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ORIGINAL ARTICLE

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Comparison of vaginal misoprostol and oral misoprostol with intracervical dinoprostone gel for labor induction at term

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OBJECTIVE(S) : To compare the efficacy and safety of vaginal misoprostol and oral misoprostol with intracervical dinoprostone gel for labor induction at term.

METHOD(S) : In our tertiary referral hospital, 25 mg vaginal misoprostol 6 hourly for a maximum of five doses and 50 µg oral misoprostol 6 hourly for a maximum of five doses were compared with 0.5mg intracervical dinoprostone gel 12 hourly for a maximum of three doses for induction of labor at term in 150 women in three groups of 50 each. Number of vaginal deliveries achieved, induction to vaginal delivery interval, requirement of oxytocin, incidence of cesarean section for fetal distress, failed induction, side effects, and neonatal outcome were compared.

RESULTS : There were no differences in the mode of delivery. Induction to vaginal delivery interval was significantly shorter and lesser number of women required oxytocin in the vaginal misoprostol group compared to intracervical dinoprostone gel group whereas the differences were not significant in the oral misoprostol group. There were no differences in the incidences of cesarean section for fetal distress, failed induction, hyperstimulation, and neonatal outcome.

CONCLUSION(S) : Vaginal misoprostol is more effective and as safe, and oral misoprostol is as effective and safe as intracervical dinoprostone gel for labor induction at term, in primigravidas and multigravidas with unfavorable cervices without previous uterine scar.

Key words: vaginal misoprostol, oral misoprostol, intracervical dinoprostone gel, induction of labor at term.

Introduction

Induction of labor at term with an intention of achieving vaginal delivery is a common and accepted obstetric intervention when continuation of pregnancy is deleterious to mother or fetus or both. Advent of prostaglandins revolutionized induction. Many studies have shown the advantages of using vaginal prostaglandins in cervical priming and labor induction in terms of reduced induction-delivery interval and lower operative rate compared to oxytocin alone [1,2]. Dinoprostone (PGE_2) is the drug of choice and is accepted for labor induction at term. Although safe and effective it is expensive and requires refrigeration for storage.

Misoprostol, a synthetic analogue of PGE_1, which was originally used in prevention and treatment of peptic ulcer, has been shown to be effective in cervical priming and labor induction. It is inexpensive, can be stored at room temperature and has few systemic side effects [3,4].

Several studies have shown that misoprostol used vaginally, orally or sublingually is effective in labor induction and reduces the induction-delivery interval and oxytocin requirement. At the same time concerns were expressed about the increased incidences of hyper stimulation and cesarean for fetal distress [5-7].

This study was undertaken to compare the efficacy and safety of misoprostol, administered vaginally and orally with our

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standard induction protocol using intracervical dinoprostone gel for labor induction at term.

Methods

Permission was obtained from the Hospital Ethical Committee for the study. Written informed consent was obtained from all the women who participated in the study.

All women at term (37-42 completed weeks) with a singleton live fetus in cephalic presentation, with either obstetric or medical indication, for induction of labor were included in the study. Intact membranes, a Bishop score of ≤ 4 and a reassuring NST pattern were the other requirements for inclusion in the study.

Grandmultiparas, women with cesarean or other surgical scar on the uterus, those with medical contraindications for the use of prostaglandins, and those with significant maternal or fetal compromise were excluded from the study.

A total of 150 women were randomized into three groups of 50 each. One group received 0.5mg intracervical dinoprostone gel every 12 hours for a maximum of three doses (PGE_2 group). The second group received vaginal misoprostol 25 mg every 6 hours for a maximum of five doses (Vaginal PGE_1 group). The third group received 50mg of oral misoprostol every 6 hours for a maximum of five doses (Oral PGE_1 group).

The demographic details such as the age, height, weight, parity, gestation in weeks and the amniotic fluid index (AFI) at induction were noted. Subsequent dose was withheld if the woman was in active labor, in the event of contraction frequency of 3/10 minutes or more, a non-reassuring fetal heart rate pattern or rupture of membranes.

Labor was managed according to our labor ward protocol regarding decisions for oxytocin augmentation, amniotomy and requirement for additional analgesia. Apgar score at 1 & 5 minutes and need for neonatal intensive care unit (NICU) admission were noted.

Primary outcome measures assessed were number of vaginal deliveries achieved and induction to vaginal delivery interval. Secondary outcome measures assessed were requirement of oxytocin, incidence of cesarean section for fetal distress, failed induction, side effects especially hyper stimulation, and neonatal outcome with reference to apgar less than 6 at 5 minutes, and admission to NICU.

Hyperstimulation was defined as uterine contractions lasting more than 90 seconds or frequency of 5 or more contractions in 10 minutes, with abnormal fetal heart rate tracing (late deceleration / fetal tachycardia / fetal bradycardia).

Failed induction was diagnosed when the women did not go into labor or cervix was not favorable enough for artificial rupture of membranes (ARM), at the end of induction protocol.

Birth asphyxia was defined by apgar ≤ 3 and/or requirement of NICU admission and/or need for ventilation immediately after delivery.

Statistical analysis was used to compare the results. Test of proportion was used in most instances. The significance of the difference in the induction delivery interval was determined by ANOVA test.

Results

The demographic characteristics of the women in the three groups were similar (Table 1), as also were the indication for induction (Table 2). Postdatism and pregnancy induced hypertension (PIH) were the most common indications. Majority of women had an amniotic fluid index (AFI) of more than 5 and only a small percentage (2-4%) were with an AFI of < 5 in all the three groups.

Table 1. Demographic variables

Variable	PGE_2 group (n=50) Number	Vaginal PGE_1 (n=50) Number	Oral PGE_1 (n=50) Number
Average age (years)	25	24	24
Average height (cms)	152.5	150	150
Average weight (kgs)	61	59	60
Primigravidas	29 (58%)	30 (60%)	28 (56%)
Multigravidas	21 (42%)	20 (40%)	22 (44%)
Average gestational age (weeks)	38.7	39.4	39

Table 2. Indications for induction

Indication	PGE_2 Number (Percent)	Vaginal PGE_1 Number (Percent)	Oral PGE_1 Number (Percent)
Postdatism	16 (32)	18 (36)	15 (30)
Pregnancy induced hypertension	13 (26)	11 (22)	12 (24)
Oligoamnios	7 (14)	8 (16)	6 (12)
Intrauterine growth restriction	3 (6)	3 (6)	4 (8)
Others *	11 (22)	10 (20)	12 (24)

Others * - Rh negative pregnancy, decreased fetal movements, diabetes mellitus

Table 3 shows the number of vaginal deliveries achieved and the incidence of cesarean section in the three groups. Mode of delivery did not differ significantly in the three groups.

Table 3. Mode of Delivery

Mode of delivery	PGE_2 gel Vs PGE_1 Vag N (%) Vs n (%) {p}		PGE_2 gel Vs PGE_1 Vag N (%) Vs n (%) {p}	
Vaginal deliveries	38 (76%)	42 (84%) {0.31}	38 (76%)	36 (72%) {0.64}
Cesarean section	7 (14%)	7 (14%) {0.89}	7 (14%)	5 (10%) {0.86}
Failed inductions	5 (10%)	1 (2%) {0.206}	5 (10%)	9 (18%) {0.25}

Induction to vaginal delivery interval was found to be significantly shorter and more women delivered in less than 24 hours in the vaginal PGE_1 group compared to those in the PGE_2 group, whereas the same was not significantly different in the oral PGE_1 group (Table 4).

Table 4. Induction - vaginal delivery interval

	PGE_2 vs Vag. PGE_1 M (± SD) vs m (± SD) {P}		PGE_2 Gel vs Oral PGE_1 (m±SD) vs m (± SD) {p}	
Induction - Vag. delivery Interval in minutes	1322 (± 733.74)	912 (± 641.52) {0.021}*	1322 (± 733.74)	1051 (±644.68) {0.221}
Women delivering in <24 hrs in (n%)	22 (58%)	33 (83%) {0.014}*	22 (58%)	10 (23%) {0.63}

m- mean, SD - Standard deviation, {p} p value, {p}* - significant p value
n (%) - number (percentage)

Significantly lesser number of women required oxytocin for augmentation in the vaginal PGE_1 group, whereas the difference was not significant in the oral PGE_1 group. The incidences of cesarean for fetal distress and rates of hyperstimulation were similar in the three groups. None of the cases of hyperstimulation required cesarean for fetal distress. There were no other significant side effects except that one woman developed fever (>100 degree F) attributable to vaginal misoprostol, which however settled in 48 hours. Neonatal outcome was similar in the PGE_2 and the PGE_1 groups. One neonate in vaginal PGE_1 group was born with an apgar of <6 at 5 minutes and required admission to NICU group. This was a growth-retarded infant with severe oligoamnious and born with low birth weight and meconium aspiration. The number of failed inductions in the PGE_2 group did not differ significantly from the PGE_1 group, though higher number of failed inductions was observed in the oral PGE_1 group.

The comparison of the secondary outcome measures is shown in Table 5.

Table 5. Secondary outcome measures

Variable	PGE_2 vs PGE_1 Vag. n (%) vs n (%) {p}		PGE_2 vs PGE_1 oral n (%) vs n (%) {p}	
Syntocinon acceleration	19 (50%)	10 (23%) {0.014}*	19 (50%)	16 (44%) {0.063}
Hyperstimulation	1 (2.6%)	2 (4.7%) {0.92}	1 (2.6%)	1 (2.7%) {0.96}
Apgar <6 NICU admission	Nil	1 (2.3%) {0.5}	Nil	Nil
Cesarean for fetal distress	5 (10%)	6 (12%) {0.86}	5 (10%)	4 (8%) {0.88}

n (%) - number (percentage), {p} - p value, {p}* - Significant p value

Note : For variables number 1,2 & 3, the percentages are calculated over total number of vaginal deliveries in each group. For variable 4, the percentage calculated over total number induced in each group.

NICU - Neonatal intensive care unit

Discussion

Our results show that 25 mg vaginal misoprostol administered 6 hourly for a maximum of 5 doses, when compared with the standard induction protocol of 0.5 mg intracervical dinoprostone gel 12 hourly for a maximum of 3 doses, is more effective for labor induction at term. There was a significant reduction in the induction to vaginal delivery interval with more women delivering within24 hours and also lesser number requiring oxytocin for augmentation. At the same time we found it to be equally safe. There was no increase in the incidence of cesarean for fetal distress, hyperstimulation occurred in similar numbers and the neonatal outcome was no different. Frank Chuck & Huffaker [8] have compared 50 mg vaginal PGE_1 with in intracervical PGE_2 gel every 4 hours for labor induction and have reported similar results. Agarwal et al [9] have studied vaginal PGE_1 50 mg 6 hourly vs intracervical PGE_2 gel, and have concluded that vaginal misoprostol is more effective and safe for labor induction at term.

However Le Roux et al[10] and Gary et al[6] have reported an increased incidence of cesarean for fetal distress and tachysystole with 50 mg vaginal PGE_1 when compared to vaginal dinoprostone. van Gemund et al[11] in their study comparing 25 mg vaginal misoprostol with dinoprostone, with adverse neonatal outcome as the primary outcome measure, concluded that this lower dose of misoprostol is safer with lesser neonatal admissions. Maydanli et al[12] have concluded that 25 µg vaginal misoprostol could be as effective as 50 mg for cervical ripening and labor induction.

Hence 25 mg as used in our study appears to combine efficacy with safety and could be the dosage that can be adopted in clinical practice for labor induction at term in primigravidas and multigravidas with unfavorable cervices. The safety in grand multiparas and in women with previous uterine scar cannot be commented upon as these women have been excluded from our study.

Comparing 50 mg oral PGE_1 every 6 hours for a maximum of five doses, with our standard PGE_2 protocol we found that both were equally effective and safe. Though there were a higher number of failed inductions (18% vs 10%), the difference was not statistically significant. Langnegger et al[13] compared 50 mg oral PGE_1 with PGE_2 intracervical gel every 6 hours and concluded that oral PGE_1 is as effective and safe as PGE_2 for labor induction with no difference in the frequency of fetal heart abnormality.

However, Le Roux et al[10] compared 50 mg oral PGE_1 6 hourly with PGE_2 vaginal gel and concluded that oral PGE_1 is less effective and results in fewer vaginal deliveries, but is as safe. Whereas Bartha et al[14] compared a single dose of 200 mg of oral PGE_1 with PGE_2 intracervical gel every 6 hours and Hassan [15] compared 50 mg oral PGE_1 with dinoprostone. Both concluded that oral PGE_1 was more effective with shorter induction-delivery interval. Hence there is a need to optimize the dosage of oral PGE_1 to combine efficacy with safety. Safety and efficacy along with the convenience and ease of administration, makes oral misoprostol an attractive option for labor induction at term.

Conclusion

Vaginal misoprostol used in the dosage of 25 mg 6 hourly for a maximum of five doses is more effective and as safe and oral misoprostol 50 mg 6 hourly for a maximum of five doses is as effective and safe, as intracervical dinoprostone gel 0.5 mg 12 hourly for a maximum of three doses for labor induction at term in primigravidas and multigravidas with unfavorable cervix without previous uterine scar.

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