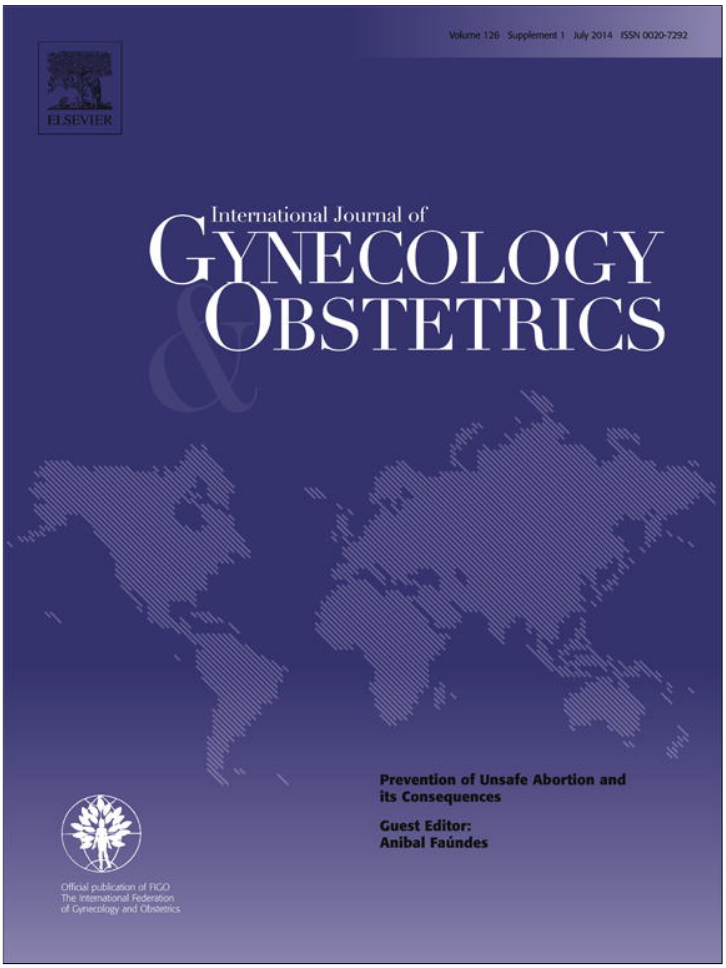

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FIGO INITIATIVE

Introduction of misoprostol for the treatment of incomplete abortion beyond 12 weeks of pregnancy in Benin

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ABSTRACT

Improving the care of women who have undergone a spontaneous or induced abortion is an important step in reducing abortion-related morbidity and mortality. Both the International Federation of Gynecology and Obstetrics (FIGO) and the World Health Organization recommend the use of manual vacuum aspiration (MVA) and misoprostol rather than sharp curettage to treat incomplete abortion. MVA was introduced into the public healthcare service in Benin in 2006 and since 2008 misoprostol has been available in 3 large maternity hospitals. The present study opted to use an oral dose of 800 μg and not to limit to pregnancies of up to 12 weeks, but to include women with second trimester abortions. After 5 years, results show that around three-quarters of the women treated with misoprostol at 13–18 weeks of pregnancy required MVA to complete uterine evacuation and approximately one-quarter had severe bleeding, confirming that the indication of misoprostol for incomplete abortion should be limited to pregnancies of up to 12 weeks.

1. Introduction

Maternal mortality has been an issue of great concern in Benin for decades. The high maternal mortality ratio has remained virtually unchanged, from 474 maternal deaths per 100 000 live births in 2001 to 397 in 2006. Accordingly, approximately 1500 women die each year in the process of giving birth. It is estimated that 15% of those deaths are related to induced, mostly unsafe, abortions [1].

In an effort to achieve the fifth Millennium Development Goal, in 2006 Benin implemented a policy for preventing unsafe abortion and improving postabortion care. Initially, manual vacuum aspiration (MVA) was introduced to replace sharp curettage, followed by the adoption of misoprostol for the treatment of incomplete abortion.

There is already ample experience on the use of misoprostol for the treatment of incomplete abortion, as reflected in publications in scientific journals and in the recommendations of the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics (FIGO) [2,3]. Most of the literature, however, refers to clinical trials in which the recommendations are strictly followed. Few publications deal with experiences in which those recommendations are applied in low-resource countries such as Benin and in hospitals in which the demand of women requesting postabortion care is heavy. In addition, to the best of our knowledge there have been no publications on the success rate of misoprostol when larger doses are used to treat an incomplete abortion beyond 12 weeks of pregnancy.

For that reason, 5 years after the introduction of misoprostol for the treatment of incomplete abortion in 3 maternity teaching hospitals in Benin using a protocol that differs from the one usually recommended, it is time to review this experience and evaluate its results, particularly in cases in which the drug was used after 12 weeks of pregnancy. The present article presents an analysis of the data collected throughout the entire period in which this pioneering experience was applied in this region.

2. Materials and methods

A descriptive, prospective study was conducted over a 5-year period in 3 maternity hospitals in Cotonou, Benin: the Obstetrics and Gynecology Clinic (CUGO) at the Hubert Koutoukou Maga National Teaching Hospital; the Lagoon Mother and Child Hospital (HOMEL); and the Ménontin Maternity Hospital.

The study population consisted of all women admitted to the 3 aforementioned hospitals between January 1, 2008, and December 31, 2012, with a diagnosis of incomplete abortion. Women were not included in the study if they had had a complete abortion that did not require active treatment or if they had severe complications requiring immediate action—a situation in which there would be no time or opportunity to collect data. They were also not included if gestational age was more than 18 complete weeks or if the woman was unable to provide information on gestational age and physical examination showed a uterine size compatible with the late second trimester.

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A team of midwives and physicians, who were either specialists in obstetrics and gynecology or residents in training, received the women consulting for incomplete abortion. The diagnosis of incomplete abortion was based on a clinical examination and on an ultrasonography scan carried out in the emergency department. Women were candidates for misoprostol treatment if they were hemodynamically stable and uterine contents at ultrasonography were less than 20 mm. They were counseled on the option of medical treatment, and informed about the other alternatives available, thus the women were given the right to choose the method they preferred. Counseling also emphasized the need to return for a follow-up visit at which they would be offered an effective contraceptive method. Together with the advantages, the women were also informed of the possible adverse effects of medical treatment, principally pain and bleeding but occasionally diarrhea, hyperthermia, and chills.

Patients who opted for medical treatment received 800 μg of misoprostol (Cytotec R; Pfizer, NY, USA) in the form of four 200-μg tablets placed under the tongue in the presence of the provider and kept in place for a period of 30 minutes.

Follow-up appointments were made for 3 days later to verify progress and for 15 days later when ultrasonography was performed to monitor uterine contents. If the uterus was empty or ultrasonography showed minimal uterine contents, but the woman was asymptomatic, the procedure was considered successful and no further treatment was given. If the uterus was not empty and the woman was bleeding or still cramping, the procedure was considered to have failed and the woman underwent MVA unless she was stable and wanted to try a second 800-μg dose of misoprostol. In the latter case she received a second dose of misoprostol and an appointment was set for 10–15 days later. If the uterus was still not empty after this second follow-up, the patient underwent MVA.

Once it was confirmed that the uterus was empty, the women were offered a contraceptive method of their choice; however, particular emphasis was placed on the advantages of long-acting reversible contraceptives (LARCs) such as the copper T 380 intrauterine device (IUD) and the Jadelle (Bayer Healthcare, Berlin, Germany) contraceptive implant.

The present paper describes the proportion of women with an incomplete abortion who were treated with misoprostol in the 3 study hospitals, and how this proportion changed over time. It also shows the distribution of these women according to gestational age at the time of the abortion, the adverse effects recorded, the results of the ultrasonography scans at the follow-up control visit, and the success rate defined by the proportion of women who did not require MVA to complete uterine evacuation. The associations between gestational age and adverse effects and between gestational age and the success rate were also analyzed, as well as which contraceptive methods were adopted by the women during the follow-up period. Evaluation of the adverse effects was based on the patient's report and on the clinical examination and ultrasound scan. The amount of bleeding was evaluated according to the number of completely saturated tampons used by each woman over a 24-hour period. Bleeding was classified as heavy if the number of tampons used over 24 hours was more than 4.

Data on the variables studied were collected prospectively using specially designed clinical forms on which the data listed above had to be recorded. The same forms were used in all 3 hospitals. The data were checked manually to reduce possible data collection errors. Excel 2007 (Microsoft, Redmond, USA) was used for data entry and cleaning. The associations between gestational age and success rate and between gestational age and the incidence of adverse effects were evaluated using Epi Info (Centers for Disease Control and Prevention, Atlanta, USA).

Every woman who elected to use misoprostol for the treatment of an incomplete abortion signed an informed consent form. The study was evaluated and approved by the Internal Review Board of the School of Health Sciences, University of Benin.

3. Results

A total of 3139 women were admitted with an incomplete abortion at the 3 participating hospitals over the 5-year period between January 2008 and December 2012. The number of patients seen at the CUGO and Homel hospitals during the 5-year period was similar (n = 1150, 36.6% vs n = 1190, 35.3%, respectively), while only 880 cases (23.1%) were attended at the Ménontin Maternity Hospital.

After examination, 630 of the 3139 women were diagnosed as having had a complete abortion requiring no treatment. Of the remaining 2509 women, 48.1% (n = 1277) were treated with MVA and 21.4% (n = 537) with misoprostol. The number of women treated with misoprostol comprised less than 10% of all the women during the first year; however, this proportion increased to 10%–20% in the different hospitals in the second year, stabilizing at around 25% in the fourth year and decreasing slightly to just over 20% in the fifth year of observation (Table 1).

The gestational age of the 537 women treated with misoprostol was: 10 weeks or less (64.1%; n = 344), 11–12 weeks (14.9%; n = 80), 13–14 weeks (13%; n = 70), and 15–18 weeks (8.0%; n = 43).

Misoprostol was administered either in a single 800-μg dose or in two 800-μg doses for a total of 1600 μg. In 55.9% of the cases (n = 300) only one 800-μg dose of misoprostol was required, whereas in 44.1% (n = 237), the women received 2 doses or 1600 μg. Most of the women who received misoprostol (94.4%) were treated as outpatients, while 5.6% (n = 30) were admitted to hospital (data not shown in tables).

Two-thirds of the women with pregnancies of up to 12 weeks used only 1 dose of misoprostol (66%); however, this proportion decreased to 34% among those with pregnancies of 13–14 weeks and to 23% for women with pregnancies of 15–18 weeks (data not shown in tables).

Gestational age was significantly associated with the success rate, defined as the percentage of cases in which MVA was not required to complete uterine evacuation. In women with pregnancies of up to 12 weeks, the success rate was 99.1%; however, this percentage dropped to only 25.7% and 27.9% in the case of women with pregnancies of 13–14 weeks and 15–18 weeks, respectively. At the ultrasound scan performed on the 15th post-treatment day, residual uterine contents were found in fewer than 5% of the women with pregnancies of up to 12 weeks. This proportion increased to 10% of women at 13–14 weeks of pregnancy and to 14% of women with pregnancies of more than 14 weeks. However, all of these cases were clinically asymptomatic and no interventions were performed (Table 2). In addition, 7.6% of women with pregnancies of up to 12 weeks and around 3% of those with pregnancies of 13–14 weeks failed to return for follow up and are presumed to have had no complications. None of the women with pregnancies of more than 14 weeks failed to return for their follow-up visit. The differences in success rates according to gestational age were statistically significant ($P < 0.001$) (Table 2).

The most common adverse effects of misoprostol treatment were pain, evaluated as severe, in 26.6% of patients (n = 143), chills in

Table 1
The percentage of incomplete abortions treated with misoprostol in the three participating hospitals in Cotonou, Benin (2008–2012).

	CUGO		HOMEL		Ménontin		Total	
Year	No.	%	No.	%	No.	%	No.	%
2008	14/116	12.1	12/156	7.7	10/112	8.9	36/384	9.4
2009	34/243	14.0	33/186	17.7	53/230	23.0	120/659	18.2
2010	49/143	34.3	45/153	29.4	26/143	18.2	120/439	27.3
2011	52/185	28.1	50/198	25.3	28/111	25.2	130/494	26.3
2012	53/214	24.8	52/192	27.1	26/127	20.5	131/533	24.6
Total	202/901	22.4	192/885	21.7	143/723	19.8	537/2509	21.4

Abbreviations: CUGO, Obstetrics and Gynecology Clinic at the Hubert Koutoukou Maga National Teaching Hospital; HOMEL, Lagoon Mother and Child Hospital; Ménontin, Ménontin Maternity Hospital.

Table 2
Presence of residual uterine contents at the follow-up ultrasound scan and subsequent management, according to gestational age at the time of abortion.[a]

Ultrasound report and management	Weeks of pregnancy							
	<12		13–14		15–18		Total	
	No.	%	No.	%	No.	%	No.	%
Clean	370	87.3	9	13	6	14	385	71.7
Residue present, but no intervention made	18	4.2	7	10	6	14	31	5.8
Residue removed with MVA	4	0.9	52	74	31	72	87	16.2
Failed to return for follow up	32	7.5	2	3	0	0	34	6.3
Total	424	100	70	100	43	100	537	100

Abbreviation: MVA, manual vacuum aspiration.
[a] Pearson $\chi^2 = 318.1.\alpha < 0.001$.

17.7% (n = 95), hyperthermia in 10.8% (n = 58), and heavy bleeding in 4.5% (n = 24).

Gestational age at the time of the abortion was also associated with the incidence of adverse effects. The proportion of women with severe pain, chills, hyperthermia, diarrhea, and heavy bleeding was significantly smaller ($P < 0.001$) in women with pregnancies of up to 12 weeks compared with those with pregnancies of 13–14 weeks or more than 14 weeks (Table 3). There was little variation in the proportion of women who complained of severe pain between women with pregnancies of 13–14 weeks (93%) and those with pregnancies of 15–18 weeks (100%). Heavy bleeding was observed only among women with pregnancies of more than 12 weeks and was present for approximately half of the woman with pregnancies of more than 14 weeks compared with only 7% among those with pregnancies of 13–14 weeks (Table 3).

Every woman treated with misoprostol elected to use some method of contraception, although the majority (70.8%) chose the combined oral contraceptive pill. Just over one-quarter (25.7%) chose a LARC method, with a preference for the Jadelle implant system (21.0%) rather than the copper IUD (4.7%). Only 2.6% chose an injectable contraceptive (depot-medroxyprogesterone acetate or Noristerat) and 0.9% (n = 5) decided to use a natural or barrier method (data not shown in tables).

4. Discussion

Misoprostol was introduced in Benin in an attempt to reduce the workload caused by the large number of women demanding postabortion care at every maternity hospital in the country. Evaluation of this experience shows that the method has been very well accepted by both providers and clients. Nevertheless, although there was a rapid increase in acceptance over the first 3 years, reaching a level of approximately one-quarter of all patients, this level has remained unchanged over the past 3 years of observation. It is important to remember that not all women with an incomplete abortion are able to use misoprostol and those with heavy bleeding, an infection, or hemodynamic instability are not eligible to use this method. Therefore, the percentage of women with an incomplete abortion who were able to choose misoprostol was affected by the severity of their complications at the time of their consultation at one of the study hospitals.

A number of different doses and dose intervals have been used to treat incomplete abortions [4–7]. By 2008, there was already a general agreement that 600 μg of oral misoprostol should be the recommended dose, with the effect expected to occur within a period of 7–10 days. On the other hand, the single dose of 800 μg reported by Demetroulis et al. [4] seemed an attractive option, as the effect appeared to be faster. In addition, one of the objectives of the present study was to verify whether a higher dose would enable incomplete abortions to be treated in the case of more advanced pregnancies. Accordingly, 800 μg was the dose selected for the present study, since this dose has already been shown to be very well tolerated and has been recommended by WHO for pregnancy termination up to the late second trimester of pregnancy [2]. When the present study was initiated, the authors were unaware of the evidence showing that endometrial thickness is not a good indicator of a need for further treatment [8] and the protocol required that a second dose of misoprostol be given whenever ultrasound suggested the presence of residual uterine contents. This explains the frequency with which the dose of misoprostol was repeated; however, if the women were completely asymptomatic and uterine contents were minimal, the clinical criteria prevailed and the protocol was not always followed.

A more important difference between the present study and other experiences that have been reported was that in the present case the medical treatment of incomplete abortion with misoprostol was not limited to the first trimester of pregnancy. It was decided to apply this method in pregnancies of up to 18 weeks as long as the women were in a stable condition and were within easy access of the hospital should any complication, particularly heavy bleeding, occur. The analysis of the study results showed that misoprostol did not work, as MVA was required to complete uterine evacuation in almost 75% of cases in which gestational age exceeded 12 weeks. In addition, all cases of heavy bleeding and most of the cases of complaints of severe pain were in women with pregnancies of more than 12 weeks of gestational age.

The success rate of 99.1% was similar to rates reported in other studies [12–14]. It could be argued that there is an assumption that there were no complications in any of the women who failed to return for their follow-up visit and there is no way of showing that these women did not, in fact, require surgical evacuation. The socioeconomic status of these patients, however, makes it highly unlikely that they would have gone to a private facility, knowing that they could receive free care at any one of the hospitals involved in this study.

Less than 10% of the women with pregnancies of up to 12 weeks reported adverse effects, which consisted principally of severe pain, chills, fever, and diarrhea, and this finding is in agreement with other reports [9–12]. The relatively high proportion (21%) of women with pregnancies of more than 12 weeks who reported heavy bleeding is another argument against the use of this treatment for incomplete abortion in cases of more advanced pregnancy. In particular, if this treatment is disseminated to places in which access to emergency care is difficult, the risk of heavy bleeding outweighs the benefits of the treatment, including its success rate.

Table 3
Incidence of adverse effects following misoprostol treatment, according to gestational age at abortion.

Adverse effects	Weeks of pregnancy								*P* value[a]
	≤12		13–14		15–18		Total		
	No.	%	No.	%	No.	%	No.	%	
Severe pain	35	8.3	65	93	43	100	143	26.6	<0.001
Chills	39	9.2	24	34	32	74	95	17.7	<0.001
Hyperthermia	16	3.8	20	29	22	51	58	10.8	<0.001
Diarrhea	18	4.2	13	19	25	58	56	10.4	<0.001
Heavy bleeding	0	0.0	5	7	19	44	24	4.5	<0.001
Total	424		70		43		537		

[a] Yates χ^2 test.

Based on these results, the current recommendation in these hospitals and for dissemination of this practice to the rest of the country is to reduce the dose of misoprostol to 600 μg orally and to limit use to patients with pregnancies not exceeding 12 weeks, in compliance with international recommendations [13].

Despite these deviations from the usual procedures for the use of misoprostol for this indication, analysis of this experience shows that it was generically quite positive, although it also shows that greater restrictions are required in limiting its indications, for gestational age in particular. The most important finding of the present study is its confirmation that misoprostol should not be used to treat incomplete abortion beyond 12 weeks of pregnancy.

Conflict of interest

The authors have no conflicts of interest.

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