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ORIGINAL ARTICLE

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Induction of labor with oral misoprostol in women with prelabor rupture of membranes at term

Datta *Mamta* Rath, Kabiraj *Manas*

Tata Main Hospital, Jamshedpur – 831001.

OBJECTIVE(S): To evaluate the efficacy of oral misprostolol for induction of labor in women with prelabor rupture of membranes (PROM) at term.

METHOD(S): Three hundred pregnant women at term with PROM, singleton pregnancy and cephalic presentation who were not in labor were taken up for study and were randomly selected for conventional expectant management for 20-24 hours followed by induction by oxytocin (control group) or oral misoprostol in the dose of 50 μg 4 hourly upto a maximum of six doses (study group). Chi square test and standard error of difference between two means [SE(d)] were used for statistical evaluation.

RESULTS : Cesarean rates were comparable in the two groups (16.7% and 18% in study and control groups respectively). Induction delivery interval was similar (10 hours 26 minutes ± 4 hours 11 minutes and 9 hours 39 minutes ± 2 hours 42 minutes in study and control groups respectively). The mean PROM - delivery interval was significantly shorter in the study group (18 hours 10 minutes ± 7 hours 20 minutes vs 29 hours 55 minutes ± 5 hours 54 minutes). Oxytocin requirement was lower in the study group (38% vs 80%). The average nursery stay was also lower in the study group (3.5 vs 6.4 days).

CONCLUSION(S) : Oral misoprostol significantly reduces the PROM - delivery interval, oxytocin requirement, and average nursery stay, and provides a cheap method of induction of labor in women with PROM.

Key words : induction of labor, PROM, misoprostol

Introduction

Prelabor rupture of membranes (PROM) affects 10% of all pregnancies. Existing views differ widely regarding the timing and method of induction of labor in PROM at term.

The advent of prostaglandin analogue, misoprostol, has given the obstetricians another alternative to the traditional use of oxytocin for active management of PROM.

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Correspondence :
Dr. Mamta Rath Datta
B2, Maharani Mansion
36, Circuit House Area,
Jamshedpur - 831 001.
Tel. 06572224845 Email : drmamtadatta@hotmail.com

Prostaglandins are used in obstetrics because of their uterotonic effect. They are used as cervical ripening agents for labor induction and control of postpartum hemorrhage.

Misoprostol is a synthetic analogue of PG E_2. When given orally, it is rapidly absorbed by gastrointestinal tract. It then undergoes deesterification to its free acid, which is responsible for its clinical activity. Peak concentration time and half life of misoprostol acid (the active metabolite) are 12 minutes and 21 minutes respectively. Total systemic bioavailability of vaginally administered misoprostol is three times greater than that of orally administered misoprostol. Misoprostol is extensively used because it is effective, inexpensive, easily stored (shelf life 2 years), not affected by ambient temperature and needs no refrigeration for its storage and no needles or syringes for administration. It has, in comparison to the other prostaglandins, minimal effects on cardiovascular system

and bronchial tree smooth muscles and so can be safely used in hypertensives and asthmatics. Vaginal application of misoprostol for induction of labor has been extensively studied. We studied the efficacy of oral misoprostol for induction of labor in PROM. We chose the oral route because of its ease of administration.

Methods

This prospective study was undertaken from August 2002 to July 2005. Three hundred women attending labor room for PROM at more than 37 weeks pregnancy, with singleton fetus in cephalic presentation and a normal cardiotocography (CTG) tracing were included in the study. They were not in labor. Those with a scarred uterus, multiple pregnancies, nonvertex presention, features of chorioamnionitis, severe gestational protinuric hypertension, medical diseases, grand multiparity and antepartum hemorrhage were excluded from the study. Those included in the study were randomly assigned to two groups.

Group I – These were given 50 μg of oral misoprostol at 4 hourly intervals upto a maximum of 6 doses. A CTG was done before each dose of misoprostol. Women who went into active labor, had vaginal examinations at 4-6 hour intervals. If after 6 doses the woman did not go into active labor, the induction was considered as failed. Once active labor set in, oxytocin was added for acceleration, if necessary.

Group II – These women were managed by the traditional conservative method of watchful expectancy for 20-24 hours following PROM after which a pelvic examination was done and oxytocin drip given for induction/acceleration of labor as the case may be. Thereafter, pelvic examination was done every 4-6 hours.

Both the groups were given antibiotics like ampicillin/ amoxyicillin and were monitored for fetal distress, tachysystoles, hyperstimulation, and progress of labor. Study was approved by the ethics committee of the hospital

Chi square test and standard error of difference between two means were used for statistical evaluation.

Results

Hundred and nine women in the study group and 116 in the control group were primigravidas (Table 1).

Table 1. Distribution of parity

Parity	Study group N=150	Control group n=150
0	109	116
1	26	19
>2	15	15

Table 2 shows that the cesarean rates were comparable in the two groups and the induction delivery intervals were also similar. However, the PROM delivery interval was significantly shorter in the study group [SE(d) = 46] and 80% women in the study group delivered within 24 hours compared to only 30% in the control group (P<0.05). Fifty seven women (38%) required oxytocin acceleration in the study group as compared to 120 women (80%) in the control group (P<0.05). On an average 3 doses of 50 μg misoprostol were required in the study group (Table 2).

Table 2. Labor outcome.

Labor outcome	Study group (PROM) N=150	Control (Expectant treatment) n=150	Test of significance
Vaginal delivery	125 (83.3%)	123 (82%)	P>0.50
Cesarean Delivery	25 (16.7%)	27 (18%)	P>0.50
Induction-delivery interval	10 hours 26 minutes ± 4 hours 11 minutes	9 hours 39 minutes ± 2 hours 42 minutes	S.E (d) = 24.5 Not significant [a]
PROM – delivery interval	18 hours 10 minutes ± 7 hours 20 minutes	29 hours 55 minutes ± 5 hours 54 minutes	S.E (d) = 46 Significant [b]
Delivered within 24 hours	120 (80%)	45 (30%)	P<0.05
Oxytocin required	57 (38%)	120 (80%)	P <0.05
Average misoprostol doses required	3	Not applicable	Not applicable

[a] Difference between the two means is 45 minutes i.e less than twice the SE (d) and hence is not significant
[b] Differene between the two means is 705 minutes i.e, more than twice the SE (d) and hence is significant.

Table 3. Neonatal outcome.

Parameter	Study group	Control group	P value
Apgar score < 7	10 (6.6%)	9 (6%)	>0.5
Meconium stained liquor	14 (9.3%)	10 (6.6%)	>0.5
Nursery admission	35 (23.3%)	96 (64%)	<0.01
Average nursery stay	3.5 ± 1.9 days	6.4 ± 2.3 days	SE (d) = 0.5. Significant [a]

[a] Difference between two means is 2.9 days i.e. more than twice the SE(d) and hence is significant.

Table 4. Comparison with other studies.

Study	Route and dose	Induction delivery interval	PROM delivery interval	Cesarean rate	Oxytocin requirement	Delivery in 24 hours	Apgar score <7 at 1 minute	Average Nursery stay
Ozden et at (2002) [5]	Vaginal, 50 µg	8.68 ± 4.4 hours	19.37 ± 7.2 hours	-	45.2%	-	6.4%	-
Shetty et al (2002) [2]	Oral, 50 µg 4 hourly Maximum 5 doses		20.5 hours	16.7%	36.7%	72%	-	-
Mozurkewich et al (2003) [4]	Oral, 100 µg 6 hourly 2 doses	- 11.9 hours		20.1%	-	-	-	-
Krupa et al (2005) [3]	Vaginal	18.9 hours	-	20%	-	44%	-	-
Cheung et al (2006) [7]	Oral; (i) 50 µg (ii) 100 µg 4 hourly Upto 6 doses	-	(i) 14.5 ± 6.2 hours (ii) 13.0 ± 6.1 hours	-	-	50%	-	-
Present study	Oral	10 hours 26 minutes ± 4 hours 11 minutes	18 hours 10 minutes ± 7 hours 20 minutes	16.7%	38%	80%	6.6%	3.5 days

Out of the 25 women who delivered by lower segment cesarean section (LSCS) in the misoprostol group, 15 (60%) had fetal distress as compared to 15 of the 27 women (55.5%) in the control group. This difference was not statistically significant. Eight women (32%) in the study group and 10 (37.3%) in the control group needed LSCS for failure to progress. The incidence of cephalopelvic disproportion (CPD) needing cesarean section was also similar in the two groups (8% and 7.4% respectively).

The incidence of babies with apgar <7 was similar in both the groups (6.6% and 6% respectively). The incidence of meconium stained liquor was 9.3% in the study group as compared to 6.6% in the control group. These differences were not significant. Thirty five babies (23.3%) in the study group were admitted to the nursery as compared to 96 babies (64%) in the control group (P<0.001). The average duration of nursery stay was significantly (P <0.01) less in the study group (3.5 vs 6.4 days).

Discussion

Majority of the women in our study were primigravidas (Table 1) The induction to delivery interval was similar in the two groups 10 hours 26 minutes ± 4 hour 11 minutes (range 3 hours 30 minutes to 20 hours) in the misoprosol group and 9 hours 39 minutes ± 2 hours 42 minutes (range 4 hours to 18 hours 20 minutes) in the group of expectant management. Women in the misoprostol group required 3 doses of 50 µg on an average. Krishnamma et al [1] have also reported an induction delivery interval of 12-14 hours with vaginal misoprostol. Table 4 gives comparison of our results with those of other workers. Mozurkewich et al [4], reported that the induction to vaginal delivery interval was similar in the misorostol and oxytocin group. The mean PROM-delivery

interval was 18 hours 10 minute ± 7 hours 20 minutes in the misoprostol group and 29 hours 55 minutes ± 5 hours 54 minute in the control group in our study and the difference was statistically significant. In our study 40% of those managed conservatively went into spontaneous labor within 24 hours. Eighty percent of women in the misoprostol group delivered within 24 hours of PROM compared to only 30% the women managed conservatively (P<0.05). Shetty et al [2], reported that 72% of women induced with misoprostol delivered within 24 hours of PROM compared to only 26.9% in the conservative group while 93.3% of the misoprostol group and 54.8% of the conservative group went into labor within 24 hours of PROM. Further they reported a PROM delivery interval of 20.5 hours in the misoprostol group as compared to 35.5 hours in he conservatively managed group. Cheung et al [7], reported a PROM delivery interal of 25.1 ± 10.5 hours with 50 μg oral misoprostol and that more than 50% of women delivered within 24 hours of PROM. In the misoprostol group in our study, 38% required additional oxytocin for augmentation. Shetty et al [2] have reported a 36.7% oxytocin requirement rate in the misoprostol group while Ozden et al [5] reported a 45.2% oxytocin requirement rate in women induced with oral misoprostol and 100% oxytocin requirement in the group managed expectantly. Hofmeyr et al [6], reviewed published articles on misoprostol for induction of labor and reported that oral misoprostol reduced the need for oxytocin.

LSCS rates were similar in our two groups i.e., 16.7% and 18% respectively (p>0.50). This is similar to that reported by Krishnamma et al [1] viz. 27.3 rate using vaginal misoprostol in women requiring induction of labor but without PROM. Shetty et al [2] reported a LSCS rate of 16.7% in the oral misoprostol group and 16.2% in the conservative management group. Krupa et al 2005 [3], reported a LSCS rate of 20% in the misoprostol group and 30.7% in the group with expectant management. The indications for LSCS were similar in both the groups in our study viz., fetal distress, failure to progress and CPD. Out of the 25 women in the misoprostol group who had LSCS, 15 (60%) had fetal distress as the cause for LSCS while out of the 27 women who had LSCS in the group with expectant management 15 (55.5%) had fetal distress as the cause for LSCS; the difference was not statistically significant. In the study by Krishnamma et al [2]. LSCS rate was 27.3% (41 out of 150 women) and out of these 17 (41.4%) had fetal distress. In our study, 6.6% of the newborns in the misoprostol group had an apgar score <7 at 1 miunte compared to 6% in the group managed conservatively. This difference is not statistically significant. Ozden et al [5] reported that in their study 6.4% of the newborns had an apgar score < 5 at 1 minute. Slightly higher incidence of meconium stained liquor was found in the misoprostol group compared to that in the control group (9.3% vs 6.6%)in our study. 23.3% of the babies in the study group went to the nursery for observation compared to 64% of the babies in the control group (<0.01). This is probably because more babies delivered within 24 hours of PROM in the study group as compared to those managed by the conservative method. The average nursery stay was significantly higher in the group managed conservatively (6.4 vs 3.5 days; SE(d)=0.5.

We did not have any incidence of tachysystole or any other untoward effect in either of the groups.

Conclusion

The PROM - delivery interval was significantly decreased with the use of oral misoprostol. The number of nursery admissions and the average nursery stay were significantly reduced with the use of oral misoprostol. The LSCS rate and perinatal outcome were comparable in the two groups. The slightly increased incidence of meconium stained liquor with misoprostol does not seem to affect the newborn adversely. Oral misoprostol is a safe, effective, easy to administer and cheap drug for active management of patients with PROM at term.

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