Comparison of oral misoprostol with intravenous oxytocin for induction of labour in premature rupture of membranes

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Abstract

Introduction: To compare the effectiveness of oral misoprostol with intravenous oxytocin for induction of labor in premature rupture of membranes (PROM) at term.

Methods: This randomized comparative study was carried out in 100 women who were at or beyond 37 weeks of gestation with cephalic presentation, had PROM more than 12 hours with bishop's score less than six. Out of 100 women 50 were induced with 50 µg of oral misoprostol 4 hours apart (max 6 doses) and other 50 received intravenous oxytocin infusion (max 3 pints).

Results: The parity, mean bishop's score of two groups were comparable. Both misoprostol and oxytocin group showed similar induction to delivery interval (8.68 hrs ± 3.22hours vs. 7.61hours ± 2.84hours, P value was 0.08). Maximum number (52%) of patients responded to single dose of misoprostol in misoprostol group. Whereas in oxytocin group 40% of primigravidae required 10 units and 47% of multigravidae required 2.5 units of oxytocin. Majority of women in both the groups delivered vaginally but oxytocin group had slightly increased number of LSCS and one instrumental delivery. Meconium stained liquor was seen more in oxytocin group than misoprostol. Neonatal outcome was comparable in both groups.

Conclusion: Oral misoprostol was as effective as oxytocin in induction of labour in term PROM with low bishop's score.

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

Introduction

Premature (Prelabour) rupture of membranes (PROM) occurs in approximately 10% of all pregnancies and 70% occur at term [1,2]. The time interval between the rupture of membranes and onset of labour i.e. latent period may extend from hours to days.

With expectant management approximately 80% of women with PROM after 37 weeks go into labour within 24 hours and 95% within 72 hours[1]. In contrary longer expectancy brings a significant risk of neonatal and maternal morbidities due to infection so it is better to do induction of labour in these women which helps to decrease latent period[3]. As supported by different studies such as the study done by Schreiber and Benedetti, which showed that the prevalence of chorioamnionitis was 2.7% before 12 hours but increased to 26.4% after 24 hours of latent period[4]. Similarly systematic review of data from 12 trials at various centers done by Philippa Middleton and colleagues had also found a lower risk of maternal infection and neonatal intensive care for women who were induced, than for those who underwent spontaneous labour[5].

Although oxytocin is widely accepted as a safe and effective initiator of uterine contractions, its success is dependent on

the favorability of the cervix at the beginning of induction thus increasing risk of caesarean section in women with unfavorable cervix. Induction with prostaglandins offers the advantage of promoting not only cervical ripening but also initiating myometrial contractility.

Misoprostol, a PGE, analog; (15deoxy-16-hydroxy methyl PGE) is effective, inexpensive, easily stored, not affected by ambient temperature and is active both by the vaginal and the oral routes of administration[6]. In Tribhuvan University Teaching Hospital (TUTH) intravenous oxytocin was used for induction and augmentation in PROM which has been significantly replaced by per vaginal misoprostol. There is a risk of introducing ascending infection during frequent vaginal insertion of these preparations after PROM leading to increased infectious morbidity which can be avoided by convenient oral route.

Studies done with oral misoprostol for induction of labour in term PROM have shown to reduce latent phase, the induction to delivery interval and to decrease the infectious morbidity of both mother and neonate. It is also associated with increased maternal satisfaction and less hyperstimulation compared to other modalities as suggested by different literatures[7]. Thus this study has been conducted to see the effectiveness of oral misoprostol in induction of labour in comparison with intravenous oxytocin in patients with term PROM with unfavorable cervix.

Methods

The study was a prospective randomized comparative study carried out in labour room of department of Obstetrics and Gynecology, TUTH, from November 2008 till December 2009.

A hundred pregnant women, Primi or multigravidae, at or beyond 37 weeks of gestation presenting with history of PROM within 12 hours with singleton pregnancy and vertex presentation not in labour, with bishop's score less than six and reassuring Cardiotocography (CTG) were included in the study.

Women with allergy to prostaglandin and oxytocin, features of chorioamnionitis, scarred uterus, grand multipara, medical disease (such as cardiac disease, asthma, glaucoma, hypertension, uncontrolled type II diabetes mellitus) and cephalopelvic disproportion were excluded from the study. The other exclusion criteria's were intrauterine fetal death , intrauterine growth restriction, low lying placenta, moderate to thick meconium stained liquor on admission.

Approval from the institutional review board of this institute was taken and informed written consent was obtained from all women entering the study.

The duration of per vaginal leaking was noted and examination of the women included general, systemic and obstetric examination. Uterine contractions were noted for 10 minutes. PROM was confirmed if sterile speculum examination revealed pooling of amniotic fluid in posterior fornix. In doubtful cases pH of vaginal fluid was detected by litmus paper test which turned blue from yellow colour in contact with amniotic fluid. Internal examination was done to assess bishop's score, high vaginal swab was taken from all patients and CTG was done. Antibiotic (as per hospital protocol, i.e. Cefazolin 1gm iv stat followed by oral cefadroxil 500mg 12hrly for 7 days) were given to both the groups. And it was changed if required according to culture sensitivity report.

Included women were randomly assigned to two groups; misoprostol group and oxytocin group. Misoprostol group received 50µg of tab misoprostol (half tab of available 100µg) orally, repeated every 4 hourly till bishop's score of > 6 was achieved, maximum up to 6 doses. Oxytocin group received oxytocin by continuous intravenous infusion, 2.5 u in multi and 5 u in primi in 500ml (1 pint) of 5% dextrose, given in titration doses starting at 10 drops/ min and increasing 10 drops/min every half hourly (up to 60 drops/ min). After 1st pint was over next two pints containing same dose of oxytocin were given one after another at same rate as in previous pint and maximum 3 pints were used.

Fetal heart sound and uterine contractions for 10 minute was recorded just before administration of drug, immediately after and half hourly and per vaginal examination was performed 4 hourly to assess the response of either drugs in terms of cervical ripening (Bishop's score) or progress of labour.

Any one of the following outcome either Bishop's score > 6 or progression to active labour or both were observed. In such condition next dose of misoprostol withheld in misoprostol group whereas oxytocin infusion was continued at the same rate at which adequate contractions achieved till delivery.

Labour progress was monitored with the help of partograph which was maintained for each patient. In active labour oxytocin augmentation was done in misoprostol group if required. Labour was managed according to labour room protocol. The maternal side effects such as nausea / vomiting, diarrhea, fever/chills, hyperstimulation were noted. Failed Induction was considered when labour was not initiated after 6 doses of 50 µg misoprostol in misoprostol group and after 3 pints of oxytocin infusion in oxytocin group.

Maternal outcomes in terms of leaking to admission interval, induction to delivery interval, number of doses of

misoprostol and oxytocin required in concerned group, oxytocin augmentation required in misoprostol group, mode of delivery including instrumental delivery, lower segment caesarean section (LSCS) and their indications, PROM to delivery interval, any side effects or complications were noted with the help of partograph / patient's chart.

Similarly neonatal outcome such as APGAR score in 1 and 5 min, incidence and groups of meconium stained liquor, birth weight, neonatal admission and indication, neonatal sepsis presumed or proved, neonatal mortality if any was recorded from the partograph / paediatrician's record.

Data were analyzed using chi square test, independent t test, Z test with the help of SPSS computer software version 17 and PHSTAT2.

Results

The incidence of PROM was 9.11% during the study period. In terms of age, parity, period of gestation, mean bishop's score, leaking to admission interval the groups showed no significant differences. Most of the women were between 37-40 weeks of gestation (49 in misoprostol group and all in oxytocin group). Only one woman in misoprostol group was between 41-42 wks.

Maximum number of patients responded to single dose of misoprostol i.e. 26 (52%) in misoprostol group. Eighteen women (36%) required 2 doses of misoprostol and 6 women (12%) required 3 doses of misoprostol; however none of the women required more than 3 doses. Mean dose of misoprostol is 1.66 ± 0.72 in primigravida and 1.47 ± 0.63 in multigravida, (p value was 0.38). Maximum number of primigravidae (13, 39.39%) required 10 units of oxytocin among total 33 primigravidae and in multigravidae maximum number of women (8, 47%) required 2.5 units among total 17 patients. Thirty five patients (70%) who were induced with misoprostol didn't require oxytocin augmentation where as 15 patients (30%) required oxytocin augmentation.

Table 1: General characteristics of two groups

	Misoprostol	**Oxytocin**	**P value**
Mean age	25.32 ± 3.82years	25.94 ± 4.01 years	0.10
Mean period of gestation	39.2 ± 1.26 weeks	39.2 ± 1.04 weeks	0.33
Nullipara	35 (70%)	33 (66%)	0.66
Leaking duration	6.15 ± 2.83 hours	5.73 ± 2.78 hours	0.45
Mean Bishop's score	3.70 ± 1.23	3.98 ± 1.05	0.22

Table 2: Induction to delivery and leaking to delivery interval

Induction to delivery interval	**Misoprostol**	**Oxytocin**	**Leaking to delivery interval**	**Misoprostol**	**Oxytocin**
<6hr	9	13	<6hr	2	2
6-12hr	35	34	6-12hr	7	13
>12hr	6	3	12hr-18hr	29	27
			>18hr	12	8
Mean (p value 0.08)	8.67 hr ± 3.22 hr	7.61hr ± 2.84hr	Mean (p value 0.44)	14.23 ± 4.84 hr	13.97 ± 4.17hr

Table3: Indications of LSCS

Indication		Misoprostol	Oxytocin
Failed induction		-	2
Meconium stained liquor	Moderate	2	1
	Thick	-	1
Non progress of labour (NPOL)	NPOL	1	1
	Non descent of head	1	1
	Deep transverse arrest	-	1
Fetal distress (Fetal bradycardia)		1	-
Total		**5 (10%)**	**7 (14%)**

Table 4: Maternal adverse effects and complications

Adverse effect	Vomiting	Diarrhoea	Chills	Fever	Total	P value
Misoprostol	2	1	1	-	4	0.69
Oxytocin	2	-	-	1	3	
Complications	**Precipitate Labour**	**Post Delivery bleeding**	**Urinary retention**	**Fainting attack**	**Total**	**P value**
Misoprostol	1	1	1	1	4	**0.04**
Oxytocin	-	-	-	-	-	

Table5: Neonatal Outcome

	Misoprostol	Oxytocin	Total (p value)
Mean Birth weight	2987gm ± 425.08gms	2990gm ± 357.99gms	(0.43)
Apgar Score <7 in 1 min	5	7	12 (0.53)
Neonatal admission/observation	15	12	27 (0.49)
Leaking to delivery interval > 18 h	12	9	21 (0.46)
Proved sepsis	1	-	1

Delivery was achieved within 12 hours of induction in 44 patients (88%) in misoprostol group and 47 patients (94%) in oxytocin group the difference being not significant (p value 0.29). The mean induction to delivery interval was 8.67 hours ± 3.22 hours in misoprostol group and 7.61hours ± 2.84hours in oxytocin group which was also not significant statistically(p value 0.08). Fourty five women (90%) in misoprostol group and 43 women (86%) in oxytocin group had vaginal delivery. Among vaginal delivery one patient in oxytocin group had vacuum delivery applied for poor maternal effort with fetal distress in 2nd stage of labor.

LSCS was more in oxytocin group (7 i.e. 14%) than misoprostol group (5 i.e. 10%) but the difference was not significant (p value 0.53). Similarly meconium stained liquor was also noted more in women induced with oxytocin (13 i.e. 26 %) than in women induced with misoprostol (10 i.e. 20%) though not significantly different (p value 0.47).

Maximum number of patients had leaking to delivery interval of 12 to 18 hours (29, 58%

in misoprostol group and 27, 54% in oxytocin). Mean leaking to delivery interval was also comparable.

Regarding maternal side effects due to respective drugs there was no significant difference between the two groups (p value 0.69) but few maternal complications were observed only in misoprostol group (p value 0.04). There was no statistically significant difference in neonatal outcome in both the groups in terms of birth weight, APGAR score, neonatal admission, neonatal mortality.

Discussion

As success of induction depends on favorability of the cervix, LSCS rate is seen more frequently in oxytocin group than misoprostol in women with unfavorable cervix which is consistent with different trials because misoprostol helps in ripening of cervix along with initiation of uterine contractions. Hussaini et al[8] randomly allocated women with term PROM to receive either oral misoprostol or oxytocin infusion. They showed that vaginal delivery was seen in 92.3% in misoprostol group and 87.7% in oxytocin group with LSCS in 7.7% and 12.3% respectively8. Comparable to above results 90% in misoprostol group and 86% in oxytocin group had vaginal delivery in the present study and LSCS was more in oxytocin group (14%) than misoprostol group (10%). Inclusion of unfavorable bishop's score in the study population probably is responsible for the higher LSCS rate in oxytocin group than misoprostol group.

However in another study done by Mozurkewich et al[9] higher rate of LSCS (20.1% in misoprostol group and 19.9% oxytocin group) was observed which could be because of the study population as only nullipara had participated unlike the present study including both primigravidae and multigravidae . In addition they had used only two doses of misoprostol 6 hours apart but in this study up to 3 doses of misoprostol was used[9].

In oxytocin group inductions failed in 2 cases and were delivered by LSCS whereas none of the

inductions failed in misoprostol group in the present study, comparable to study done by Suk Ngai et al[10].

In the present study only 1 patient (2%) in oxytocin group had vacuum delivery and none in misoprostol group. However, Crane et al have reported higher rate of instrumental delivery in both the groups (19.23% in misoprostol, 18.86% in oxytocin). This could be because of longer PROM to recruitment interval (12.26 ± 8.83hour in misoprostol and 15.75 ± 11.7hour in oxytocin) than the present study (<12 hours) resulting in dry and difficult labor necessitating instrumental delivery[7].

Maximum number of women delivered between 6-12 hours of induction (70% in misoprostol and 68% in oxytocin group) in both groups in this study. The mean induction to delivery interval was comparable in two groups as it was 8.68 hrs ±3.22 hours in misoprostol group and 7.61hrs ± 2.84hours in oxytocin group, which was similar to the study done by Datta M R and Kabiraj M[11]. The induction to delivery interval was longer in misoprostol group but this did not reach the statistical significance in the present study. The mean bishop's score was lower in misoprostol group than in oxytocin group as well as the dose used was low (50µg) which may be responsible for this result. Hussaini et al documented significantly shorter induction to delivery interval in misoprostol group, than in oxytocin group (p value- 0.03)8. This result could have been obtained because of higher dose of misoprostol as they used 100µgm of misoprostol 2 doses 6hours apart compared to 50 µgm used in this study. Also parity and preinduction bishop's score were not mentioned so the influence of these elements could not be correlated. But in the present study women with unfavorable cervix (bishop's <6) were taken and primigravidae were more than multigravidae. In similar study done by Ellen Mozurkewich et al the induction to delivery interval was slightly longer in both the groups than the present study which can be explained by the study population as they included all nullipara[9].

In this study delivery was achieved within 12 hours in 44 patients (88%) in misoprostol group and 47 patients (94%) in oxytocin group because of which maximum number of patients had leaking to delivery interval < 18 hours (38, 76% in misoprostol group and 42, 84%). Also women with history of leaking > 12 hours were excluded from the study which minimized longer leaking to delivery interval. Datta Mamta Rath, Kabiraj Manas reported longer PROM to delivery interval than this study which could be attributed by the study methodology as they randomized women with term PROM into two groups one receiving expectant management for 20-24 hours then followed by induction by oxytocin another oral misoprostol[11].

Meconium stained liquor was seen more in women induced with oxytocin than in women induced with misoprostol (26% vs. 20%). The same finding does not hold true in the other studies done in term PROM, where meconium is seen more in misoprostol given orally than oxytocin group.[8,9] Dutta M R and Kabiraj M had observed meconium stained liquor in 9.3% of patients of misoprostol group and 4.1% of oxytocin group (p value> 0.05)[11]. Small sample size of the

present study than others does not allow us to accept this observation as conclusive.

Conclusion

The induction to delivery interval was comparable in this study comparing oral misoprostol with intravenous oxytocin. Neonatal outcome was similar and no major maternal or neonatal infectious morbidity was observed in both the groups. Thus it can be concluded that oral misoprostol was as safe and effective as intravenous oxytocin in inducing labour in women with PROM at term.

Conflict of interests None declared

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