"EFFICACY OF INTRAVAGINAL MISOPROSTOL FOR MEDICAL TERMINATION OF PREGNANCY UP TO 12 WEEKS"

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ABSTRACT

Objectives: (1) To ascertain the success of intravaginal misoprostol for medical termination of failed pregnancy up to 12 weeks. (2) To find out the side effects of misoprostol in our population.

Methodology: A descriptive study was done in Gynae "A" Unit, Lady Reading Hospital, Peshawar for a ten months (January to October 2013). Fifty women with less than 12 weeks gestation and women in whom fetal demise/pregnancy failure (missed abortion, blighted ovum) after confirmation were included in the study, were received misoprostol vaginally. The dose was repeated at three hours interval, until adequate contraction or cervical ripening achieved. First dose was 800 mcg (4 tablets) and remaining three doses were 400 mcg (2 tablets) each (maximum dose 2000 mcg).

Results: Out of 50 patients 78% were between 21-30 years, 12% were between 15-20 years, and 10% were between 31-40 years of age. Missed abortion was commonest indications for termination of pregnancy in 72% cases. Blighted ovum was the second indication in 28% cases. Outcome of misoprostol administration was successful in 68% cases. In 40% cases mild to severe per vaginal bleeding was reported during induction of abortion. Nausea and vomiting was observed in 16% patients, 12% patients had pyrexia. In 8% cases diarrhea was noted.

Conclusion: Success rate of abortion was 68%. Mild to severe per vaginal bleeding was commonest side effect of misoprostol in 40% patients. Less common side effects were nausea and vomiting, pyrexia, and diarrhea.

Key Words: Misoprostol; termination of pregnancy; medical; missed-abortions; side-effects. Prostaglandins E1.

INTRODUCTION

Misoprostol is a prostaglandin E1 analogue. It has been approved by Food and Drug Administration (FDA) to be used orally for prevention and treatment of gastric ulcers associated with the use non-steroidal anti inflammatory drugs. It also causes uterine contraction and ripening of the cervix therefore it has become an important drug in obstetrical and gynecological practice. Misoprostol can be used for medical termination of pregnancy, cervical ripening before surgical abortion, evacuation of the uterus in case of embryonic or fetal death, induction of labour and to treat post partum hemorrhage. Although, misoprostol is not approved for any of the above indication but the fact that under certain situations, off-label uses of approved products are appropriate rational and accepted medical practice, is recognized by FDA.[1]

Such "off-label" use of prescribing medicine is common in pregnancy and if it is based on several scientific evidence, it is not thought to be experimental.[2] Use of misoprostol along with mifepristone for early termination of pregnancy is FDA approved.

Medical termination with misoprostol can be done in case of missed abortion, incomplete abortion and anembryonic pregnancy. In many countries it is used in combination with mifepristone (RU-486) or methotrexate for medical termination of first trimester pregnancy. When used along with mifepristone, in women no more then 56 days pregnant, the success rate was 83 to 95 percent.[3,4,5] Combination of methotrexate and misoprostol is a safe and effective in medical termination of early pregnancy.[6,7]

When used for termination of pregnancy up to 49 days, success rate was 96 to 99 percent.[8,9,10,11,12] Vaginal misoprostol alone is effective in the medical abortion up to 9 weeks of gestation.[13]

There are different routes of administration of misoprostol: (i) sublingual (ii) oral (iii) vaginal (iv) vaginal with addition of water.[14] Vaginal route is preferred to buccal route because it is more effective, if used after methotrexate for early abortion.[15,16]

Medical termination of early failed pregnancy with 800 µg of misoprostol vaginally is effective and safe and the success rate is 84 percent.[17] Misoprostol is both safe and effective in the treatment of missed abortion.[18,19]

Misoprostol is comparable in effectiveness, safety and acceptability to manual vacuum aspiration (MVA), when used in the treatment of first trimester uncomplicated incomplete abortion.[20] Depending upon the availability, either option can be used.

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The rational of the study was to ascertain the success of intravaginal misoprostol for medical termination of failed pregnancy up to 12 weeks, to show whether misoprostol (intravaginally) can be recommended for medical termination of failed pregnancy up to 12 weeks or not. And to find out the side effects of misoprostol. What side-effects can occur, and what is the frequency of different side effects like fever, gastrointestinal side effects (nausea, vomiting, diarrhea), and continued vaginal bleeding.

METHODOLOGY

This descriptive study was conducted in Department of Obstet/Gynae of Lady Reading Hospital, Peshawar for a ten months from January 2013 to October 2013. A total of 50 women with less than 12 weeks gestation and women in whom fetal demise/pregnancy failure (missed abortion, blighted ovum) after confirmation were included in the study. Hypertensive and asthmatic, women with deranged coagulation profile, women with history of allergy to prostaglandins and Para 5 or more were excluded from the study.

Patients requiring termination of pregnancy for early pregnancy failure up to 12 weeks of gestation, were admitted in the Department of Obstet/Gyne of Lady Reading Hospital, Peshawar for further evaluation. Early pregnancy failure (up to 12 weeks) was confirmed by ultrasound scan. Missed abortion and blighted ovum cases were included in this study. First of all an informed consent was taken from all patients regarding administration of misoprostol, side effects and possible complications of drug. Women with hypertension, deranged coagulation profile, asthma previous history of allergy to prostaglandin and multiparity (Para 5 or more) were excluded from the study.

All of the selected women received misoprostol vaginally. The dose was repeated at three hours interval, until adequate contraction or cervical ripening achieved. First dose was 800 mcg (4 tablets) and rest of the three doses were 400 mcg (2 tablets) each (maximum dose 2000 mcg). Time interval between induction and complete expulsion was noted.

Side effects of the drug, for example pyrexia, per vaginal bleeding, nausea/vomiting, diarrhea was noted. Other information like obstetrical history, menstrual history and sonographic findings, indication for termination of pregnancy were also recorded.

All the studied variables like obstetrical history, menstrual history, sonographic findings, indication for termination, doses of misoprostol, and side effects of misoprostol for example pyrexia, per vaginal bleeding, vomiting/nausea, diarrhea were calculated for frequencies, percentages. Mean and $\pm$ standard deviation was calculated for age and gestational age. The results were expressed/presented through frequency tables, graphs and charts and percentages. The descriptive characteristics of the study data were expressed by using average, and standard deviation. Study data was analyzed by using computer program SPSS version 12 for windows.

RESULTS

A descriptive study of 50 cases, which was conducted in Department of Obstet/Gynae of Lady Reading Hospital, Peshawar for 10 months (from January 2013 to October 2013). Results of the study are summarized as under:

In this study majority 39 (78%) patients were between the age of 21-30 years, 06 (12%) patients were between 15-20 years of age, and 05 (10%) were between 31-40 years of age. In this study minimum age of the patients was 18 years and maximum was 40 years. Overall mean age of the patients was 26.64 $\pm$ 4.8980 years.

In 50 cases of medical termination of failed pregnancy, minimum gestational age was 6 weeks and maximum was 12 weeks, and mean gestational age for induction of abortion was 10.10 $\pm$ 2.2154 weeks.

Missed abortion was the most common indications for termination of pregnancy in majority of cases

TABLE NO. 1: VARIOUS DEMOGRAPHIC FEATURES OF PATIENTS (n=50)

DEMOGRAPHIC FEATURES	NO. OF CASES	PERCENTAGE
Age ranges:		
15-20 years	06	12%
21-30 years	39	78%
31-40 years	05	10%
Indications of termination of pregnancy:		
Missed abortion	36	72%
Blighted ovum	14	28%

TABLE NO. 2: OUTCOMES AND SIDE-EFFECTS OF MISOPROSTOL (n=50)

VARIABLES	NO. OF PATIENTS	PERCENTAGE
Outcomes:		
Successful	34	68%
Not successful	16	32%
Side effects:		
Per vaginal bleeding	20	40%
Nausea/vomiting	08	16%
Pyrexia	06	12%
Diarrhea	04	08%

that was 36 (72%) cases and blighted ovum was the second indication for abortion in 14 (28%) cases (Table No. 1).

Outcome of misoprostol administration was successful in 34 (68%) cases and was not successful in 16 (32%) cases of abortion, in whom surgical evacuation was performed.

In 20 (40%) cases mild to severe per vaginal bleeding was reported during induction of abortion. In 8 (16%) patients complain of nausea and vomiting was observed, 6 (12%) patients had pyrexia. In 4 (8%) cases diarrhea was noted (Table No. 2).

DISCUSSION

In developing countries, over 99% of deaths due to abortion occurred. Maternal deaths due to abortion are preventable. Increasing the use of misoprostol for elective abortion could have a notable impact on maternal mortality due to abortion. As a test of this hypothesis, a study estimated the reduction in maternal deaths due to abortion in Africa, Asia and Latin America. This simple modeling exercise demonstrated that increased use of misoprostol, an option for pregnancy termination already available to many women in developing countries, could significantly reduce mortality due to abortion. Empirical testing of the hypothesis with data collected from developing countries could help to inform and improve the use of misoprostol in those settings.[21]

Previous research has demonstrated the effectiveness of misoprostol for treatment of incomplete abortion; however, few studies have systematically compared misoprostol's effectiveness with that of standard surgical care. In a study it was concluded that 600 micrograms of oral misoprostol is as safe and acceptable as MVA for the treatment of incomplete abortion.[22]

In another study it was concluded that Misoprostol is as effective as MVA at treating incomplete abortion at uterine size of <12 weeks. The acceptability of misoprostol appears higher. Given the many practical advantages of misoprostol over MVA in low-resource settings, misoprostol should be more widely available for treatment of incomplete abortion in the developing world.[23]

Misoprostol treatment for early pregnancy failure is highly successful in selected women, primarily those with active bleeding and nulliparity. Clinicians and patients should be aware of these differences when considering misoprostol treatment.[24]

In this study, one of the prostaglandin E1 analogue, misoprostol had been used vaginally for the termination of pregnancy failure in patients with < 12 weeks gestation. Misoprostol is cheaper, as compared to other prostaglandins, available in Pakistan.[25]

In our study the successful abortion rate was 68% (success defined as no secondary surgical intervention provided). Comparable results with successful rate of 68% have also been reported by Naz S and Sultana N[25] in a recent local study conducted at Foundation University Medical College, Fauji Foundation Hospital, Rawalpindi.

In a prospective observational study by Shanker M, et al[26] evaluate the efficacy, safety and acceptability of misoprostol for outpatient management of missed miscarriage. They found that 77.3% of the women achieved successful complete medical evacuation. It was concluded that medical evacuation of missed miscarriage is efficacious, safe and acceptable in the outpatient setting.

A success rate of 86% has been reported by Sharma D et al[27] and found the acceptability of the method in 69.7% patients. They concluded that sublingual misoprostol is a non-invasive, effective and safe medical method for completion of abortion in missed abortion.

In few international studies conducted by Coyaji K, et al[28] reported the complete abortion rate from 86 to 92%, Schreiber CA, et al[29] reported 93%, Li TY et al[30] reported 97.8%, and Lin M, et al[31] reported 98.3%. In our study we had success rate of 68% while in these studies women received one or two doses of 400 microgram oral misoprostol at the clinic 48 hours after the administration of 200 mg mifepristone in another study and in another study all women concurrently received oral mifepristone 200 mg and vaginal misoprostol 800 microgram. These differences in success rate could be explained due to the use of misoprostol alone in our study as compared to the combined use of mifepristone and misoprostol in the studies mentioned above.

In another study conducted in Turkey by Kutlu T, et al[32] the success rate was 95% as first dose of misoprostol (200 microgram) was administered intravaginally and subsequent doses (200 microgram each) orally every following hour were administered with a maximum of six doses (1200 microgram). They concluded and believed that their low-dose combined misoprostol protocol is safe, effective and well-tolerated method with minimal adverse effects for the termination of both first and second trimester pregnancy losses.

The treatment failure was determined by no complete abortion within 48 hours. If spontaneous abortion had not occurred, or had heavy vaginal bleeding or evidence of incomplete abortion either by clinical manifestation or sonographic finding then dilatation and curettage was performed.

Vaginal misoprostol can be used for termination of pregnancy in case of anembryonic pregnancy with high successful rate of complete abortion and no serious adverse effects. It is recommended that with 800 microgram vaginal misoprostol regimen within 12 hours, the complete abortion rate was higher and the

median time to abortion was shorter than the 400 microgram regimen with no difference in side effects. This may decrease the suffering time of both physical and psychological trauma to the patient before complete abortion has occurred.[33]

In another study failure was defined as surgical intervention due to retained gestational sac 48 hours after completion of the drug protocol, severe symptoms, or suspected retained products of conception after the menstrual period. So it was concluded that Misoprostol is an effective and safe treatment for early pregnancy failure and could replace surgical curettage in over two-thirds of the patients. Mifepristone offers no advantage compared with misoprostol as initial treatment.[34]

Failure of treatment with misoprostol in our study was in 32% patients which is comparable with the national study done by Naz S and Sultana N.[25] This percentage is much higher than the studies conducted at international level done by Coyaji K, et al,[28] Schreiber CA, et al,[29] Li TY et al[30] and Lin M, et al.[31] The reason for high failure rates of treatment in this part of the world could be due to very late presentation of patients to the specialized centers, as women are restricted to their homes by traditional, cultural, and religious laws and they are not allowed to seek medical treatment from doctors and specially from male doctors. First they are usually treated by traditional birth attendants (TBAs), hakims, and quacks in their local areas and if they do not get well or improved then they are referred to specialized centers very late with various complications. The other reason could be that in our study very small sample size was selected in a limited time period.

Misoprostol is an important drug in obstetrics and gynecology because of its uterotonic and cervical-ripening activities. The side effects are dose-related, usually transitory, and well tolerated. The toxic dosage in humans is unknown, and there is no specific antidote.[35]

In our study there were few side effects of misoprostol including per vaginal bleeding during induction of abortion. Nausea and vomiting, pyrexia and diarrhea were observed in some patients. More or less same adverse side effects of misoprostol have also been reported in local and international literature.[36, 37,38]

Mild to severe per vaginal bleeding was observed in 40% patients, in few of them further treatment with misoprostol was stopped and dilatation and curettage (D & C) was performed. In contrast to our results few studies also reported per vaginal bleeding with less percentages by Naz S and Sultana N,[26] and high percentage of 66% by Radulovic N et al.[38]

CONCLUSIONS

From the results of this study it is concluded that: Success rate of abortion in this study was 68%. Mild to severe per vaginal bleeding was the common adverse side effect of misoprostol in 40% patients during the induction of abortion. Other less common side effects were nausea and vomiting, pyrexia, and diarrhea. Misoprostol is safe, efficacious and cost effective drug for induction of first trimester pregnancy failure abortions. Patients should be informed of both the risks and the possible benefits of misoprostol. Further research with large samples is necessary to determine whether the risks outweigh any possible benefits.

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