Original article

Comparison of vaginal misoprostol tablet with oxytocin infusion for induction of labor in term pregnancy

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BACKGROUND: Recently elective inductions of labor at term have increased dramatically which may be in part due to the patient and clinicians desire to arrange a convenient time for delivery. Termination of pregnancy before emerging labor pain is an important concern. Because induction of labor is one of the most commonly performed obstetrical procedures clinicians all over the world investigate to find a safe technique for mother and neonate. Labor induction with PGE1 is one of the selections. Our objective was to compare vaginal delivery, maternal, fetal, and neonatal complications in the induction of labor with oxytocin and misoprostol. **METHODS:** we selected one hundred and eight cases with term pregnancy, not in active labor, singleton pregnancy, vertex presentation, normal fetal heart rate reactivity and Bishop score of < 6, who consented to participate in the study. Fifty-four of the cases were included in misoprostol group and a 100 µg misoprostol tablet was placed in the posterior vaginal fornix. Another 54 cases were included in the oxytocin group. Labor characteristics, maternal and neonatal outcome were analyzed. **RESULTS:** The mean duration of induction to true labor pains ($p = 0.001$) and induction to labor ($p < 0.001$) in the misoprostol group was significantly shorter than the oxytocin group. Rate of cesarean section and maternal and neonatal complications were equal between the two groups. **CONCLUSIONS:** It is effective, safe, and economic to use 100µg misoprostol vaginally in term pregnancy with low Bishop scores.

KEYWORDS: Induction of Labor, Misoprostol, Oxytocin, Term Pregnancy

BACKGROUND

Induction of labor is performed with the aim of reducing maternal and prenatal morbidity and mortality, and is the most common obstetric interventional practice. Labor induction, when performed on a patient with an unfavorable cervix, is often prolonged and difficult. Moreover, failed induction requiring cesarean delivery is common. Different methods have been used for this intervention, which include catheter balloon insertion, laminaria insertion, prostaglandin analogs and oxytocin infusion, ideally combined with amniotomy.[1,2] Today, prostaglandin preparation and intravenous oxytocin are the most frequent pharmacologic choices of labor induction.[3,4] Although, oxytocin infusion is widely accepted as a safe and effective labor induction method, its success is dependent on the condition of the cervix at the beginning of the induction.[5] Therefore, cervical ripening before induction of labor is an important issue in women with low Bishop scores.

Misoprostol, a synthetic analogue of prostaglandin E1, has been widely studied in a variety of dosages and routes of administration as an alternative to oxytocin.[6] Misoprostol offers the advantage of promoting both cervical ripening and myometrial contractility, and previous studies have shown misoprostol to be safe and effective in patients with viable pregnancies.[7-10]

As the efficacy of misoprostol became more certain, clinical trials were conducted to detail the optimal route of administration. Some studies suggested that intravaginal administration of misoprostol is associated with a shorter induction-to-delivery interval, fewer number of doses, and lower oxytocin use.[11-13]

Generally, the 50 µg dose results in a shorter induction-to-delivery interval and a higher rate of vaginal delivery after one dose.[14-16]

The majority of participants in these trials have received doses of 25 µg to 50 µg of intravaginally administered misoprostol.

The purpose of this study was to compare the efficacy and safety of 100 µg intravaginally administered

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misoprostol with a maximum of two doses at 6 hour, intervals with oxytocin for labor induction at term with a Bishop score of ≤ 6.

METHODS

This was a randomized, controlled clinical trial performed from Aug. 2008 to Dec. 2009 at Beheshty University Hospital, Isfahan, Iran.

The study was initiated after approval by the Clinical Research Ethics Committee of Isfahan University of Medical Sciences, (IRCT number 201202018897N1). Written informed consent was obtained from each participant. Women were eligible for enrolment if they had a singleton live pregnancy at term (GA ≥ 38 weeks) in the cephalic presentation, low Bishop Score of cervix, an unfavorable cervix (Bishop score ≤ 6), and normal fetal heart rate tracing. Exclusion criteria were known cephalopelvic disproportion, abnormal presentation, previous cesarean delivery or other types of uterine surgery, cervical cancer, fetal macrosomia, active herpes genitalia, multiparity, and fetal anomaly.

A total of 108 identical envelopes were prepared using a computer-generated random number table by an investigator not involved in the clinical care of the patients. Subjects were divided into two groups, one group received 100 μg (one half of a 200 μg tablet) misoprostol in the posterior fornix of the vagina and one group received oxytocin for induction. Intravaginal misoprostol administration was scheduled to be repeated every 6 hours until adequate uterine activity was achieved (at least 3 contractions per 10 minutes) but none of the cases needed to use a second dose. After two doses if inadequate contraction was achieved, patients were considered as failure of prostaglandins.[3] Excessive cervical manipulation was not permitted in order to avoid the release of endogenous prostaglandins. In the misoprostol group 3 cases did not agree with this clinical trial and were dropped out of the analysis.

In the oxytocin groups, a 1 ml ampoule containing 10 units was diluted into 1000 ml of lactated Ringer solution. Oxytocin was started at 6 mu/min and was gradually increased in dose increments of 6 mu/min at 20-minute intervals to a maximum of 48 mu/min (according to Williams Obstetrics 2009) until an adequate contraction pattern was obtained.[14] In this group 3 cases were excluded from the study because of detection of an uterine anomaly in their sonography.

All of the patients in both groups were studied prospectively and consecutively. After drug insertion the patients were monitored for signs of labor, contraction of uterus, vital signs and fetal heart rate every 20 minutes. In the misoprostol group, the decision for application of the second tablet was made by assessing uterine contractions and fetal heart rate pattern. If no signs of fetal distress existed on cardiotocography and if there were less than three uterine contractions present during 10 minutes lasting less than 45 seconds the next misoprostol tablet was applied to the posterior vaginal fornix but none of the cases received second doses. All cases had optimal contraction pattern. A successful induction of contractions for labor was defined as contractions that occur at regular intervals and cause changes in cervical dilatation, effacement and station of the presenting part.

Results were evaluated between the two groups regarding maternal and fetal outcomes.

Frequency and duration of tachysystole, hypertonus and hyperstimulation syndrome were assessed. Tachysystole was defined as at least 6 contractions per 10 minutes during 2 consecutive 10-minute periods. Hypertonus was defined as a single uterine contraction lasting 2 minutes or more. Hyperstimulation syndrome was defined as the presence of tachysystole or hyper tonus associated with a non reassuring FHR pattern (fetal tachycardia, late deceleration, sever variable deceleration, or loss of FHR variability). Recognized episodes of hyper stimulation were managed by stopping oxytocin infusion, maternal repositioning, and oxygen administration by face mask. In patients with fetal distress or failed induction it was decided to perform a cesarean section. Labor induction was considered a failure if a patient did not enter the active phase of labor within 72 hours. Data collected included age, parity, gestational age, and initial Bishop scores.

Results were evaluated between the two groups regarding maternal and fetal outcomes. Maternal outcomes assessed include pattern of labor characteristic, route of delivery, and postpartum hemorrhage. Fetal outcomes were fetal distress, 1-5 minutes Apgar scores, and neonatal intensive care unit requirement.

The main hypothesis in our study was that vaginal misoprostol application would shorten delivery interval.

The primary outcome measured was the interval from the start of induction to vaginal delivery, interval from the start of induction to true labor pain, and interval from true labor pain to delivery.

The statistical analysis was performed applying the Student t-test, the chi-square test and Fisher`s exact test, where appropriate. We have considered α (type I error) as 5% in our statistical analysis.

RESULTS

Both groups had similar demographic characteristics including maternal age, parity, and gestational age (Table 1). A total of 108 women were scheduled for labor induction within the study period; 51 were placed in the misoprostol group and 51 in the oxytocin groups. Six patients were excluded from our study because of going to other hospitals (Figure 1). There were no statistical differences between the misoprostol and oxytocin group regarding Bishop scores.

Table 2 shows the characteristics of labor and delivery in both groups. The time between induction of labor and beginning of true labor pain in the oxytocin group was 14.35 hours and in misoprostol group was 9 hours. That is a statistically significant difference ($p = 0.001$). Duration between true labor pain to delivery was 13 hours in the oxytocin group and 7 hours in the misoprostol group, which was significantly shorter in the misoprostol group ($p = 0.04$). Mean time from induction to delivery in oxytocin group was 22 hours and in misoprostol group was 11.5 hours ($p < 0.001$). No significant differences were observed in the incidence of clinically significant fetal heart rate abnormalities between the two groups. No differences in the incidence of delivery type were observed between the two groups. In the misoprostol group 4 patients needed cesarean section. Two of four cesarean sections were performed for fetal distress due to placenta abruption and two for fetal distress. In the oxytocin group one patient had cesarean section for fetal distress, 4 patients for placenta abruption and 3 for thick meconium. All of the cases in the misoprostol group needed a single dose for active labor. Passage of meconium was more in the misoprostol group, but it did not affect the fetal heart rate tracing and fetal Apgar.

The neonatal results are summarized in table 3. There were no statistical differences between the misoprostol and oxytocin group with regard to 1-5 Apgar scores, the need of neonatal intensive care unit, and fetal distress. Two patients in the misoprostol group and one patient in the oxytocin group had cesarean section for fetal distress. No neonate was admitted to the NICU.

Table 1. Demographic characteristics of the patients

	Oxytocin(n = 51)	Misoprostol(n = 51)	P-value
Age (yr)	28 ± 5.3	29 ± 5.3	p > 0.05
Weight (kg)	75.7 ± 12	70.0 ± 6.6	p > 0.05
Height (cm)	161.1 ± 5.2	161.9 ± 3.8	p > 0.05
Gestation (week)	40 ± 0.9	40 ± 1.1	p > 0.05
Initial Bishops score	4.1 ± 0.7	4.0 ± 0.9	p > 0.05

Table 2. Labor and delivery characteristics of patients in two groups

	Oxytocin	Misoprostol	P-value
Mean induction-true labor interval (h) ± S.D.	14.35	9	p = 0.001
Mean true labor-delivery interval (h) ± S.D.	13	7	p = 0.04
Mean induction- delivery interval (h) ± S.D.	22	11.5	p < 0.001
FHR abnormality (n, %)	1(2%)	3 (5.8%)	p = 0.001
Vaginal delivery (n, %)	45 (86.3%)	48 (92.2%)	p = 0.001
Cesarean section (n, %)	7 (13.7%)	4 (7.8%)	p = 0.001
Postpartum hemorrhage (n, %)	4 (7.8%)	7 (13.7%)	p = 0.001

Table 3. Neonatal outcomes

	Oxytocin	Misoprostol	P-value
Apgar score at 1 minute	8.94	8.98	0.32
Apgar score at 5 minutes	9.03	9.0	0.312
Fetal distress	1	2	0.5
NICU admission	0	0	0

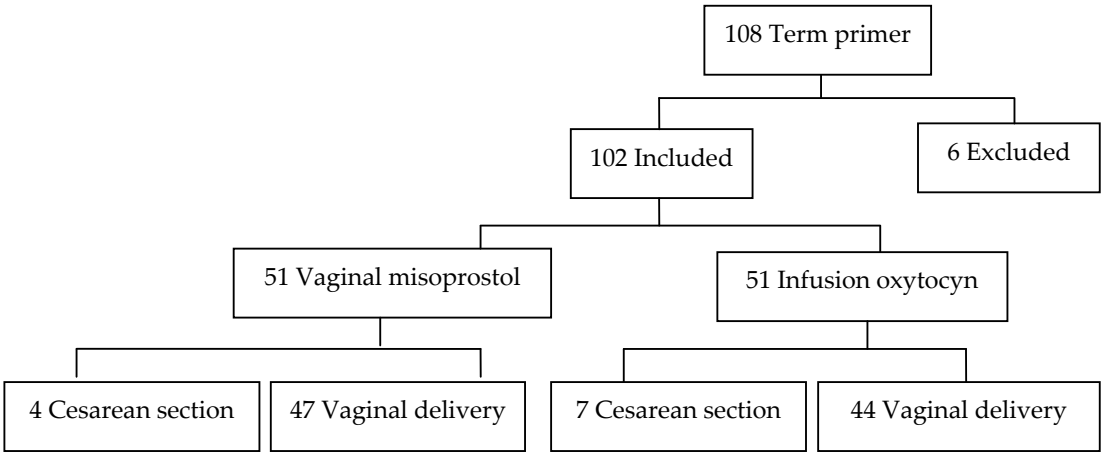

Figure 1. Flow chart of study

DISCUSSION

Prostaglandins are effective and useful agents in promoting cervical ripening and facilitating labor induction, and their use is not new. PGE2 has been used for almost three decades to promote ripening and labor induction.[17,18] However, their analogs have important disadvantages for the developing countries as they are very costly and are unavailable for clinical use in many countries. Moreover, they are unstable compounds and they need refrigeration to preserve their potency. The use of misoprostol, a prostaglandin E1 analog, has been found to be safe, effective, very stable and extremely inexpensive.[19] Margulies et al. used it to induce labor for the first time in 1992.[20] Since then large numbers of studies have been performed to describe the potential complication, to compare the various routes of administration, and define the factors affecting its efficacy and the appropriate dose. The results of these studies have shown that misoprostol is effective in cervical ripening and labor induction.[21-26]

This study was designed to compare the efficacy and adverse effects of 100 μg intravaginal misoprostol with oxytocin in term pregnant women who required induction of labor with low Bishop scores.

The results show that 100 μg of vaginal misoprostol resulted in a shorter interval from induction to delivery compared to a high dose of oxytocin. An American study also demonstrated that the average time interval until the occurrence of vaginal delivery was shorter for misoprostol (50 μg at 4 hour intervals) than for oxytocin (11 hour intervals versus 18 hour), presenting a statistical significance.[27] Many other studies have found the same results.[28,29] One other study used 100 μg intravaginal misoprostol for term pregnancy and found that it is effective for labor induction in term pregnancy without adverse effect on the mother and newborn.[30] These findings are consistent with the present results.

On the contrary, Ferguson et al. demonstrated that misoprostol (25 μg at 4 hour intervals) and low-dose oxytocin appear to be equally effective for cervical priming.[31] Moreover, Escudero and Contreras reported a shorter interval from treatment to delivery with oxytocin, compared with misoprostol.[32] Fonseca et al. found that the mean time from treatment to delivery was shorter for the low-dose oxytocin group, compared with the misoprostol (25 μg at 4 hour intervals , maximum 3 doses) group and vaginal delivery rates were also similar.[33] Differences in dosages, administration interval, and vaginal PH are suggested to be relevant in explaining the difference in outcome. The other main outcome of this study was the induction-true labor and true labor-delivery intervals; it showed that both of them were shorter in the misoprostol group.

In the current study, the rates of vaginal delivery and cesarean delivery were equal in the misoprostol group as compared to oxytocin group. In the present study the rate of cesarean delivery in both groups were lower than the above mentioned studies. This may be due to exclusion of patients with pelvic dystocia and cephalopelvic disproportion from both groups. Some comparative studies between misoprostol and oxytocin have shown that the incidence of cesarean delivery is higher in the oxytocin group.[27,34]

We found no case of uterine hyperstimulation or hypertonus, but tachysystole occurred in 3 cases in the misoprostol group and 1 case in the oxytocin group. Our study did not have the aim of determining the statistical significance of this factor.

The rates of placental abruption and postpartum hemorrhage were not statistically different. Apgar scores in both groups had no significant differences, and there was no case of asphyxia and intensive care unit admission.

CONCLUSIONS

We found that intravaginal misoprostol 100 μg safely and effectively induces labor. This drug is recommended for parturient women with Bishop score ≤ 6. Moreover, the use of this drug could produce several beneficial effects; particularly a decrease in the induction delivery interval and it is safe for mother and fetus in selected cases. However, we recommend that more studies be undertaken with more cases in order to confirm our conclusion.

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