Kamath Rajalaxmi K & Srikar SV. / Vol 4/ Issue 1 / 2014 / 70-74.

International Journal of Pharmaceutical Research & Analysis

e-ISSN: 2249 – 7781
Print ISSN: 2249 – 779X

www.ijpra.com

UTILITY OF ORAL AND VAGINAL MISOPROSTOL IN THE INDUCTION OF LABOUR: A COMPARATIVE STUDY

[*1]Kamath Rajalaxmi K and [2]Srikar SV

[1]Assistant Professor, Department of Obstetrics and Gynecology, Yenepoya Medical College, Yenepoya University, Deralakatte, Mangalore- 575001, India.
[2]Consultant Pathologist, Gowri Clinic, Balmattta Mangalore -575001, India.

ABSTRACT

This study was conducted to compare the efficiency and safety of oral (50 µg) and vaginal (25 µg) misoprostol for labour induction. In this study one Hundred patients with indications for labour induction randomly received 50 µg oral misoprostol every 4 h or 25 µg vaginal misoprostol every 4 h, using maximum four doses. Mean induction time, mode of delivery, rates of tachysystole, oxytocin use, number of doses used, failed induction rate and Intrapartum complication with fetal outcomes were compared for the two groups. Mean dose of misoprostol used for oral and vaginal misoprostol study populations were 2.34 ± 1.05 and 1.96 ± 0.91, respectively. There were two failed inductions in the oral (4%) and one failed induction (2%) in the vaginal group after a total of six doses of misoprostol. Our findings indicated that, 50 µg oral misoprostol has the potential to induce labor as safely and effectively as its 25 µg vaginal analogue. Oral ingestion of misoprostol being easier for the patient and the doctor, orally administered is more preferable than the vaginal route.

Keywords: Labour induction, Oral misoprostol, Cervical ripening agents.

INTRODUCTION

Induction of labor is the commonest obstetric procedure and in these cases cervical ripening is important. Oxytocin and prostaglandins are the commonly used agents [1]. Use of Oxytocin is a safe and effective method for labor induction. However, in patients with an unripe cervix, cervical ripening agents are often used before oxytocin administration [2]. Prostaglandins act as cervical ripening agents and also act upon myometrial contractions when used for labor induction. The prostaglandin E1 (PGE1) has been widely used for this purpose. PGE1 for labor induction has been involved in many trials with different doses and routes of administration [3,4].

A synthetic analogue of Prostaglandin E1 (PGE1) Misoprostol is currently used for prevention and treatment of gastric and duodenal ulcers [5] and is also being increasingly used for induction of labor. A number of randomized controlled trials support the efficacy of misoprostol for cervical ripening and induction of labor [6-9]. Misoprostol is relatively inexpensive, easily available and does not require refrigeration, in contrast to PGE2 preparations. There are many studies induction of labor comparing the efficacy of vaginal and oral misoprostol [10-14]. In this study, 50 µg oral misoprostol every 4 h, is compared with 25 µg vaginal misoprostol every 4 h.

MATERIALS AND METHODS

This randomized controlled trial was carried out between October 2010 and June 2011 at private hospitals in and around Mangalore city, by the investigator in the patients who visited a Clinic located in Mangalore city, for antenatal checkup, who intended to get delivered at various Private Hospitals in and around Mangalore city, of southern India. All women with a gestational age of at least 32 weeks who required induction of labor were considered for admission to the trial. Post-term inductions were considered in patients with Gestational age ≥41 weeks. Patients with premature rupture of membranes (PROM)

Corresponding Author:- Kamath Rajalaxmi Email:- gkbkrishna01@gmail.com

and IUGR cases were also included to this trial. Inclusion criteria were singleton pregnancy, cephalic presentation, reactive non-stress test, Bishop Score of <6, cervical dilatation <3 cm and uterine contractions <6 per hour. Exclusion criteria for the study included patients with a history of uterine surgery, a contraindication to vaginal birth, parity > 5 and known hypersensitivity to prostaglandins.

We divided the patients into two groups randomly: those receiving 50 μg oral misoprostol every 4 h and those receiving 25 μg vaginal misoprostol placed in the posterior fornix every 4 h. Randomization was done by picking lots of sealed numbers from a box; odd numbers were assigned to oral misoprostol and even numbers to vaginal misoprostol. Patients were counseled and informed consent was obtained before randomization. Bishop score was determined after enrolling; subjects were examined before induction and then reexamined before each dose by the same physician. A non-stress test was performed and uterine activity was assessed before administration of each dose of misoprostol. Misoprostol was repeated until adequate cervical ripening, defined as cervical dilatation ≥3 cm and cervical effacement ≥70%. The maximum total dose of misoprostol was six applications for both groups. Failed induction was considered if the woman did not go into labor or the cervix was unripe at the end of six doses. Induction with oxytocin or cesarean section was performed to those patients.

Continuous external monitor was used to monitor Foetal well-being and uterine contractions. Abnormal fetal heart rate patterns were defined as fetal tachycardia, bradycardia, late decelerations and moderate to severe degree of any type of decelerations as described by Kubli et.al 1969. Uterine tachysystole was defined as ≥6 uterine contractions in 10 min for two consecutive 10 min windows, hypertonus as a single uterine contraction lasting ≥2 min and hyperstimulation syndrome as either tachysystole or hypertonus associated with abnormal fetal heart rate patterns. To treat these contraction abnormalities, maternal position was changed to left lateral decubitus, oxygen was administered by nasal prongs and two doses of 10 mg Nifedipine were administered orally with 15 min interval.

The number of doses of misoprostol required, oxytocin need, the incidence of failed induction, the incidence of uterine tachysystole, and neonatal outcomes (Apgar scores at 1 and 5 min, presence of meconium, resuscitative measures beyond warming and drying, neonatal intensive care unit (NICU) admissions) were tabulated.Statistical analyses regarding patient characteristics and result variables were calculated and presented as mean± S.D.

RESULTS

A total of 100 subjects were included to the study. Of these, 50 were randomly assigned to receive orally and 50 vaginally administered misoprostol. No women withdrew from the study protocol after initiation of treatment. The clinical characteristics of the study population are shown in Table 1. The subjects were similar with respect to mean age, height, weight, parity, birth weight, gestational age and preinduction Bishop Score.

Induction and labor outcomes are given in Table 2. Mean dose of misoprostol used for oral and vaginal misoprostol groups were 2.34 ± 1.05 and 1.96 ± 0.91, respectively. There were two failed inductions in the oral (4%) and one failed induction (2%) in the vaginal group after a total of six doses of misoprostol. There was no significant difference for the mean induction to delivery interval in those who delivered vaginally between oral and vaginal misoprostol groups (13.06±6.0 h versus 12.5±5.0 h, respectively).The caesarean section rates for orally and vaginally administered misoprostol groups were 12 and 20%, respectively. There was no significant difference for the Intrapartum complications including, fetal distress, tachysystole, hyper tonus and hyper stimulation syndrome between two groups.

Neonatal outcomes show there was no perinatal mortality. Three infants were admitted to the NICU in the vaginal misoprostol group, two due to low birth weight and one due to neonatal sepsis. There was no significant difference for the mean 1- and 5-min Apgar scores, presence of meconium and resuscitative measures beyond warming and drying between oral and vaginal misoprostol groups.

Table 1. Characteristics of the study population [data are presented as mean Â± S.D. and n (%)]

	Oral misoprostol	**Vaginal misoprostol**
N	50	50
Age	**28.0 ± 5.5**	**26.2 ± 5.2**
Parity	**1.6 ± 0.7**	**1.7 ± 1.1**
Weight (kg)	**54.9 ± 13.4**	**56.7 ± 10.7**
Height (cm)	**141.7± 5.9**	**142.1 ± 5.3**
Birth weight (g)	**2380 ± 557**	**3090 ± 659**
Gestational age at induction (week)	**39.7 ± 1.9**	**38.8 ± 2.6**
Initial Bishop score	**3.3 ± 1.2**	**3.3 ± 1.5**
Indications for labor induction		

Post-dated pregnancy	**24 (48%)**	**17 (34%)**
Oligohydramnios	**8 (16%)**	**15 (32%)**
PROM	**9 (18%)**	**8 (16%)**
Preeclampsia	**2 (4%)**	**4 (8%)**
IUGR + oligohydramnios	**3 (6%)**	**2 (4%)**
Gestational diabetes	**4 (8%)**	**4 (8%)**

Table 2. Induction and labor outcomes [data are presented as mean Â± S.D. and n (%)]

	Oral Misoprostol (N = 50)	**Vaginal Misoprostol (N = 50)**
Number of doses	**2.34 ± 1.05**	**1.96 ± 0.91**
Failed induction	**2 (4%)**	**1 (2%)**
Induction interval (Hours)	**13.06±6.0**	**12.5±5.0**
Vaginal Delivery	**44(88%)**	**40 (80%)**
Caesarian Delivery	**6 (12%)**	**10 (20%)**
Apgar Score 1 >7	**48 (96 %)**	**45 (90%)**
Apgar Score 5 >7	**48 (96%)**	**45 (90%)**
Second stage duration (hours)	**0.6 ± 0.5**	**0.4 ± 0.5**
Newborn referral of the baby to the pediatrician	**6 (12%)**	**7 (14%)**

DISCUSSION

The ideal route and route of administration of misoprostol is still under debate despite the drug being highly effective in labour induction as shown in most studies. Many authors presume because of the 'First-Pass-Effect' vaginally administered misoprostol was more effective than oral analogue when used at same doses [10-12] and [16]. So, higher doses of oral misoprostol have been used to overcome this difference in the bioavailability of oral versus vaginal preparations. Some authors have already suggested that 200 µg oral misoprostol administration is associated with more frequent uterine hyper stimulation and higher frequency of meconium staining of the amniotic fluid and needs close monitoring during induction [17,18]. On the other hand, 50 µg oral misoprostol was found to be as effective as its 25 µg vaginal analogue for the purpose of labor induction with comparable rates of uterine tachysystole, hyper tonus and hyper stimulation [19,20] and [23].

The induction interval in those delivering vaginally in our study we found that 50 µg orally administered misoprostol is similarly effective as 25 µg vaginal misoprostol. This finding correlates with Hall R et al, [20,21] and [25], who have used similar doses. Additionally, we have observed a low incidence of failed induction for both groups (4% versus 2 %), as reported by other authors [10,14] and [17]. Mean number of doses of misoprostol required for labor induction was 3 for both groups. This number is similar to those reported in few other studies [14,20] and [25]. Recent recommendations by the WHO [26] suggest that the dosage of oral misoprostol of 25 µg every 2 hourly, and vaginal misoprostol of 25 µg every 6 hourly, show moderate degree evidence with strong recommendations for oral analogue of the drug, whereas weak recommendations for vaginal analogue. Our present study was conducted much earlier to these published recommendations by the WHO hence these recommendations were not implemented in our study.

In our study, only two patients (4 %) in the oral misoprostol group and two patients (4 %) in the vaginal group have required more than four doses of administration. So, we recommend that if the patient still has no contractions or show no change in the Bishop score after a total of four doses of oral or vaginal misoprostol administration, labor induction should be stopped unless immediate delivery is needed such as preeclampsia, growth retardation with oligohydramnios and PROM. Then the patient may be reevaluated and labor induction be tried at a later time. This will help to reduce induction interval and boosts the morale of the patient. We found oxytocin use for both oral and vaginal misoprostol patients in more than 50% of them. This finding also correlates with most authors [10,11] and [14]. A concern with misoprostol induction has been excessive uterine activity. Uterine tachysystole and hyper stimulation were seen at similar frequency for the two groups. However, the incidence of these complications were found to be significantly higher than those reported by Wing et al.[19], for 50 µg oral misoprostol (20% versus 8% for tachysystole, 12% versus 2% for hyper tonus and 8% versus 2% for uterine hyper stimulation). Differences in the patient follow-up methods may be the possible explanation, as reported rates of these complications differ significantly in the literature [17,18] and [19]. For 25 µg vaginal misoprostol administration, we have detected similar incidence of uterine tachysystole, hyper tonus and hyper stimulation as most authors [13,14] and [18]. We believe that, administration of misoprostol by either oral or vaginal routes requires adequate monitoring of the patient. Our study indicated that use of misoprostol was safe due to the fact that the neonatal outcomes were similar for the two

groups. Similar to most other studies, indicating the safety of the drug for labor induction [10,13] and [14].

CONCLUSION

Our findings indicate that, 50 µg oral misoprostol has the potential to induce labor as safely and effectively as its 25 µg vaginal analogue. Oral ingestion of misoprostol being easier for the patient and the doctor, orally administered is more preferable than the vaginal route.

REFERENCES

1. American College of Obstetricians and Gynecologists. Induction of labor. ACOG Technical Bulletin No. 217. Washington: The College, 1995.
2. American College of Obstetricians and Gynecologists. Prostaglandin E2 gel for cervical ripening. ACOG Committee Opinion-123Washington: The College, 1993.
3. Macer J, Buchanan D, Yonekura ML. Induction of labor with prostaglandin E2 vaginal suppositories .*ObstetGynecol*, 63, 1984, 664–668.
4. Keirse MJNC. Prostaglandins in preinduction cervical ripening: meta-analysis of worldwide clinical experience. *J Reprod Med*, 38, 1993, 89–98
5. Garris RE and Kirkwood GE. Misoprostol: a prostaglandin E1 analogue. *ClinPharmacokinet*, 8, 1989, 627–644.
6. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprostol for cervical ripening and labor induction: a meta-analysis. *ObstetGynecol*, 89, 1997, 633–642.
7. Fletcher HM, Mitchell S, Simeon D, Frederick J, Brown D. Intravaginal misoprostol as a cervical ripening agent. *Br J ObstetGynaecol*, 100, 1993, 641–644.
8. Wing DA, Rahall A, Jones MM, Goodwin TM, Paul RH. Misoprostol: an effective agent for cervical ripening and labor induction. *Am J ObstetGynecol*, 172, 1995, 1811–1816.
9. Mundle WR and Young DA. Vaginal misoprostol for induction of labor: randomized controlled trial. *ObstetGynecol*, 88, 1996, 521–525.
10. Shetty A, Danielian P, Templeton A. A comparison of oral and vaginal misoprostol tablets in induction of labour at term. *BJOG*, 108, 2001, 238–243
11. Bennet KA, Butt K, Crane JM, Hutchens D, Young DC. A masked randomised comparison of oral and vaginal administration of misoprostol for labor induction. *ObstetGynecol*, 92, 1998, 481–486.
12. Wing DA, Ham D, Paul RH. A comparison of orally administered misoprostol with vaginally administered misoprostol for cervical ripening and labor induction. *Am J ObstetGynecol*, 180, 1999, 1155–1160
13. Fisher SA, Mackenzie VP, Davies GAL. Oral versus vaginal misoprostol for induction of labor: a double-blind randomized controlled trial. *Am J ObstetGynecol*, 185, 2001, 906–910.
14. Kwon JS, Davies GA, Mackenzie VP. A comparison of oral and vaginal misoprostol for induction of labour at term: a randomised trial. *BJOG*, 108, 2001, 23–26
15. Kubli FW, Hon EH, Khazin AF, Takemura H. Observations on heart rate and pH in human fetus during labor. *Am J ObstetGynecol*, 104, 1969, 1190–1206
16. Toppozada MA, Anwar MY, Hassan HA, el-Gazaerly WA. Oral and vaginal misoprostol for induction of labor. *Int J GynaecolObstet*, 56, 1997, 135–139
17. Carlan SJ, Bouldin S, Blust D, Brien WFE. Safety and efficacy of misoprostol orally and vaginally: a randomized trial. *ObstetGynecol*, 98, 2001, 107–112
18. Adair CD, Weeks J, Barrilleaux S, Edwards M, Burlison K, Lewis DF. Oral or vaginal misoprostol administration for induction of labor: a randomised, double-blind trial. *ObstetGynecol*, 92, 1998, 810–813
19. Wing DA, Park MR, Paul RH. A randomised comparison of oral and intravaginal misoprostol for labor induction. *ObstetGynecol*, 95, 2000, 905–908
20. Hall R, Duarte-Gardea M, Harlass F. Oral versus vaginal misoprostol for labor induction. *ObstetGynecol*, 99, 2002, 1044–1048
21. Gómez Ponce de León R, Wing D, Fiala C. Misoprostol for intrauterine fetal death. *Int J GynecolObstet*, 99 (2), 2007, 190–193.
22. Kushwah B, Singh A. Sublingual versus oral misoprostol for uterine evacuation following early pregnancy failure. *Int J GynaecolObstet*, 106 (1), 2009, 43–45
23. Paritakul P, Phupong V. Comparative study between oral and sublingual 600 µg misoprostol for the treatment of incomplete abortion. *J ObstetGynaecol* Res, 36 (5), 2010, 978–983.

24. Montesinos R, Durocher J, León W, Arellano M, Peña M, Pinto E, Winikoff B. Oral misoprostol for the management of incomplete abortion in Ecuador. *Int J GynaecolObstet*, 115 (2), 2011, 135–139
25. Tang J, Nathalie K, Drogoman M, JPDESouza. WHO Recommendations formesoprostol use for obstetric and gynecologic indications. *Int J GynaecolObstet*, 121(2), 2013, 186–189.
26. World Health Organization (WHO) WHO recommendations for induction of labour. Geneva (Switzerland): World Health Organization (WHO), 2013, 36.