East African Medical Journal Vol. 89 No. 5 May 2012
IS MISOPROSTOL A SUITABLE ALTERNATIVE TO THE SURGICAL EVACUATION OF INCOMPLETE ABORTION IN RURAL SOUTH-EASTERN NIGERIA?
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B. CHIGBU, S. ONWERE, C. ALUKA, C. KAMANU and O. EZENOBI

ABSTRACT

***Background*: Research has demonstrated the effectiveness of misoprostol for treatment of incomplete abortion. However, few studies have focused on the feasibility of treating incomplete abortion with misoprostol at the rural clinic level in sub-Saharan Africa.**
***Objective*: To determine the effectiveness, safety and acceptability of misoprostol as an alternative to the surgical treatment of incomplete abortion at a rural clinic.**
***Design*: Open-label randomised controlled trial.**
***Setting*: A private clinic in Ekeakpara community, Osisioma Ngwa Local Government Area, Abia State, Nigeria.**
***Subjects*: Women of reproductive age presenting with incomplete abortion.**
***Results*: Regardless of treatment allocation, nearly all women had a complete uterine evacuation with either oral misoprostol or manual vacuum aspiration (misoprostol: 98.8%, MVA: 100%, P = 0.99). Misoprostol users were more likely to report that they were 'very satisfied' with the method (75.6% versus 45%, P<0.001). In the 72 hours after treatment, women using misoprostol reported heavier bleeding but lower levels of pain than those treated with manual vacuum aspiration. Women in the misoprostol group were more likely to choose that treatment again (96.9 versus 55.6%; P<0.001) and would recommend it to a friend.**
***Conclusion*: For treatment of first-trimester uncomplicated incomplete abortion at a rural facility, both MVA and 600 μg oral misoprostol are safe, effective, and acceptable treatments. Depending on availability of each method and the desires of individual women, either option may be presented to women for the treatment of incomplete abortion.**

INTRODUCTION

Approximately one in five recognised pregnancies are spontaneously miscarried in the first trimester (1) and an additional 22% end in induced abortion (2). An incomplete abortion can result from either spontaneous or induced pregnancy loss and occurs when products of conception are not completely expelled from the uterus. Incomplete abortion is closely related to unsafe abortion in many parts of the world and continues to contribute disproportionately to maternal mortality and morbidity in sub-Saharan Africa (3). Safe and effective treatment for incomplete abortion is therefore an important way to reduce abortion-related morbidity and mortality, particularly in settings like Nigeria where legal abortion is restricted. Incomplete abortion can be treated with expectant management, which allows for spontaneous evacuation of the uterus, or active management, using surgical or medical methods. Expectant management is not preferred by many providers due to its relatively low efficacy and the fact that the time interval to spontaneous expulsion is unpredictable (4). Surgical methods are highly effective for treatment

of incomplete abortion. However, these treatments require trained providers, special equipment, sterile conditions and often anesthesia, all of which are limited in many rural facilities in low-resource settings (5). A review of the recent literature on misoprostol shows that it successfully completes expulsion in between 91 and 99% of women who receive it for incomplete abortion, inevitable and missed abortion in the first trimester (6-11). These studies which were conducted in Tanzania (6), Mozambique (8), Burkina Faso (9), Uganda (10) and Ghana (11) provided evidence that a single dose of 600μg oral misoprostol is as safe and effective as manual vacuum aspiration (MVA) when used for uterine evacuation. Majority of these researches, however, took place in tertiary-care facilities and regional hospitals. The present study was designed to fill an important gap in the research by testing misoprostol for incomplete abortion treatment at a small private clinic with a large rural catchment area in another resource-poor country in sub-Saharan Africa.

MATERIALS AND METHODS

This was an open-label randomised trial to compare the safety,efficacy and acceptability of a single dose of 600μg misoprostol taken orally and MVA (the standard of care) for the treatment of incomplete abortion.

From January 2010 to December 2011, 320 women were recruited at a private clinic with existing post-abortion care services and situated at Ekeakpara, a rural community in Osisioma Ngwa Local Government Area of Abia State, Nigeria. Osisioma Ngwa has a total area of 76 sq miles and a total population (2006 census) of 219,632 (12). An incomplete abortion was diagnosed by clinical history and examination; complete evacuation was assessed using the same set of clinical techniques. Eligibility criteria were open cervical os, vaginal bleeding or history of vaginal bleeding during this pregnancy, and uterine size of less than or equal to 12 weeks' LMP. Additional eligibility criteria included willingness to return for follow up in one week, no known contraindications to misoprostol, and general good health. Women were excluded if they had signs of severe infection (foul-smelling discharge, fever > 38^{o}C, or pulse > 110/minute), or known allergy to misoprostol or other prostaglandin, suspected ectopic pregnancy and haemodynamic instability or shock.

Women who met the above criteria were given detailed information about the study and asked if they would like to participate. Consenting women were randomly assigned to one of the two study regimens. The randomisation allocation was 1:1 (600μg misoprostol tablet taken orally: MVA) and was accomplished using sequentially numbered envelopes. When a new participant was enrolled in the study, a trained nurse would open the next envelope in the numbered series and the woman would receive the treatment specified therein.

Women receiving misoprostol were counseled on the side effects of the drug and swallowed the pills in the presence of a trained nurse. Women allocated to MVA (Ipas, Chapel Hill, NC, USA) were given surgical evacuation by a trained doctor in the MVA room at the clinic using reassurance alone and no anaesthesia during the procedure. All participants, regardless of assigned treatment were given prophylactic antibiotics, and Paracetamol tablets to help manage their pain. They were observed in the clinic for a maximum of three hours after treatment and, in absence of danger signs, discharged. No admission was offered. The women and the study nurse exchanged phone numbers and they were told that they could contact the nurse at any time with any concerns.

Each woman was requested to return to the hospital seven days after treatment. At the follow-up visit, each woman's abortion status was assessed clinically by an interview, a bimanual examination and speculum examination. If the abortion was found to be complete, the woman was released from the study. If the abortion was still incomplete, the woman was offered the choice between an additional follow-up visit in one week with no further intervention during the period or immediate surgical evacuation. If after the additional week of follow-up the abortion was still not complete, the woman underwent MVA. The study protocol did not call for routine ultrasound examination (either for initial diagnosis or for determination of treatment success) or administration of prophylactic antibiotics, or haemoglobin testing.

The primary outcome measure was complete uterine evacuation after initial treatment (either misoprostol or MVA). Other outcome measures included adverse effects from the treatment assessed by observation and at an exit interview, where the participants were asked to report on the adverse effect they had experienced. Pain intensity and satisfaction was measured using a seven and five point Likert scale respectively (13). A visual analog scale using seven increasingly larger circles depicted on a card (the smallest equaling no pain, the largest the worst imaginable pain), was used to codify the pain they had in connection with their treatment. To further assess each woman's satisfaction and the acceptability of the methods, each participant was asked to indicate whether she was satisfied, very satisfied or unsatisfied with the treatment and to indicate whether she would select the treatment again or recommend it to a friend. The participants' responses to these questions were categorised and analysed quantitatively.

Data entry and analysis were done using Epi Info 6.0 (U.S. Centers for Disease Control and Prevention Atlanta, GA). Chi-square tests were used for categorical data with Fisher exact or Yates correction where appropriate and *t* test was used to compare means. Statistical significance was defined as a $P < 0.05$.

The study was conducted in accordance with the declaration of Helsinki – women were enrolled after counseling and informed consent, and the study was approved by the Ethics and Research Committee of Abia State University Teaching Hospital, Aba, Nigeria. All records were identified only by code number and initials to maintain confidentiality and locked in a filing cabinet. Women were assured that no clinical information would be released without their express permission. Assuming a 99% efficacy rate for MVA, the study was designed to have a 90% power to detect whether misoprostol was 6% less effective than MVA.

RESULTS

A total of 320 women were enrolled, and 160 women were randomised into the misoprostol group and 160 women into the MVA group (Figure 1). Each woman received the allocated treatment and no woman was lost to follow up. Table 1 details the characteristics of the study participants. There were no significant differences between women in the two groups. The average age of the participants was 29 years and majority were married. More than 90% of the women indicated they were experiencing a spontaneous abortion, but many (> 25%) had had induced abortion in the past.

Figure1
Consort flow chart

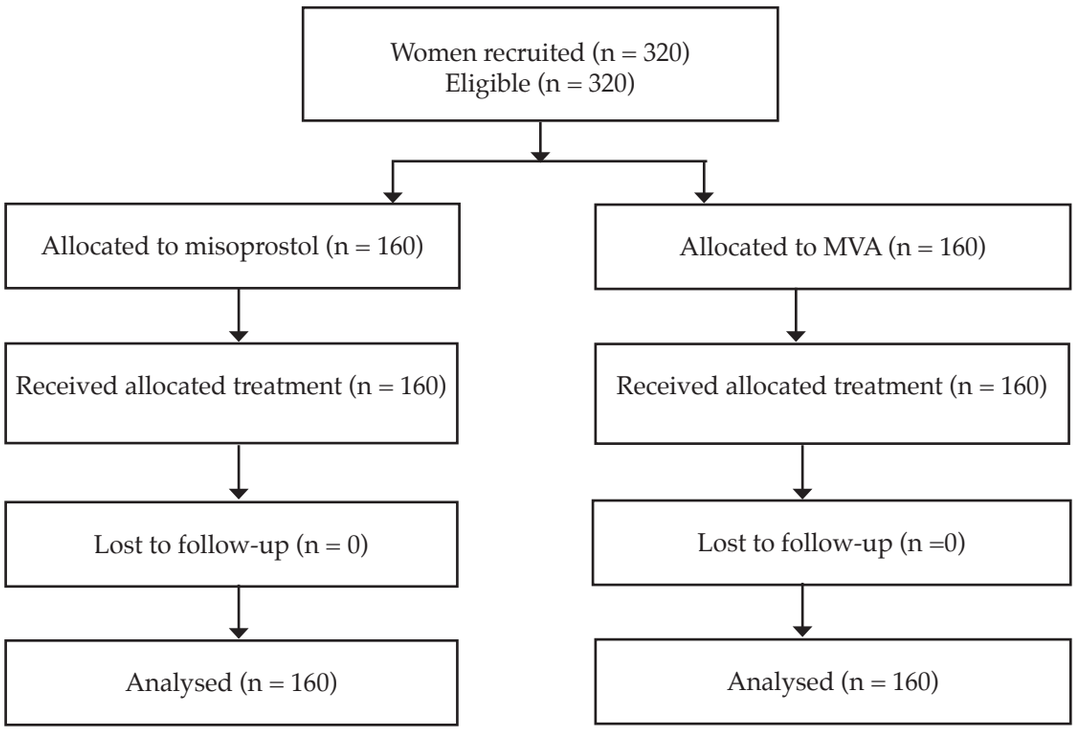

Table 1
Participant characteristics

Characteristic	Misoprostol (N=160)	MVA (N=160)	P-value
Age, years (mean, SD)	29.0±8.2	29.0±8.3	0.84*
Currently married (n %)	120 (75)	124(76)	0.91*
Parity (mean, SD)	2.1±2.1	2.0±2.2	0.62*
Previous caesarean section	6(3.8)	5(3.1)	0.99*
Previous induced abortion (n %)	42(26.3)	44(27.5)	0.94*
Previous spontaneous abortion (n %)	7(4.4)	6(3.8)	0.99*
Woman's report of current abortion (n %)			
Spontaneous	150(93.8)	152(95.0)	0.99*
Induced	10(6.3)	8(5)	0.82*

*not significant

Efficacy and adverse effects: The success rates in the two groups (defined as not requiring a secondary surgical procedure) were very high and not statistically different (misoprostol: 98.8%, MVA: 100%, P = 0.99; Table 2). The two misoprostol failures were women who presented at their first follow-up visit in seven days with retained products and requested for MVA to evacuate their uterus completely. Most women in both groups reported experiencing pain and cramps and this was significantly more in the MVA group (52.5% in the misoprostol group versus 87.5% in the MVA group, P <0.05). The reported mean pain score was significantly higher among MVA patients than misoprostol patients: 4.5 versus 3.0 (P<0.001). Women receiving misoprostol were significantly more likely to report bleeding in three days after treatment than women treated with MVA (100% versus 56.3%; P<0.001), and in subsequent days up to seven days post treatment (50% versus 6.3%; P<0.001). No patient reported bleeding in two weeks post treatment. Fever, chills, nausea, vomiting and diarrhoea were infrequently cited and tended to resolve within 24 hours. Misoprostol users made more telephone calls to study providers than MVA users (50% versus 9.4%; P<0.001).

Table 2
Efficacy and adverse effects

	Misoprostol N(%)	MVA N(%)	P-value
Success**	158(98.8)	160(100)	0.99
Failure	2(1.2)	0(0)	
Bleeding in 3 days after treatment	160(100)	90(56.3)	0.001*
Bleeding in 7 days after treatment	80(50)	10(6.3)	0.001*
Bleeding in 2 weeks after treatment	0(0)	0(0)	
Pain/cramps			
Ever	84(52.5)	140(87.5)	0.005*
Mean days	1.3	1.4	0.45
Fever			
Ever	15(9.4)	9(5.6)	0.33
Mean days	1.0	1.0	
Nausea			
Ever	8(5)	7(4.4)	0.99
Mean days	1.0	1.0	
Vomiting			
Ever	6(3.8)	6(3.8)	0.77
Mean days	1.0	1.0	
Chills			
Ever	11(6.9)	4(2.5)	
Mean days	1.0	1.0	
Diarrhea			
Ever	3(1.9)	0(0)	
Mean days	1.0	0(0)	

**Defined as not requiring a secondary surgical procedure
*significant

Satisfaction and acceptability: Women in both groups were satisfied with their treatments. Misoprostol users were significantly more likely to report that they were 'very satisfied' with the method (75.6% versus 45%, P<0.001; Table 3), and three times more likely to inform that the adverse effect of their method of treatment were 'easily tolerable'. Significantly larger proportions of women in the misoprostol group informed that they would choose that treatment again and would recommend it to a friend.

Table 3
Satisfaction and acceptability

	Misoprostol N(%)	MVA N(%)	P-value
Overall satisfaction			
Very satisfied	121(75.6)	72(45)	<0.001*
Satisfied	39(24.4)	88(55)	
Unsatisfied or very unsatisfied	0(0)	0(0)	
Tolerability of adverse effects			
Bad	0(0)	0(0)	<0.001*
Tolerable	64(40)	128(80)	
Easily tolerable	96(60)	32(20)	
Would choose method again			
Yes	155(96.9)	89(55.6)	<0.001*
No	5(3.1)	71(44.4)	
Would recommend to a friend			
Yes	155(96.9)	92(57.5)	<0.001*
No	5(3.1)	68(42.5)	

*significant

DISCUSSION

This study confirms that a single dose of 600μg oral misoprostol is a safe, suitable, and effective alternative to MVA in the treatment of incomplete abortion. In this study, misoprostol was successful in evacuating the uterus in 98.8% of cases. This high success rate is comparable with the success rates reported by researchers elsewhere (6-11).

Women using misoprostol did not find the adverse effects of this method of treatment difficult to tolerate, perhaps because, in comparison with women using MVA, they experienced lower levels of pain and this finding is consistent with reports by other studies (8-11). As evidenced by greater willingness to choose the treatment method again and to recommend it to a friend, women using misoprostol appeared more satisfied with their treatment than those undergoing MVA. This is also similar to the observations by previous researchers (8-11) and confirms that misoprostol is a suitable alternative to MVA. In contrast to the observations by Dao *et al* (9), this study revealed that misoprostol users were more likely to make more phone calls to the facility to seek reassurance than MVA users. This might be because misoprostol use in postabortion care is new to the women some of whom have been treated of incomplete abortion in the past with MVA. As providers become comfortable with misoprostol for treatment of incomplete abortion, patient counselling will improve; the womens' knowledge of misoprostol will improve and success rates will generally rise.

The findings in this study provides further evidence that ultrasonography is not essential to provide misoprostol for treatment of incomplete abortion (6,9,11) making the drug a practical alternative in PAC facilities lower down in the health system hierarchy that may lack ultrasound equipment or where ultrasound is too costly. It is unlikely that every healthcare facility in a rural area in Africa will have the resources to verify incomplete abortion status through ultrasound for all presenting women. Several recent studies in low-resource settings rarely used ultrasound to diagnose incomplete abortion (<5% of diagnoses were confirmed via ultrasound) or to confirm uterine evacuation (6-8, 10). Nevertheless, because ultrasound was not used to diagnose incomplete abortion, the study population may have included women with inevitable or already completed abortion.

Women with previous Caesarean sections were not excluded in this study yet misoprostol used for incomplete abortion treatment in these women was generally safe. Given that this study was conducted in only one PAC facility, it is difficult though to generalise how the method might turn out throughout other facilities. Expert opinion indicates there is no clinical reason to with hold misoprostol for treatment of incomplete abortion in women with a previous Caesarean section (14).

The study may seem remarkable in that none of the 320 women who participated was lost to follow-up. Other similar trials which have been conducted in East , Central and West Africa had been lost to follow-up rates of 0 to 1.7% (6, 9, and 11). That this study was conducted in a small rural community with a steady homogenous population may have given it an advantage in this respect. The issue of women lost to follow up is important, as a small proportion of misoprostol users (1 in 20) (14) will require a surgical completion. As the method is introduced in new settings, information and counselling should be provided to enable women to recognise the need for additional care and where to get it.

Until recently, Post abortion care (PAC) programmes have recommended MVA for treatment of incomplete abortion and MVA has provided a highly effective means of uterine evacuation. However MVA requires skilled providers, sterilised equipment, surgical supplies, and a special room. MVA may also be complicated by cervical laceration, uterine perforation, and infrequent failure. On the other hand, medical methods for treatment of incomplete abortion require few resources and can be administered by low- and mid-level providers (14) making it a suitable alternative at the rural areas of developing countries where MVA may not be available.

As sub-Saharan Africa continues to have the highest maternal mortality and morbidity rates in the world, a single dose of 600μg oral misoprostol as a suitable alternative to MVA for post-abortion care might make an impact on reducing maternal death from abortion-related complications in rural settings. Expansion of its use in rural settings, as well as its inclusion into country-wide PAC programmes, should be aggressively pursued. The inclusion of misoprostol to the essential medicines lists in many countries, including Ethiopia, Tanzania, Nigeria, Kenya and Zambia, for the treatment of incomplete abortion (15) is therefore a laudable development.

There were several limitations to the current study. It was a hospital based study and was not multi-centred. The sample size is also small. It was not possible to thoroughly discriminate between women with inevitable and already completed abortion. We recommend a population based multi-centred study to describe the suitability of misoprostol in incomplete abortion management in Nigeria.

In conclusion, this study affirms that for the treatment of first-trimester uncomplicated incomplete abortion at a rural facility, both MVA and 600 μg oral misoprostol are safe, effective, and acceptable treatments. Depending on availability of each method and the desires of individual women, either option may be presented to women for the treatment of incomplete abortion.

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