

## MISSED ABORTION: TERMINATION USING SINGLE-DOSE VERSUS TWO DOSES OF VAGINAL MISOPROSTOL TABLETS

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### ABSTRACT

**Objective:** To determine the effectiveness of 400µg misoprostol, administered vaginally as single-dose, compared to repeating the same drug, six hours later, for termination of missed abortion.

**Methodology:** One hundred ninety eight women with missed abortion were enrolled in this study. They had presented to Prince Zeid, Prince Rashed and Queen Alia Military Hospitals from June 1, 2005 to September 30, 2006 for termination of pregnancy. The gestational ages ranged between 9-22 weeks. Ninety three women were assigned to the single-dose group (Group-I) while the rest were given two doses of 400µg misoprostol, six hours apart (Group-II).

**Results:** The success rate for Group-I was approximately 88% compared to around 94% in Group-II. In Group-I, of all the women who aborted, about 50% had complete abortion compared to 66% in Group-II. The average time interval from the start of termination to expulsion of conception was around 13 hours in Group-I and 9 hours in Group-II ( $p < 0.05$ ). Only minimal adverse effects were noted.

**Conclusion:** Two doses of 400µg misoprostol administered vaginally did not prove to be superior to a single dose for termination of missed abortion, however, more women who had a successful procedure in Group-I needed evacuation and curettage. The mean abortion time was shorter in Group-II.

**KEYWORDS:** Missed abortion, Misoprostol, Termination of pregnancy.

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### INTRODUCTION

Application of prostaglandin into the posterior vaginal fornix has been widely used as a medical means of evacuation of the gravid uterus.<sup>1</sup> Published reports indicate that the intra-vagi-

nal administration of misoprostol tablets is safe and effective when used for this purpose.<sup>1,2</sup> Misoprostol is a methyl ester of prostaglandin E<sub>1</sub>. Its intended indications were prevention and treatment of gastro-duodenal ulcer, given its effective anti-gastric secretion activity.<sup>3</sup> In addition, misoprostol was found to be a strong stimulator of uterine contractility, although it was not marketed for this purpose.<sup>3</sup> Various doses of misoprostol, routes and protocols for term labour induction, as well as medical termination of pregnancy have been used.<sup>4-7</sup>

In this study, our aim was to determine whether a single vaginal dose of 400µg misoprostol is as effective as an abortifacient in the first and second trimesters of pregnancy when compared to two doses of the same drug, given six hours apart.

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## SUBJECTS AND METHODS

This prospective study was carried out from June 1, 2005 to September 30, 2006 at Prince Zeid, Prince Rashed and Queen Alia Military Hospitals. A total of 198 women with missed abortion were initially enrolled.

The diagnosis of missed abortion was confirmed by two ultrasonic examinations, one week apart. At the first visit, an abdominal &/ or vaginal ultrasound scan was performed by a senior specialist. One week later, a repeat ultrasound scan was also performed and the diagnosis of missed abortion was confirmed. Eligible women were then admitted to hospital for the process of termination of pregnancy.

The women were considered candidates if they had a missed abortion between 9-22 weeks gestation. Exclusion criteria included a gestational age >20 weeks with previous uterine scar, hypersensitivity to prostaglandins or history of bronchial asthma.

Women whose military ID numbers were even were assigned to the single-dose group (Group-I) while the rest were given two doses of 400µg misoprostol, six hours apart (Group-II). The tablets were inserted in the posterior vaginal fornix. Two women from the second group actually aborted within the first six hours and were excluded from the study leaving a total of 196 women (93 in Group-I and 103 in Group-II).

In the ward, the women were given a thorough medical examination. Investigations included full blood count, prothrombin time, active partial thromboplastin time, fibrinogen level and liver and kidney function tests. One unit of blood was cross-matched. In Group-I, two tablets of 200µg misoprostol were then placed in the posterior vaginal fornix while in Group-II, the same dose was repeated after six hours. The procedure was considered to have failed had there been no response within 24 hours of placement of the tablets.

## RESULTS

The demographic characteristics of the women can be seen in Table-I. Out of the 93 women in Group-I, 82 (88.2%) were consid-

Table-I: Demographic characteristics of the study population

	Group I	Group II
Mean maternal age (yrs)	27.4±6	26.8±4
Mean gestational age (wks)	16.3±3	17.1±2
Mean parity	4	4
Primigravidas	32	39
Multigravidas	61	64
Previous uterine scar	9	13

ered to have had a successful termination, while in the second group, 97 women (94.2%) also has a successful termination. Successful outcome was defined as complete or partial expulsion of the uterine contents within 24 hours.

Table-II displays the mean abortion time. This was calculated as the time from administration of the misoprostol to the time of reported expulsion of the gestation. In our study it was 13±6 hours for group I compared to 9±4 for Group-II.

In Group-I, 36 patients (43.9%) had incomplete abortion and were in need of evacuation and curettage. Twenty four women in this group (66.7%) were <14 weeks pregnant compared to only 10 women (21.7%) in the "complete group" who were <14 weeks pregnant and who did not require evacuation of the uterus. In Group-II, 29 women (29.9%) had incomplete abortion and were in need of evacuation and curettage. Nineteen women (65.5%) were <14 weeks pregnant compared to only 18 women (26.5%) in the "complete group" who were <14 weeks pregnant and who did not require evacuation of the uterus. See Table-III. The women who failed to respond were discharged but were asked to return one week later for a repeat of the same procedure.

## DISCUSSION

A variety of medical and surgical techniques have been used for termination of missed abortion.<sup>1-3,8-10</sup> These methods include intravenous infusion of oxytocin, intrauterine instillation of abortifacients, extrauterine instillation of abortifacients, dilatation and evacuation and hystrotomy.<sup>1-3,8-10</sup> Numerous methods have compared these techniques for second trimes-

Table-II: Outcome of study

	Group I	Group II	P value	Overall
Success rate	82 (88.2%)	97 (94.2%)	>0.05	179 (91.3%)
Complete abortion	46 (49.5%)	68 (66.0%)	<0.05	114 (58.2%)
Incomplete abortion	36 (38.7%)	29 (28.2%)	>0.05	65 (33.2%)
Mean abortion time (h)	13±6	9±3	<0.05	----

ter abortion, yet no single method proved to be superior.<sup>1,2,10</sup>

In 2006, the miscarriage treatment (MIST) trial was undertaken to ascertain whether a clinically important difference exists in the incidence of gynaecological infection between surgical and expectant or medical management of miscarriage. Twelve hundred women of less than 13 weeks' gestation, with a diagnosis of early fetal demise or incomplete miscarriage were included. The conclusion of this study was that the incidence of gynaecological infection after surgical, expectant, and medical management of first trimester miscarriage is low (2-3%) and no evidence exists of a difference by the method used.<sup>11</sup>

Khan et al in 2004 studied the pharmacokinetics of misoprostol. They determined that vaginal misoprostol was present in the circulation longer than oral misoprostol. Rectal misoprostol had a similar pattern. Oral misoprostol had a significantly greater peak plasma concentration and a shorter duration to maximum concentration than either rectal or vaginal misoprostol.<sup>12</sup>

In 2001, Pongsatha et al concluded that repeated doses of 400µg misoprostol, administered vaginally every three hours, are optimal for mid-trimester abortion,<sup>13</sup> while Dickenson et al in 2003 decided that in second-trimester pregnancy termination, a vaginal misoprostol regimen of 400µg every six hours was two times more likely to result in delivery within 24

hours from commencement than an oral regimen of 400µg every 3 hours.<sup>14</sup>

Combination of 200µg vaginal misoprostol followed by 48 hours later by 400µg oral misoprostol was advocated by Shannon et al in 2005. They concluded that such a combination is effective, associated with rare adverse events, and acceptable for women seeking medical abortion of pregnancies of up to 49 days duration.<sup>15</sup>

In this prospective study, we tried to determine whether a single dose of 400µg vaginal misoprostol was as effective as when this drug was repeated six hours later, in terminating a non-viable pregnancy between 9 and 22 weeks gestation. Safety and cost are of paramount importance whenever we prescribe any drug. The safety of prostaglandin E<sub>2</sub>, either for termination of pregnancy or for induction of labour was demonstrated in many earlier studies.<sup>16-18</sup> However, it is by no means cheap. The other alternative, misoprostol, apart from being much less expensive, is also widely available.

Dickinson in 2005 concluded that in second-trimester abortion, the use of misoprostol in women with prior caesarean delivery was not associated with an excess of complications compared with women with unscarred uteri.<sup>19</sup> A previous uterine incision did not prove to be a problem although no women with a previous scar and who were >20 weeks pregnant were included in the study.

Table-III: Rate of complete and incomplete abortions according to gestational age.

Type of abortion	Group I (n=82)		Group II (n=97)	
Incomplete	≥36 (43.9%)		29 (29.9%)	
	<14 weeks	≥15 weeks	<14 weeks	≥15 weeks
Complete	24 (66.7%)	12 (33.3%)	19 (65.5%)	10 (34.5%)
	46 (56.1%)		68 (70.1%)	
	<14 weeks	≥15 weeks	<14 weeks	≥15 weeks
	10 (21.7%)	36 (78.3%)	18 (26.5%)	50 (73.5%)

In 1995, Borgido et al reported that in the mid 90's, before the widespread use of misoprostol, PGE<sub>2</sub> suppositories and PGF<sub>2</sub> injections were widely used for second trimester pregnancy termination. However, although efficacious, their use was associated with numerous unwanted effects like nausea, vomiting, diarrhoea and fever in many women.<sup>20,21</sup> Misoprostol, when used as 800µg twelve hourly, is also associated with the same side effects, albeit to a much lesser degree.<sup>6,7</sup> We did not have any of these unwanted effects in our study, probably due to the low dose used.

The 91% overall success rate that we achieved correlates well with other previously published studies.<sup>1-3,14-16</sup> An interesting observation in both groups was that 65 women (33.2%) had incomplete abortion and needed evacuation and curettage. Forty three women (66.2%) were less than 14 weeks pregnant, compared to only 28 women (14.3%) who were less than 14 weeks pregnant and in whom evacuation and curettage was not necessary.

Although the results of most studies seem to be encouraging, a lot more work is still needed in order to determine the best and safest method for termination of a missed abortion.

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