Original Article

# LABOUR INDUCTION WITH ORAL MISOPROSTOL IN PRE LABOUR RUPTURE OF MEMBRANES AT TERM

Umber Fatima[*], Mubashra Naz[**], Rizwan Rasul Khan[***]

[*] Senior Registrar, Department of Obstetrics & Gynaecology, UMDC, Faisalabad
[**]Asst. Professor, Department of Obstetrics & Gynaecology, UMDC, Faisalabad.
[***]Asst. Professor Department of Internal Medicine UMDC, Faisalabad.

**ABSTRACT**

**Objective:**

To assess the efficacy of oral misoprostol for induction of labour in women with pre labour rupture of membranes at term and to monitor maternal and fetal complications.

**Design:**

Quasi experimental study

**Settings**:

Department of Obstetrics and Gynecology, Divisional Head Quarter Hospital, Punjab medical and dental college, Faisalabad.

**Methods:**

Selected patients were given 50 µg of oral misoprostol after history, examination and fetal evaluation by reactive CTG.A maximum of 6 doses at 4 hourly interval were given. Oxytocin augmentation was done if required.

**Main outcome measures:**

Efficacy that included induction-delivery interval, need for oxytocin infusion, mode of delivery, failed induction, and maternal satisfaction. Fetomaternal complications including nausea and vomiting, pyrexia, uterine hyper stimulation, postpartum hemorrhage, uterine rupture, meconium staining of amniotic fluid, abnormal CTG tracing, low Apgar score at 5 minutes and still birth were secondary outcome measures.

**RESULTS:**

Mean induction-delivery interval was 12.8 $\pm$ 4.24 hours.Nineteen patients 19 (19%) had caesarean section. Failed induction was noted in 2 (2%) cases. Oxytocin augmentation was required in 36(36%) cases.

Maternal complications were nausea and vomiting 14(14%), pyrexia 9(9%) and hyper stimulation 3(3%) syndrome.

Regarding fetal complications, meconium staining of amniotic fluid was present in 19 (19%) and abnormal CTG pattern in 14 (14%), while no baby had low Apgar score at 5 minutes and there was no still birth.

**CONCLUSION:**

Misoprostol is safe and effective method of induction associated with good fetomaternal outcome when used for induction of labour in women with prelabour rupture of membranes at term.

**KEY WORDS:** Induction,Prostaglandins,Misoprostol,PROM.

## INTRODUCTION

Pre labour rupture of membranes(PROM) is defined as rupture of fetal membranes with a latent period before onset of spontaneous uterine activity.The length of this period varies in different definitions from not being specified up to 8 hours.It complicates 10% of

*Corresponding Author:*
*Dr. Umber Fatima, Senior Registrar, Dept. of Obstetrics & Gynaecology, UMDC, Faisalabad*
*Email: drrizwan218@yahoo.com*

all gestations, of which approximately 60 % occur at term[1].

There is substantial direct and indirect evidence that genital tract infection and associated inflammatory changes are responsible for many instances of PROM.Other less consistent associations might be cigarette smoking, cocaine abuse, intrauterine DES exposed women and possible nutritional deficiencies of ascorbic acid, copper, zinc, and iron[2].

The diagnosis can be made through a combination of history,physical examination and specialized testing.There are significant maternal risks associated with premature rupture of membranes and these can occur antepartum, intrapartum, and post partum with increased perinatal mortality and perinatal infections[3]. Management of PROM is still controversial and involves a balance between expectant management and intervention[4]. However induction of labour with prostaglandins compared with expectant management reduces the risk of maternal sepsis and neonatal complications.Various agents are available for induction of labour, mainly prostaglandins and oxytocin.They are used in combination and according to Bishop score[5].

Prostaglandins are the agents to soften the unripe cervix independent of uterine activity.Dinoprostone is currently the only prostaglandin approved for labour induction at term but it is expensive and heat labile. An intense cold chain is to be maintained to achieve the desirable effects[6]. Owing to hot climate in Pakistan, storage problems significantly reduce its efficacy . Exclusive vaginal route also limits the use in PROM as the risk of sepsis increases. An ulcer healing drug, misoprostol has recently received attention for labour induction. Misoprostol (Cytotec®) is a synthetic E1 methyl analogueprostaglandin. It is cheap,stable at room temperature and effective in initiating uterine contractions. The ease of multiple routes of administration ( oral ,vaginal ,sublingual and rectal)and rapid onset of action make it a better option for induction of lobour[7].

A meta-analysis of misoprostol for induction of labour showed ashorter induction-delivery interval, a decrease in caesarean section rate for cervical dystocia and an increased rate of vaginal delivery within 24 hours.Allthese features make the oral misoprostol an effective and cheap alternative for labour induction specially in third world countries[8].

The advantage of oral misoprostol with particular reference to prelabour rupture of membranes is the avoidance of repeated vaginal examinations to minimize the risk of maternal and fetal sepsis[9].

Misoprostol is not yet licensed for use in reproductive health despite the extensive evidence of being cheap and effective compared with dinoprostone.The review of trials has found that there is not enough evidence about the safety of oral misoprostol for labour induction and more research is needed. This study strengthened the existing evidence regarding safety and efficacy. The rationale of the study was to determine the efficacy of oral misoprostol for induction of labour in women with premature rupture of membranes at term and to monitor maternal and fetal complications.

## MATERIAL AND METHODS

The study was conducted in department of obstetrics and gynecology, Divisional Head Quarter Hospital, Faisalabad from April 2006 to April 2007.

Pregnant patients with rupture of membranes admitted in labour ward during study period were included in study after informed consent and strictly following inclusion criteria(Pregnant women at term ≥ 37 weeks with singleton pregnancy , cephalic presentation ,rupture of membranes , reactive CTG(cardiotocography) trace, and Bishop score less than 4).Exclusion criteria included symptoms and signs suggestive of chorioamnionitis, prior uterine surgery(caesarean section, myomectomy), bad obstetric history and other contraindications to vaginal delivery like placenta previa and cephalopelvic disproportion. The study gained approval from institutional ethical review committee.

Detailed history of presenting complaints particularly duration of rupture of membranes and obstetric history were obtained. General

physical examination was carried out to rule out clinical signs of chorioamnionitis. Abdominal examination for presentation, engagement of fetal head and fetal size were recorded. Sterile per speculum examination was performed to confirm the rupture of membranes. Once all the inclusion and exclusion criteria for study were fulfilled, vaginal examination under sterile condition was performed to assess the Bishop score. Maternal evaluation was done by recording blood group and Rh factor, Random blood sugar level, urine C/E, blood C/E, HBsAg and HCV testing. Fetal evaluation was done with CTG and ultrasound with biophysical profile. After recording a reactive CTG trace, selected patients were induced with 50 µg of oral misoprostol at 4 hourly interval. A maximum of six doses were given or until labour was established. After establishment of uterine activity augmentation with oxytocin infusion was started if required. Labour was monitored by recording uterine activity half hourly. Fetal surveillance was done by observing color of liquor, intermittent auscultation of fetal heart and CTG. Non responders were subjected to caesarean section. Observations regarding efficacy like induction - delivery interval, need for oxytocin infusion, mode of delivery, failed induction and maternal satisfaction were recorded. Main outcome measure including maternal complications like nausea and vomiting, pyrexia (> 38 $^{\circ}$C), uterine hyperstimulation(non reassuring fetal heart rate tracing in presence of tachysystole or hypertonus),postpartum hemorrhage and uterine rupture were observed and recorded. Fetal complications includingmeconium staining abnormal CTG trace, low Apgar score at 5 minutes and still birth were recorded on attached proforma designed for this purpose.

Data analysis was computer based using SPSS version 10.Descriptive statistics were used for data presentation and to describe the observations regarding efficacy, mode of delivery, failed induction, maternal satisfaction and fetomaternal complications

**Table 1 Demographic data of study population**

| S.No. | Parameters | Description |
|---|---|---|
| 1 | Age (years) | 26.34 $\pm$5.28 |
| 2 | Gestational age(weeks) | 39 $\pm$1.72 |
| 3 | Parity status<br>Nulliparous<br>multipara | <br>61 %<br>39% |

**Table No. 2 Dosage of Misoprostol**
n=100

| No. or Doses Required | Frequency | Percentage |
|---|---|---|
| 1 dose | 35 | 35 |
| 2 doses | 39 | 39 |
| 3 or more doses | 26 | 26 |

**Table No. 3 Induction – Delivery Interval**
n=100

| Time (hours) | Percentage of patient | Mean (hours) |
|---|---|---|
| <12hours | 73 | 10.7$\pm$SD |
| >12 hours | 27 | 18.5$\pm$ SD |

Mean + Std. Deviation = 12.8 + 4.24

**Table No 4 Main outcome measures**

| S. No. | Main outcome measures | frequency | Percentage |
|---|---|---|---|
| 1 | Mode of delivery Vaginal delivery | 81 | 81 |
| | Caesarean section | 19 | 19 |
| 2 | Failed induction | 2 | 2 |
| 3 | Need of oxytocin | 36 | 36 |
| 4 | Maternal satisfaction | 75 | 75 |

**Table No. 5 Maternal Complications Secondary outcome measures**
n=100

| Maternal Complication | Frequency | Percentage | Total Cases |
|---|---|---|---|
| Nausea and vomiting | 14 | 14 | 100 |
| Pyrexia (>38$^{o}$ C) | 9 | 9 | 100 |
| Uterine hyperstimulation | 3 | 3 | 100 |
| Postpartum hemorrhage | 0 | 0 | 100 |
| Uterine rupture | 0 | 0 | 100 |

**Table No. 6 Fetal complication Secondary outcome measures**
n=100

| Fetal Complication | Frequency | Percentage |
|---|---|---|
| Meconium staining of amniotic fluid | 19 | 19 |
| Abnormal CTG tracing | 14 | 14 |
| Low apgar score at 5 minutes | 0 | 0 |
| Still birth | 0 | 0 |

## RESULTS

Demographic characteristics of patients are demonstrated in table 1.Mean age of patients was 26 years and mean gestational age 39 weeks. Among 100 patients, 61 (61%) were nulliparous, 39 (39%) were multiparas (table 1). All these patients received 50 µg of oral misoprostol, maximum 6 doses 4 hours apart. Thirty five (35%) required 1 dose of misoprostol , 39 (39%) 2 doses and 26 (26%) required 3 or more doses(Table 2).Mean induction to delivery interval was 12.8 ± 4.24 hours (Table 3).Regarding mode of delivery , 81 (81%) patients delivered vaginally and 19 (19%) underwent caesarean section (Table 4).Out of 81 vaginally delivered patients 79 (79%) had spontaneous vaginal delivery while 2 (2%) delivered by outlet forceps due to maternal exhaustion.Indications for caesarean section were failed induction in 2 cases (10.5%) and fetal distress in 17 (89.5%) noted by meconium staining of liquor and abnormal CTG patterns.

Augmentation with oxytocin infusion was required in 36 (36%) subjects (Table 4).Augmentation was done with oxytocin when uterine activity was established after oral misoprostol evident by cervical dilatation of 4 cm or more. Seventy five (75%) patients were satisfied by their method of induction (Table 4). Secondary outcome measures included maternal complications and fetal complications. l. Hyperstimulation syndrome was noted in 3 (3%) cases. Nine subjects (9%) had intrapartum pyrexia (> 38$^{\circ}$C), while nausea and vomiting was noted in 14 (14%) patients.No patient had postpartum hemorrhage or uterine rupture with oral misoprostol induction.( table 5)Fetal / Neonatal outcome was good (Table 6) with no intrapartum still birth. Meconium staining of amniotic fluid was noted in 19 (19%) patients. Abnormal CTG patterns during labour were

recorded in 14 (14%) cases. All babies were delivered with good Apgar score at 5 minutes.No neonate had features suggestive of meconium aspiration and no admission to NICU was recorded. (table 6)

## DISCUSSION

Present study provides efficacy of oral misoprostol in patients with prelabour rupture of membranes at term. Study includes active management of labour in PROM using misoprostol as a drug for inducing labor.Recent trials show that maternal and neonatal infectious morbidity is significantly reduced by induction of labour, compared with expectant management. Using oral misoprostol for labour induction, reduces the frequency of vaginal examinations and use of intravenous line only later in labour and therefore the patients may not have felt restricted in early stage of labour. This may partly explain the increased satisfaction in this group.

Mean induction to delivery interval was 12.4 hours in present study comparable to 11 hours in a comparative study conducted by Nagpal MB in Lady Hardinge hospital in New Delhi with oral misoprostol and prostaglandin E2. The study also showed similar results in terms of mode of delivery and feto maternal complications[10].

Oral misoprostol reduced the need for oxytocin in the management of women with ruptured membranes at term.

In the current study, oxytocin augmentation was required in 36 % cases ,similar to study by Levy R where 37% inductions with misoprostol required such augmentation.Levy R also noted that misoprostol also reduces the need for oxytocin augmentation (28.1%) in cases of ruptured membranes at term[11].

In present study, 81% of patients delivered vaginally which is comparable to a study conducted in Liver pool,UK on oral /vaginal misoprostol by Bricker L .The study achieved successful vaginal delivery in 86% of patients in misoprostol group[12].

Results of present study revealed failed induction in 2% cases which is not consistent with local and international studies. The study conducted in Bahawalpur Victoria hospital Pakistan revealed 10% rate of failed induction[5]. This variation in resultsmay be due to the fact that there is no universally accepted definition of failed induction. Various studies have defined this term differently. In some, patients were labeled to have failed induction who failed to achieve active phase of labour whereas in other studies those who had no change in Bishop score after misoprostol administration were taken as cases of failed induction. In present study, those cases who had no changes in Bishop score despite 6 doses of misoprostol were considered to be of failed induction.Furthermore total dose of misoprostol used in current study was 300µg while in varius other studies it was 200 µg. So there is a great variation in dosage of misoprostol used in present and other studies resulting in highly variable rates of failed induction.

Hyperstimulation is an important concern with misoprostol induction.Uterine hyperstimulation was reported to be present in 3% of patients.AyazA reported 7% rate of maternal complications including hyperstimulation, nausea, vomiting and pyrexia etc. In our study the rates were higher, probably because we used 300µg of misoprostol[5]. Higher doses of misoprostol and vaginal insertions have a stronger association with hyperstimulation. It might explain the lower rate of maternal complications.

As misoprostol was more potent as a uterine stimulant in various trials, it is difficult to be sure whether the difference is pharmacological or purely dose related.It is suggested that there is no benefit of higher doses of misoprostol but increased incidence of meconium stained liquor, fetal distress, hyperstimulation and uterine rupture.

The frequency of fetal complications including meconium staining of amniotic fluid,abnormal CTG and low Apgar scores were noted in almost 15 % of patients that subsequently changed mode of delivery and maternal satisfaction rates as well . Owing to the fact that a relative high dose for induction was used as compare to other studies may explain this rise in rate of fetal complications[13].

Present study revealed no case of uterine rupture and postpartum haemorrhage which is in agreement to the results of a study conducted in Fatima Jinnah medical college[13].
In current study no case of low Apgar score at 5 minutes and no still birth was recorded.Similar observations were noted by Adeniji at al. with no adverse fetal/ neonatal outcomes[14]. Present study suggests that results of induction with oral misoprostol are very good.
Overall misoprostol appears to be more effective than conventional methods of cervical ripening and labour induction[15]. Uterine hyperstimulation with fetal heart rate changes following misoprostol is a matter of concern. Monitoring during labour is important when using misoprostol for labour induction to detect uterine hyperstimulation and fetal distress and early intervention is required if such a condition arises in order to achieve a good maternal and fetal outcome.
Traditional prostaglandins are expensive and syntocinone is less effective when cervix is unfavorable. Several studies have shown that induction to delivery interval is significantly shorter with misoprostol when compared to oxytocin although there is no significant difference between the two groups in the neonatal outcomes[16]. On the other hand prostaglandin E2 vaginal pessaries cost up to 1000/- rupees.A repeat insertion will costs upto 2000/- rupees.Its efficacy requires cold storage and it can only be used vaginally while a tablet of 200 µg of misoprostol costs approximately 65/- rupees.It can be broken to provide 50 µg aliquots.It is easily stored at room temperature and rapidly absorbed both orally and vaginally. Misoprostol can be used safely for labour induction with PROM at term and its cost makes it more attractive in our poor socio-economic strata.
Designing and conducting further clinical trials to investigate appropriate dosage and administration routes, as well as the drugs adverse effects profile under such circumstances is essential, and would potentially allow an application for approval to be filed with health authorities regarding its use in obstetric practice.

## CONCLUSION

Oral misoprostol is effective and potentially safe drug for labour induction in patients with PROM at term particularly in countries where repeated vaginal prostaglandin pessaries, lengthy expectant management and a high rate of cesarean deliveries cannot be afforded and in tropical areas where temperature maintenance and storage of drug is a problem.

## REFERENCES

1. Weekes CR, Mahomed K. Management of pre-labour rupture of membranes at term - a survey of current practice in Australia.Aust N Z J ObstetGynaecol. 2010;50(5):428-31.
2. DiGiulio DB, Romero R, Kusanovic JP, Gómez R, Kim CJ, SeokKS,et .Prevalence and diversity of microbes in the amniotic fluid, the fetal inflammatory response, and pregnancy outcome in women with preterm pre-labor rupture of membranes.Am J ReprodImmunol.2010 ;64(1):38-57.
3. Ip M, Peyman E, Lohsoonthorn V, Williams MA.A case-control study of preterm delivery risk factors according to clinical subtypes and severity.J ObstetGynaecol Res. 2010;36(1):34-44.
4. Omole-Ohonsi A, Ashimi A, Adeleke S.Spontaneous pre-labour rupture of membranes at term: immediate versus delayed induction of labour.West Afr J Med. 2009;28(3):156-60.
5. Ayaz A, Saeed S, Farooq MU, Ahmad F, Bahoo LA, Ahmad I.Pre-labor rupture of membranes at term in patients with an unfavorable cervix: active versus conservative management.Taiwan J Obstet Gynecol. 2008;47(2):192-6.
6. Bezircioglu I, Akin MK, Baloglu A, BicerM.The efficacy of dinoprostone vaginal insert for active management of premature rupture of membranes at term: a randomized controlled trial.ClinExpObstet Gynecol. 2012;39(3):356-8.

7. Chaudhuri S, Mitra SN, Banerjee PK, Biswas PK, Bhattacharyya S.Comparison of vaginal misoprostol tablets and prostaglandin E2 gel for the induction of labor in premature rupture of membranes at term: a randomized comparative trial.J ObstetGynaecol Res. 2011;37(11):1564-71.
8. Chitrakar NS. Comparison of Misoprostol versus Dinoprostone for pre-induction cervical ripening at-term.J Nepal Health Res Counc. 2012;10(1):10-5.
9. Malik HZ, Khawaja NP, Zahid B, Rehman R.Sublingual versus oral misoprostol for induction of labour in prelabour rupture of membranes at term.J Coll Physicians Surg Pak. 2010;20(4):242-5.
10. Nagpal MB, Raghunandan C, Saili A. Oral misoprostol versus intracervical prostaglandin E2 gel for active management of premature rupture of membranes at term.Int J Gynaecol Obstet. 2009;106(1):23-6.
11. Levy R, Vaisbuch E, Furman B, Brown D, Volach V, Hagay ZJInduction of labor with oral misoprostol for premature rupture of membranes at term in women with unfavorable cervix: a randomized, double-blind, placebo-controlled trial.J Perinat Med. 2007;35(2):126-9.
12. Bricker L, Peden H, Tomlinson AJ, Al-Hussaini TK, Idama T, CandelierC,et al Titrated low-dose vaginal and/or oral misoprostol to induce labour for prelabour membrane rupture: a randomised trial.BJOG.2008;115(12):1503-11.
13. Malik HZ, Khawaja NP, Zahid B, Rehman R. Sublingual versus oral misoprostol for induction of labour in prelabour rupture of membranes at term.J Coll Physicians Surg Pak. 2010;20(4):242-5.
14. Adeniji OA ,OladokunA,Olayemi O , Adeniji OI, Odukogbe AA, Ogunbode O ,et al.pre induction cervical ripening : transcervical Foley, s catheter versus intravaginal misoprostol .J ObstetGynaecol 2005; 25 :134-9.
15. Mozurkewich EL, Chilimigras JL, Berman DR, Perni UC, Romero VC, King VJ, Keeton KL. Methods of induction of labour: a systematic review.BMC Pregnancy Childbirth. 2011;11:84.
16. Trabelsi H, Mathlouthi N, Zayen S, Dhouib M, Chaabene K, Trabelsi K et al.Cervical ripening at term. A randomized and prospective study:Misoprotol versus dinoprostone.Tunis Med. 2012;90(5):362-9.

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We think sometimes that poverty is only being hungry, naked and homeless. The poverty of being unwanted, unloved and uncared for is the greatest poverty. We must start in our own homes to remedy this kind of poverty.

***Mother Teresa***

Anyone can become angry -- that is easy. But to be angry with the right person, to the right degree, at the right time, for the right purpose, and in the Right way – this is not easy.

***Aristotle***