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RESEARCH ARTICLE

A comparative study of the labour outcomes following induction with oral misoprostol and oxytocin in pregnant women with PROM

Disha Ajila, Ritu Sharma A

Corresponding author: Dr. Ritu Sharma A, 305, Saraswati Block, Sai Bhavani Kamshetty Enclave, Ganeshnagar, Ramnathpur, Hyderabad, Telangana, India; Email : aritusharma95@gmail.com

ABSTRACT

Objectives: This retrospective study was conducted to assess and compare the efficacy of oral misoprostol and intravenous oxytocin in the induction of labour after PROM. **Materials and method:** A total of 106 patients with singleton term pregnancy with PROM were included in the misoprostol and oxytocin groups. Misoprostol and oxytocin were administered in the standard doses. Close monitoring of the maternal and fetal status and progress of labour was done. In cases of failed induction, cesarean section was performed. The outcome was recorded. **Results and observations:** Both the groups were comparable in terms of demographic and baseline parameters. The induction to delivery time was significantly shorter in the misoprostol group (P value <0.001). The cesarean section rates were comparable in both the groups. There was no incidence of intrapartum complications in any group. The fetal outcome, in terms of APGAR scores and NICU admissions, was also comparable. **Conclusion:** Oral misoprostol is a safe and effective alternative to oxytocin, especially in cases of unfavourable cervix.

Keywords: Misoprostol, oxytocin, prelabour rupture of membranes.

Prelabour rupture of membranes (PROM) is defined as rupture of membranes prior to the onset of labour. When it occurs before 37 weeks of gestation, it is termed preterm PROM. PROM occurs in 2 to 20% of all deliveries [1]. Labour may follow soon after the rupture of membranes. However, in case of delayed labour the fetus is exposed to serious risks of infection and the ensuing complications [2]. Repeated vaginal examinations pose an added risk for maternal and fetal infections [3]. This contributes to the increased postpartum maternal and fetal morbidity and mortality. In addition, prolonged labour also affects the maternal satisfaction. Therefore, American College of Obstetricians and Gynecologists (ACOG) recommends induction of labour in cases where spontaneous labour does not occur at the time of presentation [4].

Various methods are available for the induction of labour. However, the choice of a standard method remains controversial. Oxytocin is, generally, the preferred method [5]. However, its efficacy depends on the condition of the cervix and cannot be used in cases of unripe cervix. Furthermore, it has to be administered intravenously with meticulous monitoring of the infusion rates and contraction rates.

Other viable alternatives are prostaglandin analogues. They confer the advantage of being useful in cases of unripe cervix [6]. However, most of them are administered vaginally, which increases the chances of infection and ensuing complications. Therefore, the search for an ideal agent continues. Misoprostol, prostaglandin E1, has been found to be effective when administered orally. It has the additional advantages of ease of administration and being stable at room temperature [7]. Therefore, oral misoprostol may serve as a safe and viable alternative. However, studies in this regard are scarce.

Therefore, this study was conducted to assess and

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compare the efficacy of oral misoprostol and intravenous oxytocin in the induction of labour after PROM and to evaluate the outcomes.

Materials and methods

This non-inferiority, retrospective, record based study was conducted under the Department of Obstetrics and Gynecology in A.J. Institute of Medical Sciences and Research centre. The study was conducted after obtaining approval from the Institutional Ethics Committee. Women who were diagnosed with PROM and had been admitted from June to August 2020 were included in the study, provided they met the inclusion and exclusion criteria as follows:

Inclusion criteria:

1. Singleton gestation
2. Vertex presentation
3. Term pregnancy (37 weeks and above)
4. No evidence of active labour
5. Normal FHR pattern
6. Pre-induction modified Bishop score less than 6

Exclusion criteria:

1. Previous lower section cesarean section (LSCS) or any uterine scar
2. Preterm
3. Malpresentation
4. Antepartum haemorrhage
5. Chorioamnionitis
6. Contraindications to prostaglandin use (bronchial asthma, cardiac disease)
7. Meconium stained liquor
8. Placenta praevia
9. Significant fetal heart rate decelerations (slowing of FHR below the baseline by more than 15 beats lasting for more than 15 seconds)
10. Any other condition contraindicated for vaginal delivery (CPD, cervical cancer, active genital herpes, previous pelvic surgeries, bad obstetric history).

Considering power of the study as 80% and significance level of 0.05, the sample size was calculated to be 53 in each group (Misoprostol and Oxytocin groups). A total of 106 consecutive patients admitted from June 1, 2020 who were diagnosed with PROM and met the aforementioned criteria, were included in the study. Consecutive patients were included in each group until the predetermined desired sample size was obtained.

All the included patients had received antibiotics for the prevention of infection. A routine per vaginal examination had been done for the assessment of station and presentation. The pre-induction modified Bishop score had been assessed on the basis of cervical dilatation, cervical length, station, consistency and position (table 1)[8].

In the misoprostol group, all the included patients had received 50 micrograms of misoprostol orally every 4 hours until delivery (maximum dose of 200 micrograms).

Table 1: Modified Bishop score[8]

Cervix	Score*#			
	0	**1**	**2**	**3**
Cervical dilatation (cm)	0	1-2	3-4	5+
Cervical length (cm)	> 4	2-4	1-2	<1
Station of presenting part (cms in relation to ischial spine)	-3 or above	-2	-1, 0	+1, +2
Consistency	Firm	Medium	Soft	-
Position	Posterior	Midposition	Anterior	-

*1 point is added for preeclampsia and each previous vaginal delivery.
#1 point for postdated pregnancy, nulliparity, PPROM.

Patients included in the oxytocin group had received intravenous infusion of low dose regimen of 1 to 2mU/min and increased incrementally by 1 to 2 mU every 30 mins interval to achieve and maintain moderate to strong contractions (maximum 5 contractions in 10 minutes), with an upper limit of 40mU/min.

Close monitoring of the fetal and maternal status had been done after admission in the delivery room. Uterine contractions and fetal heart rate had been monitored by continuous cardiotocography. Progress of labour had been monitored by partogram. Induction of labour was considered failed if the modified Bishop score was less than 5 or no uterine contraction was achieved 4 hours after the last dose (in the misoprostol group) or when there was a failure to enter active phase of labour within 12 hours of starting the intervention (in the oxytocin group). Such cases had undergone cesarean section. The induction to delivery time was recorded. Any complications including uterine tachysystole (more than 5 contractions in a 10 minute window) were noted. APGAR score and details of NICU admissions were considered for the assessment of the fetal outcome.

Statistical analysis: The categorical/qualitative variables were expressed as number of cases and percentages and the continuous/quantitative variables were described in terms of mean and standard deviation. The P value was calculated by 'unpaired t test' and 'paired t test' (as applicable) for quantitative data and 'chi square test' for qualitative data ('Fisher's exact test' was used when any cell value was less than 5). P value of less than 0.05 was considered to be statistically significant.

Results and observations

The baseline attributes of age, socioeconomic status, gravida status, BMI, period of gestation, duration of PROM and the pre-induction modified Bishop score were similar in the misoprostol and oxytocin groups. Most of the patients were multigravidae in both the groups (tables 2 and 3). Most of the patients were delivered vaginally, with LSCS being 16.98% in the misoprostol group and 18.87% in the oxytocin group (p value - 0.807). The intraoperative blood loss was 341.51 ± 145.73 mL in the misoprostol group and 329.25 ± 161.21 mL in the oxytocin group (p value - 0.682).

Table 2: Distribution of the study population according to the baseline attributes

Parameters	Misoprostol	Oxytocin	P value
Age (years)	24.91 ± 2.52	25.62 ± 1.99	0.107
BMI (kg/m^2)	23.48 ± 2.27	22.95 ± 2.47	0.253
Period of gestation (days)	271.47 ± 4.70	270.15 ± 5.16	0.171
PROM duration (minutes)	222.45 ± 50.42	205.47 ± 45.13	0.071
Modified Bishop	4.13 ± 0.73	4.11 ± 0.75	0.896

Table 3: Distribution of the study population according to the socioeconomic status and gravida status

Parameters	Misoprostol	Oxytocin	P value
Socioeconomic	15 (14.15%)	21 (19.81%)	0.218
status	38 (35.85%)	32 (30.19%)	
Gravida status	22 (20.75%)	24 (22.64%)	0.701
	31 (29.25%)	29 (27.36%)	

Table 4: Distribution of the induction to delivery time in the study population

Parameter	Misoprostol	Oxytocin	P value
Induction to delivery (minutes)	309.15 ± 57.74	367.45 ± 78.88	<0.001*

Table 5: Distribution of the neonatal outcome in the study population

Parameter	Misoprostol	Oxytocin	P value
APGAR 5	7.55 ± 1.05	7.64 ± 0.96	0.630
APGAR 10	8.09 ± 1.11	8.34 ± 0.92	0.219

The induction to delivery time was significantly shorter in the misoprostol group compared to the oxytocin group (p value - <0.001) (table 4). There was no incidence of contractile abnormalities, including uterine tachysystole, in any group. The APGAR score at 5 and 10 minutes was similar in both the groups (table 5). There was significant improvement in the APGAR score at 10 minutes (as compared to the score at 5 minutes) in both the groups (p value - <0.001). NICU admission was required in 16.98% of the cases in the misoprostol group and 11.32% of the cases in oxytocin group (p value - 0.422).

Discussion

PROM complicates 2 to 20% of all deliveries [1]. A delay in labour following PROM increases the chances of fetal and maternal infections and complications [9]. There is an ongoing search for ideal induction agent. Vaginally administered agents contribute to increased infection rates whereas intravenously administered agents, like oxytocin need meticulous monitoring. Therefore, the search for effective induction agent is still continuing. One such agent is oral misoprostol.

In the present study, the misoprostol and oxytocin groups were comparable in terms of age, socioeconomic status and BMI. Similar studies were conducted by Shabana A et al[10], Rashmi R and Pradhan A et al [11], Nigam A et al [12] and by Al-Hussaini T et al [13]. In all these studies, both the groups were comparable in terms of baseline characteristics. The former three studies, additionally noted that the mean ages of the two groups were closely similar to the present study. In the study by Shabana A et al[10], the mean age in the misoprostol group was 24.66 ± 3.16 years and in the oxytocin group was 25.06 ± 3.53 years. In the study by Rashmi R and Pradhan A et al [11], the mean age in the misoprostol group was 25.19 ± 3.52 years and in the oxytocin groups 24.99 ± 3.52 years. Furthermore, most of their patients belonged to lower middle class in both the groups. In the study by Nigam A et al [12], the mean age in the misoprostol group was 25.1± 2.2 years and in the oxytocin group was 25.4 ± 2.9 years.

In the present study, the two groups were also comparable in terms of the gravida status. It was further observed that most of the cases were multigravidae in both the groups. These findings were similar to the study by Shabana A et al [10] and Rashmi R and Pradhan A et al [11].

The misoprostol and oxytocin groups were also comparable in terms of gestational age, PROM duration and the modified Bishop score. Similar were the findings in the study by Shabana A et al [10] and Rashmi R and Pradhan A et al [11]. Additionally, Shabana A et al [10] also noted that the mean gestational age was more than 38 weeks in both the groups (38.51 ± 0.68 weeks in the misoprostol group and 38.47 ± 0.71 weeks in the oxytocin group). This was closely similar to the present study where the mean gestational age was more than 270 days in both the groups. Furthermore, in the study by Rashmi R and Pradhan A et al [11], it was also noted that the mean duration of PROM was about 2 hours in the oxytocin and misoprostol groups (p value of 0.773); almost similar to the present study where the mean duration of PROM was more than 200 minutes in both the groups.

It was observed that vaginal delivery was the most common mode with LSCS being required in 16.98% cases in the misoprostol group and in 18.87% cases in the oxytocin group. Shabana A et al [10] also found that most of the cases were delivered by simple vaginal delivery. CS was required

in 12% cases in the oxytocin group and 6% cases in the misoprostol group (p value - 0.48). Similarly, in another study by Rashmi R and Pradhan A et al [11], it was found that majority of the patients were delivered by vaginal delivery (85.7% in the misoprostol group and 82.9% in the oxytocin group) (p value - 0.642).

In the present study, the induction to delivery time was significantly less in the misoprostol group (309.15 ± 57.74 minutes) than in the oxytocin group (367.45 ± 78.88 minutes); p value: <0.001. This was similar to the study by Shabana A et al [10], where the induction to delivery time was 6.59 ± 1.91 hours in the misoprostol group vs 9.30 ± 2.58 hours in the oxytocin group; p value: <0.001. In another study by Rashmi R and Pradhan A et al [11], they found that the induction to delivery time was significantly less in the misoprostol group (5.0 ± 2.58 hours) than in the oxytocin group (4.33 ± 2.23 hours); p value: 0.048. Similarly, in the study by Nigam A et al [12], the induction to vaginal delivery time at term was significantly shorter in the misoprostol group (7.7 ± 2.8 hours) compared to oxytocin group (14.3 ± 4.8 hours); p value: <0.001. In the study by Al-Hussaini T et al [13], they found that the induction to delivery interval was significantly shortened in the misoprostol group compared to the oxytocin group (5.5 ± 2.9 hours vs 10.4 ± 4.8 hours) (p value - 0.02). They also observed that the duration was significantly reduced in both nulliparous and multiparous patients.

In the present study, the amount of blood loss was similar in both the groups (341.51 ± 145.73 mL in the misoprostol group and 329.25 ± 161.21 mL in the oxytocin group. In terms of maternal outcome, no intrapartum complications (including uterine tachysystole) were observed in any group.

In terms of neonatal outcome, majority of the neonates were stable. When assessed with respect to the APGAR score, it was observed that the mean score at 5 minutes and 10 minutes was comparable in both the groups. It was also observed that the mean APGAR score at 5 minutes was more than 7 in both the groups and the mean score at 10 minutes was more than 8 in both the groups. A statistically significant improvement was observed in both the groups, in the APGAR score at 10 minutes as compared to the score at 5 minutes (p value - <0.001 in each group). Furthermore, it was observed that NICU admission was required in 16.98% of the cases in the misoprostol group and 11.32% of the cases in oxytocin group. Shabana A et al [10] also found that most of the neonates were stable with APGAR score of less than 7 at 5 minutes in 8% cases in the oxytocin group and 4% cases in the misoprostol group. NICU admission was required in 8% of the cases in the oxytocin group and 4% cases in the misoprostol group. In the study by Rashmi R and Pradhan A et al [11], the mean APGAR score at 1 minute and score at 5 minutes was similar in both the groups (at 1 minute: 7.61 ± 0.82 in the misoprostol group vs 7.84 ± 0.55 in the oxytocin group; at 5 minutes: 8.80 ± 0.97 in the misoprostol group vs 8.93 ± 0.86 in the oxytocin group; p value - 0.408). They also observed that NICU admission was required in 17.1% of the cases in the misoprostol group and 11.4% of the cases in the oxytocin group. Similar were the findings in the study by Nigam A et al [12].

In another similar study by Al-Hussaini T et al [13], it was observed that intrapartum complications, including gastrointestinal symptoms and contractile abnormalities, were significantly more in the misoprostol group as compared to the oxytocin group (P value - <0.05). This may be attributed to the higher dose of oral misoprostol used in the study: 100 micrograms every 6 hours (maximum of 200 micrograms).

Limitations: They present study was limited by the OPD attendance of the patients having PROM. Therefore, the results may not be generalized.

Conclusion

Oral misoprostol significantly shortens the duration of labour without any increase in the cesarean section rates. There was also no significant adverse impact on fetal outcome. Thus, it is a safe and effective alternative to oxytocin. It may also decrease postpartum morbidity and reduce the hospital stay, in addition to improving the maternal satisfaction scores. Further studies need to be conducted in this regard.

Conflict of interest: None. **Disclaimer:** Nil.

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Disha Ajila [1], Ritu Sharma A [2]

[1] Senior Resident, Department of Obstetrics and Gynecology, AJ Institute of Medical Sciences and Research, Mangalore, India; [2] Junior Resident, Department of Obstetrics and Gynecology, AJ Institute of Medical Sciences and Research, Mangalore, India.