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Research Article

Oxytocin and oral misoprostol for labor induction in prelabor rupture of membranes

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ABSTRACT

Background: Prelabor rupture of membrane is one of the most common complications of pregnancy, and the best management option for women with this condition is debatable. This study aims to compare intravenous oxytocin with that of oral misoprostol for labor induction in women with prelabor rupture of membrane.
Methods: One hundred and forty women at Central Referral Hospital, Gangtok, India were randomized to receive either misoprostol 50 µg orally every 4 hours or intravenous oxytocin. The primary outcome measure was time from induction to vaginal delivery.
Results: The mean time±standard deviation to vaginal birth with oral misoprostol was 5.0±2.58 hours compared with 4.33±2.3 h with oxytocin which was just statistically significant (P = 0.048). There were no difference in the maternal secondary outcome, including cesarean birth (ten and twelve respectively) and gastrointestinal side effects. Neonatal outcomes including Apgar scores and admission to ICU (NICU) were not different.
Conclusions: Although oxytocin resulted in shorter induction to delivery interval, oral misoprostol is still an effective option for PROM, as delivery and neonatal outcomes were similar.

Keywords: Induction of labor, Misoprostol, Oxytocin, Premature rupture of membranes

INTRODUCTION

Premature Rupture of Membranes (PROM), defined as rupture of membranes before onset of labor, occurs in 8-10% of term pregnancy. A prolonged interval from rupture of membrane to delivery are associated with higher risk of maternal infection (such as chorioamnionitis, postpartum endometritis, and sepsis) and more seriously, neonatal sepsis.[1]

The management of term patients with PROM, especially those with an unfavourable cervix, remains controversial. Management options range from expectant management or immediate induction of labor to delayed induction with mechanical methods, vaginal or oral prostaglandin (PG), or intravenous (IV) oxytocin.[1] Results of the International Term PROM Trial suggest that immediate induction results in greater maternal satisfaction and lower risk of maternal infection than expectant treatment.[2]

Oxytocin and prostaglandins are the most frequently used pharmacological agents for induction of labor.[3] Oxytocin is the standard agent for labor induction. It is produced endogenously chiefly in the hypothalamus and released from the posterior pituitary gland.[4] Although oxytocin infusion is accepted widely as a safe and effective labor induction method, its success highly dependent on the condition of the cervix at the beginning of the induction.[3]

Oral misoprostol, a prostaglandin E1 analogue, has been shown to be safe and effective for cervical ripening and labor induction to be considered as an alternative

induction agent in PROM. Particularly in women with poor cervical score.[5]

The benefit of oral misoprostol being easy administration, inexpensive, stable at room temperature and greater maternal satisfaction as it allows ambulation in early labor and avoidance of IV induction agents.

In view of this, a randomized controlled study was done with the primary research question whether oral misoprostol for induction of labor in women with PROM differed from IV Oxytocin. Secondary outcome included mode of delivery, maternal morbidity and neonatal morbidity.

METHODS

Study design

This prospective controlled-randomized study included all pregnant women presenting with spontaneous rupture of membrane beyond 28 weeks gestation at Central referral Hospital, the teaching hospital of Sikkim Manipal Institute of Medical Science (SMIMS), Gangtok from December 2011 to December 2013.The research proposal was approved by Institute (SMIMS) Ethical Committee. All women were informed about the nature of the study and a written informed consent was obtained before starting the study.

Women were eligible if they presented with PROM diagnosed by sterile speculum examination that showed passage of amniotic fluid and had singleton pregnancy greater than 28 completed weeks of gestation with cephalic presentation. Exclusion criteria included any contraindication to vaginal birth, prior uterine surgery, active maternal vaginal bleeding, chorioamnionitis, major fetal anomalies, and contraindication or known hypersensivity to prostaglandin use.

One hundred and forty patients were randomly assigned to Group I (Oral Misoprostol) and Group II (IV Oxytocin) at random using computer generated tables for the purpose of the study, keeping in mind the inclusion and exclusion criterion. All women included in the study received antibiotics (IV Ampicillin 2gm IV after test dose followed by 500 mg IV 6 hourly), had a local examination (P/V) to confirm diagnosis of PROM, presentation, position station, and assessment of the Bishop's Score.

Subjects randomly assigned to oral misoprostol receive 50 µg at 4-hour interval until progressive labor, uterine contraction of at least three per 10 minutes, side-effects (vomiting, diarrhoea , unduly forceful uterine contraction, fall in blood pressure or tachycardia), delivery occurred , or maximum of 4 doses (200µg) achieved.

Subjects assigned to IV oxytocin group received an intravenous infusion of oxytocin starting at a dose of 2mU/min with an incremental increase of 2mU/min every 30 min until adequate contraction, side-effects (hyperstimulation or fetal distress) or maximum infusion dose of 20 mU/min was achieved. Oxytocin infusion was administered by an intravenous set using the gravity-fed counting drop technique.

Women admitted to the delivery room were monitored by intermittent auscultation, with continuous cardiotography monitoring advocated as per need. Labor progress was monitored in each woman with a partogram. The induction process was stopped whenever any fetal or maternal complications developed and cesarean section was performed. In the misoprostol group, induction was considered failed, if the modified Bishop score was <5 or no uterine contraction was achieved 4 hours after the last dose. In the oxytocin group if the women failed to enter active phase of labor within 12 hours after starting oxytocin, induction was considered failed.

Neonatal assessment included Apgar score, neurological and general physical assessment which was done by the Pediatrician.

The primary study outcome was time from onset of induction to vaginal delivery (IDI). The secondary study outcomes were the mode of delivery, maternal side effects and perinatal outcome. Assuming a 10% difference in treatment outcome between two groups, the required sample size was approximately 70 in each treatment group with a p- value of 0.05 and power of 80%, to give a sample size of 140.

Statistical data was analyzed on an intent-to-treat basis by parametric (Unpaired t test) and nonparametric statistics (Mann-Whitney U, Fisher exact and chi-square tests) using SPSS version 17.0. Continuous variables were described as mean±SD, and categorical variables were presented as absolute numbers (n) and percentage (%). Significance of outcome was expressed by the P value (>0.05 was considered nonsignificant, <0.05 was considered significant, and <0.001 was considered highly significant).

RESULTS

A total of 140 women who presented with PROM were enrolled in the study, 70 to oral misoprostol group and the other 70 to oxytocin group. Maternal demographics are presented in Table 1, with no significant difference between groups.

The number of women delivering vaginally was not significantly different between the two groups. In the misoprostol group 60 and in the oxytocin group 58 women delivered vaginally. There was a statistically significant difference between the groups in the time of IDI as the mean was lower in the oxytocin group than in the misoprostol group (4.33±2.33 and 5.0±2.58; *P* 0.048), respectively, as presented in Table 2. Also, there was a

significant difference between the study groups in the number of women delivering within 3 hours of treatment with 47.1% of oxytocin group delivering as compared to 25.7% in the misoprostol group.

The modes of delivery and the indication for cesarean section were not different in two groups. In the oral misoprostol group there were ten cesarean birth and twelve cesarean in oxytocin group (P = 0.642). The indications for cesarean was non-reassuring FHR in five, failed induction in one and abruption in two with misoprostol, and non-reassuring FHR in six and cervical dystocia in one with oxytocin.

Maternal satisfaction as much higher in oxytocin group as nearly 50% of women in the group delivered within 3 hours of induction. Maternal gastrointestinal side- effects such as nausea, vomiting and diarrhoea were not significantly different between groups. Neonatal outcomes were similar in each group (Table 3). The number of Neonatal ICU admission was slightly higher in the misoprostol group, twelve cases (17%), compared to oxytocin group, eight cases (11.8%), with a nonsignificant difference (P = 0.334).

Table 1: Demographic data of the patients in the two groups.

	Group 1 misoprostol (n= 70)	Group 2 oxytocin (n= 70)	P value	Significance
Maternal Age (years)	25.19±3.52	24.99±3.52	0.737	NS
Parity				
• Primigravida	64 (91.4%)	66 (94.3%)	0.363	NS
• Multigravida	6 (8.6%)	4 (5.7%)		
Gestational Age				
• Term	57 (81.4%)	60 (85.7%)	0.494	NS
• Preterm	13 (18.6%)	10 (14.3%)		
Socio-economic status				
• Upper Class (I)	0	0	0.447	NS
• Upper Middle class (II)	4 (5.7%)	9 (12.9%)		
• Lower Middle class (III)	34 (48.6%)	35 (50.0%)		
• Lower Middle class (IV)	28 (40.0%)	22 (31.4%)		
• Lower class (V)	4 (5.7%)	4 (5.7%)		
Duration of PROM (hour) (median IQR)	2 (0-3)	2 (1- 3)	0.773	NS
Bishop score	5.51±1.18	5.71±1.12	0.304	NS

Table 2: Induction to delivery interval in the study group.

	Group 1 misoprostol (n= 70)	Group 2 oxytocin (n= 70)	P value	Significance
Induction to delivery interval (hour)	5.0 ±2.58	4.33±2.23	0.048	S
Induction to delivery interval				
• >3 hours	18 (25.7%)	33 (47.1%)	0.031	S
• 3-6 hours	37 (52.9%)	21 (30.0%)		
• 6.1-9 hours	10 (14.3%)	11 (15.7%)		
• >9 hours	5 (7.1%)	5 (7.1%)		
Parity				
• Primigravida	5.06±2.62	4.43±2.21	0.062	NS
• Multigravida	3.00±0.82	3.75±2.87	0.274	NS
Mode of delivery				
• Vaginal	60 (85.7%)	58 (82.9%)	0.642	NS
• Cesarean	10 (14.3%)	12 (17.1%)		

Table 3: Neonatal outcome between the groups.

	Group 1 misoprostol (n= 70)	Group 2 oxytocin (n= 70)	P value	Significance
Birth weight (kg)	2.86±0.46	2.77±0.48	0.239	NS
APGAR Score at 1 min	7.61±0.82	7.84±0.55	0.056	NS
• ≤7	17 (24.3%)	11 (15.7%)	0.205	NS
• >7	53 (75.7%)	59 (84.3%)		
APGAR Score at 5 min	8.80 ± 0.97	8.93 ± 0.86	0.408	NS
• ≤7	8 (11.4%)	5 (7.1%)	0.382	NS
• >7	62 (88.6%)	65 (92.9%)		
NICU Admission				
• No	58 (82.9%)	62 (88.6%)	0.334	NS
• Yes	12(17.1%)	8 (11.4%)		
Neonatal Complications				
• Sepsis	1 (1.4%)	1 (1.4%)	1.000	NS
• Birth asphyxia	5 (7.1%)	6 (8.6%)	0.753	NS
• RDS	4 (5.7%)	1 (1.4%)	0.366	NS

DISCUSSION

In the present study, the average induction delivery interval was significantly more in the misoprostol group (5.0±2.58 hour) as compared to oxytocin group (4.33±2.23 hour); the difference between both groups was statistically significant (P = 0.048). Similar results have also been reported by Kimberly D. Butt et al where induction delivery interval was 720±382 min and 501±389 min with misoprostol and oxytocin respectively.[6] In the study by Crane et al using 75µg of oral misoprostol, they also found that women in the misoprostol group had longer induction delivery interval when compared to oxytocin group (737±426 min and 573±318 min, P = 0.04).[7]

However various other studies have found that induction delivery interval was significantly longer with oxytocin than with misoprostol. In the study by Nigam A et al , it was found that the Induction-delivery was shorter with misoprostol (7.7±2.8 hour) than (14.3±4.8 hour) with oxytocin.[8] Also, in the study of Ngai et al the induction to delivery was longer in the oxytocin group than in the misoprostol group (11.1±4.9 and 7.3±3.1 hour, respectively. This may be explained by their use of an oral dose of 100 µg misoprostol.[9]

There was no significant difference between the two groups in the mode of delivery as 60 women (85.7%) delivered vaginally in the misoprostol group and 58 women (82.9%) delivered vaginally in the oxytocin group. The incidence of cesarean section in the misoprostol group was 14.3% (10 cases) compared with 17.1% (12 cases) in the oxytocin group. These findings were in agreement with those of previous studies of Butt et al, (14.5% in the oral misoprostol group versus 13.2% in the oxytocin group); Ngai et al, (5% in the oral misoprostol group and 7.5% in the oxytocin group.), with a non-significant difference in the mode of delivery between the misoprostol group and the oxytocin group.[6,9]

Despite oral misoprostol resulting in longer time from induction to delivery, there was no adverse outcome to mothers or neonates as a result. The Apgar score, an important neonatal outcome to be considered in labor induction, was similar in both the groups at 1 min and 5 min. The incidence of babies with 5-min APGAR score less than 7 in both misoprostol and oxytocin group was 11.4% and 7.1% respectively (P = 0.382). Similar results were seen in the study by Crane et al, who found no significant difference between misoprostol and oxytocin group in Apgar scores at 5 min (10 for each at 5 min).[7] Neonatal admission to ICU (NICU) showed a non-significantly greater number in the misoprostol group (12 cases, 17%) as compared to the oxytocin group (8 cases, 11.4%). Similar results were seen in the study by Mozurkewich who found a nonsignificant trend toward greater NICU admission among infants born to mother receiving misoprostol compared with the oxytocin group (20.1% versus 12.4%); though in their misoprostol group they had a higher incidence of hyperstimulation in the misoprostol group (13.8%) versus none in our study.[10]

We did not have any incidence of tachysystole or any other untoward effects in either of the groups. However, our study population was not large enough to assess uncommon maternal and neonatal outcome.

CONCLUSION

In conclusion, intravenous oxytocin infusion resulted in shorter interval to delivery; however oral misoprostol is still an option for PROM, as overall delivery and neonatal outcomes are comparable in both the groups. Despite various advantages of oral misoprostol, intravenous

oxytocin infusion is effective and safe for labor induction in PROM.

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