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PJBS

ISSN 1028-8880

**Pakistan
Journal of Biological Sciences**

ANSI*net*

Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Vaginal Misoprostol Versus High Dose of Oxytocin for Labor Induction: A Comparative Study

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Abstract: To compare the efficacy and complications of intravaginal Misoprostol with oxytocin for induction of labor this study was carried out. One hundred and ten term pregnant women with Bishop score of ≤ 4 were randomized into two groups. Fifty five patients received 50 μg intravaginal Misoprostol 2 times at 6 h intervals (Misoprostol group), the second group received oxytocin infusion (6 mu min^{-1}) for induction of labor (oxytocin group $n = 55$). The time from induction to delivery, the route of delivery, fetal outcome and maternal complications were recorded. There was no statistically significant difference regarding demographic or clinical characteristics between two groups. Induction success within the first 12 h were 80 and 33.3% for Misoprostol and oxytocin groups respectively ($p < 0.05$). The average time from induction to delivery was 10.6 ± 3.7 and 17 ± 7.2 h in the Misoprostol and oxytocin administered groups, respectively ($p < 0.05$). The rate of vaginal delivery was significantly higher in misoprostol group (72.7%) when compared with oxytocin group (45.5%). Low Apgar score, meconium stain amniotic fluid, abnormal FHR and precipitating labor was similar in both groups ($p > 0.05$). We concluded misoprostol 50 μg vaginally (every 6 h, up to 100 μg) safely and effectively induces labor and it is recommended for parturient women with Bishop score ≤ 4 and the use of this drug could produce several beneficial effects, particularly a decrease in the incidence of cesarean delivery.

Key words: Labor induction, misoprostol, oxytocin, prostaglandins

INTRODUCTION

There are many situations in obstetrics that 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 (Cunningham *et al.*, 2005). Induction of labor in women with unripe cervixes are frequently prolonged and very often unsuccessful, resulting in a cesarean delivery (Wing, 2006).

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. 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. (Escudero *et al.*, 1997; Kramer *et al.*, 1997). Misoprostol, a synthetic prostaglandin E1, because of its proven safety and efficacy, low cost and high stability at room temperature (Cunningham *et al.*, 2005) can be used for labor induction in such cases. Misoprostol use may decrease the need for

oxytocin, achieve higher rates of vaginal delivery within 24 h of induction and reduce induction to delivery intervals (Cunningham *et al.*, 2005). There are different reports about cesarean delivery rate, meconium passage and abnormal fetal heart rate in the series of studies that misoprostol was used for induction compare to control group (oxytocin, PGE2, foley catheter). Some studies have reported a decreased cesarean delivery rate (Ramsey *et al.*, 2005; Sanchez *et al.*, 2000) while some have shown an increased rate (Cunningham *et al.*, 2005; Agarwal *et al.*, 2003) and others have reported no difference in cesarean rate between misoprostol and control group (Rozenberg, 2004; Adair *et al.*, 1998). Some studies cautioned that increased uterine hyper stimulation with adverse fetal heart rate changes during misoprostol use (Cunningham *et al.*, 2005), but there were no differences in the cesarean delivery rate for fetal distress with misoprostol compare to dinoprostone a PGE2 (Ramsey *et al.*, 2005; Rozenberg *et al.*, 2004). In addition, a dose of 50 μg intravaginal misoprostol was associated with significantly increased meconium passage (Cunningham *et al.*, 2005), while in some studies meconium passage was not increased (Ramsey *et al.*, 2005; Agarwal *et al.*, 2003).

Because of controversial reports about efficacy and complications of misoprostol and to compare the efficacy and vaginal birth intervals, cesarean delivery rate and fetal outcome after intravaginal misoprostol with regimen using oxytocin for induction of labor, this study was designed.

MATERIALS AND METHODS

After obtaining approval from our local IRB and written consent 110 pregnant women requiring labor induction for any clinical and/or obstetric reason, was selected randomly during 2005-2006 in Kashan Shabih Khani Hospital (IRAN) to receive either intravaginal Misoprostol or oxytocin infusion in a randomized trial. The inclusion criteria were: gestation age greater than 37 weeks, Bishop score less than 4, singleton gestation, intact membranes, vertex presentation, no labor occurring and normal fetal heart rate. The exclusion criteria were: pelvic dystocia, evidence of cephalopelvic disproportion, placenta previa or any unexplained vaginal bleeding, fetal malformation, previous uterine scar and any situation when vaginal delivery was not indicated and any contraindication to the use of labor induction. In each patient first the fetal heart rate was monitored to ensure fetal well-being before the onset of induction. Then randomization occurred according to random sequence that generated by computer and the investigator was unaware of the sequence.

For the women receiving misoprostol (case group), 50 µg were administered in the posterior fornix of the vagina. The dose was repeated every 6 h up to two doses (100 µg). For the women in oxytocin group (control group), high dose oxytocin (as 6 mu min⁻¹ infusion) was used.

As soon as the patients presented the desired contraction rate, monitoring of fetal heart rate was performed. Amniotomy was carried out when dilation was 2-3 cm and effacement was 40%. In the cases with spontaneous or artificial membrane rupture and in case labor occurring, second dose of misoprostol did not administer. In case labor were occurred but contractions were not sufficient, contraction augmentation was done by oxytocin. In cases with abnormal fetal heart rate, meconium passage or induction failure, cesarean section was performed. Cervical examination results, amniotomy time, labor time, meconium passage, abnormal fetal heart rate, 1 and 5 min Apgar score, cesarean delivery rates and their causes in both group of Misoprostol and oxytocin were recorded. All parturient that enrolled in this study were examined by gynecologist and all data were collected and recorded by resident during the study.

Statistical analysis was performed with Chi-Square analysis, Fisher's exact test, Kolmogrov Smirnov test and Mann-whitney and leven tests.

RESULTS AND DISCUSSION

Out of the total of 110 women, 55 were randomly allocated to the use Misoprostol and 55 to oxytocin.

There was no statistically significant difference regarding demographic or clinical characteristics between two groups (Table 1).

The most common indication for labor induction was post term pregnancy in both groups. Vaginal delivery occurred more in the misoprostol group versus in the oxytocin group which was significant. When induction success within the first 12 h was evaluated the percentage was significantly higher for the misoprostol group (Table 2).

The time from induction to vaginal delivery (h) was 10.6±3.7 and 17±7.2 for misoprostol and oxytocin group, respectively.

The main causes of cesarean delivery in Misoprostol group were dystocia and meconium passage (40%) while the same for oxytocin group was dystocia (60%) (Table 3).

When low Apgar score at fifth minute of life was analyzed, 6 cases in the misoprostol group and 4 in oxytocin group were found presenting no statistical significance.

Several studies have evaluated the use of misoprostol for labor induction. An American study demonstrated that the average time interval until the occurrence of vaginal delivery was also shorter for

Table 1: Characteristics of women according to assigned treatment

characteristics	Misoprostol (55)	Oxytocin (55)
*Age (years)	24±3.54	23±2.8
*Gestational age (weeks):	No (%)	No (%)
Post term	33 (60)	30 (54.5)
Term	22 (40)	25 (45.5)
*Parity:	No (%)	No (%)
Nulliparous	41(74.5)	45 (81.8)
Multiparous	14 (25.5)	10 (18.2)

p>0.05

Table 2: Type of delivery according to the drug used for induction

Type of delivery	Misoprostol (%)	Oxytocin No (%)	p-value
Vaginal delivery (total)	40 (72.7)	30 (54.5)	p<0.05
Vaginal with in 12 h	32 (80.0)	10 (33.3)	p = 0.00008
Vaginal with in 24 h	40 (100.0)	24 (80.0)	p = 0.0045
Cesarean delivery	15 (27.3)	25 (45.5)	
Total	55	55	

Table 3: Main causes of cesarean section in studied groups

C/S* cause	Group		p-value
	Misoprostol No (%)	Oxytocin No (%)	
Meconium passage	6 (40.0)	6 (24)	p = 0.3109
Abnormal FHR**	3 (20.0)	4 (16)	p = 0.4072
Dystocia:	6 (40.0)	15 (60)	p = 0.22
Prolonged 1st stage of labor:	2 (13.3)	9 (36)	p = 0.1582
Full dilatation arrest:	4 (26.7)	6 (24)	p = 1

*Cesarean section, **Fetal heart rate

misoprostol (50 µg at four hourly intervals) than for oxytocin (11 h versus 18), presenting statistical significance (Sanchez-Ramos *et al.*, 1993). Many other studies have been found same results (Kadanali *et al.*, 1996; Ferguson *et al.*, 2002; Sahin *et al.*, 2002; de Aquino and Cecatti, 2003; Ramsey *et al.*, 2004; Zeteroglu *et al.*, 2006). These findings are consistent with present results.

Prostaglandins like oxytocin have an effective role in myometrical 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 (Cunningham *et al.*, 2005). On the other hand prolonged labor maybe accompanied with many complications like headache, anorexia, nausea, vomiting, abdominal pain, lethargy, convulsion and even death as a result of hyponatremia due to prolong use of high dose oxytocin (Wing, 2006).

Increasing of vaginal delivery rate within 12 h is the result of labor acceleration. In our study vaginal delivery rate within 12 h was 80% for misoprostol and 33.3% for oxytocin. Some studies confirm our results (Sahin *et al.*, 2002; de Aquino and Cecatti, 2003), but there are studies that have obtained opposite results. In the study has carried out by (Adair *et al.*, 1998), the rate of vaginal delivery within 12 h was lower for misoprostol than oxytocin (45.5 versus 48.4). Differences in dosage, routes of administration, administration intervals and vaginal pH are suggested to be relevant in explaining differences in outcome. Misoprostol is more effective in acidic environment (Cunningham *et al.*, 2005).

Some comparative studies between Misoprostol and oxytocin have shown that the incidence of cesarean delivery is higher in the oxytocin group (Sanchez-Ramos *et al.*, 1993; de Aquino and Cecatti, 2003) and this was also shown in our study (45.5% for oxytocin versus 27.3 for misoprostol).

Although in this study the rates of cesarean delivery was higher in oxytocin group than misoprostol but overall, in present study the rate of cesarean delivery in both of groups were higher than mentioned above studies. This maybe due to lower bishop score (0-3) in the most of our parturient women than the other studies and early performance of cesarean section in cases with labor progress failure (dilatation 0-3) (Sanchez-Ramos *et al.*, 2000; Sahin *et al.*, 2002).

Dystocia was the most common cause of cesarean section in the both groups of our study (40% for Misoprostol and 80% for oxytocin group).

Dystocia is the consequences of multiple abnormalities that may exist singly or in combination can be mechanistically simplified into three categories include the powers (uterine contractility and maternal expulsive effort), abnormality involving the passenger (size, presentation and position of fetus) and abnormalities of the passage (the pelvis). These abnormalities often interact to produce dysfunctional labor (Cunningham *et al.*, 2005).

Because of patients with pelvic dystocia and cephalopelvic disproportion were excluded in both groups during this study, difference in cesarean delivery rate between misoprostol and oxytocin groups is the result of power variance and shows that uterine contraction for baby delivery was less in oxytocin group.

Our study showed no differences between the groups regarding abnormal fetal heart rate, meconium passage and Apgar score at fifth minute of life. Many studies 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 differences between the groups, which confirms the finding of the present study (Sanchez-Ramos *et al.*, 2002; Rosenberg *et al.*, 2003; de Aquino and Cecatti, 2003).

Finally, this study suggests misoprostol 50 µg vaginally (every 6 h, up to 100 µg) safely and effectively induces labor and it is recommended for parturient women with Bishop Score ≤4 and the use of this drug could produce several beneficial effects, particularly a decrease in the incidence of cesarean delivery.

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