Original Article

A Comparative Study of Labor Outcomes after Induction with Oxytocin and Oral Misoprostol in Pregnant Women with Premature Rupture of Membrane

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ABSTRACT

Introduction: In women having premature rupture of membrane, both oxytocin as well as prostaglandins are effective for inducing labor. The choice to implement a standard procedure remains contentious. The commonly employed method is oxytocin. Nonetheless, it must be administered intravenously while closely monitoring the administered dose and contraction rates. The oral administration of misoprostol, particularly with pre-labor membrane rupture, mitigates the necessity for recurrent vaginal examinations, hence reducing the danger of infections for both the pregnant woman and the newborn.

Aims/ objective: To compare the efficacy as well as safety of oral misoprostol versus intravenous oxytocin for labor induction in women with PROM.

Materials and Method: In the misoprostol cohort, 75 participants received 50 mcg of oral misoprostol every four hours till delivery. The maximum dosage was restricted to 200 mcg. 75 participants in the oxytocin group received an intravenous administration of a low-dose regimen of oxytocin, starting at an infusion rate of one to two mU/min. The dosage was progressively raised to 1 to 2 mU at 30-minute intervals to achieve moderate to strong contractions. The interval during induction to delivery was documented. All maternal or neonatal outcomes were documented.

Results: The mean induction to delivery time was significantly lower in misoprostol group (331.26 ± 33.73) as compared to oxytocin group (363.79 ± 39.55) ($p<0.0001$). There was less incidence of cervical tear or perineal tear and neonatal complications in misoprostol group as compared to oxytocin group but the difference was not statistically significant ($p>0.05$).

Conclusion: In cases of PROM, oral misoprostol may be effectively utilized as a substitute for the administration of oxytocin or prostaglandin vaginal pessaries/gel to initiate labor.

Keywords: Labor induction, Oral Misoprostol, Oxytocin, Premature rupture of membranes.

INTRODUCTION

Premature rupture of membranes (PROM) is defined as the rupture of membranes before to the onset of labor. Preterm PROM refers to the occurrence of premature rupture of membranes before the 37th week of pregnancy. PROM happens around between two and twenty percent of deliveries.[1] Labor may commence immediately upon the rupture of the membranes. However, if labor is delayed, the fetus faces significant risk of infection and its related complications.[2] Frequent vaginal examinations elevate the likelihood of infections for both the pregnant woman and the fetus.[3] This has resulted in a rise in postpartum maternal and fetal morbidity and mortality. Furthermore, prolonged labor affects maternal satisfaction. Therefore, in instances where natural labor does not commence upon presentation, "the American College of Obstetricians and Gynecologists (ACOG)" recommends labor induction.[4] It complicates between five and ten percent of pregnancies.[5] Around sixty percent of prelabor rupture of membranes (PROM) instances occur post 37 weeks of gestation.

In cases of women with PROM, both oxytocin and prostaglandins are effective in inducing labor.[5] The choice to implement a standard procedure remains contentious. The commonly employed method is oxytocin.[6] Nonetheless, the efficacy of its use is contingent upon the condition of the cervix, since an underdeveloped cervix inhibits its application. Additionally, it must be administered intravenously while closely monitoring the administration as well as contraction rates.

Oral misoprostol is being utilized in research to address PROM in females.[7-9] The probability of unsuccessful induction and ensuing cesarean delivery escalates by thirty to forty percent when intravenous oxytocin infusion induction is administered to women with an unfavorable cervix, and extended labor heightens the possibility of infection in both the pregnant woman and the neonate.[5]

Misoprostol is a unique orally absorbed homologue of prostaglandin E1. Drug-induced stomach ulcers is effectively treated with the dependable and cost-effective misoprostol tablets. It influences the myometrium by binding to prostanoid receptors within it. The drug does not require refrigeration prior to use. It is packaged in blisters.[10] Ten These properties render it ideal for utilization in developing countries. The vaginal route has predominated in most trials, perhaps due to its superior

efficacy with other prostaglandins and the much prolonged half-life of misoprostol when administered vaginally compared to oral intake.[11]

However, the brief the half-life of oral misoprostol could prove beneficial for labor induction, as it reduces the possibility of "uterine hyperstimulation" and minimizes tachysystole. The advantage of orally administered misoprostol, particularly with PROM, is the reduction of recurrent vaginal examinations, hence diminishing the danger of infection both for the pregnant woman and the newborn.[12] For the inducement of labor, 50–100 mcg oral misoprostol doses are given every 4–6 hours.

A dosage of 100 mcg or greater of oral misoprostol in labor induction has demonstrated efficacy, leading to an increased rate of "successful vaginal deliveries within 24 hours," as indicated by a meta-analysis from the Cochrane Library. Labor must be meticulously observed for "uterine hyperstimulation."[13] This research was done to compare the efficacy as well as safety of oral misoprostol versus intravenous oxytocin for labor induction in women with PROM. The delay from induction to delivery, rates of surgical births, and “neonatal and maternal outcomes” were among the variables assessed.

MATERIALS AND METHODS

This was an observational and prospective study conducted from December 2023 to August 2024 in Department of Obstetrics and Gynaecology in tertiary care centre of eastern India. The research was conducted in accordance with "Good clinical practice and the Declaration of Helsinki." Women with PROM who had been hospitalized to "the Obstetrics and Gynaecology inpatient department" were included in the study, provided they met the specified inclusion and exclusion criteria:

Inclusion Criteria:

Women with “a singleton pregnancy, vertex presentation of the fetus,” and a term pregnancy of 37 weeks or above, who had no evidence of active labor, a normal pattern of fetal heart rate (FHR), and “a modified Bishop score before induction” of less than 6, were included.

Exclusion criteria:

Women with a previous history of LSCS or any uterine scar, a gestational age of less than 37 weeks, “malpresentation” at the time of admission, “antepartum haemorrhage” in the current pregnancy, a history of “chorioamnionitis”, contraindications to prostaglandin use (such as bronchial asthma or cardiovascular disorders), the presence of “meconium-stained liquor, placenta praevia” detected in the current pregnancy, significant fetal heart rate decelerations (defined as a decrease in FHR below the baseline by more than 15 beats lasting for over 15 seconds), or any other contraindications for normal vaginal delivery (including “cephalo-pelvic disproportion, a history of cervical cancer or active genital herpes, a history of pelvic surgeries, or a poor obstetric history”) were excluded.

With reported time for induction to delivery of 322.04 ± 61.85 in misoprostol group and 359.57 in oxytocin group in previous study,[14] minimum sample size required for 95% power and 0.05 alpha value was found to be 142. So, 150 patients were recruited in each group to cope up with any attrition rate.

All study participants received prophylactic antibiotics to avoid infection. A regular per-vaginal examination had been done to assess the station as well as presentation of the fetus. The adjusted Bishop score prior to labor induction was assessed according to cervical dilation, cervical length, fetal station, cervical consistency, as well as position. 14

In the misoprostol cohort, all participants received 50 mcg of oral misoprostol every four hours till delivery. The maximum dosage was restricted to 200 mcg.

Study participants in the oxytocin group received an intravenous administration of a low-dose regimen of oxytocin, starting at an infusion rate of one to two mU/min. The dosage was progressively raised to 1 to 2 mU at 30-minute intervals to achieve moderate to strong contractions, characterized by "a maximum of 5 contractions in 10 minutes, with an upper limit of 40 mU/min."

Continuous observation of the fetal and maternal conditions was conducted following the patient's admission to the labor room. Uterine contractions as well as fetal heart rate were continually monitored using cardiotocography. The progression of labor was evaluated using a partogram. Labor induction was deemed unsuccessful if "the modified Bishop score" was less than 5, or if no uterine contractions were observed after 4 hours following the final dosage in the misoprostol group, and if the active stage of labor was not attained after 12 hours of initiating the oxytocin infusion. Patients were referred for cesarean section. The interval during induction to delivery was documented. All maternal problems were documented. Neonatal outcomes were evaluated.

Statistical analysis:

The data was shown in tabular format utilizing Microsoft Excel 2019. The categorical data were given as numbers with percentages, whereas continuous parameters were expressed as means +/-SD. An unpaired t-test was conducted to assess the statistical significance of the variations in continuous data, whereas Fisher's exact test was utilized to evaluate the "statistical significance of differences in categorical data." A P value below 0.05 was considered indicative of statistical significance.

OBSERVATIONS AND RESULTS

Table 1: Comparison of Baseline Demographic and Clinical Characteristics between Group M (Misoprostol) and Group O (Oxytocin)

Characteristics	Group M (n = 75)	Group O (n = 75)	P-value
Age in years, Mean ± SD	29.66 ± 2.95	28.97 ± 3.02	0.16
Primi-Gravida, n (%)	52 (69.33)	55 (73.33)	0.72
BMI in kg/m^2, Mean ± SD	24.37 ± 1.96	24.56 ± 2.09	0.57
Period of gestation in days, Mean ± SD	269.72 ± 4.98	270.41 ± 4.88	0.39
Modified Bishop Score, Mean ± SD	4.23 ± 0.90	4.20 ± 0.87	0.84

* Unpaired t test ** Fisher's exact test

Most of the patients were primi-gravida of 27-32 age of gestational age 36-38 weeks of gestational age. There was no significant difference between misoprostol and oxytocin group with respect to age, gestational age, parity, BMI or modified bishop score (p>0.05).

Table 2: Comparison of Induction to Delivery Time between Group M (Misoprostol) and Group O (Oxytocin)

	Group M	Group O
Number of Patients	75	75
Mean Induction to delivery time in minutes	331.26	363.79
Standard Deviation	33.73	39.55
Difference in Mean (M-O)	-32.53	
95% CI of the Difference	-44.3909 to -20.6691	
P-Value (Unpaired t test)	<0.0001	

The mean induction to delivery time was significantly lower in misoprostol group (331.26 ± 33.73) as compared to oxytocin group (363.79 ± 39.55) (p<0.0001).

Table 3: Comparison of Maternal Outcomes between Group M (Misoprostol) and Group O (Oxytocin)

Outcomes	Group M (n = 75)	Group O (n = 75)	P-value
Mode of delivery			
Vaginal	65 (86.67)	62 (82.67)	0.6511
Caesarean	10 (13.33)	13 (17.33)	
Other maternal complications			
Post-partum haemorrhage	3 (4.00)	2 (2.67)	>0.99
Cervical tear	0	2 (2.67)	0.50
Perineal tear	1 (1.33)	4 (94.67)	0.37

There was less incidence of cervical tear or perineal tear in misoprostol group as compared to oxytocin group but the difference was not statistically significant (p>0.05).

Table 4: Comparison of Neonatal Complications between Group M (Misoprostol) and Group O (Oxytocin)

Outcomes	Group M (n = 75)	Group O (n = 75)	P-value (Fisher's Exact Test)
Meconium aspiration	1 (1.33)	4 (94.67)	0.37
NICU admission	1 (1.33)	3 (4.00)	0.62
Neonatal death	0	1 (1.33)	>0.99

Incidence of neonatal complications was less in misoprostol group as compared to oxytocin group but the difference was not statistically significant (p>0.05).

DISCUSSION

2-20% among all pregnancies are further complicated by PROM.[6] The probability of complications as well as infection among the pregnant woman and the fetus increases if labor is postponed following PROM.[15] The ideal induction agent remains under investigation. IV agents, like oxytocin, necessitate meticulous monitoring, whereas vaginal administration increases infection rates. Consequently, endeavors to identify a dependable induction agent are in progress. Oral misoprostol constitutes one such therapeutic intervention.

The age as well as BMI were comparable among the misoprostol or oxytocin cohorts in this study. The average age in the study conducted by Shabana A et al. were 27.9 ± 2.9 years in the oxytocin cohort versus 28.5 ± 3.1 years in the misoprostol cohort.[16] In the study conducted by Rashmi R, Pradhan A, et al., the average age had been 25.2 ± 3.5 years in the misoprostol cohort versus 25.0 ± 3.5 years in the oxytocin cohort.[17] Moreover, the preponderance of those they treated in both categories was from the lower middle classes. The study conducted by Nigam A et al. reported a mean age of 25.1 ± 2.2 years for the misoprostol cohort versus 25.4 ± 2.9 years in the oxytocin cohort.[18]

The parity of each of the groups in the current phase of research was comparable. In all categories, the predominant instances were primigravidae. These findings must be acknowledged when drawing conclusions from this study. These findings are inconsistent with the results reported by "Rashmi R. and Pradhan A. et al. and Shabana A. et al." [16, 17]

The adjusted Bishop score as well as gestational age were comparable between the misoprostol versus oxytocin cohorts. The findings of the research conducted by "Shabana A et al. and Rashmi R and Pradhan A et al." were analogous. [16, 17] Moreover, the average maternal age exceeded 38 weeks across both cohorts, as per the findings of Shabana A et al. [16] This was quite analogous to the present study, in which the mean gestational ages of both groups were around 270 days.

The predominant mode of birth was vaginal, with LSCS required in 13.33% of misoprostol cases versus 17.33% of oxytocin instances. Furthermore, Shabana A et al. found that most cases were to uncomplicated vaginal births. [16] Concurrently, Rashmi R., Pradhan A., et al. found that a predominant proportion of patients delivered vaginally ("85.7% in the misoprostol cohort versus 82.9% in the oxytocin cohort"). [17]

In the present study, the induction-to-delivery interval for the misoprostol group (331.26 ± 33.73 minutes) was considerably shorter when compared to oxytocin group (363.79 ± 39.55 minutes). This was analogous to the study conducted by Shabana A et al., wherein the induction to delivery time for the misoprostol group was 6.6 ± 1.9 hours, whereas for the oxytocin group it was 9.3 ± 2.6 hours. [16] In another study, Rashmi R, Pradhan A, et al. found that the induction-to-delivery time for the misoprostol group (5.0 ± 2.5 hours) was considerably shorter than that of the oxytocin group (4.3 ± 2.2 hours). [17] The study by Nigam A et al. revealed analogous findings, indicating that the "induction to vaginal delivery time" for the misoprostol group (7.7 ± 2.8 hours) was significantly less than that of the oxytocin group (14.3 ± 4.8 hours). [18] Both nulliparous as well as multiparous patients exhibited a significantly reduced duration.

The volume of blood loss in the present study was analogous across the two groups. No group encountered any intrapartum difficulties regarding mother outcomes. The majority of the neonates exhibited stable outcomes. Furthermore, it was observed that 1 instance in the oxytocin group and 3 cases in the misoprostol group required NICU admission. The maternal and neonatal problems in both groups were comparable to those reported in other research. [13, 19]

In a separate study, Al-Hussaini T et al. discovered that the misoprostol group experienced considerably more intra-partum problems than the oxytocin group, notably GIT symptoms and electromechanical anomalies.[20] The research may have utilized a greater dosage of oral misoprostol: 100 mcg each six hours, with a maximum of 200 mcg.

The duration from "induction to delivery" and the necessity for oxytocin and antibiotics are significantly reduced when oral misoprostol is given to women with an unfavorable cervix shortly after term PROM. [7] Consequently, patients may have experienced less restriction throughout the initial phases of labor when administered oral misoprostol for induction, thereby reducing "the frequency of vaginal examinations" and the necessity for intravenous lines until late labor.

Our investigation has specific limitations. Blinding was not implemented, and "women with preterm premature rupture" of membranes were excluded, which may impact the generalizability of our findings.

CONCLUSION

Our research indicates that women receiving oral misoprostol induction for PROM experience expedited induction-to-delivery intervals and deliver healthy fetuses. In instances of PROM, oral misoprostol may be effectively utilized as a substitute for the administration of oxytocin or prostaglandin vaginal pessaries/gel to initiate labor. Besides enhancing maternal satisfaction, it may help reduce postpartum morbidity and decrease hospital durations. Further research is required in this domain.

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