Original Article

Second trimester pregnancy termination with 400 μg vaginal misoprostol: Efficacy and safety

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Summary **The present study was designed to evaluate the efficacy and safety of misoprostol (400 μg) given intravaginally repeated at 6 hourly intervals for a maximum of 6 doses for second-trimester pregnancy terminations. The study was conducted on women who had to undergo pregnancy termination between 13 and 26 weeks of gestation for various indications but mainly intrauterine death over a period of 2 years. A standard regime of 400 μg of misoprostol 6 hourly intravaginally was given until a maximum of 6 doses. Sixty women underwent second trimester terminations. The mean induction abortion interval was 11.8 h. The success rate at the end of 48 h was 96.6%. Side-effects were in the form of incomplete abortion, excessive blood loss, and fever. No patient had a uterus rupture. Intravaginal misoprostol 400 μg given 6 hourly seems to be an effective, safe, and acceptable method for second trimester pregnancy terminations.**

Keywords: Second trimester pregnancy termination, vaginal misoprostol, prostaglandin

1. Introduction

Second trimester pregnancy terminations, though a common problem in obstetrics practices, can be tricky situations. Previously, the most commonly used drug oxytocin had high failure rates because it was ineffective in stimulating a preterm uterus. Prostaglandins have been the most commonly used agents for many years up to now.

Misoprostol (prostaglandin E1 analogue) originally designed for treatment of peptic ulcer has now gained wide popularity in obstetrics. This agent is effective for cervical ripening and labor induction at term, and treatment of post-partum hemorrhage as well as first and second trimester abortions (*1*). The agent has been also used in scarred uterus (*2*). The main advantages of misoprostol are ease of administration, cost-effectiveness, and stability at room temperature (*3,4*).

More than thirty different dosages of misoprostol regimes have been described in the literature for use in obstetrics and gynacology (*5*). A review article published in contraception stressed the fact that, although misoprostol is effective for second trimester preganancy terminations especially for those with intrauterine deaths, further studies are required to establish optimal dose and requirements of second trimester terminations (*6*).

The present study was undertaken to establish efficacy and safety of misoprostol (400 μg) given vaginally and repeated at 6 hourly intervals for a maximum of 6 doses, for second trimester abortions.

2. Materials and Methods

2.1. *Study design*

The study was conducted in the Department of Obstetrics and Gynaecology at Government Medical College and Hospital, Chandigarh, India, between December 2005 and December 2007. It was a prospective study. A total number of 60 patients were included in the study.

2.2. *Subject*

The study was conducted on 60 healthy women admitted for termination of pregnancy between 13-26

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weeks of pregnancy for any indication but most commonly for intrauterine death (Table 1).

2.3. *Method*

A detailed history including age, parity, and period of gestation were noted and details of clinical examination including cervical findings were also recorded. Ultrasound (USG) was done to confirm gestational age, congenital malformation, and placental localization. Written informed consent of the patient was taken and a standard regime of moistened misoprostol (400 µg) 6 hourly intravaginally was used for a maximum of 6 dosages. Any complications including: fever, diarrhea, shivering, and excessive blood loss were recorded. Failure was noted when after 6 doses of misoprostol the patient did not go into labor. In case of failure a repeat dose of misoprostol 400 µg for 6 doses was used after giving a rest of 24 h. Before the next dose, the patient was examined and if the patient was having strong and frequent contractions, *i.e.*, more than 3 contractions in 10 min and if the cervix was more than 4 cm dilated, the next dose was deferred. All incomplete abortions were surgically evacuated. Patients with previous caesarean or any scarred uterus, multiple pregnancies, or severe anemia were excluded. After abortion the amount of blood loss was noted and products of abortion checked for completeness. All patients received prophylactic antibiotics, which included a combination of ciprofloxacin and tinidazole for 5 days. All patients were followed up for a period of 6 weeks but 5 patients did not come for follow up. No patient reported any complications in the follow up period.

3. Results

All patients were between the age group of 19 to 33 years with mean parity of 2.3. Principal indication for termination of pregnancy was intrauterine death of fetus (Table 1). Majority of the patients had a period of gestation between 16 to 18 weeks (Table 2). Mean induction abortion interval (IAI) was 11.8 ± 9.9 h at the end of 48 h (Table 3). Mean number of dosages required was 2.64 (Table 4). Success rates at the end of 24 h and 48 h were 88.3% and 96.6%, respectively (Table 5). Two patients did not abort even after 6 dosages. These patients were given a repeat dose of misoprostol after rest of 24 h. The main complications were incomplete abortion requiring surgical evacuation in 6 patients; fever in one patient, but none of the patients had rupture of the uterus. Three patients had excessive blood loss and only one required blood transfusion. No patient had sepsis.

Table 1. General characteristics of patients and indications

Characteristics of patients	
Total (*n*)	60
Median age (years)	24.5 (19-33)
Median gestation (weeks)	21.1
Indication (*n*)	
IUD	34
CMF	3
PTPROM	23

Abbreviations: IUD, intrauterine device; CMF, congenital malformations; PTPROM, preterm labor or preterm premature rupture of membranes.

4. Discussion

Second trimester abortions are painful and stressful procedures. Various agents have been used and compared with misoprostol in second trimester pregnancy terminations. Misoprostol has proved to be better than extraamniotic instillation of PGF2-α (*7*), extraamniotic instillation of ethacridine lactate (*8*), and prostaglandin E2 (*9*).

Misoprostol is now widely used for second trimester terminations. However, there is still a need to find out the best route and dose with minimum IAI along with minimal side effects and complications. A number of routes of misoprostol administration have been studied and it has been shown that misoprostol

Table 2. Gestational age distribution

Gestational age (weeks)	Number of patients
13 to 15	3
16 to 18	17
19 to 21	14
22 to 24	11
25 to 26	15

Table 3. Results of misoprostol administration

Characteristics	Results
IAI (h)	11.8
Partial failure requiring surgical evacuation (*n*)	6
Excessive blood loss (*n*)	3
Blood transfusion (*n*)	1
Failure (*n*)	2

Table 4. Number of doses of 400 µg of misoprostol required

Number of doses	Number of patients	Percent (%)
1 dose	19	31.6
2 doses	17	28.3
3 doses	12	20.0
4 doses	6	10.0
5 doses	4	6.7
6 doses	2	3.3

Table 5. Number of abortions during treatment period

IAI	Number of patients	Percent (%)
Up to 6 h	10	16.6
Up to 12 h	31	51.6
Up to 18 h	38	63.3
Up to 24 h	53	88.3
Up to 48 h	58	96.6

demonstrates a route-dependent pharmacokinetic profile and that the best absorption is through vaginal administration (*5*). Although the oral route is more acceptable (*10*), vaginal administration of misoprostol is more effective and reliable with minimal side effects (*11*). Direct vagina-to-uterus transport as described for progesterone may explain the better clinical efficacy of the vaginally administered drug (*12*). Sublingual misoprostol has a better pharmacokinetic profile, *i.e.*, peak concentrations achieved in shortest time and higher peak concentrations (*13*), but clinical efficacy is poorer as compared to vaginal misoprostol for second trimester abortions (*14*,*15*). As stated earlier, more than 30 regimes of misoprostol administration have been suggested adding to the confusion.

Further, various adjuncts to misprostol administration have been suggested including moistening of misoprostol tablets with saline (*16*) or acetic acid (*17*). A saline-moistened tablet is better than a dry one and acetic acid-moistened tablet is better (although not statistically different) than a saline-moistened one (*17*). Vaginal misoprostol along with a laminaria tent has been tried (*18*). Mifepristone given orally 36-48 h decreases the mean IAI (*19*), but increases the cost of treatment (*20*).

Mean IAI in our study was 11.8 ± 9.9 h, which was comparable to other studies using 400 μg (*14*,*21*) and was 5 h less than a study published by Dickinson *et al.* (*3*). Mean dose requirement was less than the study by Dickinson *et al.* (2.64 and 3, respectively), with a total dose requirement being 1,054 μg and 1,200 μg, respectively. This higher dose requirement and longer IAI in the study of Dickinson *et al.* could be due to an inclusion of previous caesarian sections in their study. On the other hand, complete abortion rate was similar to the previous study (*14*).

Side effects such as fever and diarrhea were minor in nature, which could be due to less frequent dosages. It has been shown in the previous study that serum levels of misoprostol could accumulate when vaginal misoprostol was repeated at an interval shorter than 6 h (*14*), therefore a 6 hourly dosage schedule seems to be more practical and associated with less chance of hypertonicity besides being more convenient with a better side effect profile. This has been supported by a previous comparative study showing that vaginal administration of 400 μg was more effective than a 200 μg regime and that side effects were lower than a 600 μg dose (*22*).

In conclusion, vaginal misoprostol for second trimester abortion seems to be a cheap, convenient, and effective choice.

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