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ORIGINAL ARTICLE

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A comparison of vaginal misoprostol versus Foley's catheter with oxytocin for induction of labor.

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OBJECTIVE(S) : To compare efficacy and safety of 50 ?g vaginal misoprostol with transcervical Foley's catheter and intravenous oxytocin for labor induction.

METHOD(S): One hundred women at term gestation, with Bishop score $\leq$ 4, with various indications for labor induction were randomly allocated to receive either 50 ?g misoprostol vaginally 4 hourly (maximum 6 doses) or transcervical Foley's catheter with intravenous oxytocin (2 mU/minute to a maximum of 32 mU/minute or till the woman goes into active labor.

RESULTS: In misoprostol group induction-delivery interval was significantly less (11.58 vs 19.45 hours) and successful induction significantly higher (98% vs 78%) as compared to catheter/oxytocin group. Eighty-eight percent women delivered within 24 hours of induction in misoprostol group whereas in the other group 72% delivered within 24 hours. Eighteen percent of women delivered with a single dose of misoprostol while 28% required the maximum dosages of oxytocin.

CONCLUSION(S) : Vaginal misoprostol is a cheap, highly effective and easy to administer agent for labor induction.

Key words : vaginal misoprostal, intracervical catheter and oxytocin, induction of labor.

Introduction

Mostly labor sets in spontaneously but for various obstetrical and medical indications it needs to be induced when the benefits to either the mother or the fetus outweigh those of continuing the pregnancy. Labor induction in the presence of an unfavorable cervix is associated with an increased likelihood of prolonged labor and increased incidence of chorioamnionitis and cesarean section. Hence, the use of cervical ripening agents prior to conventional methods of induction is now a standard practice.

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A variey of cervical ripening agents exist, yet none is ideal[1]. Oxytocin and prostaglandins are the agents most frequently used for induction of labor[2]. Although oxytocin is widely accepted as a safe and effective initiator of uterine contractions its success depends on the preinduction cervical score[3]. Prostaglandin preparations that have been registered for cervical ripening and labor induction (intracervical PGE_2 gel or PGE_2 vaginal pessary) are expensive and unstable, requiring refrigerated storage[4]. In developing countries like India, conventionally cheap and feasible method used for preinduction cervical ripening is transcervical Foley's catheter. In experienced hands it is a safe and reliable method of inducing cervical ripening and even labor. But many practitioners find it cumbersome, somewhat archaic and esthetically suboptimal besides having potential dangers of accidental rupture of membranes, cord prolapse, chorioamnionitis, and pyrexia because of infection[5]. In recent years, misoprostol, a synthetic PGE_1 analogue, originally developed as a gastrocytoprotective agent, is being

evaluted for term labor induction [6]. Advantages of misoprostol include effectiveness, low cost, stability at room temperature, and ease of administration but the main worry with its use is excessive uterine response and most of the work so far has concentrated on finding the right dosage regimens that minimise this risk while maintaining efficacy [7].

In this study, we compared the safety and efficacy of 50 ?g vaginal misoprostol with transcervical Foley's catheter and intravenous oxytocin for induction of labor.

Methods

Hundred women who presented between December 2002 and November 2004 with various indications for induction of labor with singleton pregnancy at term, in cephalic presentation, intact membranes, Bishop score $\leq$ 4 and volunteering to participate in the trial were included in the study. Those with one previous cesarean section were also included. Women with multifetal gestation, nonreassuring fetal heart tracings, thyrotoxicosis, heart disease, bronchial asthma, sickle cell disease, glaucoma and known hypersensitivity to prostaglandins were excluded from the study. The study was approved by our ethics committee.

After written informed consent, women were assigned to two groups to receive either 50 ?g intravaginal misoprostol 4 hourly for a maximum of six doses or transcervical Foley's catheter with simultaneous intravenous oxytocin as per the woman's choice. In the catheter/oxytocin group at first entry a 16F Foley's catheter was introduced just beyond the internal os and its balloon was inflated with 30 mL of sterile water. Traction was applied by taping the distal end of the catherter to the medial aspect of thigh. Simultaneouslly oxytocin infusion (Syntocinon, Cadila Health Care Ltd) was started with an initial dose of 2 mU/minute and escalated by 2mU/minute every 30 minutes till the woman went into active labor (three contractions of good intensity per 10 minutes lasting for 45-60 seconds) or the maximum dose of 32 mU/minute was reached after 8 hours. This dose was continued till onset of labor and delivery or its failure inspite of 24 hours of administering this maximum dose. If labor set in the dose being then administered was continued till delviery. If labor failed to start at the end of 24 hours of the maximum dose oxytocin drip was discontinued and the method considered as failed. Women assigned to the vaginal misoprostol group received 50 ?g misoprostol (1/2 of the scored tablet Misoprost - 100, Cipla Ltd) and the dose was repeated 4 hourly to a maximum of six doses or till the woman went into active labor as per the criteria mentioned above. If she did not go in active labor in 24 hours the method was declared as failed. The two groups were now interchanged i.e. oxytocin failures were induced with misoprostol and misoprostol failures with oxytocin (second entry). Foley's cathter was inserted only in those in whom Bishop score was still $\leq$ 4. During induciton if the woman developed tachysystole ($\geq$ 6 uterine contractions per 10 minutes for two consecutive 10 minutes), hypertonus (contractions lasting for $\geq$ 120 seconds) or hyperstimulation (tachysystole or hypertonus associated with abnormal fetal heart recordings) the next dose of misoprostol was withheld and the tablet was removed if still in the posterior fornix.

Throughout induction, fetal heart rate was monitored by a fetoscope or a doppler and uterine contractions monitored manualty. In both the groups if a woman developed fetal heart abnormalities then continuous monitoring of fetal heart was done with a tocodynamometer. Before taking any decision to terminate the pregnancy, artificial rupture of membranes was done and mode of delivery was decided depending upon the color of liquor, cervical status, and fetal heart tracings.

As per the study protocol women with second failure i.e., those who did not go in active labor inspite of the maximum dose of misoprostol or oxytocin were to be terminated by cesarean section but we found that majority of women who were failures in catheter/oxytocin group did respond to oxytocin but contractions just lacked the sufficient intensity and hence were not labelled as 'achieving active labor'. At the same time there was no obstetric indication for cesarean section and these cases were given incremental higher dosages of oxytocin ranging 40-48 mIU/minute.

The main measure of efficacy was successful induction i.e. number of women who achieved active labor within 24 hours of induction in the first entry and their induction-delivery interval. Other measures were number of deliveries within 24 hours, mode of delivery and the total dose of inducing agent required for delivery. The measures of safety included the uterine tachysystole, uterine hypertonus, abnormal fetal heart tracings, incidence of meconium passage, and the neonatal outcome. Baseline data included maternal age, socioeconomic status, parity, gestation, indication for induction, and preinduction cervical score.

Statistical analysis

Median and range were computed. Continuous variables were compared using the Fisher's Z test and discrete data with the $?^2$ test. Analysis was performed using statistical software SP SS version 11.5.

Results

At first entry, 50 women received misoprostol and 50 received transcervical Foley's catheter and intravenous oxytocin. Maternal demographic characteristics and indications for induction were similar in the two groups (Table 1).

Table 1. Demographic characteristics and indications for labor induction.

	Misoprostol (n=50)		Catheter/Oxytocin (n=50)	
Demography				
Age (yrs.)	25.0	(19-33)	26.0	(22-36)
Primigravida	27	(54)	24	(48)
Gestation (weeks)	38.50	(37-41)	38.00	(37-41.43)
Preinduction cervical score	4	(2-4)	3	(2-4)
Previous one cesarean section	5	(10)	7	(4)
Indication for induction				
Postdatism	10	(20)	11	(22)
Hypertension	24	(48)	25	(50)
Intrauterine growth restriction	3	(6)	4	(8)
Diabetes mellitus	3	(6)	3	(6)
Others	10	(20)	7	(14)

Values are exressed as median (range) or (percent).

At first entry in catheter/oxytocin group, 39 of the 50 women went into active labor while 11 were failures (first failure) as these did not achieve active labor with 32 mU/minute oxytocin. These 11 entered in the misoprostol group (second entry) and six of them had successful induction with misoprostol while five still failed to achieve active labor (second failure). These five were given incremental doses of oxytocin upto 40-48 mIU/minute and went into labor. In the misoprostol group (first entry), 49 of the 50 women achieved active labor and the one failure of this group had successful induction with catheter/oxytocin (second entry). (Figure 1). At the end of the study 51 women (50+1) were induced with catheter/oxytocin while 61 women (50+11) received misoprostol. When only first entry women were taken into consideration, success rate of misoprostol group was 98% as compared to 78% of catheter/oxytocin group (P=0.002). But this statistical significance was lost when first and second entry women were considered jointly (P=0.0847) (Table 2).

Induction-delivery interval was significantly shorter in misoprostol group than that in catheter/oxytocin group (11.58 hours vs 19.45 hours; P< 0.002). Also greater number of women (44/50) delivered within 24 hours of start of induction in misoprostol group than those in catheter oxytocin group (36/50) (P=0.045) (Table 2).

In misoprostol group 18% women (9/50) delivered with one dose and only one required maximum permitted six doses. In catheter/oxytocin group 28% (14/50) needed the maximum dose of oxytocin and 6% (3/50) needed 8-12 mU/minute dose. The median dose requirement of oxytocin was 28 mU/minute (range 8-32 mU/minute) whereas it was 100 ? g (range 50-300ug) in misoprostol group (Table 3). With misoprostol five women had tachysystole, two had hypertonus and five had hyperstimulation, but none required intravenous tocolysis, while no such complication was seen in catheter/oxytocin group (Table 2).

Table 2. Outcome of labor induction.

	Misoprostol group	Catheter/oxytocin	P-value
Successful induction (First entry)	49/50 (98) [a]	39/50 (78) [a]	0.002
Successful induction (Second entry)	6/11 (54.55) [a]	1/1 (100) [a]	
Final outcome (First and second entry)			
Successful	55/61 (90.16) [a]	40/51 (78.44) [a]	0.0847
Induction-delivery interval (hours)	11.58 (6-55.13) [b]	19.45 (5.48-40.25) [b]	<0.002
Number delivered within 24 hours	44/50 (88) [b]	36/50 (72) [a]	0.045
Median dose required	100 g (50-300) [b]	28 mU/minurw (8-32) [b]	
Tachysystole	5/61 (8.19) [a]	0	
Hypertonus	2/61 (3.3) [a]	0	
Hyperstrimulation	5/61 (8.19) [a]	0	
Scar dehiscence	1/61 (1.63) [a]	0	

[a] - Percentage [b] - Range

Table 3. Dose requirement till delivery in first entry.

Women entered (n=50)			Women entered (n=50)		
Dose of oxytocin (mU/minute)	**Delivered Number**	**Not delivered Number**	**Dose of misoprostol (?g)**	**Delivered Number**	**Not delivered Number**
1-6	-	-	50	9 (18)	-
8-12	3 (16)	-	100	27 (52)	-
14-18	8 (16)	-	150	6 (12)	-
20-24	8 (16)	-	200	3 (6)	-
26-30	6 (12)	-	250	3 (6)	-
32	14 (28)	11 (22)	300	1 (2)	1 (2)
Total	39 (78)	11 (22)		49 (98)	1 (2)

Figures in brackets represent percentages.

Table 4. Mode of delivery

	Misoprostol (n=61)	**Cateheter/ oxytocin (n=51)**	**P value**	**Failure of both entries (n=5)**
Mode of delivery				
Vaginal	41/61	27/51	0.1235	4
Normal	36/41	27/27		4
Forceps	5/41	0		0
Cesarean section	14/61	13/51	0.7544	1
Indication of cesarean section				
Fetal distress	11/14	13/13	0.3381	0
Cervical dystocia	2/4	0		1/1
Scar dehiscence	1/14	0		0

Seven women with one previous cesarean section (both first and second entry) were induced with misoprostol in each group (Table 2). One woman had scar dehiscence with mioprostol while none with oxytocin. Fetal heart abnormalities were observed in fewer women with catheter/oxytocin than with misoprostol (12/50 v/s 18/ 50) but the difference was not statistically significant (P=0.190) (Table 5).

The majority of women in both the groups delivered vaginally (41/61 in misoprostol group vs 27/51 in catheter/oxytocin group; P=0.123) and fetal distress was the most common indication for cesarean section (11/14 in misoprostol group v/s 13/13 in catheter oxytocin group, P=0.338) (Table 4) . Out of the five women who failed to go into labor (first failure +second failure) four delivered with higher dose of oxytocin (40-48 mU/minute and one had cesarean section because of cervical dystocina.

Table 5. Neonatal outcome.

	Misoprostol (n=50)	**Catheter/ Oxytocin (n=50)**	**P-value**
Birth weight (kg) mean (range)	2.8 (2.25-3.5)	2.8 (1.9-3.5)	
Apgar at 1 minutes	7	7	
Apgar at 5 minutes	9	9	
Apgar < 7 at 5 minutes	1	1	
Meconium staining of liquor	2	1	
Fetal heart abnormalities	18	12	0.1906
Admission to neonatal intensive care unit	3	1	
Live birth	49/50	50/50	
Still birth	1	0	

There were no significant differences in the neonatal outcomes between the two groups. All the neonates were born alive with apgar score of nine at five minutes. But the woman who had scar dehiscence in misoprostol group lost her fetus. Only one baby in oxytocin group and three in misoprostol group required admission to neonatal intensive care unit (Table 5).

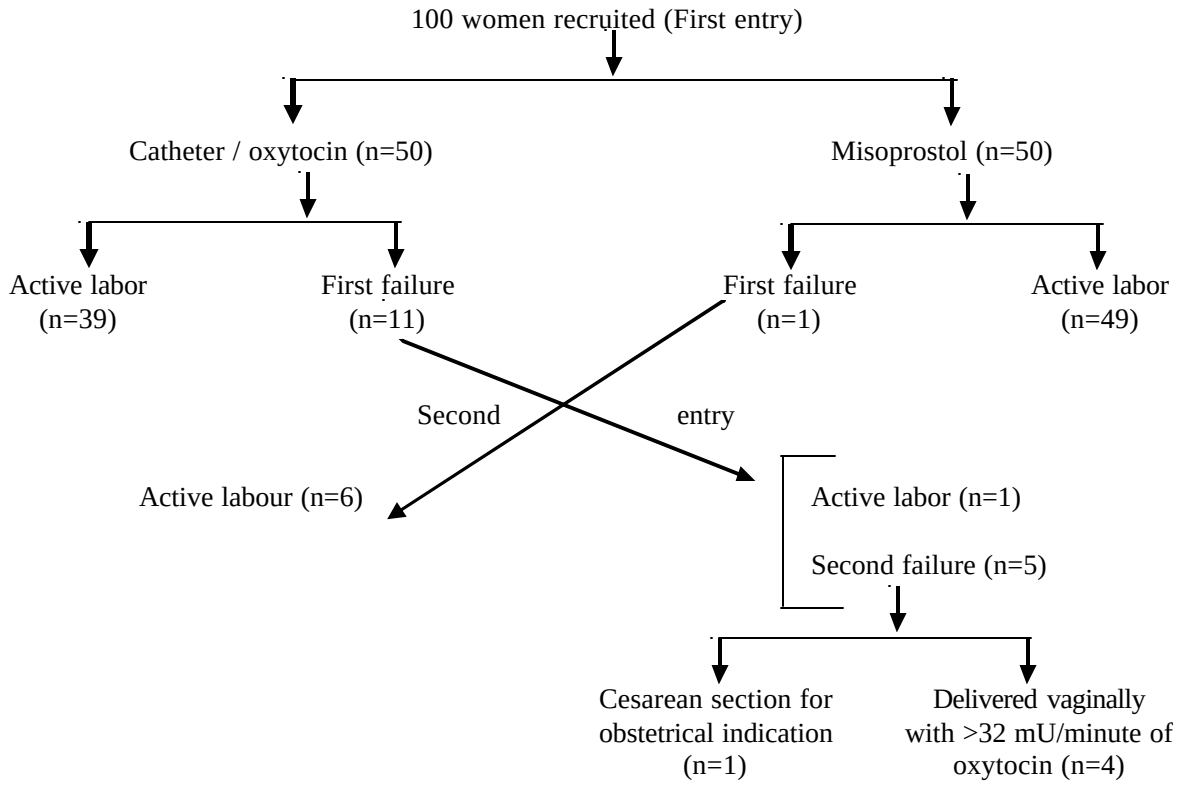

Figure 1. Schematic representation of results.

Disscussion

With 91% and 83% delivery rate within 24 hours with vaginal misoprostol and catheter/oxytocin respectively the required sample size was 274 with 80% power of detecting significance of < 0.05. However due to time constraint and limited availability of cases (our institution being unaided private tertiary center the study was confined to a sample size of hundred. Hence our study is underpowered. A large number of randomized trials suggest that vaginally administered misoprostol is an effective agent for cervical ripening or labor induction. The main concern with this agent is the incidence of excessive uterine contractions, which appears to be dose related. Higher the misoprostol dose, the shorter is the induction-delivery interval but higher is the incidence of uterine hyperstimulation [8]. In our study with vaginal misoprostol successful induction could be achieved in 98% women and with catheter/oxytocin in 78%. Other studies report that when 25 ?g vaginal misoprostol was compared with oral 50?g dose success rate was 107/110 and 95/110 respectively [9] while with 50 ?g intravaginal misoprostol it was 100% and induction-delivery interval was reduced from 18 hours to 11 hours [10]. In our study induction delivery interval was 11.58 hours with misoprostol and 19.45 hours with catheter oxytocin (P=0.002). Progress of labor is also rapid with misoprostol as compared to that with oxytocin leading to greater number of women delivering within 24 (91% vs 83%) [11]. In our study too, 88% of women delivered within 24 hours in misoprostol group compared to 72% in catheter/oxytocin group. In Caliskan et al's [12] study 91.3% delivered within 24 hours with sublingual misoprostol.

Complications are the main concern with misoprostol as inducing agent [10,13]. It appears that the incidence of uterine tachysystole is dose related as with 25 ug vaginal dose the incidence is 17% [13], with 50 ?g 37% [11], and with 100 ?g 72% [14]. In our study it was 8.19%. With sublingual route the incidence is 17.5% [11]. Inspite of relatively high incidence of uterine tachysystole it does not result in increase in cesarean rate, low apgar score, neonatal acidosis, or admission to

neonatal intensive care unit [10-14]. Our experience was similar.

During labor even 100 ?g misoprostol did not significantly increase the incidence of meconium passage which was 22% as compared to 18% with catehter/oxytocin [14]. We had 4% and 2% incidence of meconium passage in misoprostol and oxytocin groups respectively.

Vaginal misoprostol is an effective inducing agent but its use in previous cesarean section requires great caution. We observed one scar dehiscence with misoprostol. Even reducing its dose to 25 ?g had led to uterine scar disruption in two women forcing to abandonment of the trial prematurely [15]. Multiple doses of misoprostol have also caused rupture of nonscarred multiparaous uterus [16].

Conclusion

As a cervical ripener and labor inducing agent, 50 ?g vaginal misoprostol is highly effective, inexpensive and stable at room temperature. It is superior to catheter/oxytocin. In cases of previous cesarean section this powerful uterotonic should be used under the supervision of a trained personnel and with utmost caution.

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