Original Article

Misoprostol versus Manual Vacuum Aspiration for Treatment of First-Trimester Incomplete Miscarriage in a Low-Resource Setting: A Randomized Controlled Trial

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Abstract

Background: Manual vacuum aspiration is a safe and effective technology for the treatment of incomplete miscarriage but it is not widely available and affordable in rural areas particularly in low-resource countries. Misoprostol is an alternative to manual vacuum aspiration for the treatment of incomplete miscarriage. **Aim:** To compare the effectiveness, client acceptability and satisfaction, and cost-effectiveness of misoprostol with manual vacuum aspiration for the treatment of the first-trimester incomplete miscarriage. **Subjects and Methods:** This study was conducted between February 1, 2018 and August 31, 2018 at Alex Ekwueme Federal University Teaching Hospital Abakaliki, Nigeria. 100 participants were randomized to treatment with either manual vacuum aspiration or 600 μg oral misoprostol. The main outcome measures assessed at 1-week follow-up were complete uterine evacuation, client acceptability and satisfaction, and cost-effectiveness. Data were analyzed using SPSS version 25. Sociodemographic characteristics, treatment outcomes and other variables were summarized by descriptive statistics. Chi-square test was used for comparison between groups as regard categorical data while Student's '*t*' test was used for comparison between groups for continuous data. *P* value of <0.05 was regarded as statistically significant. **Results:** There was a higher failure rate in the misoprostol arm when compared with MVA. Although this difference in complete uterine evacuation rate did not reach statistical significance (81.3% versus 95.7%, RR = 4.3, 95% CI 0.98-18.9, *P* value = 0.05), more participants in the misoprostol arm would choose the method again when compared with women in the MVA group (47 versus 30, X^2 = 16.95, *P* < 0.001). The mean client satisfaction score was significantly higher among women in the misoprostol arm compared to MVA group (13.2 (2.1) versus 7.3 (4.6), *P* < 0.001). The mean cost of primary treatment was higher in the MVA group compared with misoprostol arm ($67.8 (8.9) versus 14.4 (4.0), *P* < 0.001). There was no significant difference in the mean cost of repeat uterine evacuation in both study arms (MVA, $64.9 (6.3) versus misoprostol, $65.76 (6.6), *P* = 0.86). **Conclusion:** Although medical treatment was associated with a higher failure rate, there was no statistically significant difference in the effectiveness of both treatment methods. However, medical treatment was associated with higher client acceptance and satisfaction and was more cost-effective than surgical treatment.

Keywords: *Incomplete miscarriage, manual vacuum aspiration, medical management, misoprostol, surgical management*

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Introduction

Complications of abortion is a major public health problem throughout the world as it endangers

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women's lives and contributes significantly to maternal morbidity and mortality.[1-5]

Although approximately 15% of all pregnancies end in miscarriages, there are also an estimated 46 million induced abortions annually.[2,3] Many of these are performed illegally in an unsafe environment resulting in approximately 78,000 deaths annually worldwide, with the majority of these deaths occurring as a result of septicemia and hemorrhage.[4] In addition, many more women suffer long-term morbidity from pelvic infection, uterine perforation, anemia, and infertility.[5] About 8.5% of all maternal deaths between January 1999 and December 2008 were estimated to be due to abortion complications in a study done in a tertiary health institution in Abakaliki.[6]

In Nigeria, treatment of incomplete miscarriage often involves evacuation of the uterus with manual vacuum aspiration (MVA). Uterine evacuation with MVA, highly effective technology, and useful in low-resource settings, were the "gold standard" of care for women with incomplete miscarriage until recently.[7] However, in remote areas of Nigeria, the shortage of skilled healthcare providers and equipment often limits women's access to treatment with MVA.[8] In some settings, mid-level providers face barriers to providing post-abortion care services including restrictive facility policies and lack of training opportunities.[8] Research has shown insufficient use of, inadequate access to, and low availability of uterine evacuation services in Nigeria despite the great need.[8]

Misoprostol is cheap, safe, heat-stable, easy to store, and requires no surgical skills to administer, making it attractive for use in sub-Saharan Africa.[9] In recent times, misoprostol has replaced MVA as a treatment of choice for incomplete miscarriage in the absence of sepsis or hemorrhage.[9] However, when incomplete miscarriage is complicated by genital tract sepsis or profuse hemorrhage, MVA has a clear advantage over misoprostol because its use allows immediate evacuation of retained products of conception.[9] Misoprostol use for incomplete miscarriages could decrease the burden on healthcare facilities and skilled surgical providers while also reducing the need for surgical equipment, supplies, anesthesia, and cutting costs to healthcare systems worldwide.[10] However, unlike MVA, the use of misoprostol for treatment of incomplete abortion requires ultrasound examination to confirm complete uterine evacuation.[11,12] This limits its use for post-abortion care in rural areas of developing countries where ultrasound equipment is not readily available.

In a meta-analysis, surgical treatment was significantly more effective (97%) than medical treatment (84%) when the main outcome was complete abortion but it is not known which approach is more cost-effective.[11] Most of the studies on the comparison of misoprostol and MVA for the treatment of first-trimester incomplete miscarriage focused mainly on effectiveness and client satisfaction. Few studies compared the cost-effectiveness of the treatment methods and none of these studies was done in a low-resource setting. As the economic issues have been increasingly prioritized, comparative evaluation of the costs of the two treatment methods using quantitative indicator (the success of the primary treatment) is important especially in low-resource setting like Nigeria where majority of women are of low socioeconomic status and where poverty is one of the main limiting factors to accessing healthcare.

Therefore, the aim of this study was to compare the effectiveness, client acceptability and satisfaction, and cost-effectiveness of misoprostol to manual vacuum aspiration for treatment of incomplete miscarriage in a tertiary health institution in Abakaliki.

Subjects and Methods

This is an open-label randomized controlled study conducted from February 1, 2018 to August 31, 2018 at the Gynecological Emergency Department of the Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Ebonyi State. Alex Ekwueme Federal University Teaching Hospital is a tertiary hospital within Abakaliki metropolis. It was formerly known as Federal Teaching Hospital, Abakaliki. Obstetrics and Gynecology Department is one of the ten clinical departments in the hospital. The department runs gynecology clinics, preconception, antenatal, intrapartum, and postnatal services. It is also a referral center to the surrounding maternities and hospitals. It receives a referral from the surrounding states of Cross River, Enugu, and Benue.

The study participants were women who had a diagnosis of incomplete miscarriage. Incomplete miscarriage in this study was defined by a history of amenorrhea and vaginal bleeding, an open cervical os confirmed by speculum examination, and evidence of retained products of conception on ultrasound examination. Inclusion criteria were uterine size < 13 weeks gestation on bimanual examination, clinically stable, and without signs of pelvic infection (such as foul-smelling vaginal discharge and fever, temperature > 39°C), or severe anemia (admission hemoglobin level ≤ 7 g/dl), or acute renal failure (defined as production of urine < 20 mL/h), no history of asthma, participant agrees to follow-up visit to confirm uterine evacuation and has access to a

functional telephone for follow-up contact. Moreover, women with a history of use of misoprostol prior to presentation who met other inclusion criteria were included in the study. Exclusion criteria were uterine size ≥13 weeks gestation, hemodynamic instability and with signs of infection or severe anemia, cervical injury (defined as obvious trauma to the cervix on speculum examination), history of asthma, cardiac, renal and liver diseases, and history of allergy to misoprostol.

A power analysis was performed before the study for sample size estimation based on a previous study,[12] which was used to calculate the effect size, using G*Power version 3.1.9.2 software.[13] To obtain a power of 90% at a 5% significance level with an effect size of 0.7 and the allocation ratio N2/N1 of 1, a sample of 88 participants were required. A priori power analysis showed that the sample size should be at least 44 in each study arm. By adding 10% attrition rate, the total sample size was 96.8. Therefore, 100 clients were recruited into the study and randomly assigned to each arm of the study.

At enrollment, the medical history, hemoglobin level and Rhesus antigen status were assessed and a physical examination was performed. A total of 100 consenting eligible women were randomized into two equal groups (ratio of 1:1), namely, the misoprostol group (A) and the MVA group (B). A statistician blinded to the study's objectives generated the allocation sequence by simple randomization using computer-generated random numbers. The allocation concealment was achieved by placing the allocation in sequentially numbered, opaque, sealed identical envelopes. The envelopes were secured and placed in the gynecological emergency ward from where they were drawn serially, by a nurse who was not associated with the study, until completion of the study. After obtaining written informed consent from an eligible woman, she was assigned a sequential number by the investigator who then called the nurse (keeping the envelopes) to open the corresponding envelope and assign the participant to the study group (A or B) indicated on the allocation paper in the envelope. Neither the clients nor researchers were blinded to the group assignment.

Women assigned to the misoprostol arm were given the drug orally in a dose of 600 mcg[14] (Cytotec, Pfizer pharmaceuticals, Nigeria). Women allocated to manual vacuum aspiration were transferred to the theatre where the researcher or an assistant evacuate the uterus using manual vacuum aspiration under conscious sedation. The products of conception were sent to the laboratory for histology. The research assistants were four resident doctors in obstetrics and gynecology who have spent 4 years in the department and 2 senior resident radiologists who performed ultrasound examinations.

Women in both groups were observed in the hospital for 4 h following treatment before discharge. They were given doxycycline (100 mg/12 h for 7 days) and metronidazole (400 mg 3 times daily for 5 days). Women in both groups were also provided with 500 mg paracetamol tablets to take, as needed, for pain. Information, including what should be expected following treatment and signs of possible complications requiring immediate hospital care, were given to all women. Before discharge, family planning options were discussed, and all women were scheduled for a 1-week follow-up visit and given a study card to record adverse effects experienced at home. In addition, participants were provided with the name and contact information of the study researchers to speak with in the event of complications (such as heavy vaginal bleeding, fever or foul-smelling vaginal discharge) or if they desire additional information about their treatment. The importance of the follow-up visit was stressed to all women. By day-to-day of the scheduled clinic appointment, participants were reminded of the clinic appointment and encouraged to attend a follow-up visit via phone call and text messages. Those who failed to return for follow-up were contacted via telephone to reschedule their appointments.

Treatment outcomes were determined at 1-week follow-up visit. Miscarriage status was assessed from clinical history and examination, in addition to an ultrasound scan of the uterus. Women with a closed cervical os and no vaginal bleeding with ultrasound confirmation of empty uterus were deemed to have undergone successful treatment at a one-week follow-up visit. Women with ultrasound confirmation of retained product of conception at follow-up visit underwent immediate uterine evacuation after counseling. A surgical treatment using MVA was done for all women in both study group with ultrasound confirmation of retained products of conception. Women who had reevacuation were followed up for an additional 1 week to assess complete evacuation of products of conception. Study participants were also assessed for evidence of genital tract sepsis (uterine or adnexal tenderness, pyrexia, or fouls smelling vaginal discharge) at a follow-up visit. After completion of treatment, patient satisfaction was evaluated using the Patient Perception Score Questionnaire (PPSQ). The questionnaire was modified to include information on the client acceptability of the treatment received. PPSQ is a standardized screening method for measuring client satisfaction with treatment.[15] It is a self-assessment scale which consists

of 3-item (communication, respect, and safety), with a 5-point Likert scale. Each response is rated from 1 (very unsatisfied) to 5 (very satisfied). The minimum score is 3 and the maximum score is 15. A total score for each participant was calculated by summing item responses. Siassakos *et al*. conducted a validity and reliability study for PPSQ among women with operative delivery.[15] In this study, the internal consistency of the instrument was high (Cronbach's $\alpha = 0.83$), suggesting that the PPSQ is a reliable and valid tool for the assessment of client satisfaction with the quality of healthcare. Literate patients were given the questionnaire to fill on their own while illiterate patients were assisted to fill the questionnaires by the researcher or the research assistant. A specially-designed proforma was used to collect information on the sociodemographic variables, treatment outcomes, and cost of treatment. Following the completion of the questionnaires, participants were discharged from the study after post-treatment hemoglobin concentration was determined. The participants flow through the study is shown in Figure 1.

The primary outcome measures were the complete evacuation of the uterus without recourse to surgical or medical intervention for any reason following initial study treatment, client acceptability and satisfaction with treatment method, and cost of treatment. Secondary outcomes were repeated uterine evacuation, pretreatment and posttreatment hemoglobin concentration, genital tract sepsis, and profuse bleeding after treatment requiring immediate evacuation with MVA. The cost of treatments was calculated by using the receipts of payment for each individual participants for the medications, outpatient and inpatient visits, and procedures. Only the direct hospital costs were analyzed because they give a relevant idea of the differences between the two treatments. Direct hospital costs consist of the clinical management pathway for producing the treatments and additional costs occurring during the treatment period.

Data were collected, tabulated, and analyzed using SPSS version 25, 2017 (IBM Corp, Armonk, New York, USA). Numerical variables were presented as mean ± standard deviation (SD) while categorical variables were presented as number and percentage. Chi-square test was used for comparison between groups as regard categorical data while Student's '*t*' test was used for comparison between groups for continuous data. The cost of treatment was derived from receipts of payment made to the hospital by each study participant. The total cost of primary treatment and the mean costs of primary and repeat uterine evacuation were calculated and compared for study arms. The incremental cost-effectiveness was calculated for the study. The incremental cost-effectiveness ratio (ICER) measures the additional costs for achieving an extra unit of effectiveness by adopting the experimental treatment over the standard. The ICER is calculated for the treatment by dividing the total costs of initial treatment by its effectiveness. The effectiveness was measured by complete uterine evacuation with no subsequent intervention after initial treatment. The incremental costs were compared with the incremental effectiveness (the success rate). P value < 0.05 was considered statistically significant.

The approval for the study was obtained from the Research and Ethics Committee of the Alex Ekwueme Federal University Teaching Hospital, Abakaliki (approval number: 10/08/2017-06/10/2017). All participants read and signed informed consent forms declaring that they voluntarily participated in the study. The purpose and process of the study were explained to all participants. They were informed that their participation was voluntary and that they could withdraw at any time for any reason without any penalty either personal or affecting their medical care. The written consent was obtained before a client was allowed to participate in the study after explaining the purpose and reassuring her of the confidentiality of the survey. No identifiers were used in the analysis to ensure confidentiality.

Results

100 women with incomplete miscarriage were recruited for the study with 50 participants randomly assigned to either misoprostol or manual vacuum aspiration treatment.

In the misoprostol arm of the study, 2 women did not return for follow-up visit despite several reminders sent to them to return for follow-up assessment. Hence, their outcome variables were not available for analysis. Out of the remaining 48 women, none of them discontinued their treatments.

For participants allocated to MVA arm of the study, 46 women completed their treatments and they were included in the data analysis. The remaining 4 women did not return to follow-up for assessment and they were excluded in the data analysis. All the tissues sent for histology were confirmed to be products of conception without evidence of molar gestation.

Table 1 shows a comparison of the demographic characteristics of the participants in the two study groups. Participant's age ranged from 18 to 45 years. Women in the age group of 32 to 38 years accounted for the majority in both study groups. The mean

ages were 24.8 (4.2) [95% CI 23.6–26] years and 24.6 (4.4) [95% CI 23.3–25.9] years for the misoprostol and MVA groups respectively. For the gestational age, the mean gestational age was 8.4 (2.0) [95% CI 7.8–9.0] weeks and 8.2 (2.1) [95% CI 7.6–8.8] weeks for the misoprostol and MVA groups, respectively. This showed that the two study groups did not differ in their mean age and gestational age.

Table 1: Sociodemographic comparison of the two study groups

Variables	Misoprostol (*n*=48) (%)	MVA (*n*=46) (%)	*P*
Age (years)			
18-24	8 (16.7)	6 (13)	
25-31	12 (25)	13 (28.3)	
32-38	18 (37.5)	15 (32.6)	
39-45	10 (20.8)	12 (26.1)	
Mean age (SD) years	24.8 (4.2)	24.6 (4.4)	0.82*
Parity			
0	10 (20.8)	11 (23.9)	
1	18 (37.5)	21 (45.7)	
2-4	9 (18.8)	8 (17.4)	
≥ 5	11 (22.9)	6 (13)	
Mean parity (SD)	1.4 (1.2)	1.6 (1.4)	0.44*
Gestational age (weeks)			
4-6	7 (14.6)	9 (19.6)	
7-9	31 (64.6)	24 (52.2)	
10-13	10 (20.8)	13 (28.2)	
Mean gestational age (SD) weeks	8.4 (2.0)	8.2 (2.1)	0.63*
Marital status			
Single	13 (27.1)	14 (30.4)	
Married	26 (54.2)	23 (50.0)	
Divorced	5 (10.4)	6 (13.0)	
Widowed	1 (8.3)	3 (6.6)	
Area of residence			
Urban	35 (72.9)	35 (76.1)	
Rural	13 (27.1)	11 (23.9)	
Level of education			
No formal education	3 (6.3)	7 (15.2)	
Primary	8 (16.7)	10 (21.7)	
Secondary	21 (43.8)	14 (30.4)	
Tertiary	16 (33.2)	15 (32.7)	

*Student '*t*' test was used for comparison, SD=standard deviation

The treatment outcomes of the study groups were shown in Table 2. The number of participants that returned for follow-up at 1 week were 48 (96%) and 46 (92%) in misoprostol and MVA groups, respectively. When the women who returned for follow-up at 1 week were assessed, 39 (81.3%) of the women assigned to misoprostol arm and 44 (95.7%) of those

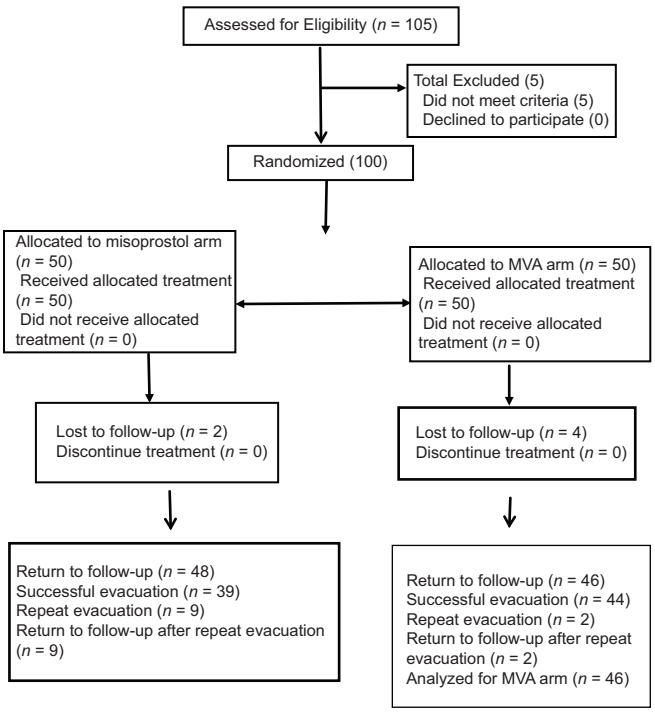

Figure 1: The CONSORT flow chart of the clients through the study

Table 2: Clinical outcomes of the study groups

Outcome	Misoprostol *n* (%)	MVA *n* (%)	RR (95%CI)	*P*
Lost to follow-up	2 (4.0)	4 (8.0)	0.5 (0.09-2.61)	0.41
Return to follow-up	48 (96.0)	46 (92)		
Complete evacuation of product of conception	39 (81.3)	44 (95.7)	4.3 (0.98-18.9)	0.05
Repeat uterine evacuation with MVA	9 (18.7)	2 (4.3)		
Return to follow up after repeat evacuation	9 (18.7)	2 (4.3)		
Complete uterine evacuation after reevacuation	9 (18.7)	2 (4.3)		
Mean pretreatment hemoglobin (SD) g/dL	9.2 (1.4)	9.4 (1.2)		0.46*
Mean posttreatment hemoglobin (SD) g/dL	8.9 (1.8)	9.0 (1.5)		0.77*
Excessive bleeding after treatment				
Yes	11 (22.9)	4 (8.7)	2.6 (0.9-7.69)	0.07
No	37 (77.1)	42 (91.3)		
Postabortion complication				
Hemorrhage after treatment	4 (8.7)	1 (2.2)		

*Student '*t*' test was used for comparison of mean, SD=Standard deviation

Table 3: Client acceptability and satisfaction in the two study arms

Parameter	Misoprostol *n* (%)	MVA *n* (%)	X^2	*P*
Would choose method again?				
Yes	47 (97.9)	30 (65.2)	16.95	<0.001
No	1 (2.1)	16 (34.8)		
Reasons for choosing method again				
Effective method	46 (95.8)	28 (60.9)	3.61	0.16
Quick and easy treatment	40 (83.3)	12 (26.1)		
To avoid uterine instrumentation	41 (85.4)	15 (32.6)		
Would recommend a method to a friend?				
Yes	46 (95.8)	28 (60.9)	17.14	<0.001
No	2 (4.2)	18 (39.1)		
Reason for recommending to a friend				
Effective method	46 (95.8)	26 (56.5)	2.63	0.27
Quick and easy treatment	39 (81.3)	18 (39.1)		
To avoid uterine instrumentation	38 (79.2)	12 (26.1)		
Mean client satisfaction score (SD)	13.2 (2.1)	7.3 (4.6)		<0.001*

*Student '*t*' test used for comparison, SD=standard deviation

Table 4: Comparison of the cost of treatment in the study groups

Study group	Cost $		95%CI	*P*
	Range	Mean (SD)		
Primary treatment				
Misoprostol (*n*=48)	10.42-20.21	14.36 (4.0)	-56.3, -50.7	<0.001*
MVA (*n*=46)	52.32-80.01	67.84 (8.9)		
Repeat evacuation				
Misoprostol (*n*=9)	51.47-78.8	65.76 (6.6)	-10.7, 12.5	0.86*
MVA (*n*=2)	52.0-79.1	64.89 (6.3)		

*Student '*t*' test used for comparison, SD=standard deviation

Table 5: Incremental cost-effectiveness (C/E) ratio for the method of treatment

Study group	Cost (C) $	Effectiveness (E) $	C/E ratio $
Misoprostol	669.14	39	17.16
MVA	2,765.30	44	62.84
Incremental	2,096.16	5	419.23

Cost consists of the sum of the cost of primary treatment of each participant in the group. Effectiveness is successful treatment with no subsequent interventions after primary treatment. Incremental is the difference in both study group

assigned to manual vacuum aspiration arm of the study had successful treatment [Table 2]. The difference in the rate of complete evacuation of products of conception in both treatment groups did not reach statistical significance [RR = 4.3, 95% CI 0.98-18.9, *P* value = 0.05]. Nine women in the misoprostol group and two in the manual vacuum aspiration group required an additional reevacuation of the uterus using MVA after the initial treatment. Of the 9 participants that had repeat evacuation in the misoprostol arm, four women had emergency uterine evacuation using MVA due to profuse bleeding following misoprostol administration and 5 had re-evacuation due to retained products of conception at follow-up visits. When women that had repeat uterine evacuation of products of conception were evaluated using abdominopelvic ultrasound 1 week later, all of them had complete evacuation of products of conception. Women treated with misoprostol reported excessive vaginal bleeding more than those treated with MVA (misoprostol, 11 versus MVA, 4; RR = 2.6 95% CI 0.9-7.69, *P* value = 0.07). These women reported bleeding which was more than expected but did not consider it as profuse enough to require representation at the hospital for assessment. However, there was no significant difference in both pretreatment and posttreatment mean hemoglobin concentration in both study groups. There were no cases of cervical trauma and genital tract sepsis in both treatment arms.

Table 3 shows client's reports of acceptability and satisfaction of the treatment methods when assessed at their follow-up visit. A significantly higher number of participants in the misoprostol arm would choose the method again when compared with women in the MVA group (47 versus 30, X^2 = 16.95, *P* < 0.001). The reasons for opting for misoprostol treatment in the future were being effective (95.8%), quick and easy treatment (83.3%), and to avoid uterine instrumentation (85.4%). Similarly, more women in the misoprostol arm would recommend the mode of treatment to a friend compared with participants in the MVA group (46 versus 28, X^2 = 17.14, *P* < 0.001). Overall, the mean client satisfaction score was significantly higher among women in the misoprostol arm compared to participants in MVA group (misoprostol, 13.2 (2.1) versus MVA, 7.3 (4.6), 95% CI -7.35, -4.45, *P* < 0.001).

The comparison of the cost of treatment in both arms of the study is shown in Table 4. The cost of primary

treatment ranged from $10.4 to $20.2 for women treated with misoprostol and $52.3 to $80 for those treated with MVA. The mean cost of primary treatment was higher in the MVA group compared with misoprostol arm (MVA, $67.8 (8.9) versus misoprostol, $14.4 (4), 95% CI -56.2, -50.6, $P < 0.001$). There was no significant difference in the mean cost of repeat uterine evacuation in both study arms (MVA, $64.9 (6.3) versus misoprostol, $65.8 (6.6), 95% CI -10.7, 12.5, $P = 0.86$).

The incremental cost-effectiveness ratio for the study is shown in Table 5. From the table, the total cost of primary treatment ($2,765.3) of incomplete miscarriage with MVA was 4 times higher than the total cost of treatment ($669.1) with misoprostol and the incremental cost (difference in cost of primary treatment in both study arm) was $2096.2. The difference in the effectiveness of both treatment methods was 5 and the ICER was $419.2. Although MVA arm had 5 successfully treated clients over misoprostol arm, this was achieved at a high cost of $2096.2 and it took a cost of $419.2 to achieve a unit change in the effectiveness of MVA over misoprostol.

Discussion

This randomized study indicates that medical treatment of incomplete miscarriages with oral 600 µg misoprostol is effective. In this study, the effectiveness of misoprostol for treatment of incomplete miscarriage was 81.3% whereas that of manual vacuum aspiration was 95.7%. Although the failure rate was higher in women treated with misoprostol when compared with those in the manual vacuum aspiration group, this difference did not reach statistical significance. The high success rate observed in the misoprostol group is similar to that reported by Fawole *et al*. in Ibadan,[3] Ibiyemi *et al*. in Ilorin,[8] Dim in Enugu,[16] and Chigbu, *et al*. in Abia.[17] Similarly, the result of this study is consistent with studies done in Uganda,[18] Tanzania,[19] Egypt[20] and Burkina Faso,[21] and also with recent Cochrane review,[6] which indicates that surgical management is more likely to induce complete evacuation of the uterus than medical management, although it did not reach statistically significant difference in these studies. The high success rate observed in the misoprostol group suggests that the medical management of incomplete abortion in a well-selected patient is an effective alternative to manual vacuum aspiration.

The incidence of complications in this study was infrequent in both treatment groups. Four women had profuse vaginal bleeding following administration of misoprostol which led to emergency evacuation of retained products of conception with MVA. Moreover, women in the misoprostol arm of the study reported excessive vaginal bleeding when compared with those treated with MVA. However, there was no significant difference in preevacuation and postevacuation hemoglobin concentrations of both treatment groups. These findings were similar to findings of studies done by Fawole *et al*. in Ibadan,[3] Ibiyemi *et al*. in Ilorin,[8] and Adisso in Benin.[22] There was no genital tract sepsis among participants in this study. This is in contrast to the findings of the study done in Uganda by Weeks and his colleagues who reported genital tract sepsis in one woman treated with misoprostol and three women who had manual vacuum aspiration.[18] The absence of pelvic infection in this study is probably due to the routine use of antibiotics for all the study participants.

In the present study, the mean client satisfaction score at a follow-up visit was higher among women treated with misoprostol [13.2 (2.1)] when compared with those treated with MVA [7.3 (4.6)]. More women in the misoprostol arm (97.9%) of the study would choose the method again when compared with those in the MVA group (65.2%). The reasons given for chosen misoprostol were being effective method (95.8%), quick and easy treatment (83.3%), and to avoid uterine instrumentation (85.4%). Similarly, for the above reasons, a higher number of women in the misoprostol arm will recommend the treatment to a friend when compared with those treated with MVA. These findings were similar to the findings of studies done by Fawole *et al*. in Ibadan,[3] Dim in Enugu,[16] and Chigbu in Abia.[17] However, the difference in client satisfaction found in this study was different from the finding of a study done in Ilorin by Ibiyemi,[8] Uganda by Weeks,[18] and that of recent Cochrane review[6] that showed that there was no difference in maternal satisfaction in the medical and surgical group. It is also different from the study done in Finland that showed that women in the manual vacuum aspiration arm were more satisfied with their treatment compared with participants in the misoprostol arm.[23] The difference in maternal satisfaction with this study is because only women with incomplete miscarriages were involved unlike some of the above mentioned studies that included other forms of miscarriage. The discomfort and fear of having manual vacuum aspiration in the MVA group and the ease of simply swallowing 3 tablets of misoprostol may have led to less client's acceptability and satisfaction among women who had MVA.

In this study, the mean cost of initial treatment of incomplete miscarriage in uneventful recovery for individual participants was smaller in misoprostol group [$ 14.36 (4.02)] when compared with MVA [$ 67.84 (8.9)]. The total cost of the primary treatment of incomplete miscarriage with MVA

was 4 times higher than the cost of treatment with misoprostol in this study. There was no difference in the mean cost of repeat treatment in both groups despite higher treatment failure among women in the misoprostol arm of the study. This shows that the misoprostol is more cost-effective than MVA in the treatment of incomplete miscarriage in our setting. Although MVA arm had 5 successfully treated clients over misoprostol arm, this was achieved at a high cost of $ 2096.16 and it took a cost of $ 419.23 to achieve a unit change in the effectiveness of MVA over misoprostol. This is a huge amount in a low resource setting where most patients are of low socioeconomic status and where out-of-pocket payment for healthcare is the norm. In this setting, poverty is one of the factors limiting access to healthcare, which often leads to high maternal morbidity and mortality from abortion. Therefore, a cost-saving, effective, and acceptable alternative to MVA such as misoprostol, may help to reduce the contribution of abortion complications to maternal mortality in the developing countries. This finding is similar to the findings of a study done in USA where the use of misoprostol for treatment of incomplete miscarriage was found to be more cost-effective when compared with MVA even with the addition of secondary costs.[24] Our findings differ from a study in Finland where primary costs of the surgical treatment were higher but the addition of secondary costs due to complications in the medical group brought the costs to the same level.[25] This difference in the cost-effectiveness with this study is because the study carried out in Finland included other forms of miscarriage which probably accounted for the difference in the outcome.

From the findings of this study, medical treatment could be recommended as the standard of care for well-motivated women with uncomplicated incomplete first-trimester miscarriages in tertiary health institution and other health institution in view of its overwhelming positives while the manual vacuum aspiration use be limited to women with complications and those unlikely to adhere to follow-up to confirm complete uterine evacuation.

The randomized controlled study design used for this study was its major strength. Unfortunately, it was not possible to apply blinding of any form in the study because of the peculiarity of its design; however, the effects of this on the study's outcome variables were likely to be very minimal. In addition, the use of a reliable and valid instrument such as PPSQ was among the strengths of this study. This is a widely used tool to determine client satisfaction with medical treatment. Client acceptability and satisfaction with treatment were assessed after the conclusion of treatment (exit interview) and this assisted to minimize or eliminated client-associated bias. Besides these strengths, the present study had a limitation. It is a single-centered study and therefore, the study outcomes could be generalized to the study area. A multicenter trial would have improved the generalization of the study outcomes. The authors recommend that a further multicenter randomized controlled trial using a similar treatment protocol should be conducted to compare client acceptability and satisfaction and cost-effectiveness in both treatment groups in low-resource settings.

Conclusion

In conclusion, for treatment of uncomplicated first-trimester incomplete miscarriage both manual vacuum aspiration and 600 μg oral misoprostol are effective treatment options although there was a higher failure rate with misoprostol. Medical treatment was associated with higher client acceptance and satisfaction and was more cost-effective than surgical treatment.

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Conflicts of interest

There are no conflicts of interest.

References

1. Gallos ID, Williams HM, Price MJ, Eapen A, Eyo MM, Tobias A, *et al.* Methods for managing miscarriage: A network meta-analysis. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD012602. doi: 10.1002/14651858.CD012602.
2. Saraswat L, Ashok PW, Mathur M. Medical management of miscarriage. Obstet Gynaecol 2014;16:79-85.
3. Fawole AO, Diop A, Adeyanju AO, Aremu OT, Winikoff B. Misoprostol as first-line treatment for incomplete abortion at a secondary-level health facility in Nigeria. Int J Gynecol Obstet 2012;119:170-3.
4. World Health Organization. Maternal mortality Fact Sheet. Updated November 2016. Available from: www.who.int. [Last assessed on 2018 Jul 27].
5. Ezegwui H, Onoh R, Ikeako L, Onyebuchi AK, Umeora O, Ezeonu P, *et al.* Investigating maternal mortality in a public teaching hospital, Abakaliki, Ebonyi State Nigeria. Ann Med Health Sci Res 2013;3:75-80.
6. Kim C, Barnard S, Neilson JP, Hickey M, Vazquez JC, Dou L. Medical treatments for incomplete miscarriage. Cochrane Database Syst Rev 2017;1:CD007223. doi: 10.1002/14651858.CD007223.pub4.
7. Adefuye PO, Sule-Odu AO, Olatunji AO, Lamina MA, Oladapo OT. Maternal deaths from induced abortions. Trop J

Obstet Gynaecol 2003;20:101-4.
8. Ibiyemi KF, Ijaiya MA, Adesina KT. Randomised trial of oral misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion at a Nigerian Tertiary Hospital. Sultan Qaboos University Med J 2019;19:38-43.
9. Dah T, Akiode A, Awah P, Fetters T, Okoh M, Ujah I, *et al.* Introducing misoprostol for the treatment of incomplete abortion in Nigeria. African J Reprod Health 2011;15:42-50.
10. Abdul MA, Palmer HO, Aminu B, Ismail H, Kadas A. Experiences in the use of misoprostol in the management of first trimester missed abortion in a low resource setting. Trop J Obstet Gynaecol 2016;33:201-4.
11. Sotiriadis A, Makrydimas G, Papatheodorou S, Ioannidis JPA. Expectant, medical, or surgical management of first-trimester miscarriage: A meta-analysis. Obstet Gynecol 2005;105:1104-13.
12. Shochet T, Diop A, Gaye A, Nayama M, Sall AB, Fawole B, *et al.* Sublingual misoprostol versus standard surgical care for treatment of incomplete abortion in five Sub-Saharan African countries. BMC Preg Childbirth 2012;12:127.
13. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39:175-91.
14. Morris JL, Winikoff B, Dabash R, Weeks A, Faundes A, Gemzell-Danielsson K, *et al.* FIGO's updated recommendations for misoprostol used alone in gynaecology and obstetrics. Int J Gynecol Obstet 2017;138:363-6.
15. Siassakos D, Clark J, Sibanda T, Attilakos G, Jefferys A, Cullen L, *et al.* A simple tool to measure patient perceptions of operative birth. BJOG 2009;116:1755-61.
16. Dim C. Comparison of sublingual misoprostol with manual vacuum aspiration in the treatment of incomplete abortion in Enugu, South-east, Nigeria: A randomized controlled study. In: Global Maternal Newborn Health Conference. October 19, 2015; Mexico City.
17. Chigbu B, Onwere S, Aluka C, Kamani C, Ezenobi O. Is Misoprostol a suitable alternative to the surgical evacuation of incomplete abortion in rural South-eastern Nigeria? East African Med J 2012;89:172-7.
18. Weeks A, Alia G, Blum J, Winikoff B, Ekwaru P, Durocher J, *et al.* A randomized trial of misoprostol compared with manual vacuum aspiration for incomplete abortion. Obstet Gynecol 2005;106:540-7.
19. Shwekerela B, Kalumuna R, Kipingili R, Mashaka N, Westheimer E, Clark W, *et al.* Misoprostol for treatment of incomplete abortion at the regional hospital level: Results from Tanzania. BJOG 2007;114:1363-7.
20. Dabash R, Ramadan MC, Darwish E, Hassanein N, Blum J, Winikoff B. A Randomized controlled trial of 400-μg sublingual misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion in two Egyptian Hospitals. Int J Gynecol Obstet 2010;111:131-5.
21. Dao B, Blum J, Thieba B, Raghavan S, Ouedraego M, Lankoande J, *et al.* Is misoprostol a safe, effective and acceptable alternative to manual vacuum aspiration for postabortion care? Results from a randomised trial in Burkina Faso, West Africa. BJOG 2007;114:1368-75.
22. Adisso S, Hounkpatin BIB, Komongui GD, Sambieni O, Perrinb RX. Introduction of misoprostol for the treatment of incomplete abortion beyond 12 weeks of pregnancy in Benin. IJGO 2014;126:S36-9.
23. Niinimaki M, Jouppila P, Martikainen H, Talvensaari-Mattila A. A randomized study comparing efficacy and patient satisfaction in medical or surgical treatment of miscarriage. Fertil Steril 2006;86:367-72.
24. Rausch M, Lorch S, Frederick M, Zhang J, Barnhart K. A cost effectiveness analysis of surgical versus medical management of early pregnancy loss. Fertil Steril 2012;97:355-360.e1.
25. Niinimaki M, Karinen P, Hartikainen A-L, Pouta A. Treating miscarriages: A randomised study of cost-effectiveness in medical or surgical choice. BJOG 2009;116:984-90.