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RESEARCH ARTICLE

Oral Misoprostol *vs* Intravenous Oxytocin Infusion for Induction of Labor in Prelabor Rupture of Membranes

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ABSTRACT

Objectives: To compare the efficacy, side effects and safety of oral misoprostol to intravenous oxytocin infusion for induction of labor in prelabor rupture of membranes (PROM).

Materials and methods: Two hundred and sixty-six women of prelabor rupture of membranes were assigned to receive either oral misoprostol 100 µg 6 hourly to a maximum 3 doses (misoprostol group, n = 142), or escalating doses of oxytocin infusion up to 20 mIU/min in primigravida and up to 10 mIU/min in multigravida (oxytocin group, n = 114).

Results: Demographic characteristics were similar in both the groups. The difference in mean induction to delivery interval (8.2 ± 6 hours in misoprostol group *vs* 12.2 ± 6 hours in oxytocin group) was statistically significant when two groups were compared. The incidence of vaginal delivery (86.1% in misoprostol group *vs* 84.2% in oxytocin group), and cesarean delivery (13.9% in misoprostol group *vs* 15.8% in oxytocin group), was almost similar in both the groups. The indication of cesarean delivery was dystocia (40% in misoprostol group *vs* 67% in oxytocin group), and fetal distress (60% in misoprostol group *vs* 33% in oxytocin group) and the difference was statistically significant ($p < 0.01$). Maternal and neonatal safety outcomes were similar for the two treatments.

Conclusion: Oral misoprostol in prelabor rupture of membrane have almost similar results as intravenous oxytocin in safety, efficacy and side effects except induction delivery interval, which is less in misoprostol group.

Keywords: Induction of labor, Misoprostol, Oxytocin induction, Prelabor rupture of membranes.

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INTRODUCTION

Prelabor rupture of membranes (PROM), which is defined as rupture of membranes before onset of labor, complicates 5 to 10% of pregnancies.[1] At least 60% of cases of PROM occur at term. Both oxytocin and prostaglandins are effective in inducing labor in women with PROM at term.[1] Several studies have demonstrated the use of oral misoprostol in women with PROM.[2-4] If induction is attempted with intravenous oxytocin drip in women with unfavorable cervix, the possibility of failed induction and subsequent cesarean delivery approaches 30 to 40% and protracted labor increases the risks of maternal and neonatal infection.[1]

Misoprostol is a unique prostaglandin E1 analog, which is rapidly absorbed orally. Tablets marketed for anti-inflammatory drug-induced gastric ulceration, are stable and cheap. Its effect on myometrium is mediated by binding to prostanoid receptors in the myometrium. The drug does not require refrigeration prior to its use. It is available in blister packing.[5] These features make it ideal for use in third world countries.

In most trials, vaginal route has been chosen, presumably because this route has been most successful for other prostaglandins and because misoprostol has a far longer half-life when administered vaginally than orally.[6] However, the short half-life of oral misoprostol may be an advantage in induction of labor, because of the less risk for hyperstimulation of uterus and less tachysystole. The advantage of misoprostol orally with particular reference to prelabor rupture of membranes, is avoidance of repeated vaginal examinations resulting in less risk of sepsis for the mother and baby.[7] Dose for oral 6 hourly resulted in misoprostol for induction labor varies from 50 to 100 mgm, every 4 hours. A meta-analysis of the Cochrane library suggested that oral misoprostol for labor induction in a dose of 100 µg or more are effective, with more successful vaginal delivery within 24 hours, but labor should be carefully watched for uterine hyperstimulation.[8]

The objective of this study was to assess the effectiveness, side effects and safety an oral dose of 100 µg misoprostol every 6 hours in women with PROM. The outcome measures studied included induction to delivery interval, operative delivery rates, and the neonatal and maternal outcomes.

MATERIALS AND METHODS

The study was conducted from December 2008 to June 2012 in the Department of Obstetrics and Gynecology, JNMC, AMU, Aligarh, Uttar Pradesh. Women were eligible for the study, if they had ruptured membranes at > 37 weeks of gestation, or at < 37 weeks of gestation with indication of termination of pregnancy, had a single fetus in cephalic presentation and were not in labor. Diagnosis was based on: (i) clinical history of passage of liquor, (ii) pooling of fluid in posterior fornix as seen by speculum examination and (iii) reduced liquor volume on sonography (AFI < 5) in selected women where clinical findings were inconclusive. No other tests of spontaneous rupture of membranes, such as pH of the vagina or the presence of ferns on microscopy were made. At the time of diagnosis of rupture of membranes, fetal heart sound was monitored and Bishop scoring was also done. If the women were not in labor, randomly allotted to induce with either oral misoprostol or intravenous oxytocin and accordingly labeled as misoprostol or oxytocin group. Prophylactic antibiotic of a penicillin group or erythromycin if the woman is allergic to penicillin, was given.

In the misoprostol group, labor was induced by 100 µg misoprostol given orally, which was repeated after 6 hours, of maximum 3 doses. The dose was not repeated if there were two or more contractions lasting for more than 20 seconds.

In oxytocin group, oxytocin was placed in 500 ml of normal saline solution and the infusion started at 2 mIU/minute. Primigravida was started with 5 IU of oxytocin, dose was escalated according to duration of uterine contraction at 30 minutes interval, maximum dose given was 20 mIU/min. Multigravida was started with 2.5 IU of oxytocin, maximum dose given was 10 mIU/min.[9]

Women were excluded from the study if they were in labor or if there was any contraindication to induction of labor or to misoprostol as previous cesarean, fetal distress or CPD. Vaginal examination was performed every 4 hours to assess the progress of labor.

The primary study outcome was the rate of vaginal delivery and the secondary outcome was assessed as induction to delivery interval, maternal and neonatal side effects, and complications. Data were compared by using student t-test and z-test for proportion.

RESULTS

Out of the 266 women of PROM 142 were assigned to the misoprostol group and 124 to the oxytocin group. Demographic characteristics were similar in both the groups, when they were compared regarding age, parity, gestational age at the time of labor induction, bishop score (Table 1). Mean induction to delivery interval in misoprostol group was 08.2 ± 6 hours and in oxytocin group it was 12.2 ± 6 hours, the difference was statistically insignificant when the two groups were compared (p = 0.006) (Table 1).

A total of 72.5% of women delivered with one dose of misoprostol, 22.22% required 2 doses, and only 2.28% required 3 doses. A total of 12.5% of women in misoprostol group required oxytocin augmentation.

One hundred and thirty-one (92.3%) in misoprostol group had vaginal delivery while 112 women (90.3%) in oxytocin group had vaginal delivery. The difference was statistically insignificant when the both groups were compared. Eleven women (7.7%) in misoprostol group had cesarean delivery while 12 women (9.7%) in oxytocin group had cesarean delivery, the difference was statistically insignificant, when the two groups were compared (Table 2). Dystocia was the cause of cesarean in four women (36.4%) in misoprostol group *vs* in eight women (66.7%) in oxytocin group, and the difference was statistically significant, when the two groups were compared (p < 0.01) (Table 2). Fetal distress was the cause of cesarean in seven women (66.7%) in misoprostol group *vs* four women (33.3%), in oxytocin group, and the difference was statistically significant when the two groups were compared (p < 0.01) (Table 2).

The complication rate was almost similar in both the groups. Hyperstimulation 2 (1.4%), cervical tear 2 (1.4%) and perineal tear 2 (1.4%) occurred in misoprostol group while in oxytocin group, hyperstimulation 1 (0.8%), cervical tear 1(0.8%) and perineal tear 2 (1.6%). In

Table 1: Demographic parameters and mean induction to delivery interval in misoprostol group and oxytocin group

	Misoprostol group	*Oxytocin group*	*p-value*
Mean age (years)	23.9 ± 4.9	24.4 ± 4.9	0.02
Parity			
0	98 (69.1%)	88 (70.9%)	0.153
≥ 1	44 (30.9%)	36 (29.1%)	0.100
Mean gestational age at the time of labor induction (weeks)	36.1 ± 4.0	37.0 ± 3.4	0.01
Mean bishop score	1.9 ± 1.6	2.3 ± 1.6	0.01
Mean induction to delivery interval (hours)	8.2 ± 6 hours	12.2 ± 6	0.006

Table 2: Mode of delivery and cause of cesarean in misoprostol group and oxytocin group (n = 266)

Mode of delivery and indication of cesarean	*Misoprostol group (n = 142)*	*Oxytocin group (n = 124)*	*p-value*
Vaginal delivery	131 (92.3%)	112 (90.3%)	0.02
Cesarean delivery	11 (7.7%)	12 (9.7%)	0.654
Dystocia	4 (36.4%)	8 (66.7%)	0.001
Fetal distress	7 (66.7%)	4 (33.3%)	0.002

Table 3: Maternal complications in misoprostol group *vs* oxytocin group

	Misoprostol group		*Oxytocin group*	
Complications	*n = 142*	*%*	*n = 124*	*%*
Nausea and vomiting	1	0.70	—	—
Chorioamnionitis	2	1.6	2	1.6
Diarrhea	—	—	—	—
Fever	1	0.70	1	0.8
Hyperstimulation	2	1.4	1	0.8
Rupture uterus	—	—	—	—
Cervical tear	2	1.4	1	0.8
Perineal tear	2	1.4	2	1.6
Postpartum hemorrhage	2	1.4	2	1.6

Table 4: Neonatal outcome in misoprostol group *vs* oxytocin group

	Misoprostol group		*Oxytocin group*	
Complications	*No.*	*%*	*No.*	*%*
Meconium	8	5.63	6	4.84
NICU admission	4	2.82	3	2.42
Neonatal death	1	0.70	2	1.61

misoprostol group, postpartum hemorrhage were occurs less than the oxytocin group (1.4 *vs* 1.6%). The incidence of complications was very less in both the groups and the difference did not reach the statistical significance (Table 3).

Meconeum aspiration occurred in eight newborns (5.63%) in misoprostol group, while in oxytocin group, it occurred in six newborns (4.84%). Four newborns (2.82%) in misoprostol group were admitted to neonatal intensive care unit (ICU) while three newborns (2.42%) in oxytocin group, were admitted to neonatal ICU. Neonatal death occurred one (0.70%) in misoprostol group and two (1.61%) in oxytocin group (Table 4). The difference was not statistically significant.

DISCUSSION

Misoprostol is safe and inexpensive agent for labor induction.[10] Among the 266 women who were included in the study, 186 (72.65%) were primigravidas. Snehamay[11] and Semuzek-Sikora et al[12] also had greater number of primigravidas.

Our study showed the induction delivery interval is significantly less in misoprostol group than in oxytocin group. Levy et al also showed the same result when they compared with placebo, oral misoprostol reduced the need for oxytocin infusion and shortened the time between induction and delivery (the difference was 8.7 hours; 95% CI: 6.0–11.3).[2] According to Sanchez-Ramos et al, there were no significant differences in the induction delivery interval, but the need for oxytocin is significantly reduced in misoprostol group.[10] The Misoprom study showed the comparable result in both the groups except postpartum hemorrhage is less common with misoprostol than oxytocin.[13] Our study also showed the postpartum hemorrhage was occurs less in misoprostol group than the oxytocin group (1.4 *vs* 1.8%). The present study showed that the rate of vaginal delivery and cesarean are comparable in both groups. These findings were comparable to other studies also.[2,8,10] Our study showed the total percentage of cesarean delivery was not significantly different, although the percentage of cesarean delivery for dystocia was lower in misoprostol group 36.4 *vs* 66.7%, $p \leq 0.01$, compatible with findings of study done by Kremer et al.[14] The complications were less in our study, because we had not repeated the dose once the contractions had started. The maternal and neonatal complications were similar in both the groups, which were comparable to other studies also.[8,10]

Oral misoprostol given to women with unfavorable cervix soon after term PROM significantly reduces the induction-to-delivery time and the need for oxytocin and antibiotics.[2] Using oral misoprostol for labor induction reduces the frequency of vaginal examinations and use of intravenous line only in late labor and, therefore, the patients may not have felt as restricted in early stage of labor.

CONCLUSION

Our study suggests that the women with PROM induced with oral misoprostol resulting in shorter induction to delivery intervals and good fetal outcome. Oral misoprostol can be used safely as an alternative to oxytocin infusion or prostaglandin vaginal pessaries/gel for labor induction in women with PROM.

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