraction within 10 min reached three contractions of 30-45 s (30 s in the latent phase and 45 s in the active phase)(1). Then it was maintained at 40 mM and increased oxytocin infusion occurred at 15 min intervals (Cunningham F G, 2014 p: No. 530).

The control group (B) received 10 units of oxytocin in 1000 cc (1 liter) ringer which was initiated by intravenous infusion at 1mL/min. The beginning time of induction was recorded and in order to also record the fetal heart rate and uterine contractions, the mother was continuously connected to fetal heart rate monitoring and tocometry from the beginning of labor. The oxytocin initiation regimen and its incremental dose were 1 mU/min. The drug was doubled at 15 min intervals until a suitable contraction pattern (3 contractions per 10 min) was obtained. The infusion dose increased to a maximum of 40 mU/min and was maintained at that limit. Oxytocin administration continued even after the optimal contraction pattern was achieved.

All interventions were performed in two equal groups and the times in this study were recorded in seconds. Meconium excretion, fetal heart condition, neonatal admission to the NICU, or neonatal resuscitation, and Apgar scores at 1and 5minwere determined by the investigator and recorded through observation.

Finally, the information was entered into SPSS software (version 20). They were then analyzed using Mann-Whitney, Chi-square, and independent t-tests. Moreover, ap-value of ≤0.5 was considered statistically significant.

Results

Based on the results, the age range of the study participants was 20-36 and 19-36 years in the control and the intervention groups, respectively. Based on the last menstrual period, the mean gestational age (week) of the control

Table 1. Frequency distribution of meconium excretion in two groups

Meconium excretion rate	control group		Intervention group		Mann-Whitney test	
	Number	Percentage	Number	Percentage	Z	P
Do not have	46	90/2	37	72/5		
Do have (thin)	4	7/8	13	25/5	2/23	0/03
Thick	1	2	1	2		

Table 2. Frequency distribution of fetal heart condition in two groups

Variable	Control group		Intervention group		Chi-square test	
	Number	Percentage	Number	Percentage	χ^2	P
Early decline	30	58/8	23	45/1	4/12	0/04
Late decline	6	11/8	8	15/7	0/33	0/56
Variable decline	10	19/6	6	11/8	1/19	0/28
Long-term decline	1	2	1	2	-	1
Beat-to-beat changes	49	96/1	49	96/1	-	1

Table 3. Mean Apgar scores at 1 and 5 min in both groups

Variable	control group		Test group		Independent t-test	
	Mean	Standard deviation	Mean	Standard deviation	t	P
First minute Apgar	9/69	0/51	9/57	0/67	0/99	0/32
Fifth minute Apgar	9/98	0/14	9/96	0/20	0/58	0/56

Table 4. Frequency distribution of neonatal need for resuscitation and hospitalization in two groups

Variable	Control group		Intervention group		Chi-square test	
	Number	Percentage	Number	Percentage	χ^2	P
The neonates who need to be revived	6	11/8	6	11/8	-	1
The neonates who need hospitalization in the intensive care unit	12	23/5	26	51	8/22	0/004

and intervention groups were 38.35±0.87 and 38.16±0.78, respectively. The majority of participants (44(86.3%) and 45 (88.2%) subjects in the control and intervention groups, respectively) were housewives with a bachelor's degree (28(54.9%) and 25 (49%) subjects in the control and intervention groups, /respectively). Furthermore, the economic status of most of them was moderate (29(56.9%) and 28 (54.9%) in the intervention and control group, respectively).

Results of the Mann-Whitney test revealed that meconium excretion was significantly higher in the intervention group than the control group (P<0.05) (Table 1). In other words, oxytocin alone causes meconium removal to a lesser extent.

Results of the chi-square test indicated that the frequency of preterm loss was significantly lower in the intervention group than the control group (P<0.05). The frequency of prolonged decline and beat-to-beat changes were quite similar in the two groups (Table 2).

Moreover, the results of the independent t-test showed that there was no significant difference between the two groups regarding the mean Apgar score at 1 and 5 min (P<0.05) (Table 3).

In addition, based on the Chi-square test results, the frequency of neonatal admission to the NICU was significantly higher in the intervention group, compared to the control group (P<0.05). Furthermore, the frequency of neonatal need for resuscitation was similar in both groups (Table 4).

Discussion

According to the results, the rate of meconium excretion in the intervention group was significantly higher than the control group. In other words, oxytocin alone causes meconium removal to a lesser extent. However, a clinical trial study titled "Comparative study of the effect of vaginal misoprostol combined with oxytocin and oxytocin alone on the preparation and induction of labor in pregnant women" which was performed by Bahadori et al. (2011) at Motahari hospital, Urmia, Iranfound no significant difference between the two groups regarding meconium excretion (14).

In addition, a retrospective study on women with a history of induction of labor was conducted by Kraft et al. (2014) at the University Hospital of Zurich which was titled "Maternal and neonatal outcome from term induction compared to two misoprostol regimens" revealed that amniotic meconium caused no significant difference between the two groups(15).

The frequency of preterm loss was

significantly lower in the intervention group than in the control group. Moreover, there was no significant difference between the two groups regarding the frequency of late and variable decelerations in the fetal heart. Frequency of long-term decline and beat-to-beat changes were quite similar in both groups. In this regard, a randomized clinical trial study was conducted by Balci et al. (2011) at the Turkish Medical University Hospital in Meram, Turkey which compared labor induction with vaginal misoprostol plus oxytocin versus oxytocin alone in first-term abdominal pregnant women(13). In the above-mentioned study, there was no significant difference in abnormal fetal heart rate of both groups. Moreover, an intervention study by Márcia Maria Auxiliadora de Cecattiet al. (2003) at Leonor Hospital, Brazil, entitled "Misoprostol compared to oxytocin to induce labor during and after pregnancy", revealed no significant neonatal outcomes(16).A randomized clinical trial by Pandey (2014) in Kanpur (India) also investigated the cord blood and cardiotocographic changes in labor induction with dinoprostone and misoprostol. The aforementioned study found FHR tachycardia> 160bpm and FHR bradycardia <110bpm for the misoprostol group which was significantly higher than the dinoprostone group. Furthermore,the variation FHR was significantly higher in the misoprostol group than the dinoprostone group(17).

The results indicated that there was no significant difference between the two groups in terms of the mean Apgar scores at 1 and 5 min. Moreover, Apgar scores at1 and 5 min were similar in both groups (vaginal misoprostol plus oxytocin versus oxytocin alone) and no significant differences were observed. Similarly, in a study conducted by Bahadori et al. (2011), no significant difference was observed between the Apgar scores at 1 and 5 min (14). In addition, an interventional study performed by Márcia Maria Auxiliadora de Cecatti et al. (2003) at Leonor Hospital, Brazil, entitled "Misoprostol compared to oxytocin for induction of pregnancy during and after pregnancy", did not find any significant neonatal outcomes(16). A randomized clinical trial conducted by Jalilian et al. (1) at Imam Reza Hospital in Kermanshah, Iran, compared the effect of vaginal misoprostol and intravenous oxytocin on the induction of labor and their complications (18). In addition, the results of the study by Kraft et al. (2014) were in line with those of the present study(15).

In this study, the frequency of neonatal hospitalization in the NICU was significantly higher in the intervention group, compared to the control group. However, Márcia Maria Auxiliadora de Cecattiet al. (2003) reported no significant neonatal outcomes in their study(16). In the study carried out by Jalilian et al. (2012), there was no significant difference between the two groups regarding the need for neonatal admission to NICU(18). The results of the study performed by Kraft et al. (2014) also indicated that at a dose of 50 µg, the need for neonatal intensive care significantly increased in neonates born to multiparous women(15). Pandey (2014) also found that the rate of neonatal admission to the NICU was higher in the misoprostol group (20%)than the dinoprostone group (15%)(17).

In addition, the present study found that the frequency of neonatal need for resuscitation was similar in both groups. Moreover, Márcia Maria Auxiliadora de Cecattiet al. (2003) reported no significant neonatal outcomes(16).

Conclusion

According to the results of this study, the rates of meconium excretion and frequency of neonatal hospitalization were significantly higher in the intervention group than the control group. Moreover, the frequency of preterm loss was significantly lower in the intervention group in comparison to the control group. In addition, there was no significant difference between the two groups regarding the frequency of late and variable decline, long-term decline ,beat-to-beat changes in the fetal heart, neonatal need for resuscitation, as well as the mean Apgar scores at 1 and 5 min.

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Conflicts of interest

There are no conflicts of interest.

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