JANUARY - MARCH 2012

MEDICAL CHANNEL

Original Article

COMPARISON OF VAGINAL AND ORAL MISOPROSTOL FOR INDUCTION OF LABOUR WITH INTRAUTERINE FOETAL DEATH.

1. KULSOOM BHATTI

ABSTRACT:

Objective: To compare the efficacy of vaginal and oral misoprostol for the induction of labor in women with intra-uterine fetal death (IUFD).
Study Design: A prospective randomized clinical trial, comparing 200ug oral and 200ug vaginal misoprostol, six hourly for a maximum of four doses for the induction of labor in women with IUFD.
Setting and duration: Department of Obstetrics and Gynecology, Ghulam Muhammad Maher Medical College Hospital Khairpur Sindh.
Main outcome measures: The primary outcome measure was the induction to delivery time, and secondary outcome measures were the number of patients requiring augmentation with oxytocin and all complications were noted.
Results: Twenty women were randomized to the vaginal route and 18 to the oral route. The induction to delivery time was shorter with vaginal misoprostol (13.5 + 8.3 hours) compared to oral misoprostol (21.4 + 13.9 hours; p< 0.05). There was no significant difference in the amount of misoprostol needed to achieve successful induction in the two groups. More women 10/18 who received oral misoprostol required oxytocin augmentation to complete the induction of labor compared with 4/20 women in the vaginal group (p< 0.05; Odds Ratio 2.8; 95% CI 1.36-4.24). There was no cases offailed induction. The systemic side effects (shivering, diarrhoea, vomiting and pyrexia) were more common with oral misopristol (44.4%) compared to vaginal misopriotol (20%). This difference gives an overall Odds Ratio of 2.2 at 95% CI of 1.6-2.8 (p< 0.05).
Conclusion: Vaginal misoprostol achieved successful induction of labor in women with IUFD in a shorter time than oral route with significantly less side effects.

Key words: Misoprostol, induction, intra-uterine fetal death, oxytocin.

Correspondence
DR.KULSOOM BHATTI
FCPS
(GYNAECOLOGY AND OBSTETRICS)
Ghulam Muhammad Maher Medical College Hospital Khairpur Sindh.
Bhattikulsoom@ymail.com
Cell no: 03083234318

INTRODUCTION:

Misoprostol is a synthetic prostaglandin E1 analogue. It was manufactured for the treatment of peptic ulcer disease,[1,2] but its off label use for labor induction has been endorsed by American College of Obstetricians and Gynecology and also by Royal College of Obstetrician and Gynecologists.[3,4] In addition, misoprostol is an effective myometerial stimulant of pregnant uterus, selectively binding to EP-2/EP-3 prostanoid receptors.[5] Misopristol is now increasingly and successfully being used for labor inductions with vaginal as well as oral routes.[6,7,8] It is economical, stable at room temperature, has easy handling and storage, rapid absorption and high potency.[1,2] Now misoprostol has gained world wide acceptance for cervical ripening.[9]

Mariani-Neto et al [10] first reported using oral misoprostol (400µg four hourly), for the induction of labor following intra-uterine fetal death. Many subsequent studies have shown that misopristol is effective, easy to use and a cheap drug for induction of labor in women with IUFD.[11] Misoprostol is rapidly absorbed orally and vaginally.

Zieman et al, in a randomized comparison of absorption kinetics of 400µg of oral and vaginal misoprostol showed that the plasma concentration of misoprostol after oral

administration, rose quickly, reaching a peak (227 pg/ml) 34 minutes after administration, fell steeply by 120 minutes and remained low for the duration of the study. In contrast, plasma concentration of misoprostol acid in subjects who received vaginal misoprostol rose gradually reaching a peak (165 pg/ml) at approximately 80 minutes after administration and declined slowly, to an average of 61% of the peak level at 240 minutes after administration.

The objective of this study was to compare the efficacy of oral versus vaginal misoprostol for the induction of labor in women with IUFD after 20 weeks of gestation.

MATERIAL AND METHODS:

Thirty eight pregnant with IUFD were asked to participate in a randomized clinical trial where the vaginal and oral routes of administration of misoprostol were compared.

The study was conducted at Department of Obstetrics and Gynecology, Ghulam Mohammad Maher Medical Hospital Khairpur Sindh. Prior to entry to the trial, confermation of IUFD was made by ultrasound examination. Written informed consent was obtained from each woman before randomization. Only women with confirmed IUFD, singleton pregnancy, cephalic presentation and parity less than five were included in the study. Women with mal presentation, fetal macrosomia, previous uterine scar, any contraindication to receiving prostaglandin and renal or hepatic dysfunction were excluded from the study.

All patients participating in the study were admitted in antenatal ward. The initial assessment included patient's demographic features (age, parity, gestational age), duration of IUFD and initial Bishop score. The gestational age was calculated from the last menstrual period and duration of IUFD from the date of last fetal movement perception.

Misoprostol 200µg was administered six hourly orally or vaginally (in the posterior fornix), for a maximum of four doses. Patients who progressed to active labor were transferred to labor ward and managed accordingly, Oxytocin augmentation was commenced six hours after the last dose in a standard regime and increased in a increments at half hourly intervals.

The primary outcome measures was the induction to delivery time, and secondary outcome measures were the number of patients requiring augmentation with oxytocin and all complications were noted. If the woman was no established labor six hours after the last dose of misoprostol, the induction was deemed a failure.

Standard statistical methods (P-value; Odds Ratio and 95% Confidence Intervals) were used to analyze the data.

RESULTS

Thirty eight women were randomized for the study, of whom 18 received oral misoprostol and 20 vaginal misoprostol, both groups were comparable with respect to maternal age, parity, gestational age at the time of fetal demise, duration of intra-uterine death, and Bishop score at commencement of induction (Table 1). There were no cases in which labor could not be induced. There were no post randomization exclusion and no women withdraw from the trial after consent has been given.

DISCUSSION:

In this study, the mean induction to delivery time was significantly shorter in the vaginal group (13.5+ 8.3) hours when compared to the oral group (21.4+ 13.9) hours. Further more significantly more women in the oral group required oxytocin augmentation 10

TABLE 1
COMPARISON OF WOMEN WITH IUFD UNDERGOING INDUCTION OF LABOR WITH MISOPROSTOL

	Vaginal administration	Oral administration	P-value
=Maternal age (Mean +SD)	25.3 + 4.2	24.7 + 5.6	NS
=Parity = P0	10	8	
P1-2	7	6	
P3-4	3	4	
=Gestational age (mean + SD, weeks)	27.4+ 5.0	28.2+ 4.5	NS
=Duration of IUFD (mean+ SD, weeks)	1.7+ 0.8	1.8 + 0.8	NS
=Initial Bishop's score			
< 4	3	2	
4-6	15	14	
> 6	2	2	

The mean induction to delivery time was 21.4 + 13.9 hours in the oral group and 13.5 + 8.3 hours in the vaginal (P< 0.05; Table 2). A higher mean dose of misoprostol was required for successful induction in the oral group (537.5 + 249 µg) than in the vaginal group (420 + 233 µg) but this difference was not statistically significant. In addition, more women in the oral group required oxytocin augmentation 10(55.6%) patients than in the vaginal group 5(25%) patients (P<0.05; Odds 2.8; 95% CI 1.36-4.24, Table 2).

TABLE 2
COMPARISON OF THE EFFECT OF INDUCTION WITH VAGINAL AND ORAL ROUTE OF ADMINISTRATION OF MISOPROSTOL.

	Vaginal	Oral	P-value
Induction to (mean+ sd)	13.5+ 8.3	21.4+ 13.9	< 0.05
Delivery time (median)	11.9	18.3	
(range)	3.6-32.7	4.0-47.9	
Oxytocin augmentation	5/20(25%)	10/18(55.6%)	< 0.05
Dose of miso prostol used (µg) mean + sd	420.0+ 233.1	537.5+ 249.7	NS

There were no major complications but only minor systemic side effects namely:

Vomiting, diarrhea, shivering and pyrexia, were more common in the oral group (44.5%), Than in the vaginal group (20%). (P < 0.05; Odds Ratio 2.2; 95% CI 1.6-2.8%,

(Table 3). There were no cases of uterine rupture seen in the study population.

TABLE 3
COMPARISON OF THE SIDE EFFECTS OF VAGINAL AND ORAL ADMINISTRATION OF MISOPROSTOL FOR THE INDUCTION OF LABOR.

	Vaginal	Oral	P-value
-Vomiting	2/20 (10%)	3/18 (16.7%)	1.7(0.0-3.6)
-Diarrhoea	1/20 (5%)	-	
-Shivering	1/20 (5%)	3/18 (16.7%)	3.3(0.95-5.65)
-Pyrexia	-	2/18 (11.1%)	
-Hyperstimulation	-	-	
-Uterine rupture	-	-	
-PPH	-	-	
Total rate of side Effects	20%	44.5%	P < 0.05

(55.6%) of 18 patients than in the vaginal group 4(20%) of 20 patients (P< 0.05). The doses of misoprostol used in this present trial were higher (200µg six hourly) than in other trials.[12]

Topazada et al [13] compared vaginal versus oral misoprostol for induction of labor in 40 women who were randomized in to two equal groups. Group A received vaginal misoprostol (100 µg) every three hours while group B patients were given the same dose via the oral route. The vaginal route of administration induced a higher success rate in a shorter time interval using a lower dose, but was associated with more abnormal fetal heart rate pattern and instances of uterine hyper-stimulation. The authors recommended the use of the vaginal approach with cardio-tocographic monitoring. The study shows that women who receive misoprostol vaginally require less dosing and experience faster induction-to-delivery time with less need for oxytocin augmentation when compared with a similar group of women receiving oral misoprostol, These findings occur with those of others.[14]

In this trial significantly more side effects were reported in the oral misoprostol group with, in order of frequency ; vomiting, shivering and pyrexia being the most common. Hofmmeyr, et al[15] in a randomized placebo controlled trial of oral misoprostol in the third stage of labor, Using oral misoprostol 400µg, found that shivering was more common in the oral misoprostol group (19% vs 5%, relative risk 3.69; 95% confidence interval 2.05-6.64). They concluded that shivering was a specific side effect of misoprostol administered orally in the puerperium.

There was no case of uterine rupture in this study, However, this study did not aim to test the safety of the different routes of administration of misoprostol.

This study concluded that vaginal route of misoprostol achieved successful induction of labor in women with IUFD in a shorter time than oral route with significantly less side effects.

CONCLUSION:

Vaginal misoprostol achieved successful induction of labor in women with IUFD in a shorter time than oral route with significantly less side effects.

REFERENCES:

1. Dodd JM, Cowther CA, Robinson JS. Oral misoprostol for induction of labor at term: a randomized trial. BMJ 2006; 332: 509-13.
2. Sarbek DV. Misoprostol for labor induction in term pregnancy clinical review. Eur Clin Obstet Gynecol 2007; 3:25-9.
3. American College of Obstetricians and Gynecologists committee opinion number 283, May2003.
4. Royal College of Obstetricians and Gynecologists. Induction of labour. Evidence based clinical guidelines no.9, 2001. Accessed. 30 May 2007.
5. Senior J, Marshall K, Sangha R, Clayton JK. In vitro characterization of postanoid receptors on human myometrium at term pregnancy. Brit. J. P harm. 1993; 108:501-506.
6. Amna M, Skindar R. Misoprostol for induction of labour: the Hyderabad experience. J Liaquat Uni Med Health Sci 2007; 2:56-9.
7. Hofmeyr GJ, Gulmezoglu AM. Vaginal misoprostol for cervical ripening and labour induction in late pregnancy. Cochrane Database Syst Rev 2001;(3): CD000941.
8. Alfirevic Z, Weeks A. Oral misoprostol for induction of labour. Cochrane Database Syst Rev 2006;(2): CD001338.
9. Luthy DA, Malmgren JA, Zingheim RW. Caesarean delivery after elective inductionin nuliparous women. AmJOG 2004; 15: 319-23.
10. Mariani-Net C, Leao EJ, Baretto EM, Kenj G, and De Aquino MM. Use of misoprostol for labour induction in still births. Rev, Paul, Med, 1987; 105:325-328.
11. Hofimeyer GJ. Vaginal misoprostol for cervical ripening and labour induction in late pregnancy. The Cochrane Library 1999; 2:1-18. (Meta Analysis)
12. Nigama A, Singh VK, Dubaya P, Pandeya K, Bhagoliwala A, Parkash A,. Misoprostol vs oxytocin fof induction of labour at term. Int J Gynecol Obstet 2004; 86:398-400.
13. Toppozada MK, Anwar MYM, Hassan HA, and El-Gazaerly WS. Oral or vaginal misoprostol for induction of labour. Int J Gynecol, Obstet, 1997; 56:135-139.
14. Bennett KA, Butt K, Crane JMG, Hutchens D, Young DC. A masked randomized comparison of oral and vaginal administration of misoprostol for labour induction. Obstet Gynecol 1998; 481-86.
15. Hofmeyr GT, Nikodem VC, Mirinda de jager, and Gelhart BR. A randomized placebo controlled trial of oral misoprostol in the third stage of labour. Britt J Obstet Gynaecol. 1998; 105:971-975.