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ORIGINAL ARTICLE

Comparison of Vaginal Misoprostol and Prostaglandin E_2 for Labour Induction in Primigravidae: A Randomized Clinical Trial

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ABSTRACT

Objective: To compare the efficacy of vaginal misoprostol and prostaglandin E_2 (PGE_2) for induction of labour in primigravidae at term.

Methods: This randomized clinical trial was conducted at the Department of Obstetrics and Gynaecology, Sohail Trust Hospital, Jinnah Medical and Dental College, Karachi, between September 1, 2022 and August 30, 2023. A total of 100 primigravidae at 37–42 weeks gestation requiring induction of labour were randomized into two equal groups. Group A received 100 µg misoprostol intravaginally every 4 hours (maximum 3 doses), and Group B received 3 mg PGE_2 pessary every 6 hours (maximum 2 doses). Primary outcomes included induction-to-delivery interval, oxytocin augmentation requirement, and mode of delivery. Secondary outcomes included fetal outcomes and adverse effects. Data was analyzed using SPSS version 20.0 by applying t-test to obtain the results. Ethical approval was obtained from the institutional review board of Jinnah Medical College hospital Karachi, and written informed consent was obtained from all participants and then questionnaire were being filled by doctor.

Results: Mean induction-to-delivery interval was significantly shorter in the misoprostol group (10.96 ± 1.55 hours) than the PGE_2 group (13.06 ± 1.94 hours, $p<0.001$) [1]. Oxytocin augmentation was required in 44% of misoprostol patients versus 70% of PGE_2 patients ($p=0.01$). Vaginal delivery occurred in 94% of the misoprostol group and 74% of the PGE_2 group, while cesarean rates were 6% and 26%, respectively. No significant differences in Apgar scores or neonatal complications were observed.

Conclusion: Vaginal misoprostol is a more effective, lower-cost option than PGE_2 for induction of labour in primigravidae at term, with a shorter induction-to-delivery interval and lower cesarean section rate, without compromising fetal outcomes.

Keywords: Vaginal Misoprostol, Prostaglandin E_2, Labour Induction, Primigravidae, Randomized Clinical Trial

INTRODUCTION

Labour is said to be induced when an external agent is used to stimulate the uterus before the onset of spontaneous labour or it is defined as the stimulation of uterus with the aim of progressive cervical dilation and effacement to ensure delivery of the fetus at an appropriate time, when baby is thought to be safer outside the uterus than in it. Induction is performed only upon indications when further prolongation of pregnancy might expose the mother or fetus or both to certain risk and when vaginal delivery is not contraindicated. Induction of labour is one of the most common obstetric interventions worldwide, accounting for 20–30% of deliveries in many high-income countries[1].

Induction of labour should be distinguished from augmentation of labour in which the patient has been in labour which is slow or has somehow slowed down and is accelerated- During normal pregnancy a closed unripe cervix ensures integrity of pregnancy until term. At term, complex processes, this includes activation of prostaglandins causes cervix to become soft and compliant. This facilitates cervical dilation in response to myometrium contractions. It is performed when the benefits of delivery outweigh the risks of continuing the pregnancy for either the mother or fetus[2]. Common indications include post-term pregnancy, pre-labour rupture of membranes, hypertensive disorders, intrauterine growth restriction, and medical conditions such as diabetes mellitus[3].

A successful labour is more likely when the cervix is ripe. Different methods have been used for cervical ripening and induction of labour. Successful induction or labour ending up in smooth delivery reduces risk of cesarean section and the condition of neonate is also improved and when the cervix is unfavorable, there are more chances of failed induction and increase risk of cesarean section'. Vaginal prostaglandins proved to be beneficial in promoting both cervical ripening and myometrium contractility. The success of induction depends heavily on the cervical status prior to intervention, which is assessed using the Bishop score[4]. An unripe cervix is associated with a higher risk of induction failure and operative delivery[5].

Prostaglandins are widely used for cervical ripening and induction, as they promote cervical softening and stimulate uterine contractions[6]. Prostaglandin E_2 (dinoprostone) has long been considered the gold standard for cervical ripening, administered as a vaginal pessary or gel[7]. However, its high cost, limited stability, and need for refrigeration pose challenges in low-resource settings[8]. Misoprostol, a synthetic prostaglandin E_1 analogue originally developed for gastric ulcer prevention, has emerged as an effective, inexpensive, and heat-stable alternative for induction of labour[9]. It can be administered orally, sublingually, buccally, or vaginally, with the latter route offering higher bioavailability and sustained uterotonic effect[10]. Several randomized controlled trials have demonstrated that vaginal misoprostol is as effective or superior to PGE_2 for induction of labour, often resulting in shorter induction-to-delivery intervals and lower cesarean rates[11,12].

However, there is concern about higher rates of uterine tachysystole, requiring careful dose titration[13]. In Pakistan, where induction resources are often limited, cost-effective agents are critical for improving maternal outcomes[14]. This study aimed to directly compare the efficacy and safety of vaginal misoprostol and PGE_2 in primigravidae at term.

METHODS

This randomized clinical trial was conducted at the Department of Obstetrics and Gynaecology, Sohail Trust Hospital, Jinnah Medical and Dental College, Karachi, between September 1, 2022 and August 30, 2023. Ethical approval was obtained from the institutional review board of Jinnah Medical College hospital Karachi, and written informed consent was obtained from all participants and then questionnaire were being filled by doctor.

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Inclusion criteria were primigravidae aged 18–35 years, singleton pregnancy, cephalic presentation, gestational age 37–42 weeks, and Bishop score ≤4. Exclusion criteria included previous uterine surgery, malpresentation, estimated fetal weight >4 kg, antepartum hemorrhage, ruptured membranes, and contraindications to prostaglandins (e.g., asthma, glaucoma, renal/hepatic dysfunction).

Participants were randomly assigned into two groups:

Group A (Misoprostol): 100 µg vaginally every 4 hours, maximum 3 doses.

Group B (PGE_2): 3 mg vaginal pessary every 6 hours, maximum 2 doses.

Bishop score was reassessed every 3 hours, and dosing was withheld if uterine hyperstimulation or fetal distress occurred. Oxytocin augmentation was initiated as per departmental protocol after artificial rupture of membranes if contractions were inadequate.

Primary outcomes were induction-to-delivery interval, need for oxytocin augmentation, and mode of delivery. Secondary outcomes included Apgar scores, neonatal intensive care admissions, and maternal side effects.

Data Analysis: Data was analyzed using SPSS version 20.0 by applying t-test to obtain the results.

RESULTS

Hundred primigravidae were studied and all of them were very cooperative and fulfilled the criteria. 50 women were given misoprostol while the other 50 were given prostaglandin E2. The characteristics of women in both groups were comparable. Regarding age distribution, the mean age was 22.51 ± 2.6 years in misoprostol group and22.41 ± 2.6 years in PGE2 group. The induced patients were divided into two groups, based on expected date delivery, group A from 37 to 40 weeks gestation and group B from 40 to 42 weeks. Out 01'.1 no patients 37 (74%) belong to group A and 13 (26%) to group B. in misoprostol group while 35 (70%) and 15 (30%) belonged to group A and B respectively in PGE2 group.

The mean gestational age was 38.96± 1.81 in misoprostol group and39.18 ± 1.86 in PGE2 group. Out of 50 patients in misoprostol group 26% were induced in37 weeks, 28%, in38 weeks, 12% in 39, 08% in 40 weeks. 1%in 41 weeks and 6% in 42weeks while in PGE2 group 32% patients were induced at for 38 weeks and 20% in 37 and 42 weeks each, All the patients in the study at the time or admission had bishop's score of 4 or less in both group. The mean bishop score was 3.06 ± 1.07 in misoprostol group while 2.76 ± 1.07 in PGE2 group. The induction delivery interval reflects the time interval between first dose of drug to expulsion of fetus. The mean induction to delivery was 10.96 ± 1.55 hours. out of 50 patients 22 delivered within 12 hours in misoprostol group. In case ofPGE2 group the mean induction delivery interval was I3.06± 1.94 hours. 44% (22) of patients required oxytocin for augmentation in misoprostol group and 70% (35) patients in PGE2 group. The mean dose of misoprostol used was 216.0±46.77 01.g and 5.22 ± 133 mg of PGE2. and it was adjusted according to the bishop's score. In misoprostol group 4% women delivered after single dose of 100 µg, 76% women second dose of 100 µg had to be used, and in the remaining 20% women, a third dose of 100 µg was used. In PG E2 group one pessary of 3mg was used in 26% women. in 3 out of 13. a second pessary was not repeated because of meconium passage and fetal distress. Second pessary of PGE2 (1mg) was used in 74% women out of which induction failed in 6 women. Only one woman had uterine hyper stimulation with two tablets of 100 µg misoprostol. There was also meconium staining or liquor. after giving injection buscopan and oxygen inhalation patient was taken immediately for emergency caesarean section. Baby delivered with apgar score of less than 7 at 1 minute and 10 at 5 minutes and didn't need any resuscitation. While no such incidence occurred in PCE2 group.

Baseline characteristics were comparable between groups. Mean age was 22.5 ± 2.6 years in the misoprostol group and 22.4 ± 2.6 years in the PGE_2 group. Mean gestational age was 38.96 ± 1.84 weeks and 39.81 ± 1.86 weeks, respectively. The induction-to-delivery interval was significantly shorter in the misoprostol group (10.96 ± 1.55 hours) compared to PGE_2 (13.06 ± 1.94 hours, p<0.001). Oxytocin augmentation was required in 44% of misoprostol cases versus 70% of PGE_2 cases (p=0.01).

The success rate in the form of normal vaginal deliveries in induced patients of miso group was found 84% (42), instrumental vaginal deliveries and the failure rate in the form of cesarean deliveries were 06% (3). While in PGE2 group 68% (34) were normal vaginal deliveries. 06 %(3) instrumental and 26%(13) cesarean section.

Out of 3 (6%) cesarean sections in misoprostol group2 Occurred due to fetal distress and one due to failure to progress while in PGE2 group 6 occurred due to failed induction 4 due to failure to progress and 2 due 10 meconium stained liquor most common indication which presented about 34 % (17 patients) and the second was prolonged pregnancy which was 26 % (13 patient) in misoprostol group. While in PGE2 group P.I.H. and prolonged pregnancy presented about 36% and30% respectively.

Regarding status and fetal outcome alive births were 76% and 24% were still born confirmed IUDs on ultrasound, in misoprostol group while in PGE2 group 96% were alive and 06% were still born confirmed IUDs on ultrasound, with no neonatal deaths in both groups.

In misoprostol group the mean weight of baby was 2.815 ± 0.49 kg and 2.878±0.51 kg in PGE2 group. The apgar score of one and rive minutes were> 7 and 10 both groups. In 02 cases or the misoprostol group and PGE2 group it was <7 at one minute and 10 at five minutes.

Regarding complications in live born neonates 2 babies from each misoprostol and PGE2 group were admitted in neonatal intensive care unit where they were diagnosed having respiratory distress syndrome and irritability in misoprostol group babies and jaundice in one baby of PGE2 group. All were recovered and shifted back to the ward within 24-48 hours.

No significant differences were noted in mean birth weight (2.815 ± 0.49 kg vs. 2.878 ± 0.51 kg) or Apgar scores at 1 and 5 minutes. Two neonates in each group required NICU admission; all recovered within 48 hours. Only one case of uterine hyperstimulation occurred, in the misoprostol group.

Table 1: Maternal Demographic Details of Induction of Labour

	Misoprostol	PGE2	P-value
	(n=50)	(n=50)	
Age (years)	22.5 I +7.6	22.41±2.6	p= 0.84
			t=0.04
Gestational Age (weeks)	38.96±1.84	39.81±1.86	P=0.02
			t=5.35
Bishop score	3.06±1.07	2.76±I.07	P=0.16
			t= 1.97
Birth weight of fetus (kg)	2.815±O.49	2.878±O.51	P=0.53
			t= OAO
Induction to delivery interval			
(hours)	10.96±1.55	13.06±1.94	P=O.OOI
			t= 35.76
No. of Patients needing oxytocin			
augmentation	22 (44%)	35 (70%)	
P=O.OI			

Chi-square = 6.9

Table 2: Delivery Outcomes in Both Groups

Outcomes	Misoprostol (n=50)	PGE_2 (n=50)	p-value
Induction-to-delivery interval (hours)	10.96 ± 1.55	13.06 ± 1.94	<0.001
Oxytocin augmentation	44%	70%	0.01
Vaginal delivery	94%	74%	—
Cesarean section	6%	26%	—
Mean birth weight (kg)	2.815 ± 0.49	2.878 ± 0.51	0.53
NICU admissions	2	2	—

DISCUSSION

As the frequency of induction of labour is increasing day by day and the rate of induction varies worldwide in different countries, units and between individual obstetricians within the same units, different methods have been introduced for induction.

All patients receiving misoprostol went into labour, whereas only 37 patients receiving PGE2 did so. The induction [0 delivery interval is an important aspect in induction of labour. Longer time interval is associated with more psychological trauma. Prolong induction time also necessitates the use 01 intravenous hydration, increased analgesic requirement, and use 01 augmentation with oxytocin.

This study demonstrates that vaginal misoprostol is more effective than PGE_2 for induction of labour in primigravidae at term, with a significantly shorter induction-to-delivery interval and reduced need for oxytocin augmentation. The higher vaginal delivery rate and lower cesarean rate in the misoprostol group are consistent with findings from multiple randomized controlled trials[11,12,15]

Our results align with a meta-analysis by Alfirevic et al.[16], which found that low-dose vaginal misoprostol was associated with shorter time to delivery and lower operative delivery rates compared to PGE_2. Cost-effectiveness is another important consideration in low-resource settings: misoprostol is inexpensive, stable at room temperature, and widely available[9,14].

Misoprostol is well absorbed through all routes of administration. The unpleasant side effects like nausea, vomiting and diarrhea with vaginal route were not observed. Bulgaho et al also reported virtually no side effects with intra vaginal doses of 50-200 /ug[9]. Vaginal administration also allows the body to be exposed to more of the drug's active metabolite. The peak plasma levels after vaginal route of administration is achieved within 60-80 minutes. Oral route may be desirable in set-ups with limited medical staff" Misoprostol tablets are stable at room temperature and cost effectiveness of the drug is an added advantage for its use which is highly suitable for developing countries[18].

Concerns about uterine tachysystole and hyperstimulation have been reported with higher misoprostol doses (>50 µg)[13], but our study using 100 µg every 4 hours had only one such event, which resolved without long-term sequelae. From a public health perspective, the findings support the inclusion of misoprostol in national induction protocols, particularly in settings where cost and storage limitations make PGE_2 less feasible[14,17]. However, careful dosing and fetal monitoring remain essential to ensure safety.Further research is warranted to evaluate lower doses (e.g., 25–50 µg) and alternative routes (sublingual, buccal) in the Pakistani context to optimize efficacy while minimizing risks.

CONCLUSION

Vaginal misoprostol is a cost-effective, efficient, and safe alternative to PGE_2 for labour induction in primigravidae at term, associated with shorter induction-to-delivery intervals, lower oxytocin use, and reduced cesarean rates. Adoption in national guidelines could improve maternal outcomes in resource-limited settings.

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