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Original Research Article

Comparison between effectiveness of sublingual misoprostol and intracervical dinoprostone gel for induction of labour in pregnant women

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ABSTRACT

Background: This hospital-based, prospective, comparative interventional study aimed to compare the effectiveness of sublingual misoprostol and intracervical dinoprostone gel for induction of labor in primigravida women.
Methods: A total of 100 patients were alternately assigned to induction with either Misoprostol 25mcg 6 hourly or dinoprostone Gel 0.5mg 6 hourly.
Results: The induction delivery interval was significantly longer in the dinoprostone group compared to the misoprostol group. The incidence of fetal distress was slightly higher in the Dinoprostone group, but the difference was not statistically significant. There were no significant differences between the two groups in the incidence of respiratory distress, birth asphyxia, and APGAR 1 MIN <6.
Conclusions: This study suggests that sublingual misoprostol (a type of prostaglandin E1, or PGE1) is more effective than intracervical dinoprostone gel (a type of prostaglandin E2, or PGE2) for cervical ripening and induction of labor.

Keywords: Sublingual misoprostol, Intracervical dinoprostone gel, Labor induction, Oxytocin augmentation, Caesarean section

INTRODUCTION

Because of their dual function of cervical ripening and producing uterine contractions, prostaglandins (PG) are attractive medications for inducing labour. Prostaglandins have been used extensively for cervical ripening, with a wide range of PG classes, dosages, and methods of administration.[1,2] Misoprostol and Dinoprostone Gel are the only prostaglandin analogues currently available for cervical ripening. Misoprostol can be administered orally, sublingually, vaginally, or rectally. Dinoprostone gel is given intracervically. Because it skips first-pass metabolism, sublingual misoprostol has a high effectiveness. Except for increased caesarean rate and hyperstimulation, researchers have demonstrated that intracervical PGE1 is as effective as PGE2. Because the intracervical route is more difficult for the patient, if another medicine, such as Misoprostol, has an easier route of administration with the same or greater efficacy as Dinoprostone gel, it can be utilised to make the induction process more convenient for the patient. Thus, the purpose of this study was to examine the efficacy of sublingual PGE1 and intracervical PGE2.

In obstetrics, induction of labour (IOL) is a common operation. The World Health Organization defines IOL as the artificial induction of labour prior to its spontaneous beginning at a viable gestational age, with the goal of achieving vaginal birth in a pregnant woman with intact membranes. IOL accounts for around 25% of all

deliveries in developed countries. The rates differ in developing countries.[3] According to the WHO Global Survey on Maternal and Perinatal Health, IOL accounted for 9.6 percent of all deliveries in 24 countries. The prevalence of IOL was also found to be rising.[4]

Over the years, a variety of mechanical and pharmacological inducing agents have been tested. An ideal inducing agent is one that induces labour in the shortest amount of time possible, with a low rate of vaginal birth failure and no increase in perinatal morbidity when compared to spontaneous labour. Because of their dual action of cervical ripening and uterine contraction inducing impact, prostaglandins have evolved as the most popular and often utilized pharmacologic agents for IOL. Prostaglandin E2 (Dinoprostone gel), a registered inducing agent in many countries, is expensive and must be refrigerated due to its temperature sensitivity. It is administered intracervically or high in the posterior fornix of the vagina and may need to be re-administered after 6 hours if necessary. Misoprostol (15-deoxy-16-hydroxy-16-methyl prostaglandin E1) is another option that comes in a variety of dosages. It is stable at room temperature, relatively inexpensive, and can be administered by a variety of ways (oral, vaginal, sublingual, buccal and rectal).

Sublingual misoprostol has a high efficacy since it skips gastrointestinal and hepatic metabolism and reduces uterine hyperstimulation by avoiding direct influence on the cervix. Furthermore, the sublingual method is less intrusive and thus eliminates the need for repeated per vaginal exams, in addition to being easier to administer. However, because prostaglandins are potent uterotonics, they can have negative maternal and perinatal results. Researchers have previously examined the efficiency of vaginal and oral PGE1 with intracervical PGE2 and found that PGE1 is just as effective as PGE2 with the exception of a higher caesarean rate and hyperstimulation.[5,6]

Misoprostol

(15-deoxy-16-hydroxy-16-methyl-PGE1) was the first synthetic analog of prostaglandin available for the treatment of peptic ulcer. Impressed by his stimulating actions on the uterus, Sánchez Ramos in 1993 used it to control various obstetric conditions. Misoprostol is available in tablets of 50, 100, 200 micrograms.

Dinoprostone

Dinoprostone (PGE2) is a synthetic preparation of natural prostaglandin E2. The PGE2 gel is available in a 2.5 ml syringe for an intracervical application of 0.5 mg of Dinoprostone.[6] PGE2 has been used for more than a decade for cervical ripening and labour induction and has been approved by food and drug administration. The local application results in direct softening of the cervix by the following mechanisms:

Softens the cervix by altering the extracellular ground substance of the cervix

Increases the smooth muscle activity of the cervix and uterus

Leads to gap junction formation that is necessary for the coordinated uterine contractions.

Very limited knowledge is available on the efficacy of sublingual PGE1 and intracervical PGE2. Hence, this study was designed to bridge these lacunae comparing effectiveness of sublingual PGE1 with intracervical PGE2 in terms of the maternal and foetal outcomes.

Aim

To compare the effectiveness of sublingual misoprostol with that of intracervical dinoprostone for induction of labour.

Objectives

To assess time taken from induction to delivery. To assess the need for oxytocin augmentation. To assess the number of caesarean sections for failed induction.

METHODS

This study is a hospital-based, prospective, comparative interventional study conducted at Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta, Assam, India. The study duration was one year, from September 4th, 2021 to September 3rd, 2022.

Study population and sampling method

The study population included all primigravida women who delivered at FAAMCH, Barpeta, during the study period, meeting the inclusion and exclusion criteria. A total of 100 patients with an indication for induction of labor were alternately assigned to induction with either Misoprostol 25mcg 6 hourly or Dinoprostone Gel 0.5mg 6 hourly. The sample size was calculated using a formula considering a power of 80%, a significance level of 1.96, a proportion of patients requiring oxytocin augmentation of 68.6%, and a difference of 16.7% between the two treatments. The total sample size was 100, with 50 patients in each group.

Inclusion criteria

The inclusion criteria were as follows: primigravida women who provided informed consent, had a singleton pregnancy, were at 37 weeks of gestation or more, and had a live fetus with cephalic presentation.

Exclusion criteria

The exclusion criteria were estimated fetal weight on scan greater than 3.5kg, amniotic fluid index less than 5cm, contraindication to vaginal delivery (such as placenta previa, unexplained vaginal bleeding, fetal malformation, and malpresentation), maternal co-morbidities (such as bronchial asthma, glaucoma, serious cardiovascular disorders, renal disease, or allergy to misoprostol), and patients not willing to participate in the study.

Data collection procedure

On the day of admission, a detailed history was taken, and a physical and systemic examination was conducted. Abdominal and pelvic examinations were performed, and Bishop's score was assessed. Routine investigations and ultrasonography were conducted. Patients provided written informed consent, and then, alternately, were given intracervical dinoprostone gel or sublingual misoprostol. The dosage of misoprostol was 25mcg, which was administered sublingually and repeated every 6 hours, while intracervical dinoprostone gel was applied and repeated every 6 hours. Oxytocin drip was started 6 hours after the last dose of induction for both drugs. The primary outcomes assessed were the time taken from induction to delivery interval and the need for oxytocin augmentation. The secondary outcomes were the mode of delivery and the number of caesarean sections for failed induction.

The data collected from the case record proforma were entered into Microsoft Excel spreadsheet version 2021 and analyzed using IBM-SPSS version 26. The normality of the data was determined using the Kolmogorov–Smirnov test. Categorical data was expressed as frequency and proportion (percentages), while numerical data was represented with mean and standard deviation for parametric data or median and IQR in case of non-parametric data. Statistical correlation in categorical data was determined using the Chi-square test or Fisher Exact test, while Pearson's correlation coefficient was used to measure the strength and direction of the linear relationship between two continuous variables. A student t-test was applied to calculate a significant mean difference for normally distributed continuous data, while the non-parametric test of Mann-Whitney U was used for non-normal continuous data. A P-value <0.05 was considered significant for all statistical comparisons.

RESULTS

The study compared the effectiveness of sublingual misoprostol and intracervical dinoprostone gel for induction of labor in pregnant women. The study included two groups of women, one receiving dinoprostone and the other receiving misoprostol. The mean age of the women in the dinoprostone group was 27 years with a standard deviation of 2, while the mean age of the women in the misoprostol group was 26 years with a standard deviation of 3. The difference in age between the two groups was not statistically significant (p=0.624). The gestational age at the time of induction was similar between the two groups with a mean of 39 weeks and a standard deviation of 1 for both groups (p=0.953).

Table 1: Comparison of dinoprostone and misoprostol groups based on mode of delivery, use of oxytocin, uterine hyperstimulation, and intrapartum fever.

		Group				
		Dinoprostone		Misoprostol		
		Count	Column (%)	Count	Column (%)	P value
Mode of delivery	LSCS	5	10.20	4	7.80	0.68
	NVD	44	89.80	47	92.20	
Use of oxytocin	No	23	46.90	41	80.40	0.001
	Yes	26	53.10	10	19.60	
Uterine hyperstimulation	No	48	98.00	50	98.00	0.977
	Yes	1	2.00	1	2.00	
Intrapartum fever	No	47	95.90	49	96.10	0.967
	Yes	2	4.10	2	3.90	

Regarding the mode of delivery, there was no significant difference between the Dinoprostone and Misoprostol groups, with 89.8% of the Dinoprostone group and 92.2% of the Misoprostol group delivering via NVD, and 10.2% and 7.8%, respectively, delivering via LSCS (Table 1).

In terms of the use of oxytocin, there was a statistically significant difference between the two groups, with 53.1% of the Dinoprostone group and only 19.6% of the Misoprostol group requiring oxytocin for labor augmentation (p-value=0.001). This suggests that

Dinoprostone may be a more effective method of labor induction in women who do not require oxytocin for labor augmentation.

There was no significant difference between the two groups in the incidence of uterine hyperstimulation or intrapartum fever.

However, the induction delivery interval was significantly longer in the dinoprostone group with a mean of 12 hours and a standard deviation of 3 compared to the misoprostol group with a mean of 8 hours and a standard deviation of 4 (p=0.001).

For the outcome of fetal distress, the incidence was slightly higher in the Dinoprostone group (12.20%) compared to the Misoprostol group (7.80%), but the difference was not statistically significant (p = 0.463). (Table 2).

Table 2: Comparison of dinoprostone and misoprostol groups based on fetal distress, respiratory distress, birth asphyxia, early onset sepsis, APGAR 1 min <6, and liquor grade.

		Group				
		Dinoprostone		Misoprostol		P value
		Count	Column (%)	Count	Column (%)	
Fetal distress	No	43	87.80	47	92.20	0.463
	Yes	6	12.20	4	7.80	
Respiratory distress	No	48	98.00	50	98.00	0.977
	Yes	1	2.00	1	2.00	
Birth asphyxia	No	48	98.00	49	96.10	0.582
	Yes	1	2.00	2	3.90	
Early onset sepsis	No	47	95.90	50	98.00	0.534
	Yes	2	4.10	1	2.00	
APGAR 1 min >6	No	48	98.00	50	98.00	0.977
	Yes	1	2.00	1	2.00	
Liquor grade	Clear	40	81.60	45	88.20	0.026
	Grade 1	2	4.10	6	11.80	
	Grade 2	5	10.20	0	0.00	
	Grade 3	2	4.10	0	0.00	

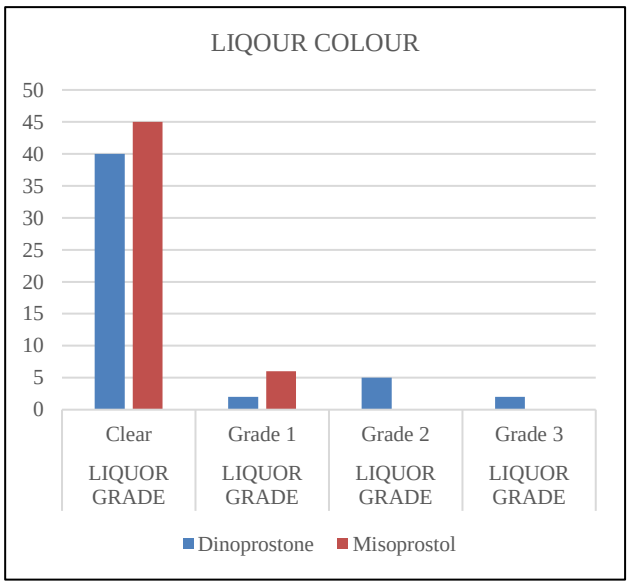

Figure 1: Comparison of liquor colour.

There were no significant differences between the two groups in the incidence of respiratory distress, birth asphyxia, and APGAR 1 MIN <6.

For early onset sepsis, the incidence was slightly higher in the misoprostol group (4.10%) compared to the dinoprostone group (2.00%), but the difference was not statistically significant (p = 0.534).

In terms of liquor grade, there was a statistically significant difference between the two groups (p = 0.026), with a higher proportion of Grade 1 liquor in the Misoprostol group (11.80%) compared to the Dinoprostone group (4.10%) (Figure 1).

DISCUSSION

Induction of labor is a common practice in obstetrics when the benefits of delivery outweigh the risks of continuing the pregnancy. Misoprostol and dinoprostone are commonly used medications for cervical ripening and

labor induction. Both of these drugs have been used extensively in clinical practice for several years, and their effectiveness and safety have been studied in numerous studies. By understanding the relative effectiveness of these two options, pregnant women can make informed decisions that are best suited to their individual needs.

A recent study published in the Archives of Gynecology and Obstetrics by Jha N et al. sought to compare the safety profiles of sublingual misoprostol and intracervical dinoprostone gel for induction of labour.[6] The study utilized a retrospective cohort design to determine the differences between the two medications. The primary outcome was a comparison of the adverse effects of the two medications. The secondary outcome was a comparison of the success rates of the two medications. The results showed that the sublingual misoprostol had a higher rate of adverse effects than the intracervical dinoprostone gel, with 8.2% of patients experiencing adverse effects compared to 7.9% of patients with dinoprostone gel. Furthermore, the success rate of the sublingual misoprostol was slightly higher than that of the intracervical dinoprostone gel, with 85.2% of patients in the misoprostol group achieving successful induction of labour compared to 84.9% of patients in the dinoprostone gel group. In conclusion, the study suggested that although there were differences in the safety profiles and success rates between the two medications, the differences were not statistically significant and both medications may be equally effective for induction of labour.

The 2016 study conducted by B Veena et al. 8 sought to analyze the cost-effectiveness of sublingual misoprostol and intracervical dinoprostone gel for induction of labour. The study used a randomized control trial to compare the two methods of labour induction, and found that overall, the sublingual misoprostol was more cost-effective than the intracervical dinoprostone gel. The study found that sublingual misoprostol required fewer doses to induce labour, had a higher success rate in inducing labour, and resulted in fewer adverse effects than the intracervical dinoprostone gel. Furthermore, the study found that the sublingual misoprostol was more cost-effective than the intracervical dinoprostone gel, with a cost savings of $49 per induction. This cost savings was attributed to the reduced use of oxytocin and other medications, as well as the reduced hospital stay for patients who were induced with sublingual misoprostol. Ultimately, this study demonstrated that sublingual misoprostol is a safe and cost-effective method of labour induction compared to intracervical dinoprostone gel (Veena et al., 2016).[8]

A systematic review and meta-analysis by Zhang et al., included 13 randomized controlled trials (RCTs) and found that there was no significant difference in the success rate of vaginal delivery between sublingual misoprostol and intracervical dinoprostone gel for induction of labor in pregnant women. However, the misoprostol group had a higher incidence of hyperstimulation and meconium-stained amniotic fluid.[9]

Another meta-analysis by Alfirevic et al. included 17 RCTs and found that both misoprostol and dinoprostone were effective for cervical ripening and induction of labor, with no significant differences in the success rate of vaginal delivery or other maternal outcomes.[10] However, the misoprostol group had a higher risk of hyperstimulation, and the dinoprostone group had a higher risk of maternal fever.

A randomized controlled trial by Agha et al. compared sublingual misoprostol with dinoprostone gel for induction of labor and found that both methods were equally effective for cervical ripening and labor induction.[11] However, the misoprostol group had a higher incidence of hyperstimulation, meconium-stained amniotic fluid, and fetal distress.

In a systematic review and meta-analysis by Di Renzo et al, which included 25 RCTs, the authors found that both misoprostol and dinoprostone were effective for cervical ripening and labor induction, with no significant differences in the success rate of vaginal delivery.[12] However, the misoprostol group had a higher incidence of hyperstimulation and meconium-stained amniotic fluid, while the dinoprostone group had a higher risk of maternal fever.

Limitations

There were several limitations to this study that should be considered when interpreting the results. Firstly, the study was conducted in a single center, which may limit the generalizability of the findings to other settings. Additionally, the sample size was relatively small, with only 100 patients included in the study, which may limit the statistical power of the analysis and the ability to detect significant differences between the two treatment groups.

There was also a lack of blinding in the study, as both patients and healthcare providers were aware of the treatment assigned to each patient, which may introduce bias into the results. Additionally, the study did not evaluate long-term outcomes such as neonatal morbidity and mortality, which may be important when considering the overall effectiveness and safety of each method of labor induction.

CONCLUSIONS

In conclusion, studies have shown that both sublingual misoprostol and intracervical dinoprostone gel are effective for the induction of labour in pregnant women. However, sublingual misoprostol has been found to be associated with a higher rate of vaginal birth within 24 hours than dinoprostone gel and require fewer doses. Ultimately, it is up to the patient and their healthcare

provider to discuss the risks and benefits of each option to determine which is the most suitable for their unique situation.

This study suggests that sublingual misoprostol (a type of prostaglandin E1, or PGE1) is more effective than intracervical dinoprostone gel (a type of prostaglandin E2, or PGE2) for cervical ripening and induction of labor. Specifically, the study found that misoprostol shortened the interval between induction and delivery, and also reduced the need for oxytocin (a hormone that helps to stimulate contractions) to augment labor.

One advantage of misoprostol is that it is a relatively inexpensive medication, and is also stable at room temperature, making it easier to store and transport compared to other induction agents that require refrigeration. In addition, the study found that misoprostol had no major adverse effects on either the mother or the fetus, and led to good outcomes for both.

It's worth noting, however, that there are some potential risks associated with misoprostol induction, including hyperstimulation (which can lead to uterine rupture), fetal distress, and meconium staining of the amniotic fluid. These risks should be carefully weighed against the potential benefits of the medication, and the appropriate dosage and administration should be determined by a healthcare professional.

Overall, the study suggests that misoprostol is a safe and effective option for cervical ripening and induction of labor, with advantages over other induction agents such as dinoprostone. However, as with any medical intervention, careful monitoring and individualized treatment are important to ensure the best possible outcomes for both mother and baby.

Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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