ORIGINAL ARTICLE

EXPERIENCE WITH THE USE OF ORAL MISOPROSTOL FOR LABOUR INDUCTION IN PRELABOUR RUPTURE OF MEMBRANES AT TERM

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ABSTRACT

Objective: To study the efficacy, safety and maternal satisfaction of oral misoprostol for medical induction of labor in patients with prelabour rupture of membrane at term (PROM).

Material and Methods: This descriptive study was carried out in the Obstetrics unit of Rehman Medical Institute, Peshawar-Pakistan, from January 2015 to December 2018. A total of 546 admitted patients were selected for the study in whom 50 microgram Misoprostol was administered orally at four hourly intervals. Labour was induced in selected patients and post-delivery complications were recorded.

Results: The age range of patients was 25.19 years.±3.529 SD, Out of 546 gravid patients, Primigravida and multigravida were 241 (44.1%) & 39(12.7%) respectively. There were more failed inductions in primigravida 71 (29.5%) patients, as compared to multigravida 39(12.7%). 436(79.8%) of women had a successful vaginal delivery compared to 110(20.1%) patients who failed IOL and underwent emergency caesarean section. The induction delivery interval was longer in primigravida with only 105(34.1%) patients delivering within 24 hours, in contrast to multigravida with 126(52.2%) achieving a vaginal delivery within 24 hours of induction.

Conclusion: In patients with PROM at term, Oral Misoprostol dose of 50 microgram every 4 hours, is safe, cheap, an effective agent for cervical ripening, significantly reduces the PROM-delivery interval & associated with low rate of CS, without adversely affecting maternal or fetal outcome.

Key words: Oral, Misoprostol, PROM, Induction, Labour.

This article may be cited as: Qamar Un Nisa. Experience with the use of oral misoprostol for labour induction in prelabour rupture of membranes at term. J Med Sci 2019; 27: (1) 30-33.

INTRODUCTION

Prelabour rupture of membranes (PROM) is a common obstetric condition in 8-10% of all pregnancies, [1] 60% of which occur at term (37-42 weeks gestation). [2] PROM is defined as rupture of membranes at least 1 hour before onset of uterine contractions. The management of a case of PROM has remained as one of the most difficult and controversial problems in obstetrics over the past several decades.[3] Studies in the period 1960-1980 showed an increased risk of maternal and perinatal morbidity and mortality, when the interval from rupture of membranes until delivery was prolong leading to advocation of immediate induction after PROM at term.[4] 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.[5] As per Cochrane review, there is no substantial difference in the induction and expectant management group regarding the maternal and neonatal outcome and women should be informed on the risk and benefit of each option to be able them to make an informed choice.[6]

Misoprostol has been used effectively for labor induction with PROM. It is stable at room temperature, inexpensive and available in more than 80 countries, making it particularly useful in resource-poor settings resulting in FDA approval.[7] Induction of labor with unfavorable cervix remains a challenge. Evidence has shown that induction of labor in women with an unfavorable cervix (Bishop Score < 6) is associated with higher rates of induction failure and increased risk of cesarean

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Date Received: 11 January 2019
Date Revised: 06 February 2019
Date Accepted: 20 February 2019

in nulliparous women, and that cervical ripening agents such as misoprostol increase cervical favorability and successful induction of labor. [8] The objective of this study was to assess the effectiveness, safety and maternal satisfaction of an oral dose of 50microgram of misoprostol every four hours in women with PROM at term. The outcome measures studied included induction to delivery interval, mode of delivery, operative delivery rates, and maternal complications.

MATERIAL AND METHOD

This study project was carried out in the Labor Ward of the Department of Obstetrics and Gynaecology of Rehman Medical Institute, Peshawar between January 2015 and December 2018.There is a well-equipped delivery suite, with an average 2000 deliveries per year. Formal approval of the hospital ethical review committee was obtained. A total of 546 pregnant women with confirmed PROM at 37–42 weeks of gestation were recruited. Fully informed written consent was obtained from all the included patients. These patients were either booked attending antenatal clinic or emergency admissions in labor room. All patients having a gestational age between 37–42 weeks with singleton fetus cephalic pregnancy presentation, PROM confirmed by visualizing a pool of amniotic fluid at a sterile speculum examination, rupture of membranes for <6 h, reassuring fetal cardiotocograph (CTG) with a Bishop score less than 4 were included in the study project. All those patients with previous uterine scar, non-reassuring CTG or meconium stained liquor, Parity ≥5, current or previous group B streptococcus carrier, evidence of chorioamnionitis, estimated fetal weight of >4 kg or <2 kg, multiple pregnancy, bad obstetric history and known contraindication to use of prostaglandin or induction of labor, presence of any pre-existing maternal medical disease e.g. cardiovascular disease or chronic renal failure were not included in the study. Prior to commencement of induction of labor, P/V examination to confirm diagnosis of PROM, fetal presentation, position, station, and assessment of the Bishop's Score was performed. All the patients were commenced on ampicillin (1gm three times a day) combination and metronidazole (100ml three times a day) on admission and continued for five days. Maternal blood was tested for CBC, C-reactive protein (CRP), blood group and Rh factor, RBS, urine R/E, HBsAg and HCV testing, high vaginal swab for microscopy, culture and sensitivity. Fetal assessment was done with CTG and ultrasound for measurement of Amniotic fluid index (AFI) & biophysical profile.

The variables observed regarding efficacy of Oral Misoprostol, included age, booking status, parity, time from onset of induction to vaginal delivery (IDI), mode of delivery (Spontaneous vaginal delivery, Operative vaginal delivery), Rate of Caesarean section, fetal heart rate abnormality, failed induction (failure to achieve a cervical dilatation of ≥3 cm after four completed doses of medication or if the modified Bishop score was <5).

The findings were recorded in a specially designed proforma. Data was analyzed using SPSS version 22. Frequency, rate and percentages were calculated for qualitative outcomes like parity, Bishop score, vaginal deliveries, cesarean section, hyper stimulation, maternal side effects, (nausea, vomiting, diarrhea). Quantitative variables like age, gestational age, induction delivery interval etc. were presented as mean ± standard deviation.

RESULTS

Out of total of 3618 patients delivered during study period, 546 patients were eligible for inclusion. A total of 81(14.8%) were less than 20 years, 344 (68%) were between 20-30 years of age, 74 (13.5%) were between 30-35 years and 47(8.6%) were more than 35 years of age. The dosages of misoprostol are presented in Table 1. The main outcome measures in the form of mode of delivery, need of oxytocin, failed inductions and maternal satisfactions are presented in Table 2. The delivery interval versus parity and Bishop score are presented in Table 3. Table 4 shows the maternal side effects associated with oral misoprostol.

Table 1: Dosage of Misoprostol

Misoprostol Doses needed	Frequency & Percentage
1 dose	212(38.8%)
2 doses	161(29.4%)
3 doses	95(17.3%)
4 doses	78(14.2%)

Table 2: Main outcome measures: (n=546)

Sr. No	Main outcome measures	Frequency
1.	• Spontaneous delivery	296 (67.8%)
	• Instrumental delivery	140 (54.6%)
	• Cesarean section	110 (20.1%)
2.	Need of Oxytocin	226 (41.3%)
3.	Failed Induction	110 (20.1%)
4.	Maternal Satisfaction	387 (70.8%)

DISCUSSION

Every obstetrician's effort has been to recognize the correct time for the delivery, and take anticipatory action to reduce the perceived materno-fetal morbidity. Stress of pregnancy and labor increases as women reach near term. Induction of labor is now more widely used than ever before.[8,9]

Prelabour rupture of the membranes (PROM) is an important clinical problem and a dilemma for the gynaecologist. In this study, only a single inducing agent

Table 3: PROM–Delivery interval (n=546)

	Parity		Bishop score		Total (n=546)
	Primigravida	Multigravida	<5	>5	
Vaginal delivery within 12 hours	44(18.2%)	161(52.7%)	64(14.6%)	141(32.3%)	205(37.5%)
Vaginal delivery within 24 hours	105(34.1%)	126(52.2%)	94(21.5%)	137(31.4%)	231(42.3%)
Failed Induction of labor	71(29.5%)	39(12.7%)	59(10.8%)	51(9.3%)	110(20.1%)

Table 4: Secondary outcome measure (Maternal complications)

Sr. No.	Maternal complications	Frequency	Percentage
1.	Nausea & Vomiting	313	57.3%
2.	Pyrexia(>38C)	54	9.8%
3.	Uterine hyperstimulation	24	4.3%
4.	Postpartum hemorrhage	49	8.9%
5.	Uterine rupture	0	0%

i.e. oral misoprostol was used for all mothers to establish its safety/efficacy, irrespective of any other inducing agent. Oral misoprostol dosing offers the theoretical advantage of avoidance of vaginal examinations and possibly enhanced patient acceptance. Absorption kinetics and bioavailability studies have demonstrated a more rapid and more pronounced onset of uterine tone after administration of oral misoprostol compared with vaginal misoprostol. Our study supports the safety and efficacy of 50 microgram of oral Misoprostol for induction of term labor with PROM.

The first published study of oral misoprostol for PROM was carried out by Ngai et al [11] in 1996. They randomly assigned 80 subjects to receive either misoprostol, 200 micrograms by mouth, or placebo after PROM. Not surprisingly, more women receiving misoprostol entered labor than those receiving placebo. Misoprostol use was associated with a shorter interval to delivery, and no difference in adverse maternal or neonatal outcomes was seen. No difference in mode of delivery was demonstrated. The Cochrane database of 2014 has a review of 75 randomized controlled trials (13,793 women) and have found oral misoprostol to be at least as effective as current methods of induction. Nine trials (1,282 women) showed that oral misoprostol was equivalent to intravenous infusion of oxytocin. There were no obvious differences in the number of women who had a vaginal birth within 24 hours, or the number of women who experienced uterine hyper stimulation with changes to the baby's heart rate, although there were fewer caesarean sections in the group of women who were given oral misoprostol.[12]

Recent trials show that immediate labor induction in patients with term PROM resulted in significant shortening of latent period and PROM to delivery interval without any increase in caesarean section rate as compared to expectant management group.[13]A recently completed UK National Institute of Health Research (NIHR) funded network and cost-effectiveness analysis included 31 induction regimes evaluated in 611 trials with over 100 000 trial participants. Titrated low-dose oral misoprostol was identified as likely to be the most cost-effective method, and also had a favorable safety profile.[14]

Repeated small doses of 50 microgram every 4 hours has been practiced with good results even in multiparous women. We were very cautious in using doses for multiparous women, being in a private hospital. Our results suggested that oral misoprostol treatment could significantly accelerate the progression from PROM to vaginal delivery within 24 hours of PROM. Mean induction to delivery interval was13±2.7 hours in our study comparable to overall median time from induction to delivery to be 15 (10.5–24.4) hours in a prospective observational study conducted at Modilon Hospital in Papua New Guinea, by Morris et al.[15] In 2015, historical cohort study, conducted by Kehl analyzed 1861 inductions of labor at term using misoprostol.[16] For the PROM group, induction-to-delivery interval was shorter (mean: 972 minutes) and Cesarean section rate was significantly lower (21.9% vs. 26.3%, p = 0.029). The difference in induction-delivery interval, in different studies, may be due to a different dosing regimen used in them.

Traditional prostaglandins are expensive and Syntocinone is less effective when cervix is unfavorable. Starting labor induction with oral misoprostol resulted in less use of oxytocin, in women with PROM at term. In current study, 41.3 % cases required oxytocin augmentation. Study by Davidsons Et al showed that >50% of women induced with misoprostol did not require oxytocin.[17]

Vaginal delivery occurred in 436 (79.8%) of patient which is comparable to a comparative study conducted by Wang Et al, on titrated oral misoprostol solution and vaginal Dinoprostone for labor induction at term pregnancy. This study achieved successful vaginal delivery

rate in 81% of patients in Misoprostol group.[18] Cesarean section was done in 20.1% of our patients. Main indication for emergency CS was fetal distress (meconium stained liquor and fetal heart rate abnormalities), Failed induction, arrest of cervical dilatation due to malposition, relative cephalopelvic disproportion or cervical dystocia. Similar results are seen in other studies.[19]

Present study revealed no case of uterine rupture which is in accordance to the results of a study conducted in Fatima Jinnah Medical College.[20] Depending upon the dose and frequency of misoprostol administration, the incidence of uterine hyperstimulation varies between 1-10%. Only 1 patient had uterine hyper stimulation, although systematic reviews.[15] have shown that misoprostol use is associated with significant hyper stimulation, which adversely affect both mother and baby. More supervised trials in local hospitals are needed to prove safety& efficacy of drug, to investigate its dosage & routes of administration. Subsequently, smaller doses like 25microgram can be tried for induction of labor, to see if it is equally effective and thereby increasing its safety.

CONCLUSION

All patients presenting with PROM at term, should be actively managed with induction of labour with oral misoprostol. This leads to significant reduction in PROM -delivery interval along with significantly better maternal satisfaction Assessment of pre-Induction Bishop's score is very crucial so as to reduce the incidence of maternal and fetal sepsis and morbidity. Women tend to view active management of prelabour rupture of membranes more positively.

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