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MANAGEMENT OF FIRST TRIMESTER MISSED ABORTIONS WITH MISOPROSTOL

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ABSTRACT

Objective: To assess the efficacy and safety of misoprostol (PGE1 analogue) for termination of first trimester missed abortions.

Material and Methods: A prospective study was carried out from November 2009 to April 2011 at Gynae A unit Khyber Teaching Hospital Peshawar. A total of 80 patients at 7-12 weeks of gestation requiring termination of pregnancy were included. Misoprostol 800ug (4 tablets) with 2-3 drops of water was placed high in vagina and then 400 ug (2 tablets) were repeated 6 hourly for 24 hours i.e for 4 doses. The primary outcome measures were complete evacuation of products of conception, mean induction to expulsion time and the occurrence of side effects.

Results: Successful abortion was observed in 72 (90%) patients. Mean induction to expulsion interval was 13.9 hours. Eight (10.5%) patients had surgical evacuation, of these patients 4 (5%) had incomplete abortion and 4(5%) had failed induction. Side effects including nausea, vomiting and diarrhea were encountered, very rarely.

Conclusion: Misoprostol is a safe, effective and economical drug for induction of first trimester abortions.

Key Words: Misoprostol, missed abortion, complete abortion.

INTRODUCTION

Several studies have shown that medical treatment is a safe, effective and acceptable alternative[1] to suction curettage. Misoprostol (15 deoxy-16 hydroxy 16 methyl PGE1) is a stable, synthetic form of prostaglandin E1 analogue. It has anti-secretory and mucosal protective properties and was originally developed in 1970's for the prevention of non-steroidal anti-inflammatory drugs (NSAID) induced peptic ulcers[2,5]. Its use for that indication however has become limited and it is now used much more widely for off-label indications in the obstetrics and gynecology.

Several clinical trials have evaluated the use of misoprostol alone for termination of early pregnancy failure.[2,3,4]. The success rate reported in most of them is 70-87.5% and depended on mode or route of administration, frequency of drug administration and also the waiting time was different to diagnose complete abortion.

In the last two decades, medical termination of pregnancy has become a safe alternative to vacuum aspiration and dilatation and curettage[4,5,6]. Recently misoprostol regimen has become more widely available and is now considered to be the gold standard for early pregnancy termination[7].

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MATERIAL AND METHODS

This prospective study was carried out from November 2009 to April 2011 at Gynea A Unit Khyber Teaching Hospital, Peshawar, Pakistan. After obtaining written informed consent from 80 patients, who were diagnosed with first trimester missed abortions (7-12 weeks gestations), were assigned to receive the intravaginal misoprostol.

The diagnosis of missed abortion or blighted ovum was confirmed by two ultrasound examinations done at interval of one week. All pregnant women of gestational age more than 12 weeks, hypersensitivity to prostaglandin and those with the history of bronchial asthma were excluded from the study. Procedure was considered as failed if there was no response within 48 hours of placement of vaginal tablets.

All eligible women were given detailed information about the protocol of medical termination of pregnancy and were then admitted in Gynea A unit. Routine physical examination and investigations were carried out. Investigations included full blood count, urine routine examination, random blood sugar, blood group and Rhesus factor, hepatitis screening, liver function tests, renal function tests and blood coagulation profile.

Misoprostol 800ug (4 tablets) with 2-3 drops of water was placed high in vagina and then 2 tablets (400ug) were repeated 6 hourly for another three

doses. Vital signs, vaginal bleeding and abdominal pain were assessed every 2 hours and adverse effects were recorded. Side effects from misoprostol were carefully evaluated and docomented in a predesigned proforma.

Induction – expulsion interval was defined as the time in hours from initiation of therapy until the expulsion of products of conception. Abortion rate was calculated for those who aborted within 48 hours. Successful outcome was defined as complete expulsion of products of conception within 48 hours. If abortion did not occur within 48 hours the procedure was abandoned and surgical intervention carried out. All those who aborted had immediate digital pelvic and then sonographic examination after 24 hours to determine whether retained products of conception were present or not. Our outcome measures included induction expulsion interval, success rate and the occurrence of side effects with vaginal misoprostol.

RESULTS

A total of 80 patients were included in the study. The demographic characteristics of patients are shown in Table 1. Table 2 shows the results of induction of abortions in patients with previous caesarean sections. The success rates were complete abortion in 72 (90%) and incomplete aboration in 4(5%) of cases.

Table 1: Demographic characteristic of women with first trimester missed abortions

Age in years	No. of patients and Percentage
16-20	21(26.25%)
21-30	34(42.50%)
31-40	16(20.00%)
> 40	09(%)11.25
Parity	
Primigravidas	03(03.75%)
1-4	26(32.50%)
5-7	34(42.50%)
> 7	17(21.25%)

Table 2: Induction in patients with previous ceaserean sections

Ceaserean Section	No. of patients and Percentage
Previous 1	11(13.75%)
Previous 2	4(05.00%)
Previous 3	01(1.25%)

Table 3: Induction – abortion Interval

Interval in hours	No. of patients and percentage
< 8	04(5.2%)
8 – 16	53(69.7%)
> 16 – 24	17(21.25%)
> 24 – 48	2(2.6%)

Table 4: Side Effects with Misoprostol

Side Effects	No. of patients and percentage
Nausea	4(5%)
Vomiting	2(2.5%)
Diarrhea	2(2.5%)
Fever	3(3.7%)
Bleeding	2(2.5%)

The induction abortion interval is shown in Table 3. Mean induction – abortion interval was 13.9 hours whereas 90% of the total cases had successful abortion. In certain cases 8 (10.5%) patients needed surgical evacuation that were patients with incomplete abortion (5%) and with failed induction (5%). The average hospital stay for induction of abortion was 30 hours. Table 4 shows, side effects with misoprostol.

DISCUSSION

In the last two decades, medical termination of pregnancy has become a safe alternative to vacuum aspiration and dilatation and curettage[8,9]. Traditional methods of surgical evacuation of uterus are associated with major morbidity in upto 1% women and minor morbidity in 10%. Recently misoprostol regimen has become more widely available and is now considered to be the gold standard for early pregnancy termination. In study successful abortion was seen in 72 (90%) patients. It is in accordance with other studies.[10,11,12,13]

Jain J K et al used 800 ug of misoprostol vaginaly for termination of first trimester abortions[15,16]. He gave three doses of misoprostol every 24 hours and his study revealed an efficacy of 80.4%. In the study we used 800ug stat followed by 400ug 6 hourly for 24 hours and our success rate was 90%. Patients expelled within 24 hours of administration misoprostol and were discharged the next day instead of waiting for 3 days thus minimizing the financial burden on patients. In another study 800ug of misoprostol was given intravaginaly first and then 400ug was given 4 hourly for upto 3 doses for terminating first trimester missed abortion[13,14]. 87.5% patients had complete abortion. The regimen using repeated doses of misoprostol alone that can be finished within one day have the advantage of requiring less hospital visits and ultrasound examinations.

For terminating 1st trimester abortion low dose regimens i.e. dose of 200-400ug every 4-6 hours were

associated with less successful outcome as compared to our regimens of misoprostol. Szymarska et al (2003)[32] reported 30.0% success rate with the use of 400ug of vaginal misoprostol and this success variation may be due to this reason. In another descriptive study where 400ug of vaginal misoprostol was given 4 hourly successful complete abortion was seen in 68% patients and with induction to expulsion interval of 12.2 hours[31], whereas in our study mean induction to expulsion interval was 13.9 hours.

Differences in initial dosage, time interval during administrations, method and routes of drug administration, population and criteria for diagnosis of incomplete abortion were suggested to be relevant in explaining differences in outcome[17,18,19]. Vaginal route appears to be the most effective followed by sublingual with oral being the least effective. Sublingual misoprostol needs a more frequent administration i.e. every 3 hours to achieve a similar effectiveness to the vaginal route[20,21,22,23].

Vaginal application of misoprostol results in slower increase and lower peak plasma concentration of misoprostol than when administered orally but overall exposure to drug is increased. Among women who were 9-11 weeks pregnant and given misoprostol before surgical abortion, Intravaginal pressure began to rise on average of 8 minutes after oral administration and 21 minutes after vaginal administration and was maximal 25 minutes after oral administration and 46 minutes after vaginal administration[24,25].

Awan AS prescribed oral misoprostol for managing first trimester missed abortion[1]. 67% patients aborted and expelled completely and did not require any type of surgical intervention. 30% patients expelled incompletely and they had evacuation and curettage. Mean expulsion time was 7.8 hours. In our study mean expulsion time was 13.9 hours but the success rate was 90%. Success rate of 92% is reported with use of sublingual use of misoprostol but the incidence of side effects is high with oral and sublingual routes.

Chills and fever are fairly common more with oral or sublingual administration of misoprostol but are transient[26,27,28]. Nausea, Vomiting, diarrhea are also common adverse reactions of misoprostol intake affecting about 35% of women. Gastrointestinal side effects are more common after oral or sublingual administration[29,30]. In our study there was 5% incidence of nausea, 2.5% vomiting and 2.5% diarrhea.

The results of the study have shown that age, parity and gestational age do not effect the success rate of medical abortion using misoprostol. Wood SL and Zhang J et al compared the efficacy, acceptability and cost of medical abortion versus surgical abortion and they concluded that surgical abortion requires 10% more personal cost than medical abortion[35,36].

CONCLUSION

Misoprostol is a safe, effective and economical drug as compared to other prostaglandins. Its use would limit the use of surgical requirements, sterilization and anesthesia. The low cost, wide availability, ease of administration and storage makes it appealing for developing countries.

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