

OUT PATIENT MEDICAL MANAGEMENT OF ANEMBRYONIC PREGNANCY USING MISOPROSTOL

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ABSTRACT

Objective: This study aims to evaluate the efficacy, safety and acceptability of misoprostol for outpatient management of anembryonic pregnancy.

Study Design: This was a prospective observational study.

Place and Duration of Study: This study was conducted in the Department of Obstetrics and Gynaecology, Khyber Teaching Hospital Peshawar from Dec. 2011 to Nov. 2012.

Patients and Methods: Over a study period of one year 100 women attending our unit with ultrasound proven anembryonic pregnancy of < 10 weeks' gestation and opting to have medical management and consented to have it on an outpatient basis were recruited for the study. All patients were given 800 µg of misoprostol intra-vaginally in the unit and advised to take two further doses of 400 µg of misoprostol, orally, 3 hours apart, the following day at home. Outcome measures included success rates, emergency admission rates, pain scores, satisfaction level, incidence rates of side – effects and number of women who would choose medical management in future.

Results: Of the 100 women with anembryonic pregnancy, over three – quarters (n = 88, 88%) of the women achieved successful complete medical evacuation. Overall 6 (6%) women presented for emergency admission. Eighty eight patients were satisfied with the management. The mean visual analogue scale (VAS) score of all women was 6.9. Eighty seven said that they would choose to have medical evacuation in a future miscarriage. A total of 85 women said they would prefer to have the treatment at home rather than in the hospital. No serious side effect was reported with misoprostol.

Conclusion: It was concluded that medical evacuation of anembryonic pregnancy is effective, safe and acceptable in the outpatient setting.

Key Words: Anembryonic pregnancy, misoprostol, outpatient.

INTRODUCTION

Early pregnancy loss is very common an estimated 15 – 20% of diagnosed pregnancies miscarry in the first trimester.¹ Anembryonic pregnancy (also known as a blighted ovum) constitutes 50% of these losses.² The fertilized egg implants into the endometrium but only the gestational sac develops and there is no embryonic development.^{1,2} It can only be diagnosed by an ultrasound scan.^{2,3} For diagnosis, the sac must be of sufficient size that the absence of normal embryonic elements is established.^{2,4} The criteria depends on the type of ultrasound exam performed. A pregnancy is anembryonic if a transvaginal ultrasound reveals a sac with a mean gestational sac diameter (MGD) greater than 13 mm and no yolk sac, or an MGD > 18 mm with no embryo. If a trans-vaginal exam is not performed, the criteria for a trans-abdominal scan is a MGD of 25 mm or more without an embryo or an MGD of 20 mm or more without a yolk sac.^{4,5}

Management options for early pregnancy loss in-

clude expectant management, medical management with misoprostol, and surgical uterine evacuation.^{6,7} In the absence of embryo pregnancy is already destabilized, and the physiological changes that eventually lead to spontaneous expulsion are under way (e.g., placental degeneration and decidual sloughing).⁸ However the patient is often asymptomatic. If spontaneous expulsion is delayed, medical management is a preferable option to evacuate the uterus, in order to avoid surgery or a prolonged wait for expulsion.⁸⁻¹⁰

Misoprostol, a prostaglandin EI analog is effective in evacuating the uterus in the case of an early failed pregnancy (anembryonic pregnancy).¹¹ It can be administered both orally as well as intravaginally.¹¹ When women choose medical management, the miscarriage process usually evolves more quickly and predictably than with expectant management. Cramping and bleeding typically occur within two to six hours of misoprostol insertion.^{11,12} Pretreatment with a non-steroidal anti-inflammatory drug before

administering the misoprostol is helpful to block the adverse effects of fever, chills, and severe cramping.^{12,13} As with expectant management, a follow-up appointment is important to document completion.¹²⁻¹⁴

Medical termination of early pregnancy with misoprostol is often done in hospital on an inpatient basis mainly due to fear of complications like excessive bleeding and pain.¹⁵ However the trend is now shifting towards its use on an outpatient basis.^{15,16} It can be managed effectively and safely in the outpatient setting with misoprostol.^{16,17} Outpatient management is preferable to termination in hospital setting because it decreases cost and lessen the burden on hospitals.¹⁶ Patients convenience and satisfaction level is high and psychologically they feel at ease in the comfort of their home with their dear ones by their side to support them.¹⁶⁻¹⁸

PATIENTS AND METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Khyber Teaching Hospital Peshawar from Dec. 2011 to Nov. 2012. A total of 100 women with an ultrasound diagnosis of an embryonic pregnancy (Blighted ovum) and with a period of gestation less than 10 weeks as calculated from Last menstrual period, were asymptomatic and who consented for the medical termination of pregnancy on an outpatient basis were enrolled to the study. The purpose of the study was explained to the patients. A detailed history was taken from each patient and a thorough physical examination was carried out so as to rule out any possibility of imminent miscarriage like painful uterine contractions, vaginal bleeding and/or open cervical os. All the patients were administered a single dose of 800 µg misoprostol (total of 4 tablets 200 microgram each) intra-vaginally deep into the posterior fornix of vagina. The tablets were moistened with water for better effect. The patients were asked to remain in lying position for about 30 minutes so as to avoid the possibility of tablets being fallen down. All the patients were asked to take two further doses of misoprostol 400 µg the next day 3 hours apart orally. Patients were informed about expected bleeding and were prescribed analgesics for pain. They were advised to return to the hospital for surgical evacuation if they had unacceptable symptoms such as severe bleeding or pain. Anti-D immunoglobulin was given to all rhesus – negative women. Patients were also counseled about the side effects like diarrhea and shivering. All women returned for a follow-up visit, including pelvic ultrasound, one week after inclusion. If they had retained intrauterine products of conception with an antero-posterior diameter above 15 mm, surgical evacuation was performed otherwise oral misoprostol was prescribed. Outcome

measures were assessed which included success rates in terms of number of complete abortion, emergency admission rates, pain scores through visual analogue scale (0 no pain 10 unbearable pain), level of satisfaction, incidence rates of side – effects, and number of women who would choose outpatient medical management in future.

RESULTS

Out of 100 patients with an embryonic pregnancy, 65 were multigravidae and 35 primigravidae. Mean period of gestation was 7.6 ± 0.5 weeks. Mean age was 25 years with a range of 21 – 30 years. Only five patients had a history of an embryonic pregnancy in the past. Eighty eight patients had complete evacuation with no ultrasound evidence of retained products at one week follow-up. Twelve patients had retained products of conception on follow-up ultrasound scan, with all having only minimal products and managed with oral misoprostol. There were 6 emergency admissions all due to heavy vaginal bleeding. None of the patient was in shock. Four were managed with intravenous fluids and observation alone with complete expulsion in the next 24 hours while two ended up in emergency evacuation of products. In both of them evacuation was done under light

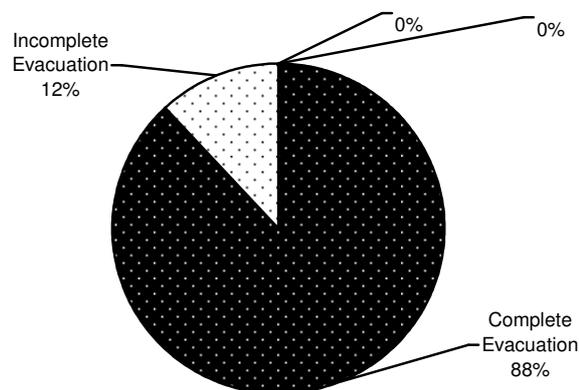


Figure 1: Effectiveness of Misoprostol.

Table 1: Patient Characteristics (data expressed as mean (SD) for age, weight and period of Gestation. For other parameters, percentages are shown in parenthesis.

Age (Years)	25 ± 2.7
Weight (Kg)	62 ± 2.3
Period of Gestation (Weeks)	7.6 ± 0.5
Previous miscarriage	N = 5 (5%)
Multigravidae	N = 65 (65%)
Primigravidae	N = 35 (35%)

sedation. Only one patient required blood transfusion.

Mean duration from administration of first dose of misoprostol to expulsion of products was 30 ± 2 hours. Five patients had expulsion before the second dose of misoprostol.

Overall 88 patients were satisfied with the management. Twenty one patients reported abdominal pain and seven diarrhea. Six patients had shivering and the rest had minor symptoms like nausea. Mean pain score on visual analogue scale was 6.9 and in nearly all patients pain responded to simple analgesics prescribed to them. Average numbers of pads used for bleeding over the first two days were 5 per day.

Table 2: *Safety of Misoprostol (Side Effects).*

Side Effect	No. of Patients
Nausea	13
Vomiting	3
Dizziness	4
Diarrhea	7
Shivering	6
Excessive bleeding requiring emergency admission	6
Abdominal cramps	21
Unbearable pain	5

Overall eighty seven women said that they would choose to have medical evacuation in a future miscarriage, while six were unsure. A total of 85 women said they preferred to have the treatment at home rather than in the hospital.

DISCUSSION

The use of misoprostol for treatment of spontaneous miscarriage is not new. Herabutya and Prasertawat¹⁹ showed that 200 µg vaginal misoprostol caused a significant increase in the passage of tissue mass when compared with a placebo (83.3% in misoprostol versus 17.1% in placebo), when given 1 day prior to suction evacuation for missed miscarriage. However, transvaginal scans were not repeated prior to the procedure and therefore the percentage of complete miscarriages induced by misoprostol was not known.

Nielsen et al¹⁰ showed that the combination of mifepristone and oral misoprostol was effective for first trimester miscarriage. They used 400 mg oral mifepristone followed by a single dose of 400 µg oral misoprostol. A total of 82% of women had an empty

uterine cavity after 5 days. However, mifepristone is only available in a few countries. The addition of mifepristone also added to the drug costs of the regimen. We demonstrated that by using misoprostol alone, the success rate was comparable with the combination of mifepristone and misoprostol. Patients can have an option of medical treatment where mifepristone is not available. The same was observed by Zalányi S.²⁰

In our study we have specifically chosen cases of anembryonic pregnancy for outpatient medical termination. Studies done so far have addressed all cases of missed abortions including those where an embryo is present. Since in anembryonic pregnancy there is only a gestational sac, this form of miscarriage is associated with less blood loss and the process of miscarriage is less painful when compared to miscarriages in which an embryo is present. It makes these cases ideal to manage on an outpatient basis.

A number of studies^{11,21} have been done to compare oral vs. vaginal misoprostol and these studies have shown that vaginal route is more effective than oral route while oral route is associated with more side effects.

In our study we used a combination of both vaginal and oral misoprostol. It was so because vaginal route is not convenient in outpatient setting. It is not preferred by women when it comes to self – application and majority find it difficult to put the tablets deep into posterior fornix. The first dose of misoprostol in our study was administered by a doctor in hospital so as to initiate the process of miscarriage in a more effective way and the next doses were oral to further enhance and thus complete the evacuation.

Misoprostol was highly effective as an abortifacient with 88% patients achieving complete abortion within 36 hours. Our results are close to Bagratee J.S. et al²² who obtained a success rate of 87%.

In our study, all women considered the side – effects tolerable and transient. Same was reported by Sifakis S et al²³ in their study. There were 6 (6%) emergency admission, which correlates with Shankat M. et al¹⁶ (6.7%) and only one patient required blood transfusion which justifies misoprostol use on an outpatient basis.

Level of satisfaction with medical management in home setting was high. Pain was reported as bearable by most of the patients and responded well to oral analgesics. Patients felt at ease away from the tense hospital environment.

It is **concluded** that Misoprostol can be effectively used for the termination of an embryonic pregnancy of less than 10 weeks period of gestation. We recommend its use on an outpatient basis because it is safe and convenient to use in this setting. Women

prefer its use in the home setting. This approach is also cost effective.

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