Trends in Clinical and Medical Sciences

PSR Press

Original Research Article

Comparative study of sublingual misoprostol (PGE1) versus intracervical dinoprostone (PGE2) for induction of labour in nulliparous postdated pregnancy

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Received: 20 January 2023; Accepted: 15 March 2023; Published: 16 April 2023.

Abstract: Objective: To compare the efficacy of sublingual misoprostol tablet and intracervical dinoprostone gel for induction of labour in nulliparous postdated pregnancy and assess the maternal and fetal outcome after induction.

Methodology: It is a prospective randomized controlled study conducted over a period of 2 years (nov 2020 to nov 2022), in dept. of obstetrics and gynecology, mkcg mch. Out of 200 cases 100 cases were given sublingual misoprostol tablet (Group 1) and rest were given intracervical dinoprostone gel (Group 2). The efficacy of both the drugs were assessed by favorability of Bishop's score at 24 hours, need of augmentation with oxytocin, drug administration to delivery interval, mode of delivery, APGAR score, NICU admission, maternal complication and number of failed induction, data was analyzed description statistics and chi square test.

Result: Mean Drug administration to delivery interval was shorter and significant (18. 53hours vs 20.42) hours, p-value 0.0018). Need for augmentation (48 vs 65, p-value 0.0125), failed induction rate (5 vs 11), post-delivery mean blood loss(436.50mL vs 516 mL, p value- 0.0173) were significantly lower with misoprostol group. NICU admission was lower in dinoprostone group (7 vs 14).

Conclusion: Sublingual misoprostol tablet is efficacious in inducing labour, with shorter drug administration to induction interval, and higher vaginal delivery rate as compared to dinoprostone gel.

Keywords: Dinoprostone gel; Misoprostol tablet; Induction of labour; Drug administration to delivery interval.

1. Introduction

Induction can be defined as an intervention intended to artificially initiate uterine contractions resulting in the progressive effacement and dilatation of the cervix which will result in the birth of the baby by vaginal route [1]. The incidence of induction of labor varies widely in different parts of the world. It is 10-15% in developing countries and 10-25% in the developed world. When the cervix is closed and unaffected labour induction is after preceded by cervical ripening, a process to soften and open the cervix. Induction is indicated when the benefits of either mother or fetus outweigh that of pregnancy continuation.

Prostaglandins undoubtedly plays an important role in cervical priming in the human. PGs may act by increasing the production of cervical fibroblast and thereby increase synthesis of collagenase and hyaluronic acid synthetase. Thus, collagenase reduces the collagen concentration and hyaluronic acid increases the GAG production. The increase in GAG production causes dispersion of collagen and stabilize the collagen fibers and thus the tissue compliance increases in the ripe cervix.

Misoprostol has been approved by the food and drug administration (FDA) solely to be taken orally for the use of non-steroidal anti-inflammatory drugs and it has also become an important drug in obstetrical

practice because of its uterotonic and cervical ripening action. ACOG has issued statements that Misoprostol is a safe and effective drug for the induction of labor, when appropriately used [2]. Misoprostol is cost-effective, can be stored at room temperature [3]. The sublingual route of misoprostol has rapid action when compared to its oral administrations [4]. Dinoprostone is a synthetic analogue of prostaglandin E2 (PGE). Dinoprostone (PGE2) is approved by the FDA in 1995 for cervical ripening and induction of labor. Dinoprostone is costlier and requires refrigeration for storage, as it is unstable at room temperature [5]. PGE2 induces collagenase, metalloproteinase, and elastin activity, thus causing separation of collagen bundles and cervical ripening [6].

An ideal inducing agent must be effective, non-invasive, economical, and safe to mother and fetus [7]. It must achieve labor in shortest possible time, with lower incidence of failure to achieve vaginal delivery and with no increase in perinatal morbidity [8].

2. Methodology

This study was a prospective randomized control study from November 2020 to November 2022, department of obstetrics and gynecology, MKCG medical college and hospital, odisha, after obtaining approval from the Institutional Ethics Committee: ethical committee permission letter number 1101/chairman-IEC, MKCG medical college, berhampur. Written informed consent was obtained prior to administration of medications.

2.1. Inclusion Criteria

singleton pregnancy, Cephalic presentation, Gestational between 40 weeks to 42 confirmed by LMP and earliest possible and available ultrasonography, AFI more than equal to 8.

2.2. Exclusion criteria

Multiple pregnancy, Abnormal presentation, Pregnancy < 40 weeks, Previous LSCS, If there is any contraindication to vaginal delivery, A cervix favourable for amniotomy, Ruptured membranes, Grand-multiparity, Antepartum hemorrhage, Pregnant women having previous uterine surgery, Cephalo-pelvic disproportion, Amniotic fluid index 8.

A total of 200 cases to be recruited and each group consisted of 100 cases. Group 1 to be administered with sublingual misoprostol tablet 25g, maximum of four doses, which is to be repeated every 4th hourly and Group 2 to be administered with intracervical dinoprostone gel 0.5 mg, maximum of two doses, repeated 6th hourly.

Maternal vitals, uterine activity and fetal heart rate were monitored clinically. Partogram was maintained for all patients and used to record all the clinical events during the course of labour. A watch for the rupture of membranes was done. If membranes not ruptured ARM was done at 3cm cervical dilatation. Per vaginal examination was done if there was rupture of membranes or once in 2 hours in active phase of labour. The pulse rate, blood pressure, temperature and urine output were recorded. Delivery particulars duration of each stage of labour blood loss at third stage of labour and baby particulars were recorded. Mother and baby were observed for postnatal complications if any.

3. Stastical Analysis

Data were analysed and all the values were expressed as mean $\pm$ standard deviation or as percentages. Statistical comparison was performed by student paired and unpaired t-test and chi-square test. Statistically significant difference ($P < 0.05$).

4. Results

In Group MISOPROSTOL the rate of improvement in Bishop's score was satisfactory, i.e., mean at 6hrs was 6.04, at 12 hrs was 8.041 and at 24 hrs was 10.28. In Group DINOPROSTONE the mean Bishop's score was 3.31 at 6hrs, 6.12 at 12hrs and 10.2 at 24 hrs. P-value for Bishop's score at 6hr, 12 hr and 24 hrs is0.69, 0.77 and 0.81 respectively, which is statistically insignificant.

In Group 1 arround 48 cases and Group 2 ,65 case required agumentation with oxytocin The chi-square statistic is 9.6186. The p-value is .0.001926. The result is significant at $p < 0.05$.

Table 1. Favourability of bishop's score

	Group	Number	Mean	Standard Deviation	Standard Error Mean	P- Value
Bishop's score at start	MISOPROSTOL (Group 1)	100	3.34	1.31	0.131	0.864 (NS)
	DINOPROSTONE (Group 2)	100	3.31	1.169	0.116	
Bishop's score at 6 hours	MISOPROSTOL (Group 1)	100	6.04	1.406	0.1406	0.690 (NS)
	DINOPROSTONE (Group 2)	100	6.12	1.430	0.143	
Bishop's score at 12 hours	MISOPROSTOL (Group 1)	96	8.041	1.722	0.175	0.774 (NS)
	DINOPROSTONE (Group 2)	97	7.97	1.720	0.174	
Bishop's score at 24 hours	MISOPROSTOL (Group 1)	17	8.5	2.43	0.572	0.393 (NS)
	DINOPROSTONE (Group 2)	24	7.87	2.271	0.463	

Table 2. Comparison of duration of labour between the misoprostol and dinoprostone group at various stages

Duration of Labour	MISOPROSTOL (67) Mean + SD	DINOPROSTONE (60) Mean + SD	P-Value
1st Stage (hr)	11.498 $\pm$ 2.319	11.575$\pm$ 2.218	0.848(NS)
2nd Stage (min)	26.149 $\pm$ 4.351	25.5 $\pm$ 4.4012	0.4058(NS)
3rd Stage (min)	7.507 $\pm$ 3.395	9.548 $\pm$3.620	0.0007(S)
DD Interval (hr)	18.730 $\pm$ 4.109	20.992 $\pm$ 3.845	0.0018(S)

Duration of 1st and 2nd stage of labour we all most same in both the groups with statistically insignificant. The mean drug administration to delivery interval was shorter in misoprostol group 18.730 hrs, which was also statistically significant.

In misoprostol group 67% delivered by natural labour. 3% patient in each delivered by outlet forceps. 5% delivered by vacuum application and 25% undergone LSCS. In Dinoprostone gel group, 64% delivered vaginaly. 2% cases in each parity delivered by outlet forceps. Vacuum application was in 6% of cases. Total 36% undergone LSCS. The chi-square statistic is 6.2345. The p-value is 0.012528. The result is significant at $p < .05$.

In the misoprostol group 25% cases were delivered by cesarean section of which 5% was done for failed induction, 14% for fetal distress, 3% for obstructed labour, 3% for non progress of labour.

In the PGE2 gel group among 36% cases were delivered by cesarean section of which 11% was done for failed induction, 12% for fetal distress, 10% for obstructed labour, 7% for non progress of labour.

Mean blood loss was less in misoprostol group as compared to dino prostone group and it was statistically significant.

69 cases of misoprostol group and 54 cases of dinoprostone group had APGAR Score ?6 at 1 minute, who were further resuscitated. The chi- square statistic is 4.7513. the P- value is 0.0292. The result is significant at $P < 0.05$.

14 cases in misoprostol group and 7 cases in dinoprostone group had APGAR Score ?6 AT 5 minutes who were further being admitted to NICU. The chi-square statistic is 2.6071. The p-value is .106388. The result is not significant at $p < .05$.

Maternal complication like fever, tachysystole was more in misoprostol group i.e., 2 cases and 11 cases respectively as compared to dinoprostone group i.e.,1 cases and 4 cases respectively.3 cases had GI symptoms and 4 cases had abdominal cramps in misoprostol group. PPH was also mare in misoprostol group i.e., 8 cases as compared to dinoprostone i.e., 3 cases. One of the side-effect of misoprostol is rupture uterus, but luckily in our study we did not had such complication.

In Group 1, 9 newborn had meconium aspiration syndrome, 6 newborn had respiratory distress, and 14 were being admitted to NICU. In Group 2, 5 newborn had meconium aspiration syndrome, 2 newborn had respiratory distress, and 7 were being admitted to NICU. There was no neonatal mortality in both the groups. The chi-square statistic is 0.2774. The p-value is .870495. The result is not significant at $p < .05$.

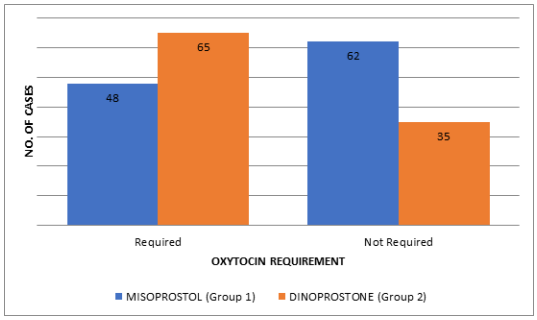

Figure 1. Agumentation with oxytocin

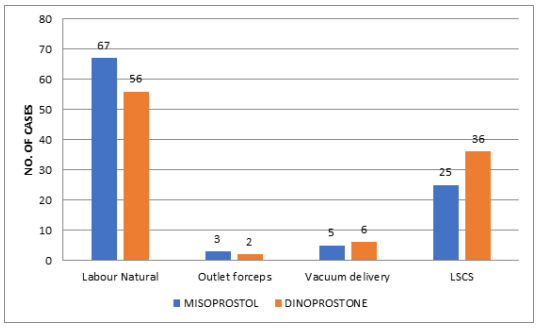

Figure 2. Mode of delivery

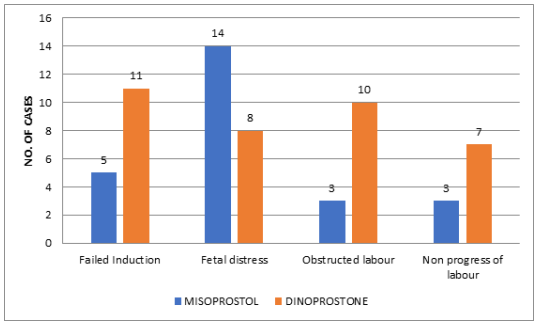

Figure 3. Indication for LSCS

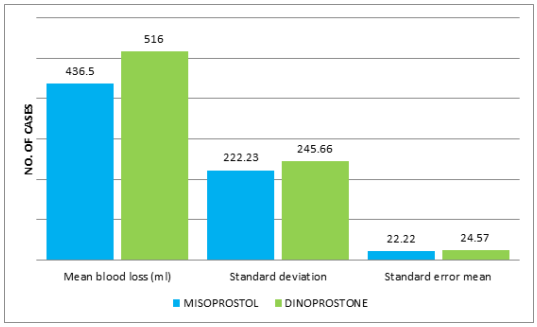

Figure 4. Mean blood loss

Table 3. Maternal complications

Maternal complications	MISOPROSTOL	DINOPROSTONE
Fever	2	1
GI symptoms	3	0
Abdominal cramps	4	2
Tachysystole	11	4
PPH	8	3

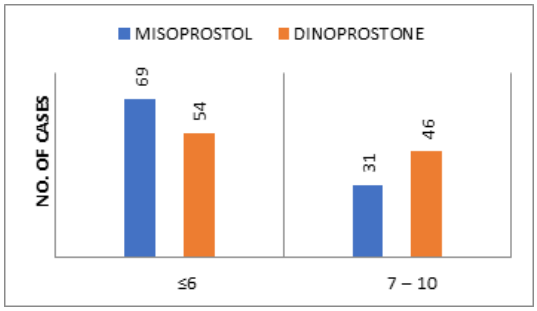

Figure 5. Apgar score at 1 minute

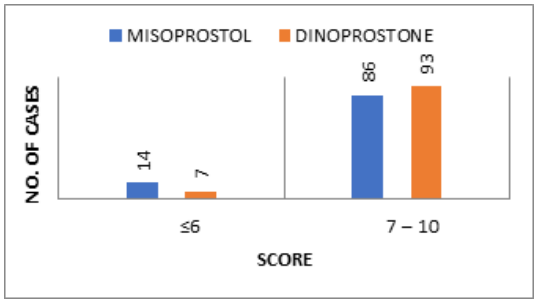

Figure 6. Apgar score at 5 minutes

Table 4. Neonatal complications

Neonatal complications	MISOPROSTOL (Group 1)	DINOPROSTONE (Group 2)
Meconium aspiration syndrome	9	5
Respiratory distress	6	2
NICU admission	14	7

5. Discussion

The mean induction to delivery interval was significantly shorter in the misoprostol group as compared to dinoprostone group, 18.73 hv/s 20.99 hours. It is comparable to Mukherjee et al (2009), (21.5 hrs vs 22.12 hrs), Jonna Malathi (2015) (14.5hrs vs 19.2 hrs). Significantly lesser percentage of patients in the Misoprostol group needed oxytocin for labour acceleration as compared to the patients in the Dinoprostone group i.e, 48% vs 65%, and is comparable with Veena et al. (2014), (46.3% vs 62.1%), Janjewal (2021), (46% vs 56%). Caesarean section rate in misoprostol group is 25% and in Dinoprostone group is 36% which comparable to Raghavan et al. (2017), (26.3% vs 35.1%), Deepika et al. (2019), (26% vs 35%). The most common indication for LSCS was fetal distress in misoprostol group i.e., 14%, whereas failed induction i.e., 11% in dinoprostone group was the common indication. Mean APGAR score at 1 minute (6 vs 6.2) of the present study is comparable with that of Yadav et al.(2017), (5.64 vs 7.58), Raidu (2021), (6.93 vs 7.04). Mean APGAR score at 5 minute (8.48 vs 8.75) of the present study is comparable with that of Yadav et al. (2017), (7.36 vs 7.68), Raidu (2021), (8.91 vs 8.98). NICU admissions were 14% and 7% in misoprostol and dinoprostone group respectively and it is comparable to Raghavan et al. (9.8% vs 8.3%), Deepika et al. (20 % vs 19%).

6. Conclusion

This study reveals that sublingual misoprostol is an effective drug for induction of labour. It has an added advantage of storage at room temperature, ease of administration even with paramedical personals, better patient compliance and acceptance, reduced oxytocin requirement, shorter duration of 2nd and 3rd stage of labour with an overall success rate of 75%. It had no major adverse feto-maternal side effects with good feto-maternal outcome if it is used in appropriate dosage for inducing labour in nulliparous post-dated pregnant ladies.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: "Authors declare no conflict of interests."

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