
A comparison of vaginal misoprostol and prostaglandin E₂ for induction of labour at term

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Abstract: Our objective was to compare the efficacy of vaginal misoprostol and tablet PGE₂ for induction of labor at term. **Methods:** In this RCT a total of 140 women at term gestation were given either misoprostol (50 mcg) or prostaglandin E₂ (3 mg) for induction of labour. The study was conducted at the Gynae/Obstetrics department, PAEC Hospital Islamabad, in a period of six months. All women requiring induction, having gestational age > 37 weeks, singleton pregnancy with cephalic presentation, bishop score < 6 and reassuring fetal heart rate tracing were included in the study. The study outcome was measurement of efficacy in terms of induction delivery interval, number of vaginal deliveries achieved within 24 hours, mode of delivery, total doses, need for oxytocin and number of successful inductions. **Results:** The mean age and average gestational age was similar in the two groups of patients. In group A (51.4%) patients required two doses while in group B (32.9%) took two doses. Similarly, (60%) patients required oxytocin in group A compared to (50%) in group B. The mean delivery induction interval was 10.8 hours (650 minutes) in group A compared to 9.01 hours (541 minutes) in group B; and this difference in two means is statistically significant. In group A (18.5%) patients required emergency cesarean section while in group B (27.1%) needed cesarean section. The major indication for emergency cesarean section in group B was fetal distress. Therefore misoprostol can play a very important role in the practice of obstetrics and gynecology in resource depleted countries where other prostaglandins are expensive and storage at low temperature is a problem.

Keywords: Misoprostol, Prostaglandin E₂, Term Pregnancy, Labour Induction

1. Introduction

Induction of labour involves artificial initiation of regular uterine contractions before spontaneous onset of labor in order to generate progressive cervical dilatation, effacement and subsequent delivery of the baby [1]. Labor induction is usually indicated when benefits of delivery to the mother or fetus outweigh the potential risks of continuing the pregnancy.

There are various medical, obstetric or social indications of labor induction [2]. The common obstetric indications include prolonged pregnancy [3], PIH, preterm rupture of membranes and maternal diabetes mellitus.

The most recent evidence base studies report the annual rate of labour induction varies from 9.5 to 33.7% of all pregnancies [4]. In Australia nearly 27% pregnant women have had their labour induced [5] for a variety of reasons. A successful vaginal birth is less likely in the absence of a ripe or favorable cervix. Therefore, cervical ripening or

preparedness for induction should be assessed before a regimen is selected. Assessment is accomplished by calculating a bishop score. When the bishop score is < 6, it is recommended that a cervical ripening agent should be used before labour induction [4].

Induction of labour at term in the presence of an unfavorable cervix is associated with an increased risk of failed induction and cesarean section. Prostaglandins have been used for labor induction. Amongst many types, prostaglandin E₂ (PGE₂) is the most commonly used and very effective agent for labor induction. It is available in various formulations including tablets, gels and passeries [7]. However, natural prostaglandins are inconvenient to use, expensive and difficult to store as they require refrigeration [8,9].

There has been a growing interest in using misoprostol, a PGE₁ analogue, as an alternative agent for labor induction. Although not approved for such use but misoprostol has been widely used for cervical ripening and induction of labor [10,11]. It can be administered through oral, vaginal and

rectal routs [12]. Advantages over other agents include its low price, stability at room temperature and availability in secured tablet form [13]. The rate of successful induction with misoprostol of up to 98.7% and with prostaglandin E₂ of up to 91.4% [3].

The aim of our study was to evaluate the efficacy of vaginal misoprostol and PGE₂ and to establish the fact that misoprostol can play a very important role in the practice of obstetrics and gynecology in resource depleted countries where other prostaglandins are expensive and storage at low temperature is a problem.

2. Methodology

Objective: To compare the efficacy of vaginal misoprostol and tablet PGE₂ for induction of labour at term. The outcome measures of efficacy include induction delivery interval, number of vaginal deliveries achieved within 24 hours, mode of delivery, total doses need for oxytocin, and the number of successful and failed inductions.

3. Hypothesis

Induction delivery interval with vaginal misoprostol is shorter than that of prostaglandin E₂.

4. Material and Methods

Study design:

Randomized controlled trial

Setting:

The study was conducted in the Gynae/Obstetrics department, PAEC Hospital, Islamabad.

Duration:

The study duration was six months from 15th July 2010 to 15 Jan 2011.

Sample size:

Sample size = 138 patients (70 patients in each group) (sample size was calculated by using WHO sample size calculator taking level of significance 5%, power of test 80%, anticipated population proportion p₁ = 98.7% [3] and anticipated population proportion p₂ = 91.4% [3].

Sampling technique:

Consecutive or purposive sampling

Sample Selection:

Inclusion criteria:

All the women requiring induction of labor for medical, obstetric or other indications with:

- Gestational age ≥ 37 weeks (by dates or ultrasonography)
- Singleton pregnancy with cephalic presentation
- Bishop score ≤ 6
- Reassuring fetal heart rate tracing

Exclusion criteria:

- Ruptured membranes
- Previous cesarean section or any other uterine scar
- Placental abruption/placenta preavia

- Fetal congenital anomalies
- Any contraindications to the use of prostaglandins

Data Collection Procedure:

After approval from the ethical committee of the hospital, all women selected for induction of labor fulfilling the inclusion criteria were recruited in the study. A written informed consent was taken from the patient after informing her about purpose of the study. All patients were randomized into two groups (group A or group B) with 70 patients in each group using computer generated random table.

History, examination and ultrasonography were done for the confirmation of inclusion criteria i.e. gestational age ≥ 37 weeks, singleton pregnancy, cephalic presentation, intact membranes and bishop score ≤ 6 , and to exclude the confounding variables. Fetal wellbeing was assessed by CTG prior to administration of every dose of misoprostol or PGE₂.

Women randomized to group A (PGE₂) received tablet PGE₂ (3 mg), placed in the posterior fornix of vagina. After 6 hours, bishop scoring was done and if patients did not progress to active labor, maximum of two doses was given (6 mg).

Women randomized to group B (Misoprostol group) received tablet misoprostol 50 mcg (1/4th of tab), placed in the posterior fornix of vagina and dose was repeated 6 hourly if patient did not progress to active labor. Maximum of 4 doses were given.

Partogram recording progress of labor was maintained. Augmentation of labor with amniotomy and oxytocin were carried out whenever indicated by partogram. Pediatrician was informed prior to delivery. If the patient was failed to enter into the active phase of labor after maximum doses of both the drugs (24 hours), Induction was considered as failed and she was offered cesarean section. All the data was recorded.

Data Analysis:

All the data was analyzed by using SPSS version 12. Mean \pm SD was calculated for age of patient (in years), gestational age (in weeks), total doses, induction delivery interval (in hours). Frequencies and percentages were calculated for gravidity, parity, mode of delivery, use of oxytocin, failed and successful induction. Student's t-test was used to compare induction delivery interval between misoprostol and PGE₂ groups. A p-value of < 0.05 was taken as statistically significant.

5. Results

A total of 140 women at term gestation were enrolled and divided into Group A, given PGE₂ (n=70) and Group B, given Misoprostol (n=70).

The overall mean age of women was 27.3 ± 3.9 years. (p-value = 0.11). In group A the mean \pm SD gestational age was 272.3 ± 11.9 days while in group B it was almost similar 272.3 ± 10.5 days (p-value = 1.0). The difference in gravidity not significant.

The indications of induction of labor were compared between the two study groups as shown in Table I. In group

A 36 (51.4%) patients took one dose of PGE₂ while 34 (48.6%) patients needed two doses. Similarly, in group B 32 (45.7%) patients took one dose of misoprostol, 23 (32.9%) patients took two, 8 (11.4%) patients took three and 7 (10.0%) patients took four doses.

These patients were augmented with oxytocin in group A 42(60%) patients were given oxytocin while in group B 35 (50%) patients were given oxytocin, this difference was statistically not significant (p-value = 0.23). The duration of labor and induction delivery interval was analyzed in the two study groups. In group A, the mean \pm SD interval between induction and delivery was 10.8 ± 1.89 hours (650.9 ± 113.8 minutes) compared to 9.03 ± 2.04 hours (541.8 ± 122.9 minutes) in group B, this difference was statistically significant (p-value = <0.001). Similarly the mean duration of active phase of labor in group A was 4.09 ± 1.43 hours (245.9 ± 86.2 minutes) compared to 3.60 ± 1.52 hours (216.2 ± 91.2 minutes) in group B, and this difference in the means between the two groups was also found to be statistically significant (p-value = 0.04).

Induction of labour was successful in almost similar proportion in both study groups. The indications for cesarean delivery. The mode of delivery was comparable. Table II.

6. Discussion

Induction at term in the presence of an unfavorable cervix is associated with an increased risk of failed induction and cesarean section [13,14].

The rate of induction depends on geographical location, at current in many centers it is more than 20% [15,16]. The potential effect of induction is an increased risk of caesarean delivery and its associated complications [17-22]. Nulliparous women with an unfavorable cervix, or low Bishop Score, particularly are at high risk of caesarean delivery [23]. In an unfavorable cervix with a low bishop score ripening of cervix is recommended, to increase the likelihood of successful induction and smooth vaginal delivery [17-19].

Many therapeutic regimens and procedures are available for performing labor induction with variable efficacy. Prostaglandin E₂ (PGE₂) given vaginally or intracervically has been found effective for cervical ripening [24]. Misoprostol a prostaglandin E₁, analogue has also gained worldwide acceptance for cervical ripening [25]. Misoprostol was marketed as a gastric cytoprotective agent but its off label use for induction has been endorsed by American College of Obstetricians and Gynecologists and also by the Royal College of Obstetrician and Gynecologists [26, 27]. Misoprostol is low priced and remains stable at room temperature, thus, suitable for the environments and communities of developing and underdeveloped countries which are cash strapped and resource less. The current study was planned to evaluate the efficacy of vaginal misoprostol and PGE₂ and to establish the fact that misoprostol can play a very important role in the practice of obstetrics and gynaecology in our settings where other prostaglandins are

expensive and storage at low temperature is an issue.

The average age of study patients was 27.3 years. This is comparable to the ages in other studies. In the study by Wasim. T and Siddiq. S which was conducted in a similar setting in Lahore it was revealed that patient's average age in PGE₂ group were 25 years and misoprostol group 26 years [28]. In a systematic review to compare misoprostol with prostaglandin E₂ in the induction of labor it was observed that the average ages of women were a bit older than our settings (29 years) [29], (29.5 years) [30] and (30.3 years) [31]. This difference could be due to the fact that in our part of the world the trend of women marriages is at an early age compared to the developed world.

The gestational age of patients in the PGE₂ group was 272.3 days (38.9 weeks) and in misoprostol group as well it was 272.3 days (38.9 weeks). In the study by Beigi A and colleagues on cervical ripening with misoprostol at term the average gestational age of patients was 39.6 weeks [32]. In the current study approximately 47% patients were nulliparous in group A and 48% patients in group B. Similarly a previous study by Beigi A et al found out that about 50% of their patients in misoprostol and placebo groups each presented with nulliparity [32]. Other studies from the western world have also presented a similar trend, except for few who have found high incidence of nulliparous women presenting for induction of labor. A study from USA reported that 83.2% of their patients were nulliparous [33]. Another study from Spain also reported a high incidence of up to 64% patients presenting as nulliparous [34].

In our study oxytocin was required by 60% cases in group A and 50% in group B. A systemic review found out in 8 comparative studies of misoprostol that it is less likely to require oxytocin when used for induction of labor compared to other prostaglandins [35].

Induction of labor was successful in a similar number in both study groups (91.4%) and (90.0%) in group A and group B respectively. Our results are comparable with Wasim T's study, where they revealed that induction was successful in 84% cases with PGE₂ and in 96% cases that had misoprostol [28].

The average duration of induction delivery interval was 10.8 hours (650.9 minutes) in PGE₂ group compared to 9.0 hours (541.8 minutes) in misoprostol group. This duration is in continuation with previous reports on the topic. In a study on oral misoprostol for induction of labor the mean induction delivery interval was 8.7.

hours [32]. A study by De Aquino MMA and Cecatti JG in Sao Paulo, Brazil the investigators compared misoprostol with oxytocin for induction of labor in term and post-term pregnancies. They revealed that misoprostol had significantly less (10.6 hours) induction delivery interval compared to oxytocin (14.8 hours) [36].

The misoprostol group required more emergency cesarean section compared to the PGE₂ group but this difference was not statistically significant. The significant indication for cesarean delivery was fetal distress in 15.7% cases in misoprostol group and 4.2% cases in PGE₂ group.

7. Conclusion

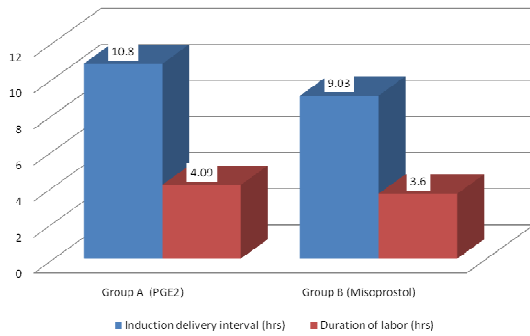


Figure 1. Comparison of mean induction delivery interval and duration of active phase of labor between study groups

In our study induction delivery interval was significantly low in misoprostol group as compare to PGE2 group. Moreover, it was as effective as PGE2 in achieving successful induction of labor in term pregnant women. The difference in the rate of cesarean section between two groups was also not significant. However, the main indication for emergency cesarean section was fetal distress in misoprostol group.

Therefore Misoprostol can play a very important role in the practice of obstetrics and gynecology in resource depleted countries where other prostaglandins are expensive and storage at low temperature is a problem.

Table 1. Indications for induction of labour in the two study groups

	Group A(PGE2) n = 70	Group B (Misoprostol) n = 70	p-value
Gestational diabetes mellitus	6 (8.5%)	6 (8.5%)	0.18
Decreased fetal movement	2 (2.9%)	2 (2.9%)	
Irregular labour pains	13 (18.5%)	15 (21.4%)	
Oligohydramnios	6 (8.5%)	13 (18.5%)	
PIH	17 (24.3%)	15 (21.4%)	
Polyhydramnios	0 (0.0%)	2 (2.9%)	
Postdate	17 (24.3%)	16 (22.9%)	
Gestational thrombocytopenia	0 (0.0%)	1 (1.4%)	
Obstetric cholestasis	2 (2.9%)	0 (0.0%)	
Bad obstetric history	3 (4.3%)	0 (0.0%)	
Conceived on treatment/ precious pregnancy	3 (4.3%)	0 (0.0%)	
Increased uric acid	1 (1.4%)	0 (0.0%)	

Table 2. Indications of cesarean section and comparison of delivery mode between the two groups

Indications of caesarean section	Group A (PGE2) n = 70	Group B (Misoprostol)n = 70	p-value
Failed induction	6 (8.5%)	7 (10.0%)	0.04
Fetal distress	3 (4.2%)	11 (15.7%)	
Failure to progress	4 (5.7%)	1 (1.4%)	
Comparison of Mode of delivery between the two groups,	Group A (PGE2) n = 70	Group B (Misoprostol) n = 70	p-value
SVD	23 (32.8%)	19 (27.1%)	0.31
SVD with episiotomy	29 (41.4%)	30 (42.8%)	
Vacuum delivery	3 (4.2%)	2 (2.8%)	
Emergency LSCS	13 (18.5%)	19 (27.1%)	
Outlet forceps delivery	2 (2.8%)	0 (0.0%)	

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