ORIGINAL PROF-1478

"PROM";
ACTIVE MANAGEMENT AT TERM WITH ORAL MISOPROSTOL

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ABSTRACT... **Objective:** To assess and compare the number of subjects in both groups (Study and comparison), who went into active labour within 24 hours and to compare the various complications (maternal & fetal) in both groups. **Study Design:** Quasi experimental. **Sampling Technique:** Convenience sampling. **Sample Size & Setting:** A total of 100 pregnant women presenting with history of leaking amniotic fluid at term (≥37 wks) to labour ward of obstetrics and Gynaecology unit, Bahawal Victoria Hospital, Bahawalpur were included in the study. **Material & Method:** The pregnant women fulfilling the inclusion criteria were enrolled as our study subjects. Rupture of membranes was confirmed by nitrazine test.The patients were randomized into two groups (50 women in study and 50 in comparison group). In study group, 50 (Ligm of misoprostol was given orally after initial assessment of mother and fetus. The dose was repeated 4 hourly, if there was no uterine activity. The number of patients going into active labour and delivering within 24 hours were noted. Different complications (maternal & fetal) faced during all procedure were also recorded and managed. In comparison group, patients were managed were also recorded and managed. In comparison group, patients were managed conservatively for 24 hours. Like in study group, number of patients gong into active labour and delivering with in 24 hours were noted. Different maternal & fetal complications occurring in this group were also recorded and managed. **Results:** A total of 100 Pregnant women were included in the study. The sample size (100 patients with PROM at term) was completed in 5 months. During that period over all 1105 deliveries were conducted, so the incidence of PROM at term in the study was 9.4%. It was observed in the study group, that all the patients (100%) went into active labour and 96% were delivered within 24 hours of PROM. While in comparison group 72% patients went into active labour and only 62% were delivered within 24 hours of PROM. The results showed that in study group 36 patients went into active labour with only one dose of oral misoprostol, 9 patients required 2 doses and 5 patients required 3 doses of oral misoprostol for going into active labour. When maternal complications were compared in both groups, 92% patients in study group had no complication while only 8% patients had to face different complications. In comparison group 86% had no complication and in 14% patients different complications occurred. Regarding fetal complications 4% fetus/neonates had to face different complications in each group. In current study there was no significant difference in the mode of delivery between the two groups. **Conclusion:** It was concluded that active management of pre labour rupture of membrances at term with oral misoprostol is a better option than the expectant management. Oral misoprostol in dose of 50 jugm is an effective agent for cervical ripening and induction of labour in PROM at term as significantly high percentage of patients delivered within 24 hours with no increase in maternal and fetal complications.

Key words: Induction of labour, PROM, Oral misoprostol.

INTRODUCTION

Premature rupture of membranes is an obstetrical conundrum poorly defined with obscure etiology, difficulties in diagnosis and associated with significant maternal, fetal and neonatal risks. Premature rupture of membranes (PROM) is defined as rupture of Eal membranes occurring prior to the onset of labour at or beyond 37 weeks .3tation.

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Its management is one of the most controversial topics in obstetrics[1]. PROM occurs in approximately 10% of all pregnancies. It is generally accepted that majority of cases occur after 37 completed weeks of gestation. It can occur at term or prior to term, in which case it is designated as preterm premature rupture of membranes. When PROM occurs remote from term (PPROM) significant risks of morbidity and mortality are present for both fetus and mother[2]. Numerous studies have addressed the issue of possible pre disposing factors responsible for occurrence of PROM. It has been studied from the stand point of infection, maternal nutrition and smoking status, local membrane insult and predisposing anatomic abnormalities.

PROM is diagnosed by speculum vaginal examination of cervix and vaginal cavity. Pooling of fluid in the vagina or leakage of fluid from the cervix, ferning of dried fluid under microscopic examination, and alkanity of fluid as determined by Nitrazine paper confirm the diagnosis. If all the fluid has leaked out an ultrasonogrphic examination may then show absence of or very low amounts of amniotic fluid in uterine cavity.

When PROM occurs at term, after confirmation of diagnosis, there are two management options. First is expectant management, treating the patients conservatively for 24 hours after PROM. Second is, active management of PROM done by using oxytocin or prostaglandin for cervical ripening. In large part, management of these patients depends upon their intrauterine infection increases with the duration of PROM. Evidence supports the idea that induction of labour (active management), as opposed to expectant management, decreases the risk of chorioamnionitis, without increasing the cesarean delivery rate [3,4].

At term, infection remains the most serious complication associated with PROM for mother and the neonate. The risk of chorioamnionitis with term PROM has been reported to be less than 10% and to increase to 40% after 24 hours of PROM[5]. Since the risk of infection with PROM is small during first 24 hours, expectant management may be considered in selected patients for first 24 hours[6]. The neonatal risks of expectant management of PROM include infection, placental abruption, fetal distress pulmonary hypoplasia and fetal or neonatal death. Fetal death does occur in approximately 1% of patients with PROM after viability who have been expectantly managed[7] and in about 1:1000 term PROM[8].

The largest randomnized control trial on pre labour rupture of membranes to date, found that active labour induction with oxytocin or vaginal prostaglandin E2 (PGE2) gel and expectant treatment resulted in similar rates of C- Section and neonatal infection[9]. Prostaglandin E2 preparations, given locally in the form of vaginal pessaries or gel have been shown to be effective both for cervical priming as well as for labour induction in women with PROM at term with unfavourable cervix and are generally superior to intravenous oxytocin, with a shorter induction to delivery interval and a lower caesarean delivery rate[10]. But these preparations tend to be unstable at room temperature and are expensive. More over there is a risk of ascending infection during application of these preparation. Misoprostol, an orally active synthetic PGE_1 analogue that is used for prophylaxis of peptic ulcer has been tried for induction of labor and cervical ripening at term in pregnancies with a live fetus [11]. In the past it was given by vaginal route but in order to avoid the risk of introducing ascending infection, many studies have been conducted with oral route. Given orally as 50 jiigm tablets, misoprostol is not associated with any gastrointestinal or other significant side effects. Because misoprostol is not as expensive as currently available PGE_2 gel or suppositories and is stable at room temperature, it appears to be a better alternative especially if it can be administered orally for this purpose.

MATERIALS METHODS

A total of 100 pregnant women (fifty in study group and fifty in comparison group) presenting with history of leaking amniotic fluid at term (≥37 weeks) to labour ward of obstetrics & gynecology unit, Bahawal Victoria Hospital Bahawalpur were included in the study. Inclusion criteria was pregnant women with pre labour rupture of membranes at term, with a single fetus in cephalic presentation, normal cardiotocogram, parity less than 5, being 150 cm or more in height with adequate pelvis on clinical elvimetry, in case of primigravida. Exclusion criteria was, patients in established labour, with signs & symptoms of chorioamnionitis (maternal

fever, tachycardia, uterine tenderness, purulent vaginal discharge, fetal tachycardia), fetal distress, malpresentation, postdate pregnancy, twin pregnancy, previous cesarean section, cord prolapse, party over 5, inadequate pelvis, or height less than 150 cm in case of primigravida and women with vaginal bleeding, proteinuric hypertension, intrauterine growth retardation and diabetes mellitus.

The pregnant women fulfilling the inclusion criteria were enrolled as our study subjects and detailed history was taken regarding rupture of membranes . General physical examination (temp, B. P, pulse) and abdominal examination was done. A fetal cardiotographic trace to confirm fetal well being was performed. Uterine contractility if any was noted. Digital examination was avoided. Diagnosis of PROM was confirmed by seeing amniotic fluid on sterile speculum and by nitrazine test. Base line investigations including complete blood examination, complete urine examination, blood grouping and RH factor were sent. Then the patients were randomized to active or conservative arm after full informed consent.

Women raundomized to active arm received 50 µ gm of oral misoprostol which was prepared by taking one fourth of a 200 µ gm tablet cytotec (searle pharmaceuticals). The dose was repeated after 4 hrs, if there was no uterine activity or if uterine contractions were less than two mild contractions in ten minutes, to a maximum of 4 doses. Before every dose a fetal CTG was done. When uterine activity suggested the onset of labour, vaginal assessment was performed and the women moved to labour ward. The management in the labour ward was according to our normal labour ward protocols. If, at the end of 4 doses of misoprostol, labour was not set in, the induction was declared as failed. However, in these patients oxytocin could be started after doing Bishop Score, (score 7 or more). At the time of delivery paediatrician was called for initial resuscitation and assessment of new born. Different complications to be faced during this induction procedure were, uterine hyper stimulation (strong uterine contractions lasting over 2 minutes, with associated fetal heart changes), tachy systole (6 or more contractions in 10 minutes) chorioamnionitis and fetal distress and these were indications for caesarean sections as well.

Women randomized to conservative arm were kept under observation for 24 hours. Continuous maternal and fetal monitoring was done. Maternal pulse, temperature and blood pressure were monitored at 4 hours interval. Detailed record of progress of labour was maintained on partogram. Fetal CTG was performed every 4 hours. If significant uterine contractions started, time was noted and the duration since rupture of membranes till this time was recorded. Further management in the labour ward was according to our normal labor ward protocol. If labour was not set in by 24 hours of the pre labour ruptures of membranes the conservative management was labeled to be failed. In these patients (failed conservative gp) a vaginal examination was performed to evaluate the Bishop's score. If it was <7, PGE_2 vaginal gel was administered into posterior fornix, that could be repeated every 6 hours for a maximum of 3 doses. If Bishop's scare was 7 or more the oxytocin infusion was started. Labour management was according to normal labour ward protocols.

RESULTS

A total of 100 pregnant women (50 in each group) were studied. In our study maximum member of patients (47%) were between 20-29 yrs and out of them 63% were primigravida and 27% were multigravida. In study group, 72% of patients went into labour with only 1 dose of oral misoprostol 18% patients required two doses and 10% required 3 doses of misoprostol, for induction of labour. With the help of oral misoprostol all the patients ie. 100% went active labour within 24 hours of PROM while in conservative management of comparison group only 72% patients went into active labour within 24 hours of PROM (Table I).

Rupture of membranes to delivery time was also short in study group i.e 48 patients (96%) delivered by either route within 24 hours of PROM while in comparison group only 62% patients were delivered within 24 hours of PROM. Acc to our results chi square is equal t o17.5761, significant at the level of 0.001 while degree of freedom is equal to 1 and table value is equal to 10.88 (Table II).

Table-I. Patients in active labour within 24 hours of PROM				
Patients went into active labour within 24 hours of PROM	Study group		Comparison	
	No of Pts.	%	No of Pts.	%
Yes	50	100	36	72
No	-	-	14	28
Total	50	100	50	100

Table-II. Rupture of membranes to delivery time				
Rupture of membranes to delivery time	Study group		Comparison group	
	No of Pts.	%	No of Pts.	%
≤24 Hours	48	96	31	62
>24 Hours	02	04	19	38
Total	50	100	50	100
X^2 = 17.5761 Significant at the level of 0.001 df = 1 Table value = 10.83				

Table III. Shows that there was no significant difference between the study and comparison groups regarding the mode of delivery within 24 hours. In active group (6%) had caesarean section while in conservative group 5 (10%) had caesarean section within 24 hours (Table III).

Table III. Mode of delivery (in comparison with time in study and comparison group).					
Time in Hours	Mode of Delivery	Study group		Comparison	
		No of Pts.	%	No of Pts.	%
< 24 Hours	Spontaneous vaginal delivery	45	90	26	52
	C - Section	03	06	05	10
> 24 Hours	-	02	04	19	38
Total	-	50	100	50	100

According to our results, in study group 46 patients (92%) had no complication during management while 04 (08%) had to face different complications. In comparison group 7(14%) had different complications (Table IV). In this table chisquare is equal to 0.9235 which is not significant.

Table-IV. Maternal complications in study and comparison group				
Complications	Study group		Comparison group	
	No of Patients	%	No of Patients	%
No Complication	46	92	43	86
Complication	04	08	07	14
Total	50	100	50	100
X2 = 0.9235 Not significant				

Table V shows the details of different complications which occurred in both groups. Chorioamnionitis was the commonest complication in conservative management.

Table-V. Details of maternal complications		
Complication	Study Group	Complications Groups
Chorioamniontis	01	05
Placutal abruption	-	-
Hyper stimulation	02	01
Tachy systole	-	-
Nausea & Vomiting	01	01
Total	04	07

Table-VI. Detail of apgar score at brith and after five minutes				
APGAR SCORE	**Study group**		**Comparison group**	
At Birth	**No of Patients**	**%**	**No of Patients**	**%**
6-8	03	06	04	08
9-10	47	94	46	92
At 5 Minute	**No of Patients**	**%**	**No of Patients**	**%**
6-8	01	02	02	04
9-10	49	98	48	96

Table-VII. Shows, there was no difference in both groups regarding the fetal/neonatal complications.

Table-VII. Foetal complications				
Complications	**Study group**		**Comparison group**	
	No of Patients	**%**	**No of Patients**	**%**
Fetal Distress	02	04	-	-
Neonatal Sepsis	-	-	2	4
Total	02	04	02	04

DISCUSSION

In the management of pre labour rupture of membranes at term, active approach appear to be desirable because a prolonged interval from PROM to delivery is associated with increased incidence of chorioamnionitis[5]. Maternal and neonatal infection and morbidity is also increased[12].

Induction of labour is a process which aims for planned delivery with a favourable maternal and fetal outcome[13]. It is important to ripen the cervix before induction in order to improve the chance of successful vaginal delivery. Vaginal misoprostol has been shown to be effective in lobour induction at doses of 50-100 ugm,[14] with lower incidence of nausea than that associated with PGE_2 tablets. In the past 15 years, a large no of trials have been reported, which assessed the efficacy and safety of misoprostol when used for induction of labour in the presence of viable pregnancy. These trials have used both vaginal & oral misoprostol [15,17,20]. The potential advantage of oral route include easy, non-invasive administration and avoidance of unnecessary vaginal examinations. Razia Mustafa and Pushpa Sirichand[19], also concluded in their study that safety and efficacy was comparable between low dose vaginal and oral misoprostol uses for induction of labour at term. However, oral route was better with respect to treatment interval, number of doses required and route of delivery. In the present study, we compared the expectant management of PROM with active management done with 50 µg of oral misoprostol. In this study the incidence of PROM at term was 9.4%, that is comparable to reported incidence of PROM (10%) in latest update given by Allahyar Jazay[6].

Although PROM has no relation with age of women but maximum number of patients (47%) were in age group of 20-29 years. Most probably because, this is the age group in which maximum number of pregnancies occur. With the use of oral misoprostol the interval between recruitment to onset of uterine activity and the recruitment to delivery were significantly reduced. A shetty et al[16] conducted the same type of study in December 2002. According to their results 93.3% patients went into active labour with in 24 hours and 72% of them were delivered within 24 hours in misoprostol group as compared with 54.8% of the patients going into active labour and 26.9% of them delivering within 24 hours in comparison group. In the current study 100% patients went into active labour within 24 hours and 96% were delivered by either route within 24 house while in comparison group only 72% went into labour and out of them only 62% were delivered by either route within 24 hours. Jehan Ara and Meher Noorani conducted a study[18] on induction of labour with oral misoprostol for prelabour rupture of membranes at term. They concluded that active management with oral misoprostol resulted in more women going into labour and delivering within 24 hours of PROM with no significant maternal and neonatal complications. Another most recent data analytic study[17], showed that in seven trials comparing oral misoprostol with placebo, women using oral misoprostol were more likely to deliver vaginally within 24 hours.

There was no significant difference in the mode of delivery

between the two groups. In active group 6% and in conservative group 10% had caesarean section. The current study showed that with the use of oral misoprostol in dose of 50 µ gm, the (12) complication (maternal & fetal) rate does not increase in comparison with control group that is similar to the results of study by A Shetty et all[16].

At term, infection remains the most serious complication associated with PROM for the mother and neonate. Seaward PG et al [5] showed that chorioamnionitis with term PROM has been reported to be less than 10% and increase up to 40% after 24 hours of PROM. In the study conducted it was 10% with the conservative management and only 2% with active management. Apgar score at the time of birth and at 5 minutes was comparable in both groups. In our study, 4% babies in the conservative group suffered from neonatal infection while none in the study group, suggesting that there was no significant difference between the neonatal complication rate in both groups[16].

CONCLUSION

We concluded that PROM at term should be managed by delivery. The active treatment does results in shorter PROM to delivery time with significantly more patients going into labour and delivering within 24 hours of PROM. There oral misoprostol in dose of 50 µ gm is effective for cervical ripening and labour induction in PROM at term. With its use there is no significant difference in mode of delivery or in maternal and fetal complications. It is cost effective. It neither requires special packing nor refrigeration prior to its use.

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CORRECTION

The amendment of the Professional Vol:14, No.03 (Jul, Aug, Sep 2007) Prof-1127 page 398 are as under;

INCORRECT

ORIGINAL **PROF-1127**

HEAVY METAL EXPOSURE;

JEWELERS AND AUTOMOBILE WORKERS.

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JEWELERS AND AUTOMOBILE WORKERS.

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