

COMPARISON OF INDUCTION OF LABOUR WITH OXYTOCIN AND MISOPROSTOL IN PATIENTS WITH PREMATURE RUPTURE OF MEMBRANE

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ABSTRACT

Objective: To compare induction of labour with oxytocin and misoprostol in patients with pre-mature rupture of membrane.

Materials and Methods: This randomized controlled trial was carried over 136 PROM patients from Sep 25, 2017 to Sep 24, 2018 which were divided in two equal groups of oxytocin and misoprostol. The patients were followed till the delivery. Induction of delivery interval was noted and compared through Statistical Package for social sciences.

Results: A total of 136 patients (68 in each group) were included in the study. Induction of laborwise distribution was significant with p -value = 0.009. The average induction of labour in Group A was observed 5.42+1.71SD while this average was 4.60+1.88SD in Group B. **Conclusion:** Oxytocin has shorter induction of delivery interval as compared to Misoprostol in patients with pre mature rupture of membrane.

Keywords: Frequency, misoprostol, oxytocin, pregnancy, premature, rupture of membranes

INTRODUCTION

Premature rupture of membranes (PROM) is defined as the rupture of fetal membranes before the onset of labor.¹ PROM complicates 8 – 10% of pregnancies, and is responsible for nearly one - third of preterm births.² PROM, especially preterm PROM (PPROM), has been associated with brief latency from membrane rupture to delivery, an increased risk of chorioamnionitis, and umbilical cord compression. As such, PROM is associated with increased risk of perinatal complications.³

Approximately 90% of women with PROM go into labor within 1 week.⁴ Five per cent of cases of PROM involve fetuses in the 1000 g to 2500 g weight category, while those weighing less than 1000 g constitute less than 0.5%. Preterm PROM, while

affecting about 5% of all pregnancies accounts for up to 30% of all preterm deliveries.⁵

Disruption of fetal membranes before the initiation of labor is termed as premature rupture of membrane (PROM). It results in spontaneous leakage of amniotic fluid. It may be before or after 37 weeks of gestation. Premature rupture of membrane that occurs before 37 weeks of gestation is referred as preterm premature rupture of membrane and premature rupture of membrane that occurs after 37 weeks of gestation is termed as term premature rupture of membrane. It occurs in approximately 5%–10% of all pregnancies, of which approximately 80% cases occur at term. It is linked to significant maternal and fetal morbidity and mortality. Current literature shows that it causes 18%–20% and 21.4% of prenatal mortalities and morbidity respectively.⁶

prematurity and its complications such as newborn respiratory distress syndrome, neonatal sepsis, necrotizing enterocolitis, intraventricular hemorrhage, periventricular leukomalacia, varying degrees

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of hypoplasia and bronchopulmonary dysplasia are directly related to premature rupture of membrane. Thus it greatly increases neonatal morbidity and mortality.⁷

Prostaglandins & Oxytocin are the most frequently used drugs for induction of labor in premature rupture of membranes. Oxytocin infusion is used widely as a safe and effective labor inducing agent. Misoprostol is a prostaglandin E1 analogue. It is given orally for a labor induction. Misoprostol is inexpensive and stable at room temperature and requires no refrigeration for its storage as other prostaglandins which is its great advantage. Due to these features its use is ideal in the third-world countries.⁸

In a study women were assigned randomly into two equal groups: groups A, which received 100 µg oral misoprostol every 4h for a maximum of three doses and group B, which received an intravenous infusion of oxytocin starting with a dose of 4mU/min with an incremental increase of 4mU/min every 30 min until a maximum dose of 32mU/min. In the misoprostol group, 47 women (94%) were delivered vaginally and three women (6%) were delivered by cesarean section, whereas in the oxytocin group, 44 women (88%) were delivered vaginally and six women (12%) were delivered by cesarean section, with a nonsignificant difference in the mode of delivery.⁹

Shah B et al. in a comparative study showed that the average time interval to the onset of labor and also to the occurrence of vaginal delivery was longer in oxytocin group as compared to misoprostol group. It was observed that the induction of delivery interval in multigravida was lesser than primigravida with unfavorable cervix in both the groups. With misoprostol it was 54.54% and 67.67%, and with oxytocin 43.45% and 52.33% in primigravida and multigravida respectively.¹⁰

Ezechi et al. randomized three hundred and forty six Nigerian women with pre mature rupture of membrane into two groups of misoprostol and oxytocine to know the safety and efficacy of misoprostol in induction of labour in pre-mature rupture of fetal membrane in Nigerian women. Their results showed that 18.1% women underwent caesarean section while 87.9% delivered vainally among the misoprotol group. On the other hand 41.4% women underwent caesarian section & 58.6% delivered vaginally in the oxytocin group.¹¹

There is no consensus among the researchers on the results of these drugs for labour induction in premature rupture of membranes. So there is no single protocol regarding the use of these drugs. This study will help in establishing fresh statistics on induction of labour with oxytocin and misoprostol in patients with premature rupture of membrane. Health professionals can take benefit from this study in managing patients with this disease by allotting appropriate resources according to the burden of the disease & thus this will help us manage this condition in a better way.

MATERIAL AND METHODS

All pregnant women presenting to department of gynecology & obstetric, Sohar Hospital, Ministry of Oman with spontaneous rupture of membrane were included in the study. Sample size was 136 (68 for each group). Proportion of interval of induction with oxytocin (c/section) was 18.6% & proportion induction of labour with misoprostol (C/Section) was 41.3% based on previous study.⁶ Significance level was 5% and power was 90% under WHO sample size calculation formula. An informed consent were taken from all the participants of the study followed by a local examination (P/V) and per speculum examination by a consultant obstetrician having not less than 3 years of experience to confirm diagnosis of premature rupture of membrane and to calculate Bishop's Score. Patients were randomly assigned to Group I (Oral Misoprostol) and Group II (IV Oxytocin) according to selection criteria. Subjects in Group I were receive 50 µg oral misoprostol at 4-hour intervals until progressive labor or uterine contractions start and delivery occurs or maximum of 4 doses (200µg) achieved. Subjects in Group II were receive an intravenous infusion of oxytocin starting at a dose of 2mU/min with an incremental increase of 2mU/min every 30 min until contraction starts or maximum infusion dose of 20 mU/min given. All the subjects were continuously monitored and the induction process were stopped whenever any fetal or maternal complications develops and cesarean section were performed. In the misoprostol group, induction were considered failed, if the Bishop score were <5 or no uterine contraction started 4 hours after the last dose. In the oxytocin group if the women failed to enter in labor within 12 hours after starting oxytocin, induction were considered failed. All the data obtained during the study period were entered

into a data form specifically designed by me for the study which is attached.

Any contraindication to vaginal birth assessed by history, clinical examination & ultrasound, Women with prior uterine surgery assessed by clinical examination & history, active maternal vaginal bleeding, chorioamnionitis, major fetal anomalies confirmed on ultrasound were excluded.

All the data obtained were analyzed with the help of SPSS software (version 19.0). Chi square Test was applied to compare outcome in both groups keeping P value < 0.05 was considered significant. All the results were presented as tables and graphs.

RESULTS

A total of 136 patients of pre mature rupture of membrane were observed, which were divided in two equal groups A & B. Patients in Group A were managed with oxytocin misoprostol while patients in group B were subjected to oxytocin.

Comparison of gestational age, bishop score and induction delivery interval in both the groups shows that gestational age and bishop score was insignificant in both the group while average inunction of delivery interval in group A was 5.4+1.71SD while 4.6+1.88SD in group B which was significant with p-value of 0.009.

Average age was 28.63 years+5.08SD. Group A contained 18(26.5%) patients in less than or equal to 25 years, 41(60.3%) patients 26-35 years and 9(13.2%) patients having ages of more than 35 years. While group B contained 23(33.8%) patients in less than or equal to 25 years, 38(55.9%) in 26-35 years and 7(10.3%) patients with age more than 35 years. Average age in group B was 27.6 yearts+5.11SD. The age distribution among the group was also insignificant with p-value 0.615.

Induction of labor wise distribution was significant with p-value = 0.009. The average induction of labour in Group A was observed 5.42+1.71SD while this average was 4.60+1.88SD in Group B. which shows that mistprotal group has longer induction of labor as that of oxitonic group. (Table 1)

Mode of delivery shows insignificant results in both the group with p-value=0.405. Majority of cases shows vaginal deliveries in both the groups. There were 9(13.2%) cases of C-section in misoprostal

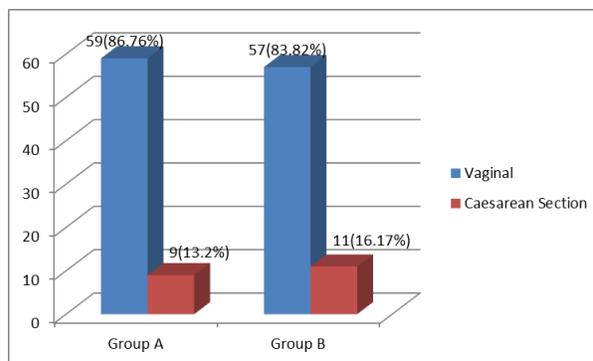


Fig 1: Comparison of mode of delivery

Table 1: Comparison of induction of labour interval

	Group	N	Mean	Std. Deviation	p-value
Induction Delivery Interval	A	68	5.4265	1.71313	0.009
	B	68	4.6029	1.88584	

Table 2: Gestational age and bishop score in both the groups

		Induction Delivery Interval				
		Group	Count	Mean	Standard Deviation	p-value
Gestational Age (in weeks)	<= 40.00	A	50	5.26	1.76	0.09
		B	57	4.65	1.91	
Gestational Age (in weeks)	41.00+	A	18	5.89	1.53	0.022
		B	11	4.36	1.80	
Bishop Score	<= 5	A	51	5.51	1.65	0.056
		B	49	4.82	1.93	
Bishop Score	6+	A	17	5.18	1.91	0.069
		B	19	4.05	1.68	

while 11(16.17%) in oxytocin group. Fig No 1

Age wise distribution of induction of labour shows that it was almost same in all age groups. The patients having less than or equal to 25 years of age have shows average of 5.78 ± 1.59 SD while 4.87 ± 2.01 SD was observed in group B.

When stratification was made over gestational age and bishop score in both the groups, it shows no significance in both the groups over induction of delivery interval except for gestational age of more than 40 weeks. (Table 2)

DISCUSSION

Spontaneous rupture of membranes before the onset of labour is known as premature rupture of membranes (PROM).¹² Premature rupture of membranes complicates 5-10% of pregnancies. The decision to manage PROM expectantly or actively is still controversial and depends on factors such as gestational age, fetal weight, lung maturity and availability of good neonatal care balanced against the chance of developing chorioamnionitis, cord compression and neonatal infection.¹³

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.¹⁴ 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.¹⁵

Oxytocin and prostaglandins are the most frequently used pharmacological agents for induction of labor.¹⁶ Oral misoprostol, a prostaglandin E1 analogue, has been shown to be safe and effective for cervical ripening and labor induction, particularly in women with poor cervical score.¹⁷

The goal of labor induction is to stimulate uterine contractions resulting in vaginal delivery.¹⁸ Our results showed higher rate of vaginal deliveries in women undergoing labor induction with misoprostol compared with oxytocin (86.76 versus 83.82%). It is noticeable that there is no significant difference between the two groups in percentage of vaginal deliveries. One group of authors in a randomized study among 210 pregnant women compared the

effectiveness of orally administered 25 µg of misoprostol every 4 hours and intravenously infused 10 units of oxytocin. The cesarean section rate, latent period and period from induction to vaginal delivery were significantly lower for the misoprostol group.¹⁹ In another study 120 patients were enrolled in misoprostol (57 cases) and oxytocin (63 cases) groups. Vaginal delivery occurred in 78.9 and 58.7% of misoprostol and oxytocin group respectively ($p < 0.05$).²⁰ Fonseca et al.²¹, by performing a randomized trial did not show a statistically significant difference between misoprostol and oxytocin group in term of vaginal delivery (87 versus 81%). Also, the total percentage of cesarean deliveries was not significantly different among these methods in Kramer's study.²²

In a recent research among 240 pregnant women it was revealed that mean induction-to-vaginal delivery time with misoprostol was shorter than Foley catheter and oxytocin (17.3 versus 20.2 hours).²³ These findings were also established in two other separate studies.^{24,25} On the other hand, results of Fonseca's et al.²¹ study support the finding that the induction-to-delivery interval with oxytocin is shorter compared with misoprostol (13.1 versus 16.3 hours). A shorter interval for oxytocin in comparison with misoprostol was also reported in another study (8.4 ± 4.1 hours versus 11.3 ± 6.9 hours, $p < 0.05$).²⁰ In our trial, the mean times from induction to active phase and induction to delivery were significantly shorter in oxytocin group than in misoprostol group.

Failed progression in the oxytocin group accounted for the most indications of cesarean section, four cases (16.2%), with (13.2%) occurrence of failed progression in the misoprostol group. This finding was in agreement with that of Zamzami²⁶, who found that all cesarean sections performed in the oxytocin group were because of failure to progress (7.4%). However, Butt et al.²⁷, found that failed progression in both the misoprostol group and the oxytocin group was the most common indication for cesarean section in both groups: six cases (10.9%) in the misoprostol group and 11.3% in the oxytocin group.

In the present study, the average induction delivery interval was significantly more in the misoprostol group (5.4 ± 1.71 hour) as compared to oxytocin group (4.60 ± 1.88 hour); the difference between both groups was statistically significant ($P = 0.009$). Butt

et al where induction delivery interval was 720 ± 382 min and 501 ± 389 min with misoprostol and oxytocin respectively.²⁷ 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, $P = 0.04$).²⁸

There was no significant difference between the two groups in the mode of delivery as 60 women (83.82%) delivered vaginally in the misoprostol group and 58 women (86.76%) delivered vaginally in the oxytocin group. The incidence of cesarean section in the misoprostol group was 13.2% (9 cases) compared with 16.17% (11 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.^{27,29}

Suk Wai Nagai (2000) compared the uterine activity of oral misoprostol with oxytocin for labour induction in women presenting with prelabour rupture of membranes at term. Intrauterine pressure transducers were introduced one hour before induction of labour in both groups of women. For those treated with oral misoprostol, mean uterine activity reached a peak 6-8 hrs. after the medication. Increase in high amplitude uterine activity was observed in the first 1 to 2 hours and persisted for the rest of labour. In the oxytocin group, the mean uterine activity rose steadily and reached the peak at 10-12 hours after treatment.²⁹

CONCLUSION

Pre mature rupture of membrane is a serious obstetrical emergency. Prompt resuscitation and identification of the causes of should be performed by a multidisciplinary team approach. Our study suggests that the use of oxitocine is more effective for induction of labor, thereby avoiding a cesarean section, and is associated with mild and selflimiting side effects. Misoprostol is cost effective and easily administered and therefore may be considered for use in low resource areas when oxytocin is unavailable.

Our sample size was not sufficient to detect differences in uncommon outcomes; thus, it is rec-

ommended that further studies include large numbers of patients. This can lead to better evaluation of the rare complications and side effects of the drugs and may also enable identification of the ideal dose.

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