International Journal of Gynecology and Obstetrics 111 (2010) 131–135

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

CLINICAL ARTICLE

A randomized controlled trial of 400-μg sublingual misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion in two Egyptian hospitals ☆

Rasha Dabash [a,*], Mohamed Cherine Ramadan [b], Emad Darwish [c], Nevine Hassanein [d], Jennifer Blum [a], Beverly Winikoff [a]

[a] Gynuity Health Projects, New York, USA
[b] El Galaa Teaching Hospital, Cairo, Egypt
[c] Alexandria University Faculty of Medicine/Shatby Maternity Hospital, Alexandria, Egypt
[d] Public Health Consultant, Cairo, Egypt

ARTICLE INFO

Article history:
Received 15 March 2010
Received in revised form 2 June 2010
Accepted 20 July 2010

Keywords:
Hemoglobin
Incomplete abortion
Manual vacuum aspiration
Misoprostol
Post-abortion care

ABSTRACT

Objective: To compare the safety, efficacy, and acceptability of 400-μg sublingual misoprostol with that of manual vacuum aspiration (MVA) in 2 Egyptian hospitals. *Methods:* Participating women were randomized to either MVA or misoprostol treatment for incomplete abortion. The primary outcome, complete uterine evacuation, was determined 1 week later, as were adverse effects, change in hemoglobin, acceptability, and satisfaction. *Results:* Complete uterine evacuation was achieved in 98.3% of women who received misoprostol and 99.7% who underwent MVA (relative risk [RR] 0.99; 95% confidence interval [CI], 0.97–1.00). A decrease in hemoglobin of 2 g/dL or more was comparably rare in the 2 groups (0.3% misoprostol vs 0.9% MVA; RR 0.34 [95% CI, 0.04–3.21]). Mean change in hemoglobin was also clinically similar (–0.5 g/dL misoprostol vs –0.4 g/dL MVA; $P<0.01$). Heavy bleeding was rare (2.4% misoprostol vs 1.6% MVA; RR 1.55 [95% CI, 0.51–4.68]) following treatment. Nearly all women (96.8% misoprostol vs 98.3% MVA) were satisfied with their treatment but those who received misoprostol were significantly more likely to prefer that method in the future (81.9% vs 62.8%; RR 1.30 [95% CI, 1.19–1.43]). *Conclusion:* The high efficacy, safety, and acceptability of 400-μg sublingual misoprostol indicate that it is analogous to surgery as a first-line treatment for incomplete abortion. Misoprostol might improve post-abortion care when resources are limited and surgical treatment is unavailable.

1. Introduction

The prostaglandin E1 analog misoprostol is inexpensive, widely available, and easy to store and use. Its strong uterotonic and cervical-ripening qualities have made it an accepted and widely used treatment for several reproductive health indications, including cervical ripening, labor induction, and incomplete abortion/failed pregnancy [1,2]. Misoprostol is an effective alternative to surgical evacuation for incomplete abortion [3–18], which is one of the most common clinical presentations of failed pregnancy in low-income countries.

A single dose of 600-μg oral misoprostol effectively evacuates the uterus following incomplete abortion in 91%–99% of cases [14–18]. One study also showed that a dose of 400 μg administered sublingually is as effective and is associated with comparable adverse effects [19]. In 2009, after reviewing data regarding its use for incomplete and spontaneous abortion, the WHO added misoprostol to its Model List of Essential Medicines for this indication—noting that, in addition to being as effective as surgery, misoprostol "in some settings may be safer as well as cheaper" [20].

In 1995, a study of Egyptian hospitals showed that post-abortion cases comprised one-fifth of hospital admissions and consumed substantial resources [21]. Egypt subsequently became one of the first countries in the region to introduce manual vacuum aspiration (MVA) as an outpatient service in lieu of dilatation and curettage under general anesthesia. Manual vacuum aspiration was piloted in selected tertiary hospitals and later expanded to additional hospitals throughout the country. Its introduction was an important step toward making post-abortion care safer, more accessible, and potentially more cost-effective. Nonetheless, more than a decade after its introduction, access to MVA and post-abortion care services remains highly centralized and limited to select hospital sites.

The aim of the present introductory study was to examine the safety, efficacy, and acceptability of 400-μg sublingual misoprostol compared with MVA in 2 hospitals to understand the potential role of misoprostol as a first-line treatment for incomplete abortion in Egypt.

☆ Clinicaltrial.gov registration number: NCT00466999.

* Corresponding author. 15 East 26th Street, No. 801, New York, NY 10010, USA. Tel.: +1 212 448 1230.
E-mail address: rdabash@gynuity.org (R. Dabash).

0020-7292/$ – see front matter © 2010 International Federation of Gynecology and Obstetrics. Published by Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijgo.2010.06.021

2. Materials and methods

Between February 7, 2007, and October 28, 2008, women presenting with an incomplete abortion and a maximum uterine size of 12 weeks of gestation were screened for eligibility at 2 large tertiary hospitals in Egypt: El Galaa Teaching Hospital, Cairo; and Shatby Maternity Hospital, Alexandria. Incomplete abortion was defined by an open cervical os confirmed by clinical examination, with either past or present history of vaginal bleeding, or evidence of retained products of conception if ultrasound was performed. Women were included if they were at least 21 years of age, lived or worked within 1 hour of the hospital, and agreed to provide contact information and return for follow-up. Exclusion criteria were as follows: known allergy to prostaglandins; symptoms of possible ectopic pregnancy; signs of hemodynamic instability; and signs of infection requiring immediate intervention.

Women consented via signature or thumbprint after information was provided verbally and in writing by study staff. Women's baseline hemoglobin (Hb) was measured instantly, using a Hemocue device (Hemocue, Ängelholm, Sweden). Participants were then randomly assigned to either MVA or 400-μg sublingual misoprostol. Randomization was based on a computer-generated sequence in blocks of 10; the sequence was prepared by Gynuity staff in New York using sequentially numbered envelopes, which were opened by providers following enrollment.

Participants randomized to the misoprostol group received 2 200-μg misoprostol tablets (Misotac, Sigma Pharmaceuticals, Egypt) to hold under the tongue for 20 minutes, after which they were instructed to swallow any remnants. Those in the surgery group underwent MVA—the standard surgical treatment in both hospitals. Pain management practices with MVA depended on provider preference, ranging from verbal anesthesia only to general anesthesia. Women in both groups were also provided with 500-mg paracetamol tablets to take, as needed, for pain and cramping. Following treatment administration, women in the misoprostol group were discharged at the provider's discretion, usually within 1 hour. Discharge following MVA treatment was variable and largely dependent on standard hospital procedure. Antibiotics were prescribed only if there were signs of potential infection. Information, including what should be expected following treatment and signs of possible complications requiring immediate hospital care, was 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.

The primary outcome was complete evacuation of the uterus without recourse to surgical intervention for any reason following initial study treatment. Secondary outcomes were a clinically significant change (at least 2 g/dL) in Hb following treatment, adverse effects, satisfaction, and acceptability. A sample of 668 women was required to detect a 1-sided difference ($\alpha = 0.05$, $\beta = 0.2$) of 4% or more, assuming a 98% efficacy with MVA. The sample was increased by approximately 5% to account for possible loss to follow-up.

Treatment outcomes were determined at follow-up. Abortion status was assessed from clinical history and examination, in addition to vaginal ultrasound when necessary. Women with a closed cervical os and no signs of an incomplete abortion were deemed to have undergone successful treatment and were discharged from the study after a brief interview and a follow-up Hb measurement. Women with signs of retained products of conception and no signs of complication were given the option of waiting an additional week before surgical evacuation. If the abortion was still not complete 1 week later, women underwent immediate surgical completion.

Women were encouraged to call the study hotline or return to the hospital if they experienced any signs of complication, as discussed in counseling. Those who failed to return for follow-up were contacted via telephone to reschedule their appointments. Women who were reachable by telephone but not willing or able to return to the hospital provided most of their follow-up data by telephone. To offset the cost of travel for the additional study visit, women received 20 LE (approximately US $4) at their follow-up visit.

Data were collected via study forms by trained physicians, nurses, and social workers and were reviewed on-site by site investigators and study coordinators before entry into SPSS version 14.0 (SPSS, Chicago, IL, USA). Data were periodically queried by Gynuity staff, who also conducted periodic monitoring visits to assess study progress and protocol compliance. The research protocol was approved by the appropriate ethics committees at both sites. Data from study sites were merged, cleaned, and analyzed on an intention-to-treat basis. χ^2 tests or t tests were used, as appropriate, to compare outcome measures. $P<0.05$ was considered to be statistically significant.

3. Results

In total, 700 eligible women were assessed, of whom 697 were enrolled and randomized to a treatment group (Fig. 1). The 2 groups did not differ statistically with regard to background characteristics (Table 1). Few women were suspected to have interfered with their current pregnancy: 2.0% in the misoprostol group and 2.3% in the MVA group (relative risk [RR] 0.8; 95% confidence interval [CI], 0.32–2.38). Ultrasound was used before randomization to confirm the diagnosis of incomplete abortion in approximately one-third of women (30.4% misoprostol vs 27.6% MVA; RR 1.10 [95% CI, 0.87–1.39]). All women received treatment as allocated, with no reports of problems in randomization or treatment administration. Outcome data were noted and analyzed for all participants, with the exception of 2 women (1 in each study group) who were lost to follow-up. Treatment outcomes were assessed via telephone for 13 women in the misoprostol group and 10 in the MVA group.

Both methods were highly effective at treating incomplete abortion (98.3% misoprostol vs 99.7% MVA; RR 0.99 [95% CI, 0.97–1.00]) (Table 2). Treatment success was determined 1 week after treatment, except for 11 (3.2%) women who opted for an extended follow-up visit after presenting with signs of continued incomplete abortion. Providers opted for ultrasound use in approximately one-fifth of cases, with recourse to ultrasound slightly more likely in women treated with misoprostol (21.6% misoprostol vs 15.2% MVA; RR 1.42 [95% CI, 1.03–1.97]).

One woman allocated to the MVA group underwent a second surgical evacuation at a private clinic following persistent pain and bleeding. The 6 failures in the misoprostol group comprised 2 women who underwent surgical evacuation following persistent heavy bleeding, 3 women with evidence of retained products of conception at follow-up, and 1 woman who underwent surgical evacuation within a few hours of misoprostol administration (owing to light–moderate bleeding) by a provider unfamiliar with the method and study protocol.

Treatment for incomplete abortion rarely resulted in a clinically significant decrease in Hb. One (0.3%) of the participants in the misoprostol group and 3 (0.9%) in the MVA group experienced a decrease of at least 2 g/dL. The mean change in Hb following treatment was significantly higher in the misoprostol group (–0.50 vs –0.39 g/dL; $P<0.01$), although it was clinically negligible. Heavy bleeding (compared with normal menses) was infrequently reported and transient (Table 3). Women treated with misoprostol were more likely to report normal (menses-like) bleeding following treatment (62.7% misoprostol vs 48.4% MVA; RR 1.29 [95% CI, 1.12–1.49]) and for slightly longer (2.26 days misoprostol vs 1.52 days MVA; $P<0.01$). Approximately 90% of women in both groups reported light bleeding (RR 0.96 [95% CI, 0.91–1.01]), which was slightly more persistent in the misoprostol group (3.23 vs 2.73 days; $P<0.01$).

Pain and/or cramps lasting approximately 2.5 days were reported by most women (87.8% misoprostol vs 75.9% MVA; RR 1.16 [95% CI, 1.07–1.24]). The medication provided during and after treatment was viewed as adequate by 89.4% in the misoprostol group and 84.4% in