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Intrauterine Extra-amniotic Misoprostol Solution is Effective for Termination of Second Trimester Missed Abortion: A clinical pilot descriptive study

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ABSTRACT

Objectives: The purpose of this study was to determine the efficacy and safety of intrauterine extra-amniotic misoprostol solution for termination of the second trimester missed abortion.

Materials and Methods: A clinical pilot descriptive study was done in Women Health Hospital, Assiut University, Egypt between March 2015 and June 2015. Fifty patients having missed abortion of gestational age between 13 to 24 weeks were included in the study. Insertion of an intrauterine Foley's catheter followed by infusion of sterile misoprostol solution through a sterile infusion set at a constant drip rate. The primary outcome was successful expulsion of the fetus in 12 hours after starting misoprostol infusion.

Results: The mean age of the study group was 27.25±4.08 years, the mean BMI was 26.35± 3.6 kg/m^2, the mean gestational age was 22.85±3.4 weeks and the mean parity was 2.5±1.5. The mean induction expulsion interval was 5.27±2.66 hours. Six cases (12%) needed analgesic. Surgical evacuation of retained contents was needed in 3 cases (6%). Side effects in the form of rigors, fever and diarrhea were recorded in 4 cases (8%). No serious maternal events were recorded.

Conclusion: Our results showed that intrauterine extra-amniotic misoprostol solution instillation appeared to be effective and safe for termination of a second trimester missed abortions.

Keywords: Misoprostol, foley catheter, pregnancy termination, second trimester

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Introduction

Second-trimester abortions constitute of 10% to 15% of all induced abortions worldwide but are responsible for two-thirds of major abortion-related complications[1, 2]. Both surgical (dilatation and evacuation) and medical induction of labor options are available, each with its own advantages and complications[3].

Medical methods for second trimester induced abortion have improved considerably during the last

decades in terms of efficacy and safety; however, a variety of regimens remain in use[4]. Induction of abortion was used frequently when the risks to the mother with expectant treatment outweigh the risks that are involved with the intervention when the fetus is dead. A range of methods, including mechanical and pharmacological methods, are available for cervical ripening, like the transcervical Foley catheters which is frequently used[5]. Cervical ripening with a Foley catheter had several advantages over pharmacological methods especially avoiding hyperstimulation[5].

Pharmacological methods, including prostaglandin E1 (misoprostol) and prostaglandin E2 preparations (dinoprostone), became a treatment of choice in many countries[6].

Misoprostol (PGE1) is increasingly used for second-trimester termination of pregnancy[1, 7]. Misoprostol is a synthetic PGE1 analog (15-deoxy-16-hydroxy-16-methyl PGE1), initially developed for the prevention and treatment of peptic ulcer it is registered for obstetric indications, including abortion, in a few countries. It is inexpensive, stable at room temperature and it is rapidly absorbed by vaginal, sublingual, buccal and oral routes[1]. Side effects are the main disadvantage of misoprostol and can occur in up to 30% of the patients[8].

Titrated oral misoprostol solution was as effective and safe for labor induction as vaginal misoprostol tablets[9]. Our hypothesis was that using misoprostol via intrauterine extra amniotic route may be more effective and associated with few side effects. To our knowledge, there are no trials that used misoprostol solution via intrauterine extra amniotic route for termination of second-trimester gestation.

Materials and Methods

Study design:

This is a clinical pilot descriptive study to assess the efficacy and safety of using misoprostol solution through intrauterine extra amniotic route for termination of a second-trimester missed abortions.

Participants:

The study group included 50 healthy women with second-trimester missed abortion (defined as abortion between 14 and 24 weeks of gestation) at Women Health Center, Assiut University, Assiut, Egypt. Gestational age was determined by last menstrual period and fetal size ultrasonic estimation. Eligibility criteria included being 14–24 weeks of gestation with missed abortion presenting with a closed cervical os and no vaginal bleeding, and being willing to follow the study protocol.

Exclusion criteria included women with a previous caesarean section, low lying placenta; known allergy to misoprostol, or oxytocin; premature preterm rupture of the membranes; history of recent asthma; a known coagulation disorder or past thromboembolic event; history of chronic adrenal failure.

After recruitment, the patients were given a detailed explanation about the study protocol and only those who agreed to participate in the study signed an informed consent. The study protocol was approved by our institutional ethical Committee of Assiut Faculty of Medicine.

All women were examined clinically to assess their general conditions before the intervention. All demographic and social data of the participants were collected and kept confidentially. Vital signs were recorded regularly and any side effect or complications were recorded and managed immediately

Intervention:

Foley's catheter introduced transcervical with direct visualization by use of a vaginal speculum under complete sterile conditions in the operative theater. Cleaning of the cervix with an aseptic solution (chlorhexidine) was done. After passing the internal os, the catheter balloon was inflated with 30 ml of sterile water, and the external end of the catheter was taped to the thigh.

Infusion set was fixed to the Foley's catheter at the opening of its drainage side after cutting part of this opening to allow tight fixation of the infusion set. Then, an infusion of 500 cc of saline was loaded by 500 microgram misoprostol (2 and half tablets of misoprostol

solved in this 500 cc of saline) and given at 20 drops per minute (2 microgram of misoprostol extra-amniotically per minute), as each milliliter of normal saline contain one microgram of misoprostol (Misotac – Segma pharmaceutical company).

This means that the dose of 20 drops per minute contains only 2 micrograms of misoprostol solution and the dose was not increased by increasing the drops. When the catheter was expelled from the vagina spontaneously, the patient will be examined and oxytocin may be started after the expulsion of the fetus and the placenta. Prophylactic broad spectrum antibiotic were every 12 hours during the procedure using third generation cephalosporin intravenously.

After starting the misoprostol infusion, blood pressure, temperature, side effects, and bleeding were monitored every 3 hours. Oral or parenteral analgesia was provided as needed. If the products of conception were passed and appeared complete (including the placenta) within 12 hours of the start of extra-amniotic misoprostol infusion, the procedure was considered complete and no further interventions were given.

If fetal expulsion did not occur within 12 hours from the start, the induction was considered a failure and the woman was offered standard evacuation. However, if the fetus was expelled but the placenta remained in the uterus after an additional 30 minutes, the woman could be given an oxytocin intravenous infusion to help placental expulsion. If placental expulsion still did not occur or there was heavy bleeding, health care provider was instructed to remove remaining products surgically.

All women were given the standard postabortion care and discharged within 48 hours.

The primary outcome measure was successful expulsion of the fetus in 12 hours after starting misoprostol infusion. Secondary outcomes included time until the expulsion of the fetus, the rate of adverse outcomes, need for another intervention either medically or surgically for completing abortion and the need for analgesics.

Statistical analysis

Analysis of data was done using the statistical package for social science (SPSS Inc., Chicago, version 18). Continuous variables were presented in terms of mean, standard deviation. Qualitative variables were expressed as number and percentage.

Table 1. Induction characteristics and outcome data.

Outcomes	No	Mean±SD
Interval from start of induction to start of contractions[1]	50	62.5±44.7 minutes = (1.04±0.74 hours)
the mean duration of interval from start of induction to complete expulsion of contents of pregnancy was[1]	50	316.5±219.7 minutes = (5.27±2.66 hours)
The need for analgesia[2]	6	12%
Need for surgical evacuation of remnants[2]	3	6%
Side effects (rigors, fever or gastrointestinal symptoms)[2]	4	8%

1 Data expressed as mean±SD

Results

Fifty-two consenting patients who fulfilled the eligible criteria were enrolled in this clinical trial. Fifty patients completed the trial and their data were included in the final analyses.

The mean age for these fifty women was 27.25±4.08. The mean BMI was 26.35±3.6. The mean gestational age was 22.85±3.4. The mean parity was 2.5±1.5. The mean duration of time from the start of induction to start of contraction was 62.5 ±44.7 minutes

(equal to 1.04±0.74 hours) and the mean interval from the start of induction to complete expulsion of contents of pregnancy was 316.5±219.7 minutes (equal to 5.27±2.66 hours). All cases (100%) were successfully expelled the abortus within 12 hours from the start of misoprostol infusion.

The mean dose of misoprostol solution was 316.5±219.7 microgram. Analgesia in the form of one vial of non steroidal anti-inflammatory analgesic was needed in 6 cases (12%). Surgical evacuation of retained contents under general anesthesia was needed in 3 cases (6%). Side effects in the form of rigors, mild degree of fever (defined as body temperature < 38) or diarrhea (defined as increased frequency of defecation of loose stools) were recorded in 4 cases (8%) and did not require any medications (Table 1).

Discussion

Termination of pregnancy is a common obstetric problem and is considered as a great challenge to obstetricians[10]. Termination of second-trimester pregnancy has been reported to be associated with 3-5 times higher morbidity and mortality risks than termination during the first trimester[11].

The prostaglandin E1 analog misoprostol is commonly used in Egypt to induce medical abortion in the second trimester[12]. Misoprostol is absorbed rapidly when administered oral, vaginal, rectal or intracervical. Different studies were performed to evaluate misoprostol, vaginal, oral, sublingual or buccal for second-trimester termination. There were different results on the success rate of pregnancy termination in 24 hours, in 48 hours, the time interval between induction and fetal expulsion and the side effects between groups. Medical abortion in the second trimester using the combination of mifepristone and misoprostol appeared to have the highest efficacy and shortest abortion time interval. Where mifepristone is not available, misoprostol alone is a reasonable alternative[13].

Although the World Health Organization recommends a combination of mifepristone and misoprostol, mifepristone is not available in some countries, including Egypt, because of its high cost and negative connotations (it is known as an emergency contraceptive and an abortifacient, with resulting ethical dilemmas in conservative Muslim societies)[14-15].

The optimal route for administering misoprostol is vaginal, as this route is associated with slower absorption lower peak plasma levels, greater exposure to the drug and greater effects on the cervix with a lower rate of gastrointestinal side effects[13, 16].

The use of a combination of intracervical Foley catheter and vaginal misoprostol for induction of second-trimester abortion was assessed in recent studies with contrary results[17-18]. Toptas et al reported in their observational study on 91 pregnancies that the efficacy of intravaginal misoprostol and Foley catheter insertion combination was comparable to that of intravaginal misoprostol alone in terms of time to abortion/birth 14.33 (11.33-17.25) hours and 12.08 (9.50-15.33) hours, respectively[17].

In contrast, Rezk et al found a high success rate with the shortest induction to abortion interval with a combined use of intracervical Foley catheter and misoprostol for termination of second-trimester pregnancy[18]. To our knowledge, no one used titrated misoprostol solution extra-amniotically via Foley catheter for pregnancy termination during second-trimester gestation. In this study, the induction to expulsion interval was 5.27± 2.66 which is shorter than the finding of Rezk et al 7.5±1.25 h in the combined group[18].

The success rate, the side effects and need of analgesia were comparable to that achieved by Rezk et al[18]. In this study, there were no major complications encountered and no maternal mortality. Limitations to this study included non-comparative randomized study, done in cases with missed abortion only and the acceptability of the intervention was not assessed by questionnaire at a follow-up visit.

In conclusion, intrauterine extra-amniotic misoprostol solution appears to be an effective and safe for termination of second-trimester gestation with shorter induction expulsion interval. Further large sample randomized clinical studies are needed to confirm our results.

Potential conflicts of interest

The authors declare no conflict of interest.

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