Oral misoprostol in the prevention of uterine bleeding after surgical evacuation of first trimester abortion: A comparative study of three uterotonic agents

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Abstract

Objective: This comparative study was aimed at determining the effectiveness of oral Misoprostol compared with intravenous Ergometrine and intravenous Oxytocin in reducing vaginal bleeding following surgical evacuation for first trimester abortions.

Materials and Methods: This was a single-blind placebo-controlled study in which patients with first trimester uncomplicated abortions were divided into three groups using computer-generated randomization table. The first group was administered oral Misoprostol, the second group had intravenous Ergometrine, and the third group was administered intravenous Oxytocin. The uterotonic agents were administered before the surgical evacuation was carried out.

Results: There was statistically significant reduction in blood loss after the evacuation in the Misoprostol group ($P < 0.000$). There was also significant reduction in the number of days of bleeding in the Misoprostol group (2.00 ± 0.86) compared with 4.43 ± 0.92 and 4.64 ± 1.06 days in the Ergometrine and Oxytocin groups, respectively ($P < 0.000$). There were, however, more gastrointestinal side effects in the Misoprostol and Ergometrine groups (60.7% and 57.1%, respectively) compared with the Oxytocin group.

Conclusion: Oral Misoprostol appeared to demonstrate superior efficacy in reducing uterine bleeding after surgical evacuation, compared to the other commonly used uterotonic agents.

Key words: Abortion, first trimester, misoprostol, uterotonic agents, uterine bleeding

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Introduction

Abortion is a common complication of pregnancy and may either be spontaneous or induced. It is difficult to estimate the precise number of abortions due to underreporting, especially in developing countries. Spontaneous abortion is said to occur in about one-fifth of pregnancies, an estimate based on hospital data.[1] Induced abortion also is difficult to estimate, particularly in countries with restrictive abortion laws such as in Nigeria and other countries in Africa. Induced abortion is underreported because it is criminalized in many countries. The high incidence of induced abortion is partly due to the low contraceptive prevalence, and as such, many unwanted pregnancies are often aborted and by unsafe methods. According to the World Health Organization (WHO), annually about 79 million unintended pregnancies, excluding miscarriages, occur worldwide.[2]

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Irrespective of the type of abortion, one of the commonest complications seen is persistent bleeding which is often due to the retained products of conception.[3] In fact, complications from abortion are common in Nigeria as over half of the women interviewed in a survey reported that they had suffered complications following abortions.[2] Complications from abortions resulted in the death of over 3000 women annually in Nigeria.[2]

To prevent persistent uterine bleeding after abortion, evacuation of the retained products of conception is usually carried out. This may be medical or surgical evacuation. After surgical evacuation of the retained products of conception following abortions, uterotonic agents such as Oxytocin and Ergometrine have traditionally been used to control uterine bleeding. In fact, the two uterotonic agents were the ones recommended by the Nigerian Federal Ministry of Health.[4]

Misoprostol, a synthetic prostaglandin E1 analogue, has been extensively used for cervical ripening prior to the induction of labor and even to induce labor and for the control of postpartum hemorrhage.[5-9] Its use to control uterine bleeding after surgical evacuation of the uterus following first trimester abortion has not been widely studied in our environment.

Objectives of the study

The objectives of this comparative study are to compare the safety, tolerability, and clinical effectiveness of oral Misoprostol, intravenous Oxytocin, and intravenous Ergometrine in the management of uterine bleeding after surgical evacuation of first trimester abortion.

Materials and Methods

This was a single-blind placebo-controlled study. Approval for the study was obtained from the Ethics and Research Committee of the Obafemi Awolowo University Teaching Hospitals Complex. A total of 84 women who had missed abortion, inevitable or incomplete spontaneous abortion, and induced abortion without sepsis or organ perforation between 6 and 12 weeks of pregnancy were randomized into one of three arms: Oral Misoprostol or intravenous Oxytocin or intravenous Ergometrine. Excluded from the study were hemodynamically unstable patients, patients with septic abortion, and those with glaucoma or with known hypersensitivity to the three agents. Patients with hypertension and women who refused to give consent were also excluded from the study.

Each woman had adequate pre-operative counseling and evaluation. Informed consent was obtained from each woman. The women were randomized into each arm of the study by computer-generated table of random numbers.

Patients in each arm were administered the following according to the group:
Group 1: Oral Misoprostol 400 μg
Group 2: Intravenous Ergometrine 0.5 mg
Group 3: Intravenous Oxytocin 10 IU.

Women in Group 1 (oral Misoprostol) had 1 ml of normal saline administered intravenously as placebo, while the women in the Oxytocin and Ergometrine arms of the study were administered two lactose tablets as placebo.

Each patient was asked to empty her bladder and was placed in lithotomy position. The vagina, vulva, pubis, perineum, and inner aspects of the thighs were cleaned with chlorhexidine solution and sterile drapes were applied. Bimanual pelvic examination was done and the findings were noted. A Cusco's speculum was introduced to retract the vaginal walls, thereby exposing the cervix. The anterior lip of the cervix was held with a sponge holding forceps, gentle downward traction applied, and the area between the smooth cervical epithelium and the vaginal epithelium was identified. A 3.5-cm, 22-G needle mounted on a 10 ml syringe containing 0.5% lignocaine solution without adrenaline was used to inject 2 ml of the anesthetic solution just under the epithelium not deeper than 3 mm at 2, 5, 7, and 10 O'clock positions. At the conclusion of the set of injections, 2 min was allowed for the anesthetic agent to show its effect. An appropriate sized suction cannula was selected and introduced into the uterine cavity with uterine sounding done to determine its depth. This was then connected to the Manual Vacuum Aspiration syringe after a vacuum had been created in it. The vacuum was released and the products of conception were evacuated by a gentle rotary and in and out motion of the cannula until gritty sensation was felt and foamy blood came out of the uterine cavity. An appropriate Oxytocin agent was then administered. Weighed sterile pads were placed over the perineum after the procedure. All products were then sent for histopathologic examination.

Blood loss from each patient was determined within the first 6 h postoperatively using gravimetric methods with a digital weighing scale Model: Adventurer Pro AV313C manufactured by Ohaus Corporation, Pine Brook, NJ, USA with standardized sterile fixed-sized gauze pads of size 10 × 10 cm of known weight in grams, which was applied as vaginal packs immediately after the procedure and removed 6 h later and re-weighed in grams. This gave the amount of blood loss in milliliters. The patients were discharged home within 24 h after the surgical evacuation and were seen within 1 week after discharge at the outpatient clinic to determine if there were any complications and to determine the duration of bleeding. Women who could not attend the outpatient clinic were followed up by telephone calls.

Information obtained at the end of the study was processed by Statistical Package for Social Science (SPSS) version 17.

Descriptive statistics such as means, frequencies, and proportions were used to summarize variables depending on the variable type. The mean estimated blood loss and duration of bleeding were compared between the three study groups using the one-way analysis of variance (ANOVA) and the level of significance was set at 0.05.

Results

There was statistically significant reduction in the mean volume of blood loss after the evacuation in the Misoprostol group with mean blood loss of 29.3 ± 4.0 ml, compared with a mean loss of 38.5 ± 5.2 ml and 34.3 ± 6.4 ml in the Ergometrine group and the Oxytocin group, respectively ($P < 0.05$) Table 1. There was also a significant reduction in the number of days of vaginal bleeding in the Misoprostol group (2.00 ± 0.86 days) compared with 4.43 ± 0.92 and 4.64 ± 1.06 days in the Ergometrine and Oxytocin groups, respectively ($P < 0.05$) Table 2.

There was also a positive correlation between the gestational age and amount of bleeding ($P = 0.02$), but there was none between gestational age and the number of days of bleeding ($P = 0.187$).

Gastrointestinal side effects were the most common side effects, and these were more in patients in the Misoprostol group [17 (60.7%)] compared with 16 (57.1%) and 5 (17.9%) in the Ergometrine and Oxytocin arms, respectively. This was statistically significant ($P < 0.001$).

Discussion

The demographic characteristics of patients in each arm of the study as well as the indications for surgical evacuation were not statistically different [Tables 3 and 4]. The blood loss within the first 6 hours after surgical evacuation was less in the Misoprostol group. In a similar study carried out at the Women Health Centre, Assiut University, Egypt, by Shokry *et al.*, oral Misoprostol was effective in reducing the prevalence and amount of vaginal bleeding after surgical evacuation for first trimester abortion, compared with the group that had no Misoprostol.[10] Similar results were obtained in this study despite using lower dosage of Misoprostol compared to the Egyptian study. Also, unlike the Egyptian study, this study compares the efficacy of oral Misoprostol with that of other uterotonics agents, and to minimize cost, a single oral dose of 400 μg of Misoprostol was used.

One of the reasons for persistent uterine bleeding after abortion is the retained products of conception.[3] Stronger uterine contraction induced by Misoprostol may lead to complete uterine evacuation, thereby leading to reduced

Table 1: Comaprison of volume of blood loss post-evacuation by one-way ANOVA (in ml)

	n	Mean	Std. deviation	Std. error	95% confidence interval for mean		Minimum	Maximum
					Lower bound	Upper bound		
Misoprostol	28	29.2500	4.03343	0.76225	27.6860	30.8140	21.00	34.00
Ergometrine	28	38.4643	5.18175	0.97926	36.4550	40.4736	31.00	48.00
Oxytocin	28	34.3214	6.41210	1.21177	31.8351	36.8078	21.00	49.00
Total	84	34.0119	6.46304	0.70518	32.6093	35.4145	21.00	49.00

F statistics=21.238 and *P*<0.000

Table 2: Comparison of duration of uterine bleeding post-evacuation by one-way ANOVA (in days)

	n	Mean	Std. deviation	Std. error	95% confidence interval for mean		Minimum	Maximum
					Lower bound	Upper bound		
Misoprostol	28	2.0000	0.86066	0.16265	1.6663	2.3337	1.00	4.00
Ergometrine	28	4.4286	0.92009	0.17388	4.0718	4.7853	2.00	6.00
Oxytocin	28	4.6429	1.06160	0.20062	4.2312	5.0545	3.00	7.00
Total	84	3.6905	1.52865	0.16679	3.3587	4.0222	1.00	7.00

F statistics=66.684; *P* value=0.000

Table 3: Demographic characteristics of the study groups

Demographic data	Misoprostol group	Ergometrine group	Oxytocin group	*P* value	Outcome
Age (years)	26.5±2.9	26.3±3.6	27.1±5.3	0.71	Not significant
Gestational age (weeks)	9.6±1.4	8.9±2.3	9.1±1.4	0.23	Not significant
Body mass index (kg/m^2)	24.3±3.5	25.7±3.4	25.4±4.2	0.33	Not significant
Gravidity	2.7±1.3	2.4±1.2	2.9±1.5	0.49	Not significant
Parity	1.8±1.2	1.4±1.2	1.9±1.6	0.36	Not significant

Table 4: Indication for surgical evacuation in the three groups

	Clinical data: Indication			Total
	Incomplete	Missed	Inevitable	
Study group				
Misoprostol	25	2	1	28
Ergometrine	25	1	2	28
Oxytocin	26	1	1	28
Total	76	4	4	84

bleeding and risk of uterine infection. Though the other uterotonic agents used in this study (Ergometrine and Oxytocin) also induce strong uterine contractions, they may be less potent because they need stringent storage conditions like constant refrigeration which may not be readily available in developing countries, especially in the rural areas where majority of the populace resides with little access to constant power supply. Oxytocin and Ergometrine lose their potencies when exposed to direct sunlight and due to poor storage conditions.[7] The WHO has in fact drawn attention of practitioners in the developing countries to these shortcomings.[8] Another major disadvantage in the use of both Oxytocin and Ergometrine is that they are administered parenterally unlike Misoprostol which is effective when administered orally.

Conclusion

This study showed that a single oral dose of Misoprostol is better than parenteral administration of either Oxytocin or Ergometrine in reducing the amount and duration of vaginal bleeding after surgical evacuation of a first trimester abortion. Oral Misoprostol was, however, associated with more gastrointestinal side effects.

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