

# Vaginal Misoprostol for Medical Evacuation of Early Pregnancy Failure

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**OBJECTIVE** – To evaluate the efficacy of vaginal misoprostol in bringing about evacuation of uterus in early pregnancy failure. **METHODS** – A prospective observational clinical trial was carried out on 60 patients admitted with missed abortion or blighted ovum of less than 14 weeks gestation during the period from October 1999 to July 2001. Four hundred micrograms of misoprostol was placed into the posterior vaginal fornix and the patients were examined 24 hours later. If there was no response, ie., no expulsion of products of conception the same dose was repeated after 24 hours. The primary outcome was complete expulsion of uterine contents within 24 hours of initial or repeat misoprostol. Side effects were also noted. **RESULTS** – Out of the 60 patients, 46 (76.7%) expelled their products completely with misoprostol, out of whom 43 (71.7%) expelled with single dose administration thus showing that the insertion of the second dose of misoprostol was not of much use in bringing about expulsion in cases who did not respond to the first dose. The mean insertion-expulsion time was  $9.7 \pm 5.6$  hours. Even in the failed group of 14 patients (23.3%), 10 (71.4%) showed favorable cervical changes, which made subsequent evacuation much easier without dilatation. **CONCLUSION** – The use of 400 µg of vaginal misoprostol for early pregnancy failure resulted in complete expulsion of the products of conception in 71.7% of the patients after single dose and in 76.7% after two doses thus reducing the need for surgical treatment. When complete drug induced expulsion did not occur within 24 hours of the second dose of misoprostol, the cervical ripening property of misoprostol helped in performing surgical evacuation without dilatation.

**Key words** : missed abortion, blighted ovum, misoprostol

## Introduction

Early pregnancy failure (also known as missed abortion or blighted ovum) is a common problem in obstetrics and gynecology. Approximately 10% to 20% of clinically recognised pregnancies are diagnosed as non-viable in the first and second trimesters. Treatment of early pregnancy failure usually consists of waiting for spontaneous expulsion or surgical evacuation. Expectant management has the disadvantage of uncertainty as to the timing of expulsion. Surgical methods have attendant complications like hazards of anesthesia, cervical laceration with the possibility resulting in incompetent cervix, uterine perforation, hemorrhage, infection, Asherman's syndrome etc<sup>1</sup>. The major drawback of D and C is the need for a surgical procedure.

Misoprostol is a prostaglandin E<sub>1</sub> analogue, 15-deoxy, 16-hydroxy, 16 methyl PGE<sub>1</sub>, which is rapidly absorbed from the gastrointestinal tract. Comparing the pharmacokinetics of vaginal and oral administration of

misoprostol, it was reported that due to prolonged serum concentration in the vaginal group, the vaginal administration could be dosed at longer intervals than oral administration<sup>2</sup>. The sustenance of plasma levels of misoprostol upto four hours when administered vaginally is due to the fact that it bypasses presystemic gastrointestinal and hepatic metabolism that occurs with oral administration. The side effects with misoprostol include fever, abdominal cramps, diarrhea, nausea and vomiting, vaginal bleeding etc. which are more common with oral than with vaginal route<sup>3</sup>.

Considerable savings in resources can be made if routine curettage can be avoided and a medical rather than surgical approach adopted. These savings are potentially large if a significant proportion of the patients can be assessed, treated and monitored without hospital admission<sup>4</sup>. The present study was undertaken to study the efficacy of vaginal misoprostol in evacuation of early pregnancy failure and to study the complications, if any, due to misoprostol.

## Material and Methods

The present study was a prospective observational clinical trial conducted on 60 patients admitted with missed abortion or blighted ovum of less than 14 weeks gestation during the period of October 1999 to July 2001. The permission of the Hospital Research Council was

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obtained to conduct this study. The diagnostic criteria used in transvaginal ultrasonography were embryonic pole  $> 5$  mm with no cardiac activity or irregular intrauterine gestational sac with a maximum diameter of 15 mm or greater with no embryonic pole or no growth on ultrasound (USG) over a minimum period of one week. Patients with excessive vaginal bleeding (soaking more than a pad per day), with dilated cervix, with contraindications to prostaglandins and those who insisted on D and C were excluded from the study.

Each patient's informed written consent was obtained for inclusion in the study. A thorough examination including vaginal examination noting uterine size and cervical status was done and 400  $\mu$ g of misoprostol (two tablets of 200  $\mu$ g each) were inserted into the posterior vaginal fornix after breaking the tablets into half as the tablets have an inert covering. The patients remained in the hospital and were reviewed 24 hours later and if there was no expulsion of products, the same dose of misoprostol was repeated. Side effects due to misoprostol were noted. The products of conception were sent for histopathological examination. Repeat transvaginal sonography was done in all patients to rule out retained products of conception. In unsuccessful cases with products not expelled within 24 hours of repeat misoprostol, cervical changes were noted and surgical evacuation done. The patients were covered with antibiotics viz., co-trimoxazole and metronidazole. At discharge, they were requested to report for checkup after two weeks or earlier if there were any problems.

## Results

The study included 60 patients with a mean gestational age of  $12.1 \pm 2$  weeks. The mean uterine size was 8 weeks. The mean sac size was 18 mm by ultrasonography. Out of the 60 patients, 43 (71.7%) expelled the products completely with a single dose of misoprostol and 3 (5%) more expelled after the second dose. Only 18.2% of those who failed to expel the products with the first dose did so with the second dose. Thus the second dose of misoprostol was not of much use in bringing about expulsion in cases who had not responded to the first dose (Table I). The mean insertion expulsion time was  $9.7 \pm 5.6$  hours (Fig.1).

Even in the failed group of 14 (23.3%) patients, 10 (71.4%) showed favorable cervical changes, which made subsequent evacuation much easier without further cervical dilatation.

The commonest side effect noticed with misoprostol was vaginal bleeding, severe bleeding with passing of clots occurring in 5%. No patient required blood transfusion or oxytocics to control bleeding. The mean fall in Hb, was 0.4 gm%; only two patients (3.3%) had a fall of more than 2 gm% (one had 2.2 gm% and one 2.4 gm%). Moderate and severe abdominal pain was reported by six (10%) patients but unbearable pain requiring narcotic analgesia was present only in one patient. Minor side effects included vomiting in five (8.3%), diarrhea in one (1.7%), fever subsiding with oral paracetamol in two (3.3%) and chills without fever in one (1.7%). Side effects like vaginal bleeding and abdominal pain were found to be significantly less in the failed group. No case of postabortal infection was noted.

## Discussion

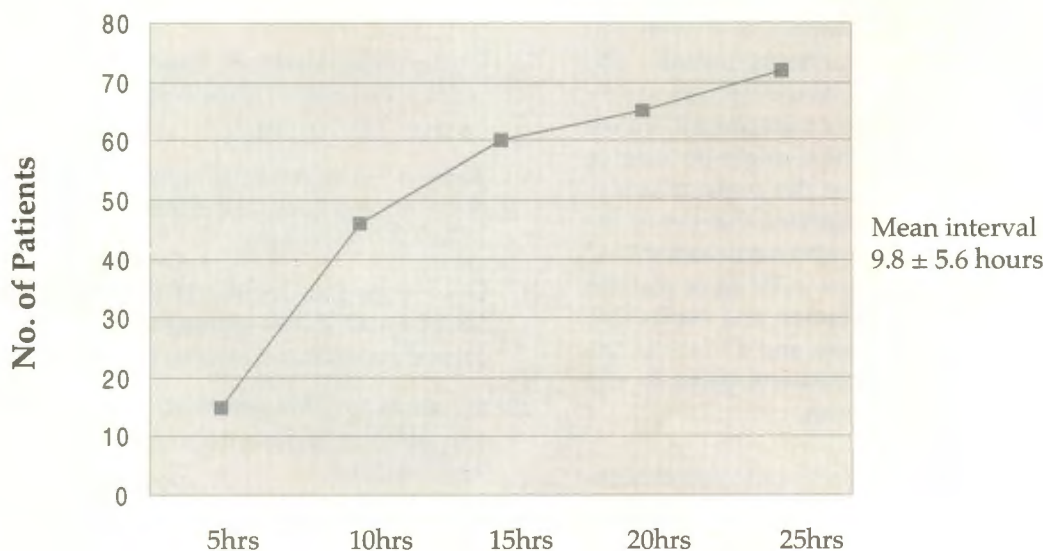


Fig 1. Insertion expulsion interval

The first report of using misoprostol for early pregnancy failure was by El Refaey et al<sup>5</sup> in 1992. Sixty women of less than 13 weeks of gestation received 600 mg of mifepristone followed 48 hours later by 600 µg of oral misoprostol. Eight women i.e., 13% (95% CI) aborted in the 48 hours interval between mifepristone and misoprostol treatment. Forty-three aborted within 4 hours of receiving misoprostol and an additional four women aborted after receiving a second dose of misoprostol. Thus 90% (90% CI) of women completely aborted during the time from initiation of treatment to 24 hours after misoprostol<sup>5</sup>.

For patients with abnormal pregnancy, the support of the decidual lining is usually already unstable and thus pretreatment with mifepristone or methotrexate may be unnecessary<sup>6</sup> and misoprostol alone may be sufficient which causes expulsion of these abnormal products of conception. In the present study, vaginal route of misoprostol was chosen because various studies have demonstrated that misoprostol is more efficacious and has fewer side effects when administered vaginally rather than orally, although the latter is more practical. We used a comparatively low dose of misoprostol to reduce the side effects.

Creinin et al<sup>7</sup> reported success rates of 88% with two doses of 800 µg vaginal misoprostol and 25% with two doses of 400 µg oral misoprostol 24 hours apart. The vaginal dose of misoprostol used was two to four times the dose in the present study with more side effects. The ultrasound criteria used to define successful evacuation were the same as in our study. The results of the present study are comparable to those of Zalanyi<sup>8</sup> who reported 72% expulsion rates with two doses of 200 µg vaginal misoprostol four hours apart. The successful evacuation rate in our study is significantly higher than 57% expulsion rate reported by De Campos et al<sup>9</sup> with two doses of 600 µg misoprostol at four hours interval. The waiting period was 24 or 48 hours in our study (depending on one or two doses of misoprostol) unlike 10 to 12 hours in their study which might be a factor involved in the better results of the present study. Herabutya and Prasertsawat<sup>10</sup>, reported that out of the 84 women with a missed abortion who were randomized to receive either vaginal misoprostol 200 µg or placebo the day before the planned dilatation and aspiration, (83.36%) in the misoprostol group and 17.14% in the placebo group expelled the products prior to the scheduled dilatation and aspiration.

The present study, confirms the safety and low incidence

of serious side effects with misoprostol at the described dose. The low cost is evident as 400 µg tablets cost less than Rs. 50 whereas surgical evacuation costs much more depending on the treatment center. The patients were satisfied with the treatment, as a surgical procedure was very often avoided. The regimen has become popular among clinicians and patients, as it avoids a considerable number of operations and even when expulsion does not occur adequate cervical dilatation for surgical evacuation is provided. Many similar studies have been undertaken by different authors but a recommended dose and route is yet to be established.

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