
To Assess The Efficacy Of Two Regimens Of Misoprostol For Second Trimester Pregnancy Termination-A Randomized Comparison

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Abstract

Objective

:- The purpose of this study was to compare the efficacy and side effects of oral and vaginal misoprostol regimens for second-trimester pregnancy termination.

Study Design

:- We performed a randomized clinical trial in patients who were at 19-23 weeks gestation who were admitted for medical termination of pregnancy. All patients received 800

m gm of vaginal misoprostol and were assigned randomly to 400

m gm of oral misoprostol or 400

m gm of vaginal misoprostol every 8 hourly up to a maximum of 4 doses. Efficacy and side effects were compared. The mean induction abortion interval was compared in both groups.

Results

:- Hundred women were assigned randomly, 50 women to vaginal misoprostol and 50 to oral misoprostol. Induction abortion interval and hospital stay were shorter for vaginal group. Side effects were more in oral group.

Conclusion

:- After an initial 800

m gm dose of misoprostol, a regimen of 400

m gm of vaginal misoprostol every 8 hourly to a maximum of 4 doses is more effective than a similar regimen of oral misoprostol.

INTRODUCTION

Prostaglandins have been recognized as effective abortifacients

for several decades⁽¹⁾. Misoprostol, a new synthetic analogue of prostaglandin E1, has several advantages over other prostaglandins which include low cost, easy storage at room temperature and favourable side effect profile⁽²⁾. The therapeutic potential of misoprostol as an abortifacient was clearly demonstrated in a randomized study in 1987 and in many subsequent trials all over the world⁽³⁾. There have been continuous attempts to find out an ideal method for second trimester pregnancy termination. Second trimester abortions are important from public health point of view because they are responsible for more than half of preventable deaths. The optimal dose and route of administration however have yet to be defined^{(4),(5),(6)}.

The results of using drug by vaginal route have been highly encouraging and side effects and complications reported have been minimal. As the hospital stay is minimized, this results in decongestion of hospital beds which are perpetually overcrowded in our country.

As no such study was conducted in Kashmir Valley regarding the comparison between the oral and vaginal routes of administration of misoprostol for induction of second trimester pregnancy termination, an endeavour was made to critically evaluate these two routes. Before initiating this study, the protocol at the University of Connecticut Health Centre for second trimester pregnancy termination consisted of 400 µgm of vaginal misoprostol every 12 hours. The mean induction time to delivery of these historic controls was 26.0 + 4.5 hours.

We sought to shorten the time by increasing the initial vaginal dose to 800 µgm and then compare the efficacy and side effects of 400 µgm of oral misoprostol every 8 hourly to the same dose of vaginal misoprostol.

METHODS

We performed a randomized controlled trial of women in the age-group of 18-40 years with a parity ranging from primigravidae to gravida 4 and above, who underwent medical termination of pregnancy at our institution at 19-23 weeks of gestation between January 2006 to January 2008. Indications for termination included sonographic diagnosis of foetal structural abnormality, chromosomal abnormality, premature preterm rupture of membranes, or intrauterine

foetal death. Patients were offered a surgical evacuation or a medical induction of labour. Patients were excluded from study if (1) they had a known scarred uterus due to instrumentation (2) they had a known contraindication to prostaglandins or (3) patients with history of glaucoma, mitral stenosis and inflammatory bowel disease. After admission and other formalities, the patients were explained the procedure and informed consent was taken. All patients received initial dose of 800 µgm of vaginal misoprostol and then 50 patients were assigned randomly to 400 µgm of oral misoprostol (Group A) and 50 patients (Group B) were given 400 µgm of vaginal misoprostol every 8 hourly. Misoprostol tablets (200 µgm) were placed in posterior vaginal fornix. No other intervention were used.

The primary outcome measure was induction abortion interval which was defined as time from placement of the first dose of misoprostol until delivery of foetus. A failed induction was defined as failure to deliver by 48 hours after the first dose of drug.

Secondary outcome measures included the length of hospital stay, total number of misoprostol doses that were required for induction, the third stage of labour and side effects of medication.

The frequency of side effects which included abdominal pain, fever (>100.4° F), nausea, vomiting, diarrhoea and headache were based on patient report and charted on data sheets by assigned nursing staff. Patients received hyoscine butyl bromide for abdominal pain. Antiemetics, antipyretics and anxiolytics were administered as indicated.

After delivery of foetus, all patients received 20 units of syntocinon in 5% dextrose. When placenta was expelled within 1 hour of expulsion of foetus, abortion was considered complete. Postpartum curettage was performed if the placenta did not expel within 1 hour and was removed manually or expulsion was considered incomplete on the basis of clinical signs and symptoms and after USG diagnosis of retained products of conception. This was considered as incomplete abortion. The statistical analysis of the data was done by using test statistic, Chi Square Test. The Chi Square Test was modified by Yates Correction for the tables having cell-frequency <5. The tests were referenced by p values for their significance. The p value <0.05 were taken to be significant. The analysis of the data was done by using statistical package for social sciences (SPSS, ver 10.0) by Chicago USA for windows.

RESULTS

During the study period, 100 women were assigned randomly to two groups. 50 women received oral misoprostol (Group A) and 50 women received vaginal misoprostol (Group B) after initial 800 µgm loading dose.

Maternal age, parity, gestational age and indication for termination were similar in both groups.

Table 1 with p value in all.

Figure 1

Table I- Maternal characteristics and indications for induction

Characteristic	Group A	Group B	P value
Maternal age (yrs) Mean ± S.D	24.62 ± 5.20	26.25 ± 4.28	0.632
Median Parity (Range)	1 (1-6)	1 (1-5)	0.900
Gestational Age (wks) Mean + S.D	22.13 ± 2.24	21.74 ± 2.15	0.715
Indication for induction %	%	%	
i. IUD	24 (48%)	27 (54%)	0.548
ii. Preterm premature rupture of membranes	14 (28%)	10 (20%)	0.349
iii. Congenital malformation & Ors	12 (24%)	13 (26%)	0.817

The mean induction abortion interval in oral group (Group A) was 32.15 + 6.12 hrs and in vaginal group (Group B) was 16.12 + 6.10 hrs. Statistically, the difference was highly significant between the two groups (p value = 0.000) with regard to mean induction abortion interval.

The mean length of third stage of labour, number of induction failures and need for post partum curettage in the oral and vaginal groups were not statistically significant but, after receiving the third dose, 16 (32%) patients in Group A and 40 (80%) patients in Group B expelled the foetus. Statistically the difference was highly significant between the two groups (p value = 0.000). Thirty-eight patients in Group B and 14 patients in Group A stayed for two days in the hospital. Ten patients in Group B and 33 patients in Group A stayed for 3 or more days in hospital which was statistically highly significant (p value = 0.000).

There were no adverse outcomes such as uterine rupture or dehiscence, hemorrhage that required transfusion of blood products or hysterectomy.

The two groups were assessed for the incidence of side effects. There was a trend towards more frequent nausea, vomiting, diarrhea and fever in oral group than vaginal group. Abdominal pain was reported more in vaginal group. All this was not statistically significant.

Table II Results with p value in all.

Figure 2

Table II – Results

characteristic	Group A	Group B	P value
Third Stage (min)	57.62 ± 9.25	58.45 ± 7.60	0.684
Median doses (range)	4 (2-4)	3 (2-4)	0.001*
Hospital stay Mean ± S.D	3.60 ± 1.25	2.25 ± 1.12	0.001*
Failed induction (No) (%)	3 (6%)	2 (4%)	0.645
Postpartum curettage (No) (%)	9 (18%)	6 (12%)	0.401

DISCUSSION

Misoprostol while as being accepted as a labour inducing agent is also known to be safe and efficacious agent for medical termination in second trimester because of cervical ripening and uterotonic properties. Before misoprostol’s widespread use in mid-1990’s, other prostaglandins such as PGE2, vaginal suppositories and PGF2α injections were most commonly used for second trimester pregnancy termination. Although efficacious, these were associated with side effects such as nausea, vomiting, diarrhea and fever in high percentage of patients⁽⁷⁾. Pre-medication with antiemetics, antipyretics and anti-diarrheals is often required. We found that side effects of misoprostol are much better tolerated than other prostaglandins for pregnancy termination in second trimester. The published results of various authors like Jan E Dickenson⁽⁸⁾, Pak Chung Ho⁽⁹⁾, Miriam Ziemann⁽¹⁰⁾, Babbington W⁽¹¹⁾, Eric A Schaff⁽¹²⁾, are all pointing towards more effectiveness of misoprostol administered vaginally than orally for termination of second trimester pregnancy. No wonder in our present series we also achieved similar encouraging results with regard to the effects of misoprostol via vaginal than the oral route.

Among the objectives of the study was also to compare and analyze the age, parity, gestational age, indication for termination, number of patients expelling foetus completely, third stage with its complications and side effects. All these were similar in both the groups and thus statistically

insignificant. But the mean induction abortion interval of 32.15 + 6.12 hrs in oral compared to the mean induction abortion interval of 16.12+ 6.10 hrs in vaginal group showed a statistical difference which was highly significant (p value= 0.000). This is in contrast to the findings published by Deborah M. Feldman et al 2003. Although the mean length of third stage of labour and the number of induction failures and need of postpartum curettage in the oral and vaginal groups was not statistically significant, but the finding that after receiving third dose, 16 (32%) patients in Group A and 40 (80%) in Group B expelled the foetus revealed statistically that the difference was highly significant between the two groups (p value= 0.000).

Thirty-eight patients in Group B and 14 patients in Group A stayed for two days in the hospital which again was highly significant. These findings were in contrast to the findings of Deborah M Feldman⁽¹³⁾.

Based on these observations, it is concluded that the vaginal administration of misoprostol is superior to oral administration of misoprostol due to the achievement of complete termination more quickly, less number of doses required and shorter hospital stay, so less expenditure associated with it. The above observed effect is due to improved pharmacokinetics associated with vaginal administration. Moreover, the drug is easily available as it has been licensed for use in India.

It is, therefore, recommended that when second trimester pregnancy termination is to be done by medical method, vaginal administration of misoprostol should be the preferred route.

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