

Misoprostol versus Oxytocin for Labour Induction in Women with Rupture of Membranes -A Prospective Randomised Study.

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ABSTRACT

Background: Misoprostol and oxytocin are commonly used to induce labor, particularly in women with prelabour rupture of membranes at term, to avoid complications. **Aim:** To compare oral misoprostol and oxytocin for labour induction in women presenting with prelabour rupture of membranes at term. **Methods:** Our study included 100 women reported to department with prelabour rupture of membranes. They were randomly assigned to one of the two groups; misoprostol or oxytocin group. We compared the pattern of uterine activity, the time period between induction to delivery, duration of labour and mode of delivery between the two groups. **Result:** In both the groups, an increase in uterine activity within one hour of labour induction was observed. Peak uterine activity was reached 6-8 hours and 8-10 hours in oral misoprostol and oxytocin groups respectively. The time period between induction to delivery, mode of delivery and the perinatal out come were similar for the two groups. **Conclusion:** Oral misoprostol caused earlier peak uterine activity, but was not as effective in induction of labor when compared with oxytocin.

Keywords: Labour, Misoprostol, Oxytocin, Prelabour rupture of membranes.

INTRODUCTION

The main objective of labor induction is to stimulate uterine contractions prior to the natural onset of labor, as uterine contractions and a proper cervical ripening are the two key factors in labor and vaginal delivery. Premature rupture of membranes (PROM) or pre-labor rupture of membranes is rupture of membranes prior to the onset of labor. Prolonged duration of time from the occurrence of PROM to delivery has to be avoided or else it may lead to histologic chorioamnionitis and funisitis, leading to increased maternal and neonatal morbidity.^[1,2]

Hence, an active approach should be initiated immediately. Various treatment options have been tried of which intra venous oxytocin is the most frequent regimen used, but it has a disadvantage of requirement of continuous assessment for dosage control.^[3,4]

Prostaglandin preparations like misoprostol are used with great success for cervical ripening and induction of labour, but carry a risk of introducing ascending infection, if it is applied as vaginal

preparation and gastrointestinal side effects if taken orally. Oral misoprostol has advantages of easy administration, cost effectiveness, stable at room temperature, reducing post-partum hemorrhage and superior maternal satisfaction due to its early labor and averting intravenous procedure.^[5-9]

We carried out this randomized study to compare oral misoprostol and oxytocin for labour induction in women presenting with prelabour rupture of membranes at term.

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MATERIALS AND METHODS

We carried out this prospective, randomized study in the department of Obstetrics and Gynecology, from January 2016 to December 2016. Our study included 100 women reported to department with PROM.

After explaining the patients about the study and obtaining approval from the Institutional ethics committee, a written informed consent was obtained from the patients. A detailed case history was recorded of all the patients. We calculated the sample size based on the expected difference of the induction to delivery interval between the two groups based on study of Ngai et al.^[8]

Inclusion criteria

1. Patients with PROM after 37 weeks of gestation,
2. Membranes ruptured for more than 12 hours and without signs of labour,
3. Cases with no clinical evidence of infection,
4. Cephalic presentation and
5. A singleton pregnancy.

Exclusion criteria

1. Women with a previous uterine scar,
2. Women with Meconium stained amniotic fluid,
3. Women who are allergic to prostaglandins,
4. Women with active maternal vaginal bleeding, chorioamnionitis and major fetal anomalies.

Women were examined by a sterile speculum. A baseline Bishop score was obtained to assess the readiness of the cervix for induction. The admitted women were randomly assigned to one of the two groups (misoprostol or oxytocin) according to Meinert criteria.^[10]

Group A: Oral misoprostol 100 µg, followed by repeated doses 100 µg every 4 hours for a maximum of three doses. Oxytocin infusion was given for patients in whom active labour did not begin with oral misoprostol alone.

Group B: Intravenous oxytocin dose of 1 mIU/min. If optimal uterine contractions did not occur, the dosage was doubled every 15 minutes up to a maximal dosage of 32 mIU/min.

After inserting intrauterine pressure transducer (Sonicaid, Utah, USA), all the patients were connected to a fetal heart rate monitor and the progress of labour was assessed by either regular uterine contractions or progressive cervical dilatation. If there was no considerable change in the cervix after 12 hours of adequate uterine contractions or no progressive increase in cervical dilatation after 2 hours in the active phase of labour, failed induction was considered.

All the data observed was stored in the recording unit. The printout on the strip (paper speed 1 cm/min) gave starting time and duration of monitoring, presence or absence of monitoring gaps, poor connection and end of transmission. In order to assure consistency of interpretation, two interpreters were used. Scheerer et al method of data

interpretation was used to evaluate uterine activity.^[11] According to the amplitude of ≤ 5 mm on the tocograph tracing; the observed patterns were divided into two groups;

- A. Low amplitude, high frequency pattern (1 to 2 minute intervals).
- B. High amplitude (≥ 6 mm), Low frequency pattern (30 seconds).

On hourly basis, the fraction of time occupied by any contractions and the number of high amplitude contractions were recorded in all patients. The following maternal characteristics were compared between the groups

- i. Maternal vital signs,
- ii. Parity and Gestational age,
- iii. Baseline Bishop score,
- iv. Time interval from PROM to delivery, induction to delivery, duration of labour and mode of delivery,
- v. Analgesic requirement,
- vi. Maternal and fetal morbidity and
- vii. Cord pH.
- viii. Occurrence of side effects,

The observed data was recorded and statistically analyzed, discontinuous variables by chi-square test and Fisher's exact test and continuous variables by Student's t test and Mann Whitney U test for the skewed data, using SPSS version 17.0.

RESULTS

110 patients were included in our study, 10 were excluded as they did not meet the inclusion criteria. All of the patients had normal vaginal delivery. Out of 100 included women, 90 were nulliparous and 10 multiparous and were distributed equally between the misoprostol and oxytocin groups. Maternal characteristics were comparable in both the groups [Table 1, Figure 1].

Table 1: Maternal characteristics in the misoprostol and oxytocin groups.

Character	Misoprostol Group Mean (SD)	Oxytocin Group Mean (SD)
Age	27.8 (3.0)	30.2 (4.0)
Gestation at ROM (weeks)	38.2 (1.5)	38.8 (1.8)
Median Bishop Score	5.3 (3-8)	5.4 (3-9)
ROM to recruitment interval (hour)	20.6 (6.3)	20.3 (7.2)
Percentage of primigravida (n)	82.5 (33/40)	82.5 (33/40)

ROM = Rupture Of Membranes SD=Standard Deviation

Epidural analgesia was given to 4 and 5 patients in misoprostol and oxytocin groups respectively, whereas intramuscular pethidine or inhaled Entonox was given to others. The type of analgesia used was comparable between the two groups and probably had no effect on the pattern of labour.

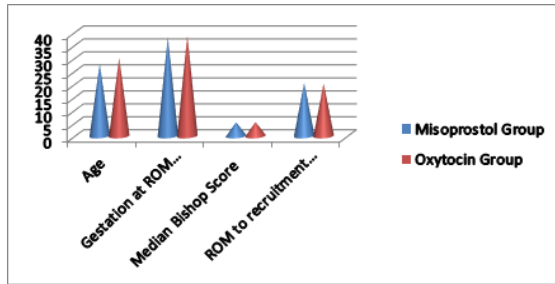


Figure 1: Maternal characteristics in the misoprostol and oxytocin groups.

The mean hourly high amplitude contraction frequencies and the fraction of time of uterine activity for both the two treatment groups showed statistically significant increase in activity (Friedman analysis of variance, $P < 0.001$). However, the misoprostol group showed a higher time of total uterine contraction in the first 4 hours.

The outcome of labour as compared between nulliparous and multiparous women are analyzed [Table 2]. Among 100 women, 90 (90%) were nulliparous and 10 (10%) were multiparous. Among nulliparous women, the difference between both the groups in relation to first and second stage was significant (4.5 h vs 9.8 h, $P = 0.026$ and 0.5 h vs 1.3 h, $P = 0.012$ respectively). The overall duration of labour was significantly shorter in the misoprostol group (5.6 h vs 10.4 h, $P = 0.004$). In misoprostol group, the induction to delivery interval was shorter, but the difference was statistically insignificant.

Whereas, in the multiparous women: the first, second and third stages of labour and the overall duration of labour were similar between the two groups. This might be due to very few multiparous women in our study. There was no finding of women suffering from uterine hyperstimulation.

Table 2: Outcome of labour in the misoprostol and oxytocin groups.

	Misoprostol Group	Oxytocin Group	P Value
Nulliparous			
First Stage (hours)	4.5	9.8	0.026*
Second Stage (hours)	0.5	1.3	0.012*
Third Stage (minutes)	2.5	3.7	0.63
Duration of labour (hours)	5.6	10.4	0.004*
Induction to delivery (hours)	7.1	10.9	0.26
Multiparous			
First Stage (hours)	2.5	4.6	0.14
Second Stage (hours)	0.3	0.2	0.26
Third Stage (minutes)	0.8	9.1	0.06
Duration of labour (hours)	3.2	5.7	0.36
Induction to delivery (hours)	3.6	7.3	0.05

* = Significant (< 0.05)

There was no significant difference in the mode of delivery between the two groups [Table 3]. Caesarean delivery was carried out in 4 patients of each group. The indications of section in the misoprostol group were cephalopelvic disproportion and oxytocin group was cephalopelvic disproportion and failed induction in 2 cases each.

Table 3: Mode of delivery in the misoprostol and oxytocin groups.

Mode of delivery	Misoprostol Group Number (Percentage)	Oxytocin Group Number (Percentage)
Spontaneous	35 (70)	27 (67.5)
Vacuum extraction	6 (20)	8 (20)
Low forceps	2 (5)	2 (5)
Caesarean section	2 (5)	3 (7.5)

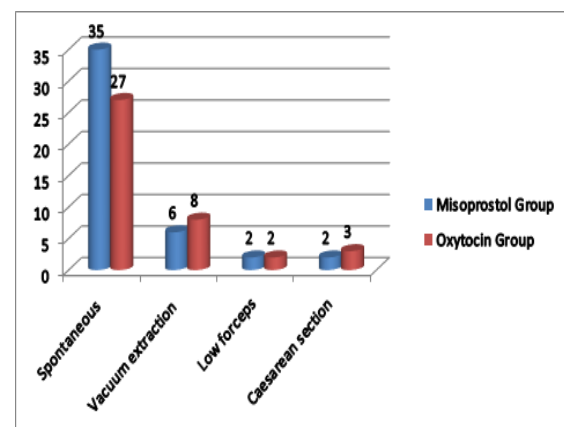


Figure 2: Mode of delivery in the misoprostol and oxytocin groups.

The neonatal outcome in both groups was comparable [Table 4]. The vaginal swab showed positive culture of Group B streptococcal infection in one and three women in the misoprostol and oxytocin groups, respectively. Patients were given antibiotic treatment.

Table 4: Neonatal outcome in misoprostol and oxytocin groups.

Outcome	Misoprostol Group	Oxytocin Group
Apgar < 7 at 5 minutes	0	0
Mean Birth weight in gm (SD)	3186 (424)	3328 (469)
Neonatal infection (n)	2	2
Umbilical artery pH	7.1 (0.3)	7.1 (0.3)
Admission to special care neonatal unit (n)	4	6

SD= Standard Deviation; n = number

DISCUSSION

PROM is a general sign for labour induction. Most commonly used drugs for this purpose are oxytocin and prostaglandins. Many studies have shown oxytocin to be a safe and efficient drug to initiate uterine contractions, but its utility depends on cervix

condition and ineffective in women with PROM and an unfavorable cervix, thus necessitating caesarean section. This disadvantage can be overcome by prostaglandins, which have property of promoting both cervical ripening and myometrial contractility, but may cause excessive uterine contractility, leading to perinatal and maternal morbidity and may increase the risk of ascending infection.^[16]

Regarding the exact dosage of drugs for labor induction, very few studies have been carried out. To be effective for labour induction, vaginal misoprostol is used at doses of 50-100 pg. Ngai et al showed that oral misoprostol 200 pg improved the Bishop score and reduced need of oxytocin infusion for labour induction.^[17]

Windrim et al compared vaginal dinoprostone and oral misoprostol for labour induction in patients with intact membranes. They did not find any statistically significant difference in the time between induction and delivery among the two groups and suggested that oral misoprostol can be considered as an option for labour induction. Even though we used a higher dose of oral misoprostol in our study (100pg) than that of Windrim et al (50pg), we did not notice any complaint of uterine hyperstimulation, but our patients presented with ruptured membranes, thus the response might be different from those with intact membranes.^[18]

We found a significant increase in uterine activity with both misoprostol and oxytocin. The time required for attaining maximum uterine activity with misoprostol and oxytocin was 6-8 hours and 8-10 hours respectively. Zieman et al found that the plasma concentration of misoprostol ascended rapidly, peaked between 12.5 and 60 minutes after administration, fell steeply by 120 minutes, and then remained low for the duration of their study. This might be due to misoprostol initiating the endogenous prostaglandins secretion which stimulates spontaneous onset of labour.^[19]

Very low caesarean section rate in our study may be due to less sample size. But the use of misoprostol reduced the duration of first and second stages of labour in nulliparous women, and oxytocin for augmentation of labour. This reduces the stress to the patients as well as the risk of maternal and neonatal infections. Regarding cost effectiveness, misoprostol is cheap when compared with intravenous oxytocin.^[18-20]

CONCLUSION

Oral misoprostol is as efficient as oxytocin for labour induction in women presenting with PROM at term, but also reduces the duration of labour in nulliparous women and complications like chorioamnionitis. We recommend further studies on

a larger sample to exactly determine the optimal regimen for labour induction in women with prelabour rupture of membranes at term.

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