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A randomized controlled study comparing 600 versus 1200 μg oral misoprostol for medical management of incomplete abortion

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Abstract

Objectives: Although a number of studies have shown misoprostol's promise as a nonsurgical treatment for incomplete abortion, few have systematically examined treatment protocols. This study documents the effectiveness of 600 versus 1200 μg oral misoprostol for this indication.

Methods: From May 2002 to January 2003, 300 women with incomplete abortion were recruited at a large tertiary facility in Vietnam and randomized to either a single-dose (600 μg) or a repeated-dose (600 μg×2) regimen of oral misoprostol for the treatment of their condition.

Results: Misoprostol effectively evacuated the uterus for nearly all women (94.6%; $n=279$), with most reporting bleeding for 4 days (±2.3) and pain/cramps lasting 1 day (±1.0). Women indicated that the side effects were tolerable (96%) and that their experience was satisfactory (95%).

Conclusions: Oral misoprostol (600 or 1200 μg) offers a safe, effective and acceptable treatment for incomplete abortion. Larger studies to assess the advantages and disadvantages of misoprostol as compared with standard surgical care are needed to assess its role in postabortion care programs worldwide.

Keywords: Misoprostol; Incomplete abortion; Postabortion care; Vietnam

1. Introduction

Medical management of incomplete abortion using misoprostol is slowly gaining attention as an easy-to-use, feasible, low-cost means of effectively evacuating the uterus after spontaneous miscarriage or incomplete induced abortion. Although the method is increasingly used, relatively few studies have carefully assessed specific treatment protocols with ample samples to draw a clear conclusion about the efficacy of misoprostol for this indication. Indeed, a review of misoprostol for reproductive health indications concluded that there is insufficient evidence to support the use of misoprostol for treatment of incomplete spontaneous abortion [1].

To date, published studies have shown varying efficacy rates testing regimens ranging from 400 to 1200 μg misoprostol for incomplete abortion, usually administered vaginally [2–10]. Chung et al. [3] administered 400 μg misoprostol oral every 4 h to a maximum dose of 1200 μg and found that 50% of their cohort did not require additional surgical care. Later, a team from the same institution studied repeated doses of 800 μg misoprostol delivered either orally or vaginally with slightly higher success rates approximating 60% [4]. Importantly, both of these studies assessed efficacy on the day following treatment. Other studies in which the investigators chose to assess efficacy 3–15 days following initial treatment have reported markedly higher success rates. For instance, Gronlund et al. [5] compared the use of 400 μg vaginal misoprostol with expectant management and surgical evacuation and achieved a 90% success rate in the misoprostol arm at assessment on Days 8 and 14 (success was 82% for expectant management and 97% for surgical evacuation in this study). Similarly, Ngai et al. [6]

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achieved complete uterine evacuation for 83% of women in a small study with 400 μg vaginal misoprostol in which the final outcome was assessed 15 days after treatment. These studies are encouraging and support further exploration of appropriate protocols for misoprostol as a treatment for incomplete abortion.

The present study compares the completion rates among women randomized to receive misoprostol 600 μg as a single dose or that repeated for a total of 1200 μg. This research was also conducted in Thailand and showed a nonsignificant difference in the completion rate with the two regimens (single dose, 66.3%; repeated dose, 69.9%) [10]. However, the overall success rates between the two study sites (Site A, 42.6%; Site B, 85.1%) were significantly different. In an effort to address the conflicting success rates at the two sites, we felt that a second, larger study was needed to evaluate the effectiveness of these two treatment regimens.

In Vietnam, the standard of care for treatment of incomplete abortion is aspiration with or without local anesthesia. Prior to treatment, most women are given atropine and sedated, often with valium. This method works well but can be time consuming and, as aspiration must be performed by skilled surgical providers with access to surgical equipment, uncomplicated success is often provider and facility dependent. Often, resource-poor countries do not have ample facilities and providers to give this care adequately. Unlike missed abortion, which is often difficult to diagnose in places with limited access to ultrasound technology, incomplete abortion is easily diagnosed, however its treatment, either by electrical vacuum aspiration or by manual vacuum aspiration with or without anesthesia, can place unnecessary strains on health care infrastructures. The other treatment option—expectant management—is not widely practiced in Vietnam. This is because many providers and women are reluctant to wait to assess the need for treatment when reliable care (such as surgical aspiration) is available. Reducing the number of surgically treated incomplete abortions promises to reduce the burden for trained surgical providers while also broadening access to care at several levels of the health care delivery system.

2. Methods

From May 2002 to January 2003, 300 women presenting with diagnosed incomplete abortion were recruited at a large tertiary facility in Ho Chi Minh City in Southern Vietnam. Incomplete abortion was defined using the following criteria: transvaginal ultrasound evidence of substantial debris in the uterus (defined as echogenic mass > 12 mm), a past or present history of vaginal bleeding during pregnancy and an open cervical os, with or without products of conception present in the cervical or vaginal canal. Ultrasound was used only when there was suspicion that the uterus had been emptied (i.e., where the choriodecidual reaction in the uterine cavity measured <11 mm). If products of conception were seen or felt at the external os, ultrasound was not performed. Additional eligibility criteria included age of 18 years or older, living or working within 1 h of the study hospital, no known contraindication to misoprostol and general good health. All women would have received surgical evacuation of the uterus using aspiration with or without anesthesia if misoprostol had not been available.

All eligible women were counseled and given detailed information by study staff at the facility about the protocol. Women who expressed interest in participating and gave written informed consent were randomized to one of two treatment arms: (1) a single dose of 600 μg oral misoprostol or (2) 600 μg misoprostol oral repeated in 4 h for a total of 1200 μg misoprostol. The treatment group was assigned by opening the next study envelope in a computer-generated random sequence set up by staff at the Population Council. Ethical approval for this study was obtained from the Population Council's Institutional Review Board as well as Hung Vuong Hospital's Ethical Review Committee.

At the request of the local study investigators, all women swallowed their misoprostol in the presence of study staff at the hospital. Women in the single dose group could leave the hospital shortly after misoprostol administration whereas women in the repeated dose group were asked to remain at the hospital to administer their second misoprostol dose in the presence of a study investigator. These women were released shortly after administering the second misoprostol dose. Before leaving the hospital, women were given eight 500 mg paracetamol tablets to manage any pain, counseled about the side effects of misoprostol and scheduled to return to the hospital for follow-up care 2 days later. Women were also asked to complete a diary card to record any side effect and use of pain medication. They were also told that they could return to the hospital or contact the study providers at any time if they had any additional questions or concerns.

At the follow-up visit, each woman's abortion status was assessed. Women with retained products in the uterus (i.e., intrauterine echoic mass > 12 mm, dilated cervix and/or heavy bleeding on study Day 3) were offered the option of waiting an additional week to see if these products would evacuate on their own. If they agreed, they were given a second follow-up appointment on study Day 7 after initial treatment. Women who did not want to wait were given an immediate surgical completion. All women with retained products on study Day 7 were given surgical completions. Once their abortion was completed, women were interviewed to gauge their acceptability of the treatment.

The primary outcome measure for this study was complete uterine evacuation without recourse to surgical intervention at any point for any reason during the study period. In addition to this primary outcome, we sought to assess women's satisfaction and their acceptability of the method. All women were asked to respond to a series of qualitative questions during an exit interview. During these interviews, women were asked to name the methods' best and worst features and to indicate whether they would select the method again and recommend it to a friend. Additional