

ORIGINAL ARTICLE

SUCCESS AND SAFETY OF MISOPROSTOL FOR TREATMENT OF EARLY PREGNANCY FAILURE

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Background: Early pregnancy failure is a common complication in pregnancies. It can be managed medically as well as surgically. Lately there has been an emphasis on medical management of early pregnancy failure. Misoprostol, a Prostaglandin E1 analogue has been found to be safe and effective in treatment of early pregnancy failure. **Methods:** This was a descriptive cross-sectional study that was conducted at the department of gynaecology and obstetrics, Ayub teaching hospital Abbottabad from Jan 2015 to Dec 2016. A total of 81 pregnant women with early pregnancy failure were enrolled in the study. Misoprostol was administered in a dose of 800 µg PO and repeated every 3 hours for a maximum of three doses if and when required. **Results:** Misoprostol was effective in 60 (74.07%) patients and it resulted in complete expulsion of products of conception. The remainder needed surgical evacuation. There was a low incidence of side effects with nausea being the most common (4.94%) followed by PV bleeding (3.70%), abdominal cramps (3.70%) and diarrhoea (2.47%). **Conclusion:** Misoprostol is a safe and effective treatment option for the management of early pregnancy failure.

Keywords: Abortion; Pregnancy failure; Misoprostol

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INTRODUCTION

Failure of pregnancy in first trimester is a distressing situation for women and their families. The incidence of early pregnancy failure is 15% in pregnancies that are clinically recognizable.^{1,2} Early pregnancy failure is a broad term that includes different types of abortions (i.e., complete, incomplete or inevitable spontaneous abortion), blighted ovum and missed abortions that occur during the first 14 weeks of gestation.³ It is estimated that 25% of all women will have early pregnancy failure in their lifetime.^{4,5}

Surgical evacuation or dilatation and curettage is the standard form of treatment for early pregnancy failure worldwide.^{5–7} However, surgical management of early pregnancy failure has perils of its own, namely: costs of hospitalization and surgery, complications of anaesthesia, complications of surgery, risk of bleeding and infection during the procedure and possibly reduction in fertility as a result of uterine adhesions.⁷ Medical management of early pregnancy failure has therefore been suggested as a suitable alternative for surgical evacuation.^{7–9}

The commonly used agents for medical management of early pregnancy failure are mifepristone and misoprostol.² Mifepristone, which is an anti-progestin agent, is currently the drug of choice for medical management of EPF.¹⁰ When mifepristone is unavailable, Misoprostol is used.¹¹ Misoprostol is a synthetic analogue of prostaglandin E-1 originally used for treatment of NSAID-induced gastric ulcers.^{7,12} Over the period of time,

Misoprostol is being used for many indications in obstetrics and gynaecology including early pregnancy failure. A number of studies have established efficacy of Misoprostol in treatment of missed abortions.^{13–16} The efficacy of Misoprostol has been reported to be more than 70% in treatment of early pregnancy failure.⁵

There is a lack of consensus on the optimal dose of Misoprostol for treatment of early pregnancy failure.^{5,17,18} Misoprostol can be administered intra-cervically/vaginally or orally; there is conflicting evidence of efficacy of either route of administration.^{19,20} Misoprostol use is associated with a number of adverse effects, most common of which is prolonged heavy vaginal bleeding. Less common side effects include nausea, diarrhoea, vomiting and shivering.¹⁵ Since Misoprostol is the preferred agent of choice for treatment of early pregnancy failure at our setup. This descriptive cross-sectional study was designed to document the success and safety of Misoprostol in treatment of early pregnancy failure. In view of dearth of studies from this region, we believe this study will help provide a basis for future studies regarding optimal usage of Misoprostol.

MATERIAL AND METHODS

The study was conducted at the labour room, Department of Obstetrics and Gynaecology, Ayub Teaching Hospital, Abbottabad from Jan 2015 to Dec 2016. The study design was a descriptive cross-sectional study and non-probability consecutive

sampling was used to enrol study participants who comprised of women aged 20–40 with singleton pregnancy presenting with early pregnancy failure. A sample size of 81 was arrived at using 70% success rate of Misoprostol in early pregnancy failure⁵, 95% confidence interval and an absolute precision of 10%. Women with multiple pregnancies, with pre-existing hypertension, airway disease, diabetes mellitus etc were excluded from the study. For the purpose of this study, success of Misoprostol was defined as complete expulsion of products of conception within 24 hours of intravaginal administration of Misoprostol 800 µg (max 3 doses). The safety of Misoprostol was judged in terms of incidence of side effects such as per vaginal bleeding, nausea, vomiting, diarrhoea or abdominal cramps.

The women presenting with early pregnancy failure were managed in the labour room according to the protocols of the department. Misoprostol was administered as 800 µg sublingual dose every 3 hours for a maximum of three doses as per WHO guidance.¹¹ The data was recorded on a pro forma for later analysis. Data that were obtained included age, period of gestation, parity, outcome of Misoprostol administration and surgical evacuation, if required.

The data obtained were entered into and analysed using SPSS 20. Mean±SD was obtained for numerical variables such as age of patients, gestational age and parity. Frequencies and percentages were obtained for categorical variables such as outcome of Misoprostol administration and the need for further surgical evacuation. The outcome, i.e., was stratified according to age of patients, the gestational age and parity to see effect modifications. Post stratification chi-square test was applied and a *p*-value less than 0.05 was taken to be significant.

RESULTS

There were 81 study participants with a mean±SD age of 25.44±2.76 years with a range of 21–30 years. Similarly, the mean±SD period of gestation and parity were 7.58±2.61 weeks and 2.57±1.02 with a range of 3.4–12.5 weeks and 1–4 respectively. The mean±SD BMI of study participants was 23.86±1.72 with a range of 21–26.70.

The efficacy of Misoprostol in this study was 74.07% with a successful expulsion of products of conception in 60 out of 81 study participants and surgical evacuation was required in the remaining (25.93%). The most common side effect was nausea which was present in 4 (4.94%) followed by vaginal bleeding and abdominal cramps in 3 (3.70%) patients each and diarrhoea in 2 (2.47%) patients. When the efficacy of Misoprostol was stratified according to age,

gestational age and parity of the study participants, no statistically significant association was found.

DISCUSSION

Our study shows that Misoprostol administered in doses of 800 µg to a maximum of three doses is an effective option for treatment of early pregnancy failure. Misoprostol appears to be a safe alternative to surgical evacuation with a relatively low occurrence of adverse effects.

The reported efficacy of Misoprostol varies from 13–100% in literature.⁴ This variation in success rates can be attributed to a number of factors such as the specific type of pregnancy failure, the sample size of the study, the dose and frequency of dosing as well as the criteria used to define a successful outcome of the study.

In a secondary analysis of data from a multi-centre trial which compared surgical and medical management of early pregnancy failure, factors that were associated with overall success of Misoprostol administration included nulliparity, Rh blood type, and vaginal bleeding or lower abdominal pain in the preceding 24 hours.²¹ In contrast, parity was not found to be significantly associated with success of Misoprostol administration.

Majority of the patients in this study required more than one dose of Misoprostol. Single dose of Misoprostol for the treatment of early pregnancy failure has also been studied,^{22–25} and has been found to be superior to multiple doses. However, many patients needed multiple doses of Misoprostol in our study and further research is needed to determine if this trend is prevalent in local population.

Misoprostol can be administered sublingually or vaginally. We administered sublingual Misoprostol to our patients however, vaginal route has been found to be superior to other routes of administration with less occurrence of side effects.^{23,24} However, buccal Misoprostol is no less effective than the vaginal route.²⁶ The use of Misoprostol was associated with a relatively low incidence of side effects in this study. Similar trends have been reported elsewhere.^{5,27,28}

To sum up, the use of Misoprostol is an effective treatment modality for the management of early pregnancy failure. It is easily available and its advantages include ease of administration, rapid onset of action and a relatively low incidence of side effects.

There were a number of limitations of this study, though. The small sample size was the foremost limitation and results should be interpreted with caution. The efficacy of Misoprostol was stratified against a limited number of variables and effect of multiple doses of Misoprostol, when needed, was not measured in this study. The debate about best route of administration of Misoprostol is still unanswered as we did not attempt to determine the efficacy or superiority of routes of

administration of Misoprostol. Additionally, large trials evaluating the cost effectiveness of Misoprostol when compared with surgical management should be conducted to ascertain the actual benefit.

AUTHORS' CONTRIBUTION

QN: Conceived study, collected data and did literature review and data analysis. SH: Collected data and helped in data analysis. RS: Collected data and did literature review. MMN: Helped in statistical analysis and discussion of results. ZP: Helped in data collection and preparation of results.

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