Original Article

Medical Treatment of Missed Miscarriage before 24 Week of Gestation at Liaquat University Hospital

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ABSTRACT

OBJECTIVE: The objective of this study was to determine the safety and efficacy of misoprostol in termination of missed miscarriage under 24-weeks gestation.

METHODOLOGY: This descriptive observational study was conducted on 100 cases of missed miscarriage in the Department of Gynecology, Liaquat University Hospital, Hyderabad for the period of one year i.e. from 1st January 2007 to 31st December 2007.

Women with missed miscarriage of less than 24-weeks of gestation requiring termination of pregnancy were included in this study whereas Women with other types of miscarriage like incomplete, threatened miscarriages, gestational trophoblastic disease, liver disease and disturbed coagulation profiles were excluded from the study

RESULTS: Mean age of the patients was 26.79±4.82 years. Fifty three (53%) women had no previous history of miscarriage. Average gestational age was 14.75±4.96 weeks. Forty four (44%) patients needed surgical treatment while 56% had complete miscarriage with medical (misoprostol) treatment.

CONCLUSION: Misoprostol has proven to be a safe and effective method for the management of missed miscarriage.

KEYWORDS: Missed miscarriage, Gestational age, Misoprostol.

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INTRODUCTION

The terms miscarriage and abortion are synonymous and denote the expulsion of the fetus before the age of viability or before the end of 24th week.[1] Missed miscarriage is defined as pregnancy failure which is identified before expulsion of fetal and placental tissues in less than 24 weeks gestation, as after the 24th week of pregnancy the fetus is considered to be viable.[1,2] It is estimated that between 10 and 15 percent of confirmed pregnancies end in miscarriage, and that 25 per cent of women will experience an early pregnancy loss in their reproductive lifetime.[1] Each year about 30-million induced miscarriages are carried out, emphasizing the need of a safe and effective way of making it a global issue for the gynecologists and the patients.[3,4] There are two methods for termination of pregnancy, the surgical methods and the medical method.

Surgical miscarriage up to 63-day by vacuum aspiration or dilatation and curettage has been the method of choice since the 1960's with advantage of avoiding prolong hospital stay, immediate return to normal life and it ensures completeness of procedure in most of the cases. However it requires skills, anesthesia, and there is increased risk of complications of surgery and anesthesia. It is also not a very suitable method for termination of second trimester pregnancy. Medical miscarriage became an alternative method of first trimester pregnancy termination, with the availability of prostaglandins in the early 1970s and antiprogesterones in 1980s. The most widely researched abortifacient drugs are prostaglandins, mifepristone, methotrexate, mifepristone with prostaglandins and methotrexate with prostaglandins.[5]

Efficacy of prostaglandins E1 (cytotec) is tested throughout the world including Pakistan. Misoprostol, an E1 prostaglandin analogue, is approved in more than 85 countries since its first marketing in 1985, so far it is approved only for treatment of gastric ulcer.[6] Misoprostol (cytotec) was first used in obstetrics in 1993 for labor induction, since then it has been used for different indications like ripening of cervix and control of postpartum hemorrhage.[7,8] In a study it was concluded that medical management of missed miscarriage with either oral or vaginal misoprostol is highly effective and highly acceptable, with shorter induction to miscarriage interval and greater acceptability.[9,10] In third world countries though the drug is not licensed for use of pregnant woman but worldwide it is being used on women for ripening of cervix.[11] The optimal dose of vaginal misoprostol for termination in second trimester lies between 50-µg and 1200-µg and higher dose may be needed to cause miscarriages

early in the second trimester, whereas lower dose may be sufficient in late second trimester.[12]
In missed miscarriage of 4-12 weeks gestation 2-tab (400-µg) oral or vaginal, repeated every 4-hours until expulsion or 4-tab (800-µg) vaginally every 24-hours until expulsion.[13] Prostaglandin E2 is effective in miscarriage or termination of pregnancy with fewer side effects, but it is costly and large dose is required. Therefore there is need for a cheap and effective alternative agent. The purpose of this study is to determine the safety and efficacy of misoprostol inpatients with missed miscarriage before 24 weeks of gestation.

MATERIAL AND METHODS

This descriptive observational study was conducted on 100 cases of missed miscarriage in the Department of Gynecology, Liaquat University Hospital, Hyderabad for the period of one year i.e. from 1st January 2007 to 31st December 2007
Women with missed miscarriage of less than 24-weeks of gestation requiring termination of pregnancy were included in this study whereas Women with other types of miscarriage like incomplete and threatened miscarriages, gestational trophoblastic disease, liver disease and disturbed coagulation profiles were excluded from the study
A well informed consent was obtained from the patients fulfilling inclusion criteria. They were evaluated by detailed history and clinical examination. Baseline investigations including ultrasound, blood grouping, prothrombin time, activated partial thromboplastin time, bleeding time, clotting time, complete blood picture and liver function test were done. Data were collected on specially designed proforma. Upto 12 weeks of gestation 800ug of misoprostol (four tablets) every three hour maximum three doses were used vaginaly. While from 13-24 weeks 400ug of misoprostol (two tablets) every three hours with maximum three doses were used. Next dose was omitted if women started to abort on first or second dose. Efficacy was defined by the percentage of women were assessed without need for surgical intervention while safety in terms of massive hemorrhage needing surgical intervention, infection, excessive vomiting needing I/V medication.
Statistical analysis was performed through SPSS version 10.0. All numeric response variables like age, gestational age, induction to miscarriage time interval and dose used were presented by mean±SD. All categorical variables like parity, need of surgical evacuation, side effects and complications were presented by frequencies and percentages. No statistical test was applied.

RESULTS

A total of 100 women who underwent the trial of Misoprostol as medical treatment for termination of missed miscarriage were included in the study.
Mean age of women were 26.79±4.82 years. Out of 100 women, 53 women had no history of miscarriage, 31 had single miscarriage, 9 women had 2 miscarriages, 4 women had 3 miscarriages and 3 women had more than one miscarriages even 1 women had 9 miscarriages (**Table I**).
Most of the women (49%) had gestational age between 6 to 12 weeks followed by 28 women had gestational age 13 to 18 weeks and 23% had 19 to 24 weeks of gestation. Average gestational age was 14.75±4.96 weeks. In 76% of patients induction - miscarriage time were between 12 to 24 hours **(Table I)**.
Most of the women 44%required dose of 800 µg **(Table II)**.
Out of 100 women who underwent medical treatment of Misoprostol for termination of missed miscarriage, 44 needed surgical evacuation while 56 did not require surgical treatment **(Table III)**. Proceeding of surgery was the commonest complication faced in 29 women followed by retained products of conception in 23 women and hemorrhage occurred in only 1 woman.
Abdominal pain and vomiting were equally common side effects of Misoprostol which occurred in 27% women while nausea in 18% women **(Table III)**.

TABLE I:
DEMOGRAPHIC CHARACTERISTICS (n = 100)

Characteristics	Frequency	Percentage
Mean age = 26.79±4.82 years		
Mean Gestation ±SD= 14.75±4.96 weeks		
Induction to miscarriage interval		
12-14 hours	76	76%
25-24 hours	17	17%
37-48 hours	06	6%
>48 hours	01	1%
No of miscarriage		
None	53	53%
1	31	31%
2	9	9%
3	4	4%
>4	3	3%

TABLE II: DOSE DISTRIBUTION (n = 100)

Dose	Frequency	Percentage
600 µg	20	20%
800 µg	44	44%
1200 µg	20	20%
1600ug	14	14%
2400ug	2	2%

TABLE II: EFFICACY'S AND COMPLICATIONS OF MEDICAL TERMINATION (n = 100)

Misoprostol	Frequency	Percentage
Complete miscarriage with medical treatment	56	56%
Need surgical treatment	44	44%
Complications		
Hemorrhage	01	1%
Vomiting	27	27%
Abdominal pain	27	27%
Infection	18	18%

DISCUSSION

Misoprostol has been used safely and effectively for cervical ripening and labor induction in patients with fetal death. Mariani-Neto and associates first reported the use of oral misoprostol (400-µg every 4 hours) for induction of labor following fetal death.[14,15] The authors reported their experience with 20 patients with fetal demise. All patients delivered successfully with a mean interval to delivery of 552 minutes. The mean dose of misoprostol was 1000-µg. some other studies have assessed the safety and efficacy of misoprostol in the management of fetal death[16,17].

Recent studies mainly focus on the optimization of misoprostol dosing regimens by comparing various dosages, dosing intervals, and routes of administration[18-20]. The dosage of misoprostol ranged from 100 to 1200-µg with dosing intervals of 3 to 12 hours. The efficacy of misoprostol is improved when a higher dose (400-µg to 800-µg) is given at shorter intervals (3 to 4 hours). However, women preferred the oral route because it was less painful, gave more privacy, and was more convenient.[21]

In this study, tried to determine the efficacy of misoprostol in terms of dosage and success rate, in terminating a non-viable pregnancy less than 24 weeks gestation. Safety and cost are of paramount importance whenever any drug is prescribed. The safety of prostaglandin E2 for termination of pregnancy was demonstrated in many earlier studies.[22] However, it is by no means cheap. The other alternative, misoprostol, apart from being much less expensive, is also widely available.

Various local and international studies and some trials have been conducted in recent years to determine the efficacy and safety of misoprostol in the management of missed miscarriage.

The mean gestational age observed in our study was 14.75±4.96 weeks. A similar study reported the mean gestational age of 17.14 weeks, while the mean gestational age reported in a comparative study was 16.7 weeks[23,24]. Both studies report no significance of gestational age for the success or failure of the treatment. Mean time taken from administration of misoprostol till expulsion in our study was 24.96±9.74 hours, ranging between 12 hours and >48 hours. In a double-blind placebo-controlled trial it was observed that 15.6% women took 7-days to expel the products of conception[25]. This time is far more than observed in our study, the probable reason for which can be the dose administered was 200µgx3 (on 1st day, 2nd day and 7th day). Another study reported much less time than our study. The authors reported mean induction-expulsion interval of 7.17±3.6 hours[26]. Again this variation seems to be associated with higher dosage repeated at shorter intervals, which was 400µg repeated after every four hours.

The dose of misoprostol administered in this study was 400µg stat dose followed by 200µg after every 6 hours up to 1000µg. various patterns of dosage and interval are adopted in different studies. The choice of the pattern depends upon the consultant, hospital and socio-cultural status of the patient. Dosage pattern seems to be directly proportional to the induction-expulsion time, as reported by many studies[24,25]. The literature deficits the studies that evaluate the pattern of administration. However, several studies are conducted to compare the safety and efficacy of different routes of administration. No study correlates the pattern of dose and interval with the success or failure of treatment regimen.

The success rate achieved in this study was 56%. This is similar to 53.1% reported in a study conducted at Fatima Memorial Hospital, Lahore – Pakistan; and close to 68% success rate observed in a study conducted at Fauji Foundation Hospital, Rawalpindi – Pakistan[24,27]. The success rate reported by western studies however differ significantly from local studies. The results of a randomized controlled trial conducted at the University of Calgary, Canada, reported the success rate of 80%.[28] Another trial conducted by Demetroulis C et al, reported the success rate of 82.5% [29]. Bagratee JS et al, achieved 88.5% success rate in their trial[25]. In another study Success rate of misoprostol in miscarriage have been reported from 87-97%.[30]

Some side effects of misoprostol were observed in this study. Abdominal pain was reported by 27% of the patients. A multi-centre study conducted in Jordan observed no side effects[23]. In contrast to that another study reported abdominal pain in 82.5% women, among them 75% required analgesia[29]. Same study reported nausea complained by 15% women and vomiting by 7.5% women, which is in contrast to 18% nausea and 27% vomiting reported in this study. Once again the difference in dosage is most likely seems to be the reason behind the variation of results.

CONCLUSIONS

This study concluded that the success rate is high in the cases of missed miscarriage using vaginal misoprostol in our setup. Misoprostol has proven to be a safe and effective method for the management of missed miscarriage. It is also as cost effective as efficient to treat missed miscarriage with misoprostol. More work is still needed in this regard to provide better maternal health care services.

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