Second Trimester Medical Termination of Pregnancy with Combined Intracervical and Intravaginal Misoprostol: Comparative Analysis with Intravaginal Misoprostol—A Pilot Study

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Abstract

Context Intravaginal placement of misoprostol has been used extensively to terminate second trimester pregnancies. Intracervical misoprostol is an alternative method of termination of pregnancy for women in this period of gestation.

Objective To assess the efficacy and safety of combined intracervical and intravaginal misoprostol in the management of mid-trimester medical termination of pregnancy and to compare it with intravaginal misoprostol.

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Materials and Methods In this IRB approved prospective study, twenty-two women (mean age 25.4 ± 3.2 years, range 23–32 years; mean BMI 22.3 ± 3.4 kg/m²; mean parity 2.1 ± 1.4 , average gestational age 17.9 ± 2.4 weeks) underwent second trimester termination of pregnancy at our institution. Patient cohort was randomized into two treatment protocols depending on the drug used and route of administration. Induction-abortion interval, need for surgical evacuation, completeness of abortion and side effects if any were documented.

Results Mean induction-abortion interval for intravaginal group and combination group was comparable ($t = 7.9 \pm 1.8$ and 6.5 ± 3.5 h, respectively). Three patients required surgical evacuation for incomplete abortion ($n = 2$ after vaginal misoprostol and one after intracervical–intravaginal misoprostol). Number of patients aborting within 6 h was more in the intracervical–intravaginal group (36.3 %). Patients with intracervical misoprostol complained of abdominal pain more often than

those in other groups. Excessive bleeding and uterine rupture was not seen in any patient.

Conclusion Intracervical misoprostol is an effective method of medical treatment of second trimester pregnancy failure. Its short induction to abortion interval and acceptable safety profile makes induction via the cervical route acceptable for second trimester abortion.

Keywords Second trimester termination · Misoprostol · Medical termination of pregnancy · Intracervical misoprostol

Introduction

Medical induction has become the mainstay in the management of second trimester abortion [1, 2]. Reasons for this include the non-requirement of anesthesia or a skilled operator, and the abortus is usually delivered intact which aids in genetic diagnosis. Misoprostol is a useful agent for both first and second trimester termination of pregnancy [3–5]. This agent is readily absorbed after sublingual, buccal, vaginal and rectal administration. However, data are lacking on the pharmacokinetics of intracervical misoprostol for medical abortion [6]. Intracervical administration could potentially allow for better absorption of the drug due to dense vascularity of the cervix. Further, it may allow for better local drug action, thereby reducing the overall dosage and by decreasing the incidence of side effects of misoprostol.

The purpose of this pilot study is to determine the efficacy and safety of intracervical administration of misoprostol in the management of second trimester pregnancy termination and to compare it with other treatment protocols that exist in practice. The authors reviewed records of 22 patients at our institution who underwent mid-trimester termination of pregnancy, the results of which are given below.

Materials and Methods

Study Design

The authors conducted a prospective study at a single academic medical center. Our study was compliant with guidelines set by the Human Research Committee of our Institutional Review Board (IRB). Written informed consent was obtained from all subjects.

Patient Selection

Between December 2014 and July 2015, we studied women admitted for second trimester termination of

Fig. 1 Flowchart study outline

pregnancy. The study cohort was recruited from the community at large. Indications for performing a medical termination of pregnancy were as per guidelines of MTP Act of India. Termination was done for one or more of the following reasons: in order to save the life of the woman, to prevent grave injury to mental and physical health of woman, in view of substantial risk if child was born and it would suffer from such mental or physical abnormalities it would be handicapped, pregnancy due to rape or if it were caused due to failure of contraception. Excluded were patients hypersensitive to prostaglandins or in whom this group of drugs was contraindicated, severe anemia ($Hb < 5 \text{ g \%}$), low lying placenta, scarred uterus, coagulation disorder, current uncontrolled hypertension, cardiac disorder, jaundice or renal disease. Those women satisfying the aforementioned criteria were admitted to the emergency ward.

History and physical examination was recorded, and an ultrasonographic evaluation was done to confirm the gestational age of the fetus, placental localization and uterine abnormalities. Patients were subsequently randomized into two groups: Group I patients received 600 µg misoprostol placed within the posterior fornix of the vagina. Group II patients were given 200 µg intravaginal misoprostol and 200 µg intracervical misoprostol. Induction-abortion interval, need for surgical evacuation, completeness of abortion and side effects if any were documented for the groups (Fig. 1).

Results

A total of 22 women were included in the study (mean age 25.4 ± 3.2 years, range 23–32 years; mean BMI $22.3 \pm 3.4 \text{ kg/m}^2$; mean parity 2.1 ± 1.4). The mean gestational age was 17.9 ± 2.4 weeks as determined by ultrasonography. Average age, parity and gestational age were comparable in those patients undergoing abortion

Table 1 Demographic data of study population

	Intravaginal misoprostol	Intracervical + intravaginal misoprostol
Number	11	11
Mean age	24.3	26.4
Mean parity	2.0	2.2
Gestational age	17.2 ± 1.8	19.4 ± 3.9

Table 2 Induction abortion interval for two groups used in the study

Time period (in hours)	Intravaginal misoprostol	Intracervical + intravaginal misoprostol
0–5	3	4
5–10	7	7
10–15	1	–
15–20	–	–
20–25	–	–

Table 3 Side effects of the two induction strategies for second trimester termination of pregnancy

	Intravaginal misoprostol	Intracervical + intravaginal
Abdominal pain	2	4
Nausea/vomiting	1	1
Fever	–	–
Retained placenta	2	1
Bleeding	1	2

with intravaginal and a combination of intravaginal and intracervical misoprostol (Table 1). The average induction-abortion interval for intravaginal misoprostol was 7.9 ± 1.8 and 6.5 ± 3.5 h for misoprostol placed in the

vagina and cervix. Eighty percent of women in the intravaginal group aborted along with the placenta, while 10 of 11 in the group where both intravaginal and intracervical misoprostol was used aborted completely.

All patients in the second group aborted within 10 h. Abdominal pain was seen more often with intracervical misoprostol ($n = 4$). In contrast, this was less frequently observed with intravaginal drug administration ($n = 2$). Bleeding during and after delivery of the abortus and placenta was more common with intracervical misoprostol ($n = 2$). However, this side effect was seen in only 10 % of women in whom the drug was placed intravaginally. None of the patients with bleeding needed blood product supplementation. Nausea and vomiting were seen in only one patient in each group. This complaint subsided with injectable antiemetics. Fever was not noted in either of the groups (Tables 2 and 3; Fig. 2).

Discussion

Mid-trimester abortion has gained significant importance primarily due to its ethical and medicolegal aspect. Reasons for second trimester termination include increased surveillance of antenatal defects in the fetus as well as improvement in sonographic technology. However, for academic gynecologists, the debate still exists on the most favorable method of termination of pregnancy for women in this period of gestation. Ghorab et al. [7] found intracervical administration of misoprostol to be effective and well tolerated for mid-trimester termination with fewer side effects and no complications. In their study, all women in the intracervical group aborted within 20 h and 18 (90 %) within 13 h with a mean induction-abortion interval of 10.3 ± 4 h. Paz et al. studied twenty women with early pregnancy failure who received intracervical misoprostol

Fig. 2 Bar chart performance of intravaginal misoprostol and combined intravaginal–intracervical misoprostol for second trimester termination of pregnancy

via an endometrial sampling cannula. The authors noted that the mean time of induction of pharmacologic treatment to abortion was 13.6 h [8]. Abortion within 24 h occurred in 16 (80 %) women, and complete abortion was achieved in 14 (70 %) cases.

The authors in this study selected a dose of 600 µg for intravaginal misoprostol for the control group, as this is the dose commonly employed for second trimester termination of pregnancy. For intracervical placement, a dose level of 200 µg was selected as higher doses have the potential to cause tetanic uterine contractions and the possibility of uterine rupture. Intravaginal placement appears to be easier; however, there is a possibility of reduced absorption of drug in the case of vaginal dryness or reduced vascularity. Intracervical insertion of misoprostol has a better likelihood of the drug staying in situ if the patient is ambulatory but can be tedious if the cervical os is closed.

The results of our small study demonstrate the efficacy of the intracervical administration of misoprostol with the 24-h abortion rate of 80 % and with the mean time from the first dose to abortion of 10.3 ± 4 h. Further research for determining the maximal safe intracervical dosage needs to be undertaken. Additionally, more work needs to be done to compare intracervical with other common sites of administration of misoprostol such as the oral and sublingual routes.

Conclusion

Intracervical misoprostol is an effective method of medical treatment of second trimester pregnancy failure. Its short induction to abortion interval and acceptable safety profile via cervical route makes this method of induction acceptable for second trimester abortion. Further studies with a

larger patient cohort are needed to establish this method of abortion.

Compliance with Ethical Standards

Conflict of interests All authors have no conflict of interest.

Ethical Standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5).

Informed Consent Informed consent was obtained from all patients for being included in the study.

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