International Journal of Gynecology and Obstetrics xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

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

www.figo.org

CLINICAL ARTICLE

Prospective study of home use of mifepristone and misoprostol for medical abortion up to 10 weeks of pregnancy in Kazakhstan

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ARTICLE INFO

Article history:
Received 3 November 2015
Received in revised form 10 February 2016
Accepted 16 May 2016

Keywords:
Home use
Kazakhstan
Medical abortion
Mifepristone
Misoprostol

ABSTRACT

Objective: To evaluate the efficacy of at-home medical abortion in Kazakhstan. *Methods:* A comparative, non-randomized study was undertaken at three clinics in Kazakhstan between October 10, 2013, and November 27, 2014. Women who sought medical abortion and had an intrauterine pregnancy of up to 70 days were enrolled. All participants took 200 mg mifepristone followed by 600 μg sublingual misoprostol 24–48 hours later. Women were offered the choice to take mifepristone at the clinic or at home; all took misoprostol at home. Abortion completion was assessed at an in-clinic follow-up appointment scheduled for all participants 2 weeks after mifepristone administration. *Results:* Of 290 enrolled women, 185 (63.8%) chose to self-administer mifepristone at home. Three (1.0%) of 289 women included in outcome analyses required surgical intervention for incomplete abortion. Therefore, the overall success rate was 99.0% (95% confidence interval 97.0%–99.7%). No serious adverse events occurred. *Conclusion:* Outpatient medical abortion with mifepristone and misoprostol is safe and effective up to 70 days of pregnancy. This service should be offered to women in Kazakhstan.
ClinicalTrials.gov: NCT02018796

1. Introduction

Mifepristone and misoprostol have been widely used for medical termination of early pregnancy. Many clinical care guidelines, including the WHO 2012 safe abortion guidance [1], recommend outpatient medical abortion up to 63 days since the last menstrual period (LMP), including taking misoprostol at home to maximize the convenience and acceptability of the service. Recent evidence shows that medical abortion is safe, effective, and acceptable as an outpatient service up to 70 days after the LMP [2–6], and the option to take both mifepristone and misoprostol at home is safe and desired by a substantial proportion of women [7–11]. In some countries—e.g. Australia, Moldova, and India—mifepristone and misoprostol are available for purchase at pharmacies with a prescription after the initial medical abortion consultation, and women do not need to return to the clinic to take either medication [12].

Kazakhstan is the largest country in Central Asia, with a population of more than 17.6 million [13]. Abortion is available in Kazakhstan on request during the first 12 weeks of pregnancy and with permission up to 22 weeks. In 2009, the Government of Kazakhstan updated national guidelines to include medical abortion using mifepristone and misoprostol, mandating the service be provided on an outpatient basis up to 7 weeks since the LMP (≤49 days) and on an inpatient basis for pregnancies between 8 and 22 weeks. The current medical abortion regimen in the first trimester is 200 mg mifepristone, followed in 36–48 hours by 600 μg oral, sublingual, or vaginal misoprostol [14,15].

The outpatient medical abortion service is burdensome for women in Kazakhstan because they are required to complete four in-person visits: 1) clinical assessment, vaginal smear, blood analysis, and laboratory testing for syphilis, HIV, and rhesus factor; 2) administration of mifepristone; 3) administration of misoprostol; and 4) follow-up assessment. Additionally, women with pregnancies of 8–10 weeks are unnecessarily undergoing an inpatient treatment when they could be at home, which would reduce cost to the health system. The aim of the present study was to evaluate the efficacy and acceptability of a simplified medical abortion service in Kazakhstan up to 70 days of pregnancy, using the locally approved regimen [15].

2. Materials and methods

A comparative, non-randomized trial was conducted from October 10, 2013, to November 27, 2014, at three sites in Kazakhstan: the Consultation and Diagnostics Department of the Perinatal Center No. 3 and the Consultation and Diagnostics Department of the Perinatal Center No. 1, both in Astana, and the City Polyclinic No. 9 in Almaty. Women who sought medical abortion and had an intrauterine pregnancy

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http://dx.doi.org/10.1016/j.ijgo.2016.02.018
0020-7292/

of 70 days or less (measured since the LMP) were asked to participate in the study. A woman was eligible for the study if she was eligible for medical abortion, able to provide written consent and contact study staff or a medical center in an emergency, and willing to provide contact information and comply with the study protocol. Exclusion criteria were presence of an ectopic pregnancy or undiagnosed adnexal mass, chronic renal failure, concurrent long-term corticosteroid therapy, allergy to mifepristone or misoprostol, hemorrhagic disorders or concurrent anticoagulant therapy, inherited porphyria, or presence of an intrauterine device that had not been removed. The Bioethical Committee of the Scientific Center of Obstetrics, Gynecology, and Perinatology of the Ministry of Health of the Republic of Kazakhstan approved the study protocol. All study participants provided written informed consent before undergoing study procedures.

Study providers assessed the length of pregnancy by collecting participants' menstrual histories and conducting a clinical examination and/or ultrasonography. Required laboratory testing was performed during the initial assessment visit.

The current medical abortion regimen in Kazakhstan was used: women took 200 mg mifepristone (Zizhu Pharmaceutical, Beijing, China) followed by 600 μg sublingual misoprostol (Zizhu Pharmaceutical) 24–48 hours later (some clinical protocols allow 24–48 hours although the guidelines stipulate 36–48 hours). Women had the option to take mifepristone at the study clinic or at home. If the woman chose to take mifepristone at home, providers helped her to pick a time to do so, not exceeding 70 days since the LMP. All women took misoprostol at home 24–48 hours after the mifepristone dose. Women could return to the clinic or request a surgical completion at any time. Sites did not dispense or prescribe analgesics, but encouraged women to use nonsteroidal anti-inflammatory drugs to manage pain during the treatment. Women were also given a home study card to record the time and date of mifepristone and misoprostol administration, number of missed days of work and/or school, and number of hours of childcare needed.

Study providers assessed the women's abortion outcome at the clinic during the follow-up visit, which was scheduled for 12–15 days after mifepristone administration. Providers assessed abortion completion by collecting clinical history and/or performing ultrasonography, and conducted an exit interview with the woman once the abortion was deemed to be complete. If the abortion was not successful or incomplete, providers offered the woman additional misoprostol or surgical completion. All incomplete and ongoing pregnancies were verified using ultrasonography. Women whose abortion was not complete were asked to come back for an extended follow-up visit. Women were considered lost to follow-up if they did not return and providers were unable to reach them within a month of study enrollment. For women who did not return to the clinic for follow-up, study providers ascertained whether their abortion was complete on the telephone by asking questions about current state of health, bleeding during the abortion procedure, and current pregnancy symptoms.

The primary goal of this study was to estimate the efficacy of abortion regimen. Successful abortion was defined as complete abortion without surgical intervention at any point during the study. Secondary outcomes were the acceptability of the reduced visit service to women, and occurrence of adverse effects and complications. Additionally, the women's choice in location of mifepristone administration (in clinic or home) was assessed, and the two groups were compared for adherence to the follow-up schedule, and number of missed days of work and/or school.

On the basis of previous studies [16–18], an efficacy rate of 95% was expected with a 95% confidence interval (CI) of 3%. A sample of 203 women was calculated to be sufficient to assess the efficacy of the regimen. The sample size was increased to 350 to allow providers to gain expertise in the method, but recruitment stopped at 290 women because of time constraints.

Analysis was conducted using SPSS version 19.0 (IBM, Armonk, NY, USA). Fisher exact test and Mann-Whitney *U* test were used to compare characteristics of the two groups. Two-tailed *P* values of less than 0.05 were considered statistically significant. The Fisher exact (Clopper-Pearson) method was used to calculate a 95% CI for success rates.

3. Results

Among the 290 women enrolled, the median pregnancy length was 45 days (range 34–69). Pregnancy length was 49 days or less for 221 (76.2%) women; 16 (5.5%) presented in the 10th week of pregnancy. At least one previous abortion was reported by 148 (51.0%) women.

Overall, 185 (63.8%) chose to take mifepristone at home (home group) and 105 (36.2%) chose to take the drug in the clinic (clinic group). There were no statistically significant differences in baseline characteristics between the two groups (Table 1).

The top three reasons for choosing to take mifepristone at home were schedule flexibility (reported by 57 [30.8%] of the 185 women), compatibility with duties (57 [30.8%]), and the need to miss fewer days of school or work (59 [31.9%]). The top three reasons for the choice in the clinic group were the presence of the physician or clinic staff (reported by 87 [84.5%] of 103 women), anxiety/fear and feeling safe in the clinic (58 [56.3%]), and feeling more comfortable taking mifepristone in the clinic (23 [22.3%]).

All women in the home group took mifepristone at the scheduled time, and no woman took mifepristone past 70 days of pregnancy. Furthermore, all women in both groups reported taking misoprostol at the scheduled time, except for one woman in the home group who took it 20 minutes earlier than scheduled.

One woman in the home group decided not to terminate her pregnancy before she took mifepristone and was withdrawn from the study. A total of 23 (7.9%) did not return to the clinic for follow-up, but all were contacted by phone. The proportion of women who did not return to the clinic for follow-up did not differ between the home group (14/184 [7.6%]) and the clinic group (9/105 [8.6%]; $P = 0.94$). Among the 221 women with pregnancies of less than 49 days, 21 (9.5%) did not return, compared with 2 (2.9%) of 68 women with pregnancies of 50–70 days ($P = 0.12$).

Overall, 289 women were included in outcome analyses (only the woman who was withdrawn was excluded). Three (1.0%) of the 289 women were found to have an ongoing pregnancy at the first follow-up visit. Two chose a repeat dose of misoprostol: one (42 days since LMP) completed her abortion successfully, whereas the second woman (53 days since LMP) went on to undergo surgical intervention for incomplete abortion. The third woman (67 days since LMP) chose surgical completion of her abortion. Additionally, 4 (1.4%) other women received a repeat dose of misoprostol (incomplete abortion for 3, missed abortion for 1); three successfully completed the process and one required surgical intervention. Overall, three of the 289 women received a surgical intervention, resulting in a success rate of

Table 1
Participant characteristics (n = 290).[a]

Characteristic	Home group (n = 185)	Clinic group (n = 105)	*P* value
Age, y	29 (19–44)	28 (16–42)	0.13
Gravidity	3 (1–14)	3 (1–11)	0.72
Parity	1 (0–4)	1 (0–4)	0.73
Length of pregnancy, d[b]			
≤49	139 (75.1)	82 (78.1)	0.67
50–56	23 (12.4)	13 (12.4)	>0.99
57–63	13 (7.0)	4 (3.8)	0.39
64–70	10 (5.4)	6 (5.7)	>0.99
Previous surgical abortion	72 (38.9)	41 (39.0)	>0.99
Previous medical abortion	35 (18.9)	21 (20.0)	0.88
Employed	101 (54.6)	56 (53.3)	0.90
Student	24 (13.0)	11 (10.5)	0.58

[a] Values are given as median (range) or number (percentage), unless indicated otherwise.
[b] Measured as time since last menstrual period.

Please cite this article as: Platais I, et al, Prospective study of home use of mifepristone and misoprostol for medical abortion up to 10weeks of pregnancy in Kazakhstan, Int J Gynecol Obstet (2016), http://dx.doi.org/10.1016/j.ijgo.2016.02.018