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To compare the safety, efficacy and tolerance of intravaginal PGE 1 tab with intravaginal PGE 2 gel in induction of labour

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Abstract

Induction of labour is an intervention designed to artificially initiate uterine contractions leading to progressive dilatation and effacement of the cervix and birth of the baby. There are various methods of induction of labour. Locally applied PGs have been thought to be most physiological in initiating the process of labour by promoting both cervical ripening and myometrial contraction the present study was carried out to compare the efficacy, safety and tolerance of intravaginal misoprostol (PGE1) tablets with intravaginal dinoprostone (PGE2) gel for cervical ripening and labour induction at term. A randomized control study was carried out. Two hundred women with unfavorable cervix were randomly allocated in two groups of 100 women each for misoprostol group and dinoprostone group respectively. Success of induction, mean induction to delivery interval, mode of delivery, maternal complications and Apgar score were analyzed. Statistical analysis was done by unpaired one tailed test and chi square test. The mean induction to active phase of labour was 11.61 hrs in misoprostol group and 14:29 hrs in dinoprostone group, mean induction to delivery interval was 15:07 hrs in misoprostol group and 18.11hrs in dinoprostone group. 86% of women in misoprostol group delivered vaginally as compared to 75% in dinoprostone group. No significant difference in the maternal and fetal outcome w was noted. Intravaginal tablet misoprostol 25 mcg every 6hrs for maximum of 100 mcg is an effective, safe, tolerable, low cost and simple method of cervical ripening and induction of labour at term.

Keywords: Induction, Labour, Misoprostol, Dinoprostone, Active phase.

Introduction

Induction of labour is an intervention designed to artificially initiate uterine contractions leading to progressive dilatation and effacement of the cervix and birth of the baby. The success of induction of labour depends upon the status of cervix which is assessed objectively by cervical scoring system as designed by Bishop's EH. There are various methods of induction of labour.

Various pharmacological and non-pharmacological methods have been tried for induction of labour. Pharmacological methods available for induction of labour include Oxytocin, locally or systemically applied prostaglandins (PGs), Relaxin, Mifepristone and various others. Locally applied PGs have been thought to be most physiological in initiating the process of labour by promoting both cervical ripening and myometrial contraction. Dinoprostone (PGE_2) gel has been explored and used most widely.[1-3] Various modes of administration have been studied and intracervical administration has been widely recommended. Misoprostol (PGE_1 analogue) is one of the few drugs whose use has been taken up very enthusiastically by obstetricians. Labour induction with misoprostol is being investigated intensively all over the world. It has been used by oral, vaginal or sublingual route.[4-7] There are various studies that report its excellent efficacy, minimal side effects and low cost.

In this study, cervical ripening and induction of labour using intravaginal dinoprostone gel was compared with intravaginal misoprostol tablets to assess the efficacy and safety in induction of labour.

Material and Method

This randomized control study was carried out at Lata Mangeshkar Hospital, Nagpur, which is a tertiary care hospital attached to medical college. Permission from Institutional Ethics Committee was obtained.200 consecutive admitted women from the labour ward and obstetric wards who were fulfilling inclusion/exclusion criteria and willing to participate in the study were enrolled in the study after taking written informed consent. The women were randomized into two groups by block randomization method. Study group A included 100 women who were induced with intravaginal tablet Misoprostol 25 mcg 6 hourly till labour was established, the maximum dose being 100 mcg. Comparative group B included 100 women who were induced with intravaginal Dinoprostone gel 0.5 mg, 8 hourly for maximum of three doses.

Inclusion criteria were Gestational age (GA) of 37 -42 weeks, Single live fetus, Cephalic presentation, Adequate pelvis, Reactive fetal heart rate on Non-Stress Test (NST), Bishop's score $\leq$ 4 and women not in labour.

Exclusion criteria was previous LSCS, multiple pregnancy, polyhydramnios, placenta previa, premature rupture of membranes (PROM), and history of asthma, glaucoma, Heart disease.

Thorough general examination and systemic examination was carried out. Obstetrical examination was done to assess the fundal height and fetal presentation. Ultrasonography (USG) was done to rule out placenta previa and to confirm presentation of the

fetus. NST was done to assess the well being of the fetus. Vaginal examination was performed to assess Bishop's score and to rule out cephalopelvic disproportion.

Women fulfilling the selection criteria were randomised and were subjected to induction of labour. **Group A**: under all aseptic precautions, vulva and vagina was cleaned and moistened tablet misoprostol 25 mcg was introduced in the posterior fornix. This was repeated six hourly till active labour was established, maximum dose being 100 mcg. **Group B**: under all aseptic precautions, vulva and vagina was cleaned and 0.5 mg PGE2, prepacked in the sterile prefilled ready-to-use syringe was introduced in the posterior fornix. This was repeated eight hourly till active labour was established. Maximum 3 doses were used.

Active phase of labour was considered with regular uterine contraction and cervical dilation of at least 3-4 cm. Success of induction was considered when patient entered active phase within 24 hours of start of induction. On entering active phase, depending upon uterine contractility, ARM and/ or oxytocin augmentation was done and titrated every 30 minutes till adequate contraction of 3-4/ 10 min, each lasting for 45 sec were established. Progress of labour was determined on partograph by per vaginal examination done every 4 hourly/ SOS. Fetal heart rate was monitored during labour by intermittent auscultation. Side effects due to both the drugs were noted. In case of hyperstimulation or tachysystole the tablet was removed and tocolysis given, by the time the patient was being prepared for LSCS.

The success of induction was determined at the end of 24 hrs. Those who did not enter the active stage of labour till then were considered as failure of induction but any improvement in Bishop's score was recorded. Statistical analysis was done by unpaired one tailed t test and chi square test.

Results

200 primigravida women who met the inclusion/exclusion criteria were enrolled in the study. Indication for induction of labour were comparable in both the groups, common indications being postdated pregnancy and PIH in both the groups(Table 1).

Table 1: Indication for induction of labour

Indication for induction of labour	Group A (Misoprostol)	Group B (Dinoprostone)
Postdated Pregnancy	44	46
PIH	36	33
Post dated + PIH	4	5
IUGR	8	11
Oligohydramnios	6	4
GDM	2	1

Induction was successful and active stage was reached within 24 hours in 96 women in group A as compared to 93 Women in group B. Out of 96 women with successful induction, 86 women delivered vaginally in group A, as compared to 75 out of 93 women in group B who delivered vaginally. Mean change in the Bishop's score at 24 hours in women who did not deliver within 24 hours was 6.5 in Misoprostol group and 4.85 in women receiving Dinoprostone gel (Table 2).

Table 2: Success of induction & mode of delivery

Outcome of induction	Group A	Group B
Successful induction	96	93
Vaginal births	86	75
Caesarian births	10	18
Failed inductions	4	7
Mean change in Bishpps score in patients with failed induction	6.5	4.85

The mean induction to active phase interval (Table 3) was 11.61 ± 5.28 hrs in Misoprostol group and 14.29 ± 5.71 hrs in Dinoprostone group. The difference was statistically significant (p=.001). The mean induction to delivery interval (Table 3) was 15.07± 6.38 hrs in Misoprostol group and 18.116.03 hrs in Dinoprostone group. Misoprostol group also had higher number of successful vaginal delivery as compared to Dinoprostone group. (89.58% and 80.64% respectively) but the difference was not statistically significant (p value- 0.08).

Table 3: Induction to active phase & delivery interval

Labour	Group A	Group B	P value
Induction to active phase interval in hrs.	11.61±5.28 hrs	14.29±5.71 hrs	0.001
Mean induction to delivery intervals in hrs.	15.07±6.38 hrs	18.11±6.03 hrs	0.0004

Most of the women in Misoprostol group developed effective uterine contraction with ARM and oxytocin augmentation was required in only 6% women but oxytocin augmentation was required in 38women in Dinoprostone group and the difference was statistically significant (Table 4).

Table 4: Method of augmentation of labour

Method of augmentation	Group A	Group B
ARM	80	37
ARM + Oxytocin	6	38

In Misoprostol group 7 women landed in LSCS for fetal distress while in Dinoprostone group5 women underwent LSCS for fetal distress, while 12 women had prolonged labour as the indication for LSCS (Table 5). There was no maternal complication associated in

Misoprostol group. Only 1 women receiving Dinoprostone gel had hyperstimulation.

Table 5: Indication for LSCS

Indication for LSCS	Group A	Group B
Fetal distress	7	5
Prolonged labour	2	12
Deep transverse arrest	1	1

Neonatal outcome was good in both the groups and none of the babies in both groups had Apgar score less than 7 at 5 minuets (Table 6).

Table 6: Neonatal Outcome

	Group A	Group B
Apgar Score <7		
At 1 min	3	9
At 5 min	0	0

Discussion

Over the last two decades, the incidence of induction of labour has increased dramatically. An ideal method must encompass its efficacy and safety for the mother and fetus, short induction - delivery interval, minimum side effects and convenience to women and medical staff. The present randomized control study was aimed at comparing the efficacy, safety and tolerance of intravaginal Misoprostol with intravaginal Dinoprostone for cervical ripening and labour induction at term. The efficacy and safety of dinoprostone gel has already been established by various studies;[1,2,3] no difference was found in our study either.

In various studies different doses and routes of Misoprostol have been used for induction of labour. Misoprostol has been used by oral, sublingual and vaginal route.[4,5,6,7] We used vaginal route as it is the safest route and also because the tablet can be removed from vagina in case of hyperstimulation.

We found higher success of induction with Misoprostol group similar to study by Patil[8] and study by Sushilkumar.[9] There was less induction to delivery interval and more number of vaginal deliveries in 24 hours in Misoprostol group as compared to Dinoprostone group. These results were similar to those obtained by Wing et al,[10] but Sanchez-Ramos et al[3] reported much shorter induction delivery interval, probably this difference was observed because they used higher doses. Vaginal deliveries occurred more frequently in Misoprostol group. The proportion of women who underwent caesarean section was higher in Dinoprostone group. This finding was consistent with the study done by Sanchez-Ramos et al.[11] However Mundle and Young and Wing et al[12,10] found higher rate of caesarean section in Misoprostol group.

Most common indication for caesarean section in Misoprostol group was fetal distress,[7] while in Dinoprostone group more number of caesarean section were done for prolonged labour[12] followed by fetal distress.[5] This was consistent with the findings of Sanchez-Ramos and Danielian et al.[11,13]

Oxytocin augmentation was required in 8 women of Misoprostol group while 38 women were augmented with oxytocin in Dinoprostone group. Similar findings were seen in the study by Danielian et al, Nanda et al, CN Sheela and Gupta N et al.[13,14,15,16] Only one women had hyperstimulation of uterus in dinoprostone group. This was contrary to the findings of Patilkamal P et al and Surg Cdr Sushilkumar et al.[8,9] In both these studies, tachysystole and hyperstimulation was frequent in Misoprostol group.

In those patients where induction failed, there was an improvement in Bishop's score. The mean change in the Bishop's score in both the groups were similar, 6.5 ±2.3 from 2.5 in Misoprostol group and 4.86 ±2.9 from 1.42 in Dinoprostone group. This was consistent with the findings of study by Ramsey et al.[17]

Neonatal outcome was good and Apgar score was more than 7 in both the groups at the end of 5 minutes in both the groups but the study by Gupta N et al[16] observed slightly less Apgar score in Misoprostol group as compared to Dinoprostone group.

Conclusion

In conclusion, although both Misoprostol and Dinoprostone appear to be effective agents for labour induction, Misoprostol is better as it has more success rate, shorter induction to delivery interval, requires less oxytocin augmentation, less incidence of LSCS and no maternal or fetal complications. Misoprostol is more cost-effective and stable at room temperature than the comparable commercial Dinoprostone prostaglandin preparations which require storage in refrigerator. Because of ease of administration of a tablet as compared to gel, induction is easier with Misoprostol compared to Dinoprostone gel. In case of hyperstimulation and fetal distress, the removal of tablet Misoprostol is possible as against Dinoprostonegel. These results make misoprostol superior to dinoprostone for induction of labour especially in developing and tropical countries.

Therefore intravaginal tablet Misoprostol 25 mcg every 6 hours for maximum of 100 mcg should be used an effective, safe, tolerable, low cost, simple method of cervical ripening and induction of labour at term.

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