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Original Research Article

Comparison of vaginal and oral misoprostol, for the induction of labour in women with intra-uterine foetal death

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ABSTRACT

Background: Misoprostol is a prostaglandin E1 analogue, a methyl-ester of prostaglandin E1 additionally methylated at C-16. Misoprostol is an effective myometrial stimulant of pregnant uterus, selectively binding to prostanoid receptors. The objective of the study was to compare the efficacy of vaginal and oral misoprostol for the induction of labour in women with intra-uterine foetal death (IUFD).
Methods: A prospective randomised clinical trial, comparing 50µg oral and 50µg vaginal misoprostol, six hourlies for a maximum of four doses for the induction of labour in women with IUFD. All patients with IUFD after 28 weeks without previous uterine surgeries, without contraindications for prostaglandins are included in the study. The study was conducted in the Department of Obstetrics and Gynecology MVJ Medical College and Research Hospital, Hoskote. Bangalore from June 2012 to June 2015. It is a tertiary institution serving predominantly rural population. The primary outcome measure was the induction to delivery time, secondary all complications were noted.
Results: Twenty-five women were randomised to the vaginal route and twenty-five to the oral route. The induction to delivery time was longer with vaginal misoprostol 10.5±4.03 compared to oral misoprostol (9.58±4.9). There was no significant difference in the amount of misoprostol needed to achieve successful induction in the two groups. 3 patients needed oxytocin augmentation to complete the induction of labour. There were no cases of failed induction. The systemic side effects (shivering, diarrhoea, vomiting and pyrexia) were more common with oral misoprostol (44.5%) compared to vaginal misoprostol (20%).
Conclusions: Oral misoprostol achieved successful induction of labour in women with IUFD in a shorter time than vaginal misoprostol. Both routes are equally effective in termination of pregnancy. Sublingual route is easy to administer, patient compliant, no need for internal examination, less chance of labour dysfunction, less chance of post-partum sepsis.

Keywords: Intra-uterine foetal death (IUFD), Induction

INTRODUCTION

Misoprostol is a prostaglandin E1 analogue, a methyl-ester of prostaglandin E1 additionally methylated at C-16. Misoprostol is an effective myometrial stimulant of pregnant uterus, selectively binding to prostanoid receptors.[1] Mariani-Neto et al, first reported using oral misoprostol (400µg four hourly), for the induction of labour following IUFD.[2] All the 20 patients delivered. Many subsequent studies have shown that misoprostol is effective, easy to use and a cheap drug for induction of labour in women with IUFD.[3-5] However, the preferred route of administration of misoprostol is still uncertain. Three trials compared oral and vaginal misoprostol using

different doses and their results were inconsistent.[6-8] Misoprostol is rapidly absorbed orally and vaginally.[9] Zieman et al, in a randomised 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.[9] In contrast, plasma concentration of misoprostol 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 labour in women with IUFD.

METHODS

50 pregnant women with IUFD were asked to participate in a randomised clinical trial where the vaginal and oral routes of administration of misoprostol were compared. The study was conducted at mvj medical college and research hospital. Prior to entry to the trial, confirmation of IUFD was made by ultra sound examination. Written informed consent was obtained from each woman before randomisation. Only women with a confirmed IUFD, singleton pregnancy, cephalic presentation and parity less than five were asked to participate.

Women with a malpresentation, foetal macrosomia, previous uterine scar, any contra indications to receiving prostaglandin and renal or hepatic dysfunction were specifically excluded.

All patients participating in the study were admitted in antenatal ward. The initial assessment included patients' demographic features: (age, parity, gestational age), duration of IUFD and an initial Bishop score. The gestational age was calculated from the last normal menstrual period and the duration of IUFD from the date of last foetal movement perception. 25 patients were given Misoprostol 50 micro grams was administered 4 th hourly sublingually and 25 patients are given 50 mcg vaginally (in the posterior fornix), prior to each dose modified bishop score is assessed for a maximum of five doses, or until labour was established. If labour is not established after 4 hours of last dose the same procedure is repeated after 24 hours.

Patients who progressed to active labour were transferred to labour ward and managed accordingly. The primary outcome measure was the interval between induction to uterine contraction induction to delivery time, mode of delivery and secondary outcome measures all complications and adverse effects. Standard statistical methods (p-value; odds Ratio and 95% Confidence Interval) were used to analyse the data. The study was conducted, following approval by the Ethics Committee.

RESULTS

50 women were randomised for the study, of which 25 received oral misoprostol and 25 vaginal misoprostol. Both groups were comparable with respect to maternal age, parity, gestational age at the time of foetal demise, duration of the intra-uterine death, and Bishop Score at commencement of induction (Table 1).

Table 1: Comparison of women with IUFD undergoing induction of labour with misoprostol.

	Vaginal	Oral
Maternal age	26.3±4.9	24.7±5.6
Parity		
Primi	12	13
Multi	13	12
Gestational age	27.4±5.0	29.2±4.5
Initial Bishop's score		
<4	17	12
4-6	5	10
>6	3	3
Response to drugs	2	2
Failed inductions	0	0

Table 2: Comparison of the effect of induction of labour with vaginal and oral route of administration of misoprostol.

Effect of induction	Vaginal	Oral
Induction to delivery time	10.5±4.03	9.58±4.9
Induction to pain interval	3.37	2.37

Table 3: A comparison of side-effects of vaginal and oral administration of misoprostol for the induction of labour.

	Vaginal	Oral
Vomiting	2/25	3/25
Diarrhoea	1/25	
Shivering	1/25	3/25
Pyrexia		1/25
Hyper stimulation		
Uterine rupture		

The mean induction to delivery time was 9.58±4.9 hours in the oral group and 10.5±4.03 hours in the vaginal. Oxytocin augmentation in required in 3 cases. There were no major complications but only minor systemic side effects namely: vomiting, diarrhoea, shivering and pyrexia, these were more common in the oral group than in the vaginal group Table 3. There were no cases of uterine rupture.

DISCUSSION

In this study, the mean induction to delivery time was significantly shorter in the vaginal group 10.5±4.03 when compared to the oral group 9.58±4.9. The doses of

misoprostol used in this present trial were similar (50µg 4th hourly) than in other trials.[6,8] Wing et al, in a randomised clinical trial comparing 50µg misoprostol administered orally and 25µg misoprostol intra-vaginally, 220 subjects were randomised, 110 in each arm of the study. Significantly fewer subjects who received the oral preparation (30.9%) were delivered vaginally within 24 hours of initiation of induction, in comparison with those who received the vaginal preparation (47.3%).[7] The average interval from start of induction to vaginal delivery was nearly six hours longer in the oral treatment group (mean and SD 1737.9±845.7 minutes) than in the vaginal treatment group (mean and SD 1393.2±767.9) (p=0.005). Orally treated patients required significantly more doses than vaginally treated patients (orally administered doses; mean and SD=3.3±1.7; vaginally administered doses: mean and SD=2.3±1.2) with a p-value <0.0001. Furthermore, oxytocin administration was necessary in 83 of 110 (75.4%) orally treated subjects and in 65 of 110 (59.1%) vaginally treated subjects (p=0.01). These authors concluded that oral administration of 50µg doses of misoprostol appears less effective than vaginal administration of 25µg doses of misoprostol for cervical ripening and labour induction. They recommended further investigation to determine whether orally administered misoprostol should be used for cervical ripening and labour induction. Adair et al, on the other hand did not find any significant difference in the efficacy in a randomised double blind trial comparing 50µg of vaginal misoprostol and 200µg of oral misoprostol for labour induction.[8] The most important side effects of misoprostol are nausea, vomiting and dose dependent diarrhoea, stomach-ache and flatulence.[10] 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. Hofmeyr et al, in a randomised placebo controlled trial of oral misoprostol in the third stage of labour, using oral misoprostol 400µg, found that shivering was more common in the misoprostol group (19% vs. 5%, relative risk 3.69;95% confidence interval 2.05-6.64).[11] They concluded that shivering was a specific side effect of misoprostol administered orally in the puerperium. Lumbiganon et al, reported misoprostol dose-related shivering and pyrexia in the third stage of labour.[12] Comparing misoprostol 400µg versus misoprostol 600µg both shivering and pyrexia (temperature >38°C) were more common in the 600µg misoprostol group (28% and 7.5% for shivering and pyrexia, respectively) compared with 400µg misoprostol (19% and 2%). There was no case of uterine rupture in this study. Misoprostol causes potent uterine contractions and these can lead to hyper-stimulation of the uterus and eventually to uterine rupture. In the case of IUFD, uterine rupture is still of concern.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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