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Immediate Versus Delayed Oral Misoprostol for Induction of Labour in Premature Rupture of Membranes at Term: A Randomized Control Trial

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Abstract

Background: Premature rupture of fetal membranes (PROM) occurs in approximately 5-10% of all pregnancies, of which approximately 80 % occur at term (Term PROM). If active management of term PROM is supported with induction, then it is associated with reduced maternal infective morbidity without increasing the caesarean section or operative vaginal birth rates. **Objective:** To compare the time of onset of labour among immediate versus delayed administration of oral misoprostol for induction of labour in premature rupture of foetal membranes at term gestation. **Material and Methods:** This study was conducted in Department of Obstetrics and Gynaecology, Command Hospital Air Force, Bangalore as a randomized comparative interventional study on 60 patients with confirmed PROM at term 37 to 40 weeks gestation. These patients were randomly divided into two groups by using computer generated random system of allocation after fulfilling the inclusion and exclusion criteria. Group A (immediate) received misoprostol within 6 hours of PROM and Group B (delayed) received misoprostol after 6 hours of PROM. Augmentation of labour if required was done with oxytocin infusion. **Results:** The present study showed that mean time interval from PROM to delivery was 14.2±3.30 hours in immediate group of induction and 23.04±5.44hrs in delayed group of induction and p value is 0.00 (p value <0.001) which is highly significant. Early induction of labour with oral low dose misoprostol 25 microgram in term PROM patients is always better than expectant management for better obstetric outcome. There were no maternal complications in the immediate group of induction, 2 cases with intrapartum fever, 2 cases with GIT symptoms and one case had PPH, and one patient underwent LSCS in delayed group.

Keywords: Immediate and Delayed; Misoprostol; PROM.

Introduction

Spontaneous pre-mature rupture of foetal membranes (PROM) is defined as the rupture of foetal membranes before the onset of labour, which can complicate 5 to 10% pregnancies, with 60% of them occurs at term.[1] There is controversial to manage PROM at term.[2] One of the method believes in the conservative or expectant management, in which an expectant period of 12–24 hours after the incident is observed to allow a good number of women to go into spontaneous labour with high vaginal delivery rate.[2] The other method believes in immediate induction of labour, in which labour is induced immediately after admission irrespective of the duration of rupture of membranes.[2]

The time interval between rupture of membranes and the onset of labour is termed the "latency period", the time interval between rupture and delivery is termed the "interval period". (3) About 80% of women at term will go into spontaneous labour within 24 hrs. and 10-25% will have a latent period of >24 hrs. If the latent period is >24 hrs. the chances of infection increase. Therefore, the management of such patient is induction of labour.[4]

Misoprostol synthetic analogue is rapidly absorbed when given orally and becomes extensively bound to plasma

proteins. When administered vaginally peak plasma levels are reached more slowly (80±27 min) than with oral administration (37±17 min) and are sustained upto 4 hours, probably because of the obligatory hepatic pass that occurs with oral, but not with vaginal administration, and it has been found in many studies to be efficient and safe in ripening the cervix and inducing labour when administered orally with 25-50µg tablets every 4–6 hours.[5]

The aim and purpose of this study was to compare the time interval taken from the induction of labour till the delivery.

Methodology

This prospective study was conducted on 60 pregnant women with premature rupture of membranes at term (37-40 weeks) in Department of Obstetrics and Gynaecology, Command Hospital Air Force, Bangalore. All eligible patients who gave consent, were allotted into test group and control group through a computer-generated random system of allocation of group on patients' admission, and will be administered with the tab Misoprostol 25micrograms 2hourly till the patient goes into active labour or till maximum of 24 doses till 48 hrs whichever is earlier. As per random allocation, 30 patients with immediate (within 6 hours) tab misoprostol administration (Test / Immediate Group A) and rest 30 patients with delayed (after 6 hours) administration (Control / Delayed Group B) was successful. Oral Tab Misoprostol will not be administered in case of onset of active Labour, tachysystole, hyperstimulation, foetal distress. Augmentation of labour if required will be done with oxytocin infusion.

PROM was confirmed by history (i.e. sudden gush or trickling of watery fluid per vagina) and clinical examination by sterile speculum if not immediately obvious (i.e. pooling of fluid in the posterior fornix of vagina or leakage of fluid from the cervical os). Inclusion criteria included term pregnancy ≥ 37 weeks confirmed by LMP and/or early sonography; singleton live pregnancy; vertex presentation; no contraindications for vaginal delivery; not in active labour, admission CTG shows no abnormality. Exclusion criteria included Abnormal NST, Antenatal patients with contra-indications to vaginal delivery/induction of labour, PPROM/ EROM, PROM in > 40 weeks POG, Post LSCS pregnancy, Meconium-stained liquor, Malpresentations, Multiple gestations, Heart disease, Bronchial asthma, Allergies to Prostaglandins, Antepartum haemorrhage with placental previa, Patient unwilling for induction.

If study subjects came to hospital after 6 hours of PROM, they were started with antibiotic after sensitivity test and were continued for 3 doses after delivery unless evidence of sepsis was seen, where it was given for a longer time along with a broader cover. Induction to delivery interval and PROM to delivery interval were noted. Maternal pulse, blood pressure, foetal heart rate and its variations were checked frequently. The onset of any complications like foetal distress, foetal heart rate variations, and chorioamnionitis (clinical) were looked for. Progress of labour was monitored. If there was any evidence of foetal jeopardy or any other obstetrical complications, labour was cut short by instrumental delivery or caesarean section as required.

The maternal outcomes included duration from ROM to the onset of labour pain; duration from ROM to delivery; number of doses used for induction, vaginal delivery rates; operative delivery rates (C.S); maternal morbidity and mortality (e.g. postpartum haemorrhage, vaginal or cervical tears and chorioamnionitis).

Statistical analysis: Data were entered in MS Excel sheet and tabulated. It was processed using statistical package for science and society (SPSS 20.0) for windows. Qualitative data were expressed in the form of frequency, rates and percentages, proportion were compared with Chi-square or Fischer's exact test. Quantitative data were expressed in the form of mean and standard deviation. P value was considered significant when < 0.05 and considered highly significant when < 0.01.

Results and Discussion

Sixty women participated in the study. Thirty women had immediate (within 6 hours) induction of labour with oral misoprostol, and the same number of women had delayed (after 6 hours) induction with oxytocin infusion after an expectant period of 24bhours. Of the total deliveries of induced patients in both groups there was only one patient in the delayed group who underwent LSCS accounting for 3.3% and rest all patients in both the immediate and delayed group had induced vaginal delivery without any instrumental delivery.

Premature rupture of the membrane (PROM) is a common and challenging problem in perinatal medicine today. Management of PROM has gone through various stages ranging from masterly inactivity to immediate intervention. In spite of it, management of Term PROM still lacks a standard protocol for management.

General characteristics:
Maximum women were in the age group of 21-25 years (50% in immediate group and 53.3% in delayed group). Highest age was 32years. Lowest age was 21 years. Most of the patients were in 38- 40 weeks of gestation. 56.7- 60% were primigravida (table 1).

Anjana Devi et al. (6) and Umed Thakor (7) studies found majority of PROM patients belonged to 20-29 years age group, this may be because of high probability of child bearing during this period. However, a contradictory study conducted by Hannah et al (8) found a higher incidence of PROM in multigravida. This may be attributed to increased incidence of ascending infection in multigravida which is an important cause of PROM and is more common in developing countries. Incidence of PROM is 8% between 37week 1 day to 40 completed weeks as observed by Kodkany and Telang. (9)

Table 1: General characteristics of the study subjects.

variables	Immediate Group (30)	Delayed Group (30)	chi square test p value
Age (Years)	No. (%)	No. (%)	
21 - <26	15 (50)	16 (53.3)	4.39
26 - <30	11 (36.7)	14 (46.7)	0.11
30 - 35	4 (13.3)	0 (0)	-
Gravida			
Primi	17 (56.7)	18 (60)	0.07
Multi	13 (43.3)	12 (40)	0.79
Gestational age (in weeks)			
37 --≤ 38	5 (16.7)	11 (36.7)	3.32
38 – ≤39	12 (40)	12 (40)	0.132
39 - 40	13 (43.3)	7 (23.3)	

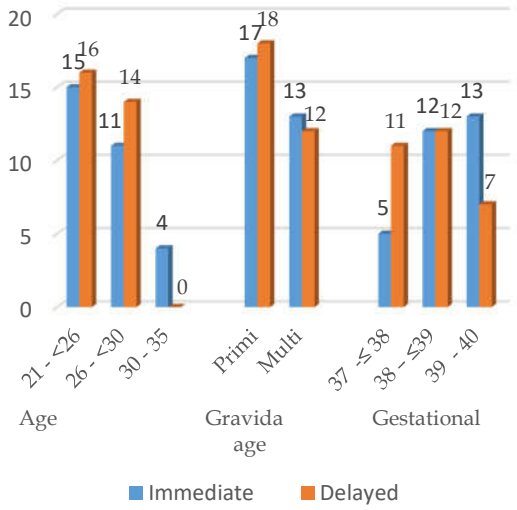

Fig. 1: General characteristics.

High vaginal swab (HVS) culture showed 6.6% growth of E. coli / Streptococci among immediate group and 16.6% among delayed group (p value >0.05). Kodkany and Telang (9) study also showed similar results with HVS culture negative cases accounting for 85% and 7% E. coli growth. 56.6% of subjects among immediate group and 75.6% of subjects among delayed group had antenatal risk factors (GDM, Anaemia, gestational hypertension, Rh negative, HBS ag, hypothyroidism) (p value >0.05). This is similar to the study done by Anjana Devi.[6] which showed that 15% had GDM as associated risk factors and 33.4% had no known antenatal risk factors.

There was not much difference in the Bishop's score among both groups. These results are in accord with results obtained by Shetty and co-workers (2002) (10) and Kunt et al. (2010) (11). Need of misoprostol doses was more among delayed group but which was statistically not significant (p value >0.05). Pitocin was needed to induce labour in immediate group whereas three subjects among delayed group needed Pitocin for labour augmentation. Different results were obtained by Javaid et al. (2008) (12) who found that there was less requirement of augmentation with oxytocin in the immediate induction group 40% than expectant management group 60%.

Table 2: Antenatal factors and dose of misoprostol

Variables	Immediate Group (N=30)	Delayed Group (N=30)	P Value
Risk Factors			
GDM	6 (20%)	5 (16.7%)	
GHTN	2 (6.7%)	4 (13.3%)	
Anemia	8 (26.7%)	9 (30%)	
Obesity	3 (10%)	3 (10%)	0.1008
Hypothyroidism	1 (3.3%)	1 (3.3%)	
RH Negative	2 (6.7%)	1 (3.3%)	
HBSAG Positive	1 (3.3%)	1 (3.3%)	
No Risk Factor	13 (43.3%)	7 (23.3%)	
Bishop's Score			
2 – 3	10 (33.3%)	12 (40%)	
4 – 5	19 (63.3%)	17 (56.7%)	0.77
6	1 (3.3%)	1 (3.3%)	
Misoprostol Doses			
2-4	13 (43.3%)	8 (26.7%)	
4-8	17 (56.7%)	19 (63.3%)	0.1.1
8-24	-	3 (10%)	
Pitocin			
Required	-	3 (10%)	0.163
Not Required	30 (100%)	27 (90%)	

Time interval between PROM to induction till the delivery: (table 3 and table 4)

Immediate group subjects were induced within 6 hours whereas delayed group after 6 hours. Time interval between induction of labour to start of contraction was almost similar among both groups (p value >0.05). The time interval between the contraction till the delivery was within 2-12 hours among 96.7% of immediate group and 83.4%of delayed group, which was not statistically significant. The time interval between PROM to delivery was 6-12hours in immediate group and 12-36 hours in delayed group and which was statistically significant (p value <0.001).

These results are in accordance to results obtained by Mahmoud Farouk Midan et al (2012),[13] Shetty et al. (2002) (10) and supported by results obtained by Crane et al. (2003).[14] Interval periods were also significantly different between the two groups; the interval periods were very

less in the immediate induction group than the delayed induction group.

The mean duration in the immediate induction group was 14.22±3.30 hours while it is 23.04±5.44 in the delayed induction group. These results are in accordance with that obtained by Mahmoud Farouk Midan et al (2012)[13] and supported by results obtained by Ngai et al. (2000). [15]

Table 3: Time intervals between various measures

Time interval	Immediate Group (n=30) No. (%)	Delayed Group (n=30) No.	P value
PROM to induction			
< 1 hr	1 (3.3)	-	
1 - 2 hrs	4 (13.3)	-	
2 - 4 hrs	17 (56.6)	-	0.00
4 - 6 hrs	8 (26.6)	-	
6 - 12 hrs	-	22 (73.3%)	
12 -24 hrs	-	8 (26.6%)	
Induction to contraction			
1 - 2 hrs	1 (3.3)	-	
2 - 4 hrs	12 (40)	14 (46.7)	0.6
4 - 6 hrs	10 (33.3)	6 (20)	
6 - 12 hrs	7 (23.3)	10 (33.3)	
Contraction to delivery			
2 - 4 hrs	2 (6.7)	5 (16.7)	
4 - 6 hrs	8 (26.6)	5 (16.7)	
6 - 12 hrs	19 (63.3)	15 (50)	0.16
12 -24 hrs	1 (3.3)	5 (16.7)	
Induction to Delivery			
4 - 6 hrs	2 (6.7)	-	
6 - 12 hrs	14 (46.7)	12 (40)	0.56
12 - 24 hrs	14 (46.7)	16 (53.3)	
24 - 36 hrs	-	2 (6.7)	
PROM to Delivery			
6 - 12 hrs	5 (16.7)	-	
12 - 24 hrs	25 (83.3)	22 (73.3)	0.001
24 - 36 hrs	-	8 (26.7)	

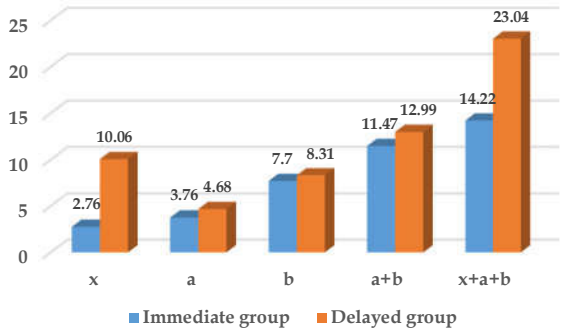

Fig 2: Various time intervals.

Only one patient among delayed group has to undergo caesarean section, whereas all subjects delivered by vaginal mode. (Table 5)

Table 5: Mode of delivery among both groups.

Delivery	Immediate Group	Delayed Group
Vaginal	30 (100)	29 (96.7)
LSCS	0(0)	1(3.3)
Total	30(100)	30(100)

Conclusion

In short, this study showed that immediate induction of labour for women with term PROM had relatively lower time intervals from PROM to delivery as compared with delayed induction after 24 hours of conservative management. However, larger scales, multicentric randomizes studies are needed before drawing a final conclusion.

Limitations

Numbers of study participants were less; further studies are required with a greater number of subjects for better statistical correlation.

Conflicts of interest: None

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