ORIGINAL ARTICLE

A Randomised Comparison of Oral and Vaginal Misoprostol for Medical Management of First Trimester Missed Abortion

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Abstract

The present study was done to compare the safety and efficacy of misoprostol administered orally and vaginally for medical management of first trimester missed abortion. 100 women with diagnosed missed abortion were taken for this prospective study. Group A comprised of 50 women who were given oral misoprostol and another 50 in-group B were administered vaginal misoprostol. Clinical outcome, time taken for expulsion, number of doses required, side effects and cervical permeability were compared in two groups. Eighty percent in group B and 36% in group A had successful clinical outcome (p=0.000008). 16.6% in group A and 22.5% in group B expelled with a single dose while 50% and 77.5% expelled with complete schedule. Mean duration of expulsion was significantly higher in group A as compared to group B. Nearly ninety percent of women in both groups had good cervical permeability. Side effects were more common in group A. Hence vaginal misoprostol was found to be more effective and safer as compared to oral misoprostol.

Key Words

Misoprostol, First Trimester, Missed Abortion

Introduction

An increasing proportion (10%) of unsuccessful pregnancies are now diagnosed on routine first trimester ultrasonography and designated as missed abortions (1). Pregnancies clinically presenting as missed abortions have so far been treated by surgical evacuation of the uterus. Although considered safe, quick and effective yet it remains invasive procedure and there is considerable evidence that it is associated with certain risks such as cervical trauma, uterine perforation and intrauterine adhesions (2). The awareness of risk and need for general anesthesia prompted the search for alternatives such as expectant and medical methods. Misoprostol, the new synthetic analogue of PGE1 has radically changed the approach to first trimester missed abortion. The therapeutic potential of misoprostol as an abortifacient has clearly been demonstrated in a randomized study (3). Misoprostol is active and safe both by oral and vaginal routes but the latter has been found to be better in many trials. Oral route has the disadvantage of decreased bioavailability and more gastrointestinal side effects. Uterine contractility increases continuously for 4 hours after vaginal administration. Greater effect on the uterus by vaginal route is probably due to direct access to myometrium via cervical canal and by transfer of drug from the perivaginal venous plexus to uterine arterioles. When complete drug induced expulsion does not occur within 12 hours, the cervical priming properties of misoprostol are helpful to perform surgical evacuation (4).This drug has a lower cost, is stable at room temperature with fewer side effects as compared to PGE2 analogues (5).

The present study has been designed to compare the safety and efficacy of oral versus vaginal misoprostol for medical management of missed abortion.

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Material and Methods

This study was carried out in the department of obstetrics and gynecology, SMGS Hospital, Government Medical College, Jammu, J&K in the year 2002-2003. A total of 100 women consented to participate in the study. The specified inclusion criteria were a period of gestation less than 13 weeks, haemodynamically stable women with hemoglobin more than 10gm%, closed cervical os, axillary temperature of less than 37.5^0 C, no previous history of inflammatory bowel disease or allergy to misoprostol. All women satisfying the inclusion criteria were chosen and subjected to undergo TVS for confirmation after a thorough general physical and systemic examination. These women were then randomized (permuted block method) to receive either oral misoprostol (GroupA) or vaginal misoprostol (GroupB). In group A 400 microgm of misoprostol was given orally and repeated every four hours for a maximum of three doses if required. In group B 600 microgm of misoprostol was inserted in posterior vaginal fornix and the second dose was repeated after 4 hours. Over the next 10-12 hours, complete, incomplete or no expulsion was documented by TVS. Absence of echogenic structure measuring less than 15 mm in AP diameter suggested complete abortion. Nothing was given by mouth except medication for pain relief until complete expulsion or surgical evacuation. Information was obtained regarding the various side effects. Rh-negative women were given 150 microgm of anti D immunoglobulin. Surgical evacuation was performed in case of heavy vaginal bleeding or when TVS did not document a complete expulsion after 10-12 hours of commencement of treatment. The primary outcome evaluated was drug induced complete expulsion of the conceptus. Secondary outcome evaluated were side effects, induction expulsion interval, number of doses required and permeability of cervical canal in those women who required surgical evacuation. A good cervical permeability was defined as the ability to pass a No 8 Hegar dilator.

Results

Two groups were compared in age, gravidity, residential status and period of gestation. There were no significant statistical differences (Table I). Successful clinical outcome was seen in 36% women in group A while it was 80% in group B. This difference was statistically highly significant (Table II). 16.6% in group A and 22.5% in group B expelled after a single dose while 50% and 77.5% expelled with complete schedule. This difference between the two groups was again found to be significant (Table III). Mean duration of expulsion was significantly higher in group A as compared to group B (Table IV). Nearly 90% of women in both the groups had good cervical dilatation prior to surgical evacuation (Table V). Although the incidence of side effects such as nausea, vomiting, diarrhoea, severe pain, hyperpyrexia and excessive blood loss was higher in-group A but the differences were not very significant.

Table 1. Baseline characteristics of women

	GROUP A (n-50) No (%)	GROUP B (n-50) No (%)
Age (years)		
15-20	9 (18)	8 (16)
21-25	25 (50)	21 (42)
26-30	14 (28)	17 (34)
31-35	2 (4)	4 (8)
		X^2 = 0.27, df = 2, p= 0.87
Gravidity		
1st	21 (42)	19 (38)
2nd	8 (16)	15 (30)
3rd	12 (24)	8 (16)
4th	9 (18)	8 (16)
		X^2 = 3.08, df = 3, p= 0.37
Residence		
Urban	32 (64)	29 (58)
Rural	18 (36)	21 (42)
		X2 = 0.37, df = 2, p= 0.53
Period of gestation (wks.)		
6-8	9 (18)	7 (14)
8-10	10 (20)	10 (20)
10-12	18 (36)	15 (30)
12-13	13 (26)	18 (36)
		X2 = 0.60, p= 0.89

Table II. Clinical Outcome

Outcome	Group A (n-50) No. (%)	Group B (n-50) No. (%)
Successful	18 (36)	40 (80)
Unsuccessful	32 (64)	10 (20),

X^2 = 19.86, df = 1, p= 0.000008

Table III. Relationship of number of doses and outcome in successful cases

Outcome	Group A No. (%)	Group B No. (%)
1	3 (16.6)	9 (22.5)
2	6 (33.3)	31 (77.5)
3	9 (50)	---
Total	18	40

X^2 = 0.26, p= 0.56

For the purpose of analysis dose 2 and 3 have been clubbed together.

Table IV. Time interval between first dose and spontaneous expulsion

	Group A Mean (SD)	Group B Mean (SD)
Time interval (hours)	9.83 (2.09)	8.15 (2.85)

t = 1.98, p = 0.01

Table V. Effect of misoprostol on cervical permeability in unsuccessful cases

Permeability	Group A No. (%)	Group B No. (%)
Permeable	28 (87.5)	9 (90)
Non- Permeable	4 (12.5)	1 (10)

p=0.75, Fisher's Exact 0.65

Table VI. Incidence of side effects

Side effects	Group A (n-50) No. (%)	Group B (n-50) No. (%)
Nausea	25 (50)	20 (40)
Vomiting	6 (12)	3 (6)
Diarhoea	5 (10)	5 (10)
Severe pain	8 (16)	5 (10)
Hyperpyrexia	2 (4)	2 (4)
Excessive blood loss	6 (12)	3 (6)

Discussion

The present study suggests that vaginal misoprostol is more effective than oral misoprostol and that it requires fewer dosages with less side effects. In the present series of 100 women majority were between 21-25 years. Our observation is in consonance with EI-Rafaey *et al.* (6) who too did not observe any difference in age. The number of primigravidas was higher in both the groups, 42% in-group A and 38% in-group B. The difference was insignificant (p=0.37). Creinin *et al.* also observed no difference related to gravidity (7). Maximum patients in both groups belonged to urban area, 64% in-group A and 58% in-group B. It probably points towards the fact that urban population is more aware of antenatal care during first trimester. Lawrie *et al.* (8) observed that women in oral treatment group had pregnancy of 7-11 weeks while vaginal group was between 7-12 weeks. In present study the missed abortion was detected at slightly higher gestational age. This may be because of low availability/acceptability of ultrasonography during first trimester. The clinical outcome in current study shows that 36% of women in-group A and 80% in-group B had successful outcome. These results are nearly similar to those of Creinin *et al.* but the sample size of their study was small twenty (7). Our results of vaginal misoprostol are also comparable to that of Zalanyi, who reported 88% successful expulsion within 10 hours (9). EI-Rafaey *et al.* (6) in their study found that 93% of women expelled with vaginal misoprostol while 78% did so with oral misoprostol ($p < 0.001$). The difference between two groups in our study is quite significant. This may be because of use of mifepristone in combination with oral misoprostol in their study. Ayres-de-Campos *et al.* (10) reported success rate of 56.8% with vaginal misoprostol whereas our study has much higher success rate. This may be due to different dosages, regimens, population selection criteria, sample size as well as different ultrasound criteria used to define success. Creinin *et al.* (7) observed in their study that 1 out of 12 (8.33%) women in oral group expelled after first dose and another 1 after repeat dose. In vaginal group 5 out of 8 (62.5%) expelled after single dose while 2 did so after second dose. Our study shows much higher expulsion rate after single dose

(Table III). The disparity between two studies may be because of different dosages of misoprostol and small sample size of their study. Administration-expulsion interval has an important bearing on acceptability. In the present study we observed that the mean time interval of expulsion in group A was 9.83 with SD of 2.09 while in group B it was 8.15 with SD of 2.85. This difference was highly significant. Like other prostaglandins, misoprostol too has common adverse effects like nausea, vomiting, abdominal pain, shivering and fever that are dose dependent. Although GI tract symptoms were reported more frequently, hemorrhage was the most serious complication. One woman in vaginal group bled heavily and required blood transfusion. Hemorrhage requiring blood transfusion is a recognized complication of both medical as well as surgical induction of abortion. Although uncommon, yet the possibility highlights the need for vigilance and ready access to medical help. Hyperpyrexia, another uncommon side effect was observed in another 2 women requiring injectable paracetamol. Pain was experienced by almost all but it was severe in 16% in group A and 10% in group B. Our results were consistent with those of EI Rafaey *at al.* (6). One of the aims in present study was to assess cervical permeability in patients who required surgical evacuation. Nearly 90% of women in both the groups had permeable cervices. Our study is similar to that of Ayres-de-Compos *et al.* (10) who reported 94.5% permeability among their 74 patients who were given 600 microgm of vaginal misoprostol. Our results are also comparable to Lawrie *et al.* (8) who used oral and vaginal misoprostol for cervical dilatation prior to surgical evacuation and found no significant differences between the two groups. Herabutya *et al* (11) similarly suggested misoprostal (600 μg) administered at 12 hour interval to be associated with fewer adverse effects and as effective as a 6 hour interval. Regimen of repeated doses of vaginal misoprostal every 3 hours over a period of 9 hours has been suggested suitable for women requesting of pregnancy upto 8 weeks of gestation (12). Kovavisarch (13), however suggested intravaginal misoprostal 800 μg to be more effective than 600 μg (dose used in the present study) for the termination of an early failure with no significant differences in the effects. It thus appears that use of misoprostol for medical management of midtrimester abortion is an effective, cheap, safe and convenient alternative to surgical evacuation and it also provides adequate cervical dilatation in unsuccessful cases requiring surgical evacuation. Its popularity has also been enhanced because of its easy availability, affordability and more importantly, predictable and favourable results.

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