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Maternal and Neonatal Outcomes of Induction of Labor with Vaginal Misoprostol Versus Intravenous Oxytocin

Mervat G. Zaghaloul*

Abstract:

Background: There are many different situations in obstetrics where there is the need for labor induction in women with unripe cervices. This indication stems from a situation where the continuation of pregnancy may be life-threatening for the mother and/or fetus. **Objective:** To compare maternal and neonatal outcomes of induction of labor with vaginal misoprostol versus intravenous oxytocin. **Methods:** A follow up study was conducted at the delivery unit of Ismailia University Hospital. The study subjects included two equal groups of women, group I (50) who received vaginal misoprostol and group II (50) who received oxytocin infusion. A structured interviewing schedule and an observation checklist were developed, validated and used to collect data related to maternal and neonatal outcomes. **Results:** Uterine contractions of longer duration (>70-90 seconds) and strong intensity were found to be significantly higher in the misoprostol group compared to the oxytocin group (p<0.01). Within the first 12 hours, the misoprostol group recorded statistically significant higher rates of normal fetal heart rate and of vaginal delivery compared to the oxytocin group (p=0.003, 0.008 respectively). On the other hand, the incidence of cesarean delivery was higher in the oxytocin group compared to the misoprostol group. **Conclusion and Recommendations:** Misoprostol 25µg vaginally (every 4 hours, up to 200 µg) is more safe and efficient for cervical ripening than oxytocin infusion. It is recommended for parturient women with Bishop score ≤4.

Key words: Apgar Score; Labor Induction; Labor Progress; Vaginal Misoprostol; Oxytocin

INTRODUCTION

According to Fraser and Cooper (2003),[1] induction of labor is indicated when the benefits to the mother or the fetus outweigh those of continuing the pregnancy, due to prolonged or post-term pregnancy, pre-eclampsia, medical problems as hypertension, diabetes, renal and respiratory diseases, placental abruption, unstable lie, premature rupture of membranes, maternal request, suspected fetal compromise, intrauterine fetal death and intrauterine growth restriction.

On the other hand, there are many

*Lecturer of Maternity, Obstetrics and Gynecological Nursing, Faculty of nursing, Port-Said University.

different situations in obstetrics where there is need for labor induction in women with unripe cervices. This indication stems from a situation where the continuation of pregnancy may be life-threatening for the mother and/or fetus. Such induction is frequently prolonged, exhausting and very often unsuccessful, resulting in a cesarean section.[2,3]

Prior to induction the state of the cervix is assessed using a Bishop score.[4] When the total score is greater than eight the cervix is said to be favorable and the prognosis for induction will become good.[5]

There are different mechanical and pharmacological techniques for cervical ripening before induction of labor. Among the pharmacological agents used for labor induction, oxytocin and prostaglandins are the most common.[6,7]

Oxytocin is a synthetic form of the naturally occurring posterior pituitary hormone used to initiate uterine contraction in a term pregnancy and it has been widely used in obstetric practice. It has possible side effects including nausea, vomiting, uterine hypertonicity, tetanic contraction, uterine rupture (with excessive dose), cardiac arrhythmias and fetal bradycardia.[8]

Misoprostol (Cytotec) is a synthetic prostaglandin E_1 (PGE_1) analog that has been found to be a safe and inexpensive agent for cervical ripening, that makes it softer, initiates its dilatation and effacement and stimulates uterine contractions.[9] It's dosages starting by taking 50 to 100 mg orally or inserting 25 to 50 mg (1/4 to 1/2 of a 100 mg tablet) intra-vaginally into posterior fornix and repeated every 3 to 6 hours as needed to a maximum of 300 to 400 mg in a 24 hours or until an effective contraction pattern is established. A higher dose of misoprostol is more likely to result in adverse reaction such as: nausea and vomiting, diarrhea, fever, hyperstimulation of the uterus and passage of fetal meconium.[10]

Several studies have shown that

continuous intravenous infusion of oxytocin is less efficient, particularly when there are unfavorable cervical conditions, leading frequently to a cesarean section, because of induction failure.[11,12] But misoprostol is of proven safety and efficacy, low cost and high stability at room temperature**.** Its use may decrease the need for oxytocin, achieve higher rates of vaginal delivery within 24 hours of induction and reduce induction to delivery intervals.[3,13]

The nurse plays an important role in assessing safety of the mother and her fetus during induction and in preparing the woman for administering uterine stimulants and monitoring the mother and fetus during the labor process.[14] Furthermore, maternal vital signs should be assessed and recorded at regular intervals, at least every hour and the frequency increases according to clinical signs and symptoms particularly as active labor progresses. Hourly assessment of maternal vital signs is more than reasonable for women receiving oxytocin or any induction agent.[15] Finally the nurse needs to be familiar with institutional policies about induction and augmentation of labor. The nurse should be aware of her local labor ward protocols and policies for induction of labor, and follow the regimen of induction.[16] Because of controversial reports about efficacy, safety and complications of vaginal misoprostol versus oxytocin infusion for induction of labor during third trimester for unfavorable cervix, this study was designed to compare maternal and neonatal outcomes of induction of labor with vaginal misoprostol versus intravenous oxytocin.

METHODS:

Study design: Follow-up study design

Setting:

The study was conducted at the delivery unit of Ismailia University Hospital.

Subjects:

A convenience study sample of 100 women attending the above mentioned

setting was recruited over a period of eight months starting on October 2009 till the end of May 2010.

Inclusion criteria:

- Multipara (2 or 3); in labor on admission with intact membranes.
- Singleton live fetus of gestational age >38weeks, with normal fetal heart rate and vertex presentation.
- Unfavorable cervix (Bishop score less than ≤ 4).
- Indicated labor induction for any clinical and/or obstetric reason with either vaginal misoprostol or intravenous oxytocin.
- No fetal or maternal distress during first stage of labor.
- History of normal pregnancy without medical or obstetrical complications.

Exclusion criteria included: pelvic dystocia; evidence of cephalopelvic disproportion; placenta previa or any unexplained vaginal bleeding; fetal weight >4Kg or malformation; previous uterine scar or any situation where vaginal delivery was not indicated or any contraindication to the use of labor induction.

Full participants included 100 eligible women subjected to induction of labor; 50 with vaginal misoprostol and 50 with intravenous oxytocin.

Tools of data collection

The tools used for data collection consisted of:

1. An Interviewing questionnaire to collect the following data:

a. General characteristics of women such as age, education and occupation and data related to the admission to labor room.

b. Past and present obstetric history including: number of gravida, para, abortions, live births, still births, and neonatal deaths, history of previous pregnancies and previous postnatal complications. In addition, date and time of admission, of last menstrual period, and the expected date of

delivery were also inquired.

2. Observational checklist:

The Partogram (labor progress record) is a graphical representation that was used in collecting data related to progress of labor and included:

- Maternal pulse, blood pressure (BP), and temperature.
- Duration, frequency and interval of uterine contractions.
- Cervical dilatation and effacement.
- Fetal heart rate changes by C.T.G.
- Doses of misoprostol given (frequency and interval).
- Type of intravenous (IV) infusion (dose of oxytocin given).
- Intra-partum complications such as fetal distress and maternal distress.

3. ***Bishop's score (cervical assessment):***

It was developed by Bishop (1964),[4] and included five factors namely; cervical dilatation, effacement, consistency, position and the station of the presenting part. Each factor is scored on a scale from 0-2, and the Bishop score ranges between 0-10. A bishop score > 6 identifies a favorable cervix, while a score ≤ 4 identifies an unfavorable one.

4. Neonatal assessment record using Apgar score:

It is a simple method to assess the condition of the newborn, performed in the first minute and after five minutes of fetal expulsion. It is based on assessment of five physical signs namely; heart rate, respiratory effort, reflex irritability, muscle tone, and color. For each vital sign, the baby is given 2, 1 or 0 points, and the points are then totaled.[3,8]

Pilot study:

A pilot was conducted on ten pregnant women to test the research feasibility clarity and objectivity of the tools as well to estimate the time needed for data collection.

Methods:

- All women who fulfilled eligibility criteria were subjected to one of the following induction of labor procedures:

Women in the vaginal misoprostol group (n=50) received 25 µg misoprostol tablets, administered in the posterior fornix of the vagina. The dose was repeated every 4 hours, until a pattern of at least 3 contractions every 10 minutes was obtained. When this ideal pattern of contractions was reached, misoprostol was no longer administered. However, some women failed to reach this contraction pattern within four hours after the administration of the maximum dose of 200 µg.

- Women in the oxytocin group **(**n=50) received an intravenous oxytocin infusion given in 500 ml of 5% dextrose (2 mU/min oxytocine), which was doubled at 30-minute intervals until the appropriate contraction pattern was obtained. The infusion dose was increased to a maximum of 20 mU/min; at that point it was then maintained constant even after the ideal pattern was reached. Failure to reach an effective induction contraction pattern was identified by the time that 15 IU of oxytocin had been infused.

As soon as patients of both groups presented the desired contraction rate, monitoring of fetal heart rate and intrapartum uterine activity was performed. Amniotomy was carried out when the Bishop score was greater than 7 and cervica**l di**lation was greater than 6 cm.

Ethical considerations:

An official permission to conduct the study was obtained from the responsible authority of the study setting. The purpose of the study was explained to every parturient woman and an oral consent to participate in the study was obtained. The interview was conducted individually and women who met the eligibility criteria were invited to voluntarily participate in the study. Those who accepted were carefully informed of the aims and procedures of the study and then asked to sign the informed consent form.

Limitations of the study:

Some mothers were excluded from the

study due to failure of induction of labor and were subjected later to cesarean section.

Statistical analysis:

Data entry was done using Epi-Info software package, while statistical analysis was done using The Statistical Package for Social Sciences (SPSS-11.0). Data was summarized using mean, standard deviation and frequency tables. Chi-square, fisher exact test and student's *t*-test were used to compare between vaginal misoprostol and oxytocin infusion groups as regards studied outcomes and a $p < 0.05$ was considered significant.

RESULTS

Table 1 demonstrates no statistically significant differences between the misoprostol and oxytocin groups as regards age, education, or job status. The mean age of women in the two study groups were 29.4 ± 3.76 and 27.9 ± 4.27 years respectively. Concerning the level of education, the majority of misoprostol and oxytocin groups (64.0% and 60.0%) had university level of education. As for the job status the majority of the studied groups were housewives.

Table 1. Distribution of the study subjects according to their general characteristics

Characteristics	Misoprostol Group (n=50)		Oxytocin Group (n=50)		X^2	*p*-value
	No.	%	No.	%		
Age (years):						
20-	8	16.0	16	32.0		
25-	15	30.0	14	28.0	3.744	0.0279*
30-35	27	54.0	20	40.0		
Mean ± SD	*29.4 ± 3.76*		*27.9 ± 4.27*		*t*-test	*0.0653*
Level of education:						
Illiterate or *just* read & write	18	36.0	20	40.0		
University	32	64.0	30	60.0	0.170	0.9823
Occupation						
Housewife	34	68.0	41	82.0		
Working	16	32.0	9	18.0	2.613	0.4552

***** Significant at $p<0.05$

Table 2 illustrates the distribution of the studied subjects according to progress of labor. Concerning the characteristics of uterine contractions the table points to statistically significant differences between parturient women in the two studied groups. Uterine contractions with an interval of 2 minutes, with longer duration (>70-90 sec.) and strong intensity were significantly more represented in the misoprostol group (90.0%, 82.0% and 86.0% respectively) compared to the oxytocin group (42.0%, 66.0% and 76.0% respectively).

Mean initial Bishop score in the vaginal misoprostol group was 3.18 ± 1.17, while it was 3.00 ± 1.50 in the oxytocin group. Table 2 also shows a statistically significant difference between the mean **o**nset of active labor (11.92 ± 10.15) in the vaginal misoprostol group compared to that in the oxytocin group (8.25 ± 6.71, *p*-value= 0.03).

Table 2. Distribution of the studied subjects according to progress of labor

Progress of labor	Misoprostol Group (n=50)		Oxytocin Group (n=50)		X^2	*p*-value
	No.	%	No.	%		
Characteristics of uterine contraction:						
- Interval (minutes):						
2 minutes	45	90.0	21	42.0		
3 minutes	5	10.0	29	58.0	25.668	*p*<0.001**
- Duration (seconds):						
60-70	9	18.0	17	34.0		
>70-90	41	82.0	33	66.0	31.818	*p*<0.001**
- Intensity of uterine contraction:						
Moderate	7	14.0	12	24.0	33.731	*p*<0.005**
Strong	43	86.0	38	76.0		
Initial Bishop score:						
(mean±SD)	3.18 ± 1.17		3.00 ± 1.50			
Onset of active labor (hour):						
(mean±SD)	11.92+10.15		8.25 + 6.71		*t*-test	0.03*

***** Significant at *p*<0.05
****** Significant at *p*<0.01

Table 3 shows a statistically significant difference between the two groups in relation to fetal heart rate (X^2= 18.778, p= 0.003). Thus more women (36.0%) in the oxytocin group had fetal heart rate below normal rate compared to women in the misoprostol group (8.0%). Meanwhile, spontaneous rupture of membrane was higher (72.0%) among women in the misoprostol group than that in the oxytocin infusion group, (40.0%, p<0.001).

Table 3. Distribution of the study subjects according to fetal heart rate and rupture of membrane

	Misoprostol Group (n=50)		Oxytocin Group (n=50)		χ^2	*p*-value
	No.	%	No.	%		
Fetal heart rate:						
<120 b/m	4	8.0	18	36.0	18.778	0.003**
120- 160 b/m	46	92.0	32	64.0		
Rupture of membranes:						
Spontaneous	36	72.0	20	40.0	31.710	*p*<0.001**
Artificial	14	28.0	30	60.0		

** Significant at p<0.01

Table 4 demonstrates percent distribution of the study subjects according to mode of delivery. The table shows statistically significant differences between the two groups as regards mode of delivery and type of induction of labor. Women in the intravaginal misoprostol group recorded higher percentage of normal delivery (54.2%), and low percentage of normal delivery with tear (14.3%) and with episiotomy (25.7%) compared to women in the oxytocin infusion group (44.4%, 14.8% and 40.7% respectively). However, women delivered by episiotomy with tear in the intravaginal misoprostol group rated 5.7% compared to none of women in the oxytocin infusion group.

Table 4. Distribution of the study subjects according to mode of vaginal delivery

Mode of vaginal delivery	Misoprostol Group (n=35)		Oxytocin Group (n=27)	
	No.	%	No.	%
Normal vaginal delivery	19	54.2	12	44.4
Normal with tear	5	14.3	4	14.8
Episiotomy	9	25.7	11	40.7
Episiotomy with tear	2	5.7	0	0.0

Table 5 shows distribution of the study subjects according to labor outcomes. It clearly illustrates that the rate of vaginal delivery success was significantly higher in the misoprostol group compared to the oxytocin group (p<0.001). Among women with vaginal delivery, induction success within the first 12 hours was 40.0% and 33.3% for the misoprostol and oxytocin groups respectively (p-value = 0.008).

Increasing the interval from induction to vaginal delivery (>18 hours) was 60.0% for the misoprostol group and 66.6% for the oxytocin group. The table also illustrates that the incidence of cesarean delivery is higher in the oxytocin group. Using misoprostol for cervical ripening and labor induction represented a reduction in the risk of having a cesarean in misoprostol group compared to the oxytocin group (30.0% and 46.0% respectively).

Concerning maternal complications, table 5 clarifies that postpartum hemorrhage in the misoprostol group was 4.0% compared to 6.0% in oxytocin infusion group.

Table 6 shows the distribution of the study subjects according to main causes of cesarean section. It was observed that the main causes of cesarean delivery in misoprostol group were dystocia and prolonged first stage of labor (40.0% and 13.33% respectively), compared to 65.21% and 39.13 % for the oxytocin group.

Also table 6 showed that a caesarean section was indicated for abnormal fetal heart rate patterns in 20.0% of the Misoprostol group compared to 34.78% in

the oxytocin group. However, the difference between the two groups was not significant (*p*-value =0.4072).

Table 7 shows no significant differences between the two groups as regards apgar score at both first and fifth minutes of life.

Table 5. Distribution of the study subjects according to labor outcomes

Labor outcomes	Misoprostol Group (n=50)		Oxytocin Group (n=50)		*p*-value
	No.	%	No.	%	
Type of delivery:					
-Total vaginal delivery	35	70.0	27	54.0	*p*<0.001**
Interval within 12 hours	14	40.0	9	33.3	0.008**
Interval >18 hours	21	60.0	18	66.6	0.020*
-Cesarean section delivery	15	30.0	23	46.0	0.05*
Postpartum hemorrhage	2	4.0	3	6.0	1.00

* Significant at *p≤0.05*
**Significant at *p*<0.01

Table 6. Distribution of the study subjects according to main causes of cesarean section

Causes of cesarean section	Misoprostol Group (n=15)		Oxytocin Group (n=23)		*p*-value
	No.	%	No.	%	
Fetal distress	2	13.33	6	26.08	03109
Abnormal FHR patterns	3	20.0	8	34.78	0.4072
Prolonged first stage of labor	2	13.33	9	39.13	0.1582
Full dilatation arrest	4	26.67	6	26.08	0.1
Cervical dystocia	6	40.0	15	65.21	0.22

FHR, fetal heart rate
Total exceeds 100% because of more than one cause.

Table 7. Distribution of the studied women according neonatal Apgar score

Apgar Score	Misoprostol Group (n=50)		Oxytocin Group (n=50)		*p*-value
	No.	%	No.	%	
1 minute (<7)	5	3.3	4	10	1.00
5 minute (<7)	0	0	0	0	---

DISCUSSION

There are many situations in obstetrics where there is the need for labor induction. Generally, induction is indicated when the benefits to either the mother or the fetus outweigh those of continuing the pregnancy.[3]

The present study was designed to compare maternal and neonatal outcomes of induction of labour with vaginal misoprostol versus intravenous oxytocin. Findings revealed that the intravaginal misoprostol is an effective drug in cervical ripening and labor induction, a finding that is in agreement with previous studies.[13,16]

The present study revealed that the socio-demographic characteristics of the two groups were similar with no significant differences, a finding that indicates control of the effect of confounding variables. Similarly, De Aquino and Cecatti, (2003)[2] reported non-significant differences between misoprostol and oxytocin groups concerning conditions for labor induction, age, parity, race, marital status, family income, initial Bishop Index and number of prenatal visits.

An important factor related to the efficacy of vaginal misoprostol versus intravenous oxytocin for induction of labor is the uterine contraction. The results of the current study showed that the vaginal misoprostol group had significantly more strong intensity of uterine contractions compared to the oxytocin group. In agreement with this finding Song, (2000)[17] reported that misoprostol alone induced sufficient uterine contractions and induction-delivery interval was half of that with oxytocin.

Prostaglandins like oxytocin have an effective role in myometrial contraction during active phase of labor. On the other hand they lead to further extracellular matrix degradation and increase levels of hyaluronic acid with concomitant increase in water. It can be envisioned that they also add to the relatively rapid changes in the

cervix leading to cervical thinning, softening and relaxation, which allow the cervix to initiate dilation. Labor acceleration have many advantages like decrease the rate of mother exhaustion, uterine atony and postpartum bleeding.[3,18,19]

However, Sunkel, (2002)[20] mentioned that misoprostol was shown to have a higher rate of vaginal delivery within 24 hours, shorter induction to delivery interval, and lower cesarean section rates than oxytocine infusion, although it increased uterine tachysystole and hyperstimulation (>12 contractions within 20 sec).

In support, Aquino and Cecatti, (2003)[2] illustrated that the cesarean section rate, latent period and period from induction to vaginal delivery were significantly lower for the misoprostol group. Concerning uterine tonus alterations, tachysystole was significantly more common in the misoprostol group. However, no significant differences were found between the two groups as regards hypoxia and neonatal morbidity.

Concerning the fetal condition and its relation to the types of labor induction, findings of the current study demonstrated that women in the intravaginal misoprostol group were significantly more likely to have normal fetal heart rate and spontaneous rupture of membranes compared to the women in the oxytocin infusion group. This is in congruence with Abdel-Aleem, (2006)[21] who reported that uterine hyperstimulation without associated fetal heart rate changes were more common with misoprostol than oxytocine infusion. In disagreement Tabasi et al., (2007)[13] reported non-significant differences between the two groups regarding abnormal fetal heart rate.

Similarly Abdel-Wahab, (2007)[22] recorded that using misoprostol as a method of Labor induction leads to uterine hyperstimulation without fetal heart rate (FHR) changes. Also uterine hyper-stimulation syndrome (tachysystole or hypertonus with FHR changes such as persistent decelerations,

tachycardia or decreased short term variability) may occur.

In partial agreement with the present study, Rosenberg et al., (2003)[23] have shown that when perinatal results are evaluated by means of Apgar score, cord pH, admission to intensive care unit, number of days of hospitalization and meconium passage, there are no significant differences regarding induction of labor with either vaginal misoprostol, or oxytocin.

The present study demonstrated that the average time interval until the occurrence of vaginal delivery was statistically significantly shorter for the misoprostol group than for the oxytocin group. This is in agreement with Sanchez et al., (2000)[24] and Ramsey et al., (2005)[25] who reported that the average time interval until the occurrence of vaginal delivery was shorter for misoprostol (50 µg at four hourly intervals) than for oxytocin (11 hours and 18 hours).

The results of the present study showed that the higher rate of vaginal delivery within 12 hours in the misoprostol group compared to the oxytocin group is the result of labor acceleration. Some studies does not support this finding.[25,26] In a previous study the rate of vaginal delivery within 12 hours was lower for misoprostol than oxytocin.[26] Thus, differences in dosage, routes of administration, administration intervals and vaginal pH are suggested to be relevant in explaining differences in the outcomes. Misoprostol was found to be more effective in acidic environment.[3]The results of the present study showed that the incidence rate of cesarean delivery is higher in the oxytocin group than the misoprostol group. This finding is in agreement with Balic et al., (2010)[27] who stated that some comparative studies between misoprostol and oxytocin have shown that the incidence rate of cesarean delivery is higher in the oxytocin group.

The results of the present study showed that dystocia was the most common cause of indicated cesarean section in both groups yet, higher in the oxytocin group compared to the misoprostol group (65.21% and 40% respectively). This finding agrees with several studies.[13,28,29] who mentioned that the percentage of cesarean deliveries for dystocia may be due to lower bishop score (0-3) in the most of their parturient women and early performance of cesarean section in cases with labor progress failure (dilatation 0-3).

Finally, this study indicates favorable outcomes regarding the use of intravaginal misoprostol as a modifying agent of the unfavorable cervix and it has proved to be a safe and effective drug to use for induction of labor than intravenous oxytocin.

CONCLUSION

This study supports the safety and effectiveness of intravaginal misoprostol compared with oxytocin infusion in labor induction. It is recommended for parturient women with Bishop Score ≤4.

Use of misoprostol for labor induction result in a shorter time intervals to delivery, more uterine tachysystole and hyper-stimulation but without abnormal fetal heart rate changes. In addition, reduction in the incidence of cesarean delivery is more likely to be encountered.

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