Original Article

First Trimester Termination of Pregnancy – Role of Sublingual Misoprostol

1. Farida Wagan 2. Razia Tariq Qureshi 3. Mehboob Wagan 4. Sabreena

1. Assoc. Prof. Obs & Gynae, PUMHS, Nawabshah 2. Asstt. Prof. Obs & Gynae, PUMHS, Nawabshah 3. Assoc. Prof. of Pharmacology, LUMHS, Jamshoro 4. Sen. Registrar, PUMHS, Nawabshah

ABSTRACT

Objective: The objective of this study was to evaluate the efficacy acceptability and dose of misoprostol sublingually in the management first trimester pregnancy failure.

Study Design: Observational Study

Place and Duration of Study: This study was conducted in the Department of Obstetrics and Gynaecology at Peoples Medical College Hospital Nawabshah from 01.01.2010 to 31.12.2010.

Patients and Methods: A total 150 patients with the diagnosis of missed and incomplete miscarriage upto 13 weeks gestation. All eligible women who consented were counseled and given detail information protocol.

Results: A total of 150 patients with missed miscarriage 119 (79.33 %) and incomplete miscarriage 31 (20.66 %).The mean age group 28.34 years ,mean parity 4.79 and mean gestational age 8.61 weeks. Efficacy was 92 %, 127 (84.66 %) had complete miscarriage by the end of 7 days with 2 doses of misoprostol 600ug sublingually 3 hours apart. 23 (15.33 %) require 3rd dose of misoprostol and 11 (7.33 %) underwent surgical evacuation. Patients satisfaction was 94 % (141 patients).

Conclusion: Misoprostol prove with benefit of efficacy, safety and acceptability in first trimester pregnancy failure. In low resources countries achieve infection haemorrhage and uterine damage can for two commonly reported on consequences of post surgical care. Misoprostol treatment can prove to be a rewarding step towards reducing morbidity and mortality.

Key Words: Misoprostol, First trimester pregnancy termination, Sublingual route.

INTRODUCTION

Termination of pregnancy is one of the common procedures in gynaecological practice.

Medical management of early pregnancy failure is an effective, safe and cost effective alternative to surgical method and suitable for women not wanting hospital admission or unfit for general anaesthesia[1]. The synthetic prostaglandin, misoprostol (PGE1 analogue) has largely replaced all other technique for pregnancy[2].

Misoprostol, prostaglandin E1 analogue, is safe option and gaining popularity because of its uterotonic and cervical priming action. It is inexpensive and stable at room temperature. Sublingual route avoids first pass effect through the liver, has the shortest time to peak concentration that is 30 minutes as compared to 75 minutes in vaginal route and greatest bioavailability as compared to other routes, due to high vascularity of buccal mucosa. It also avoids painful vaginal administration and is more convenient to take and acceptable by women[3,4,5]. The main drawback is gastrointestinal side effects, shivering and hypothermia[5].

First trimester miscarriage is one of the most common complications of pregnancy occurring in 10 – 15 % of clinically recognize pregnancies[6].

South-Asia being highly populated resource constrained and underdeveloped region, holds almost one third (30 %) of world's maternal deaths and approximately 13 % of them are related to abortions and its procedures[7].

Different studies have evaluated efficacy of misoprostol in early pregnancy failure with success rate ranging from 13 – 100 % which is influenced by many factors as diagnosis sac size, and number of dose. Efficacy rate 90 % when compared to manual vaccum aspirator in two other study documented[8,9].

Misoprostol is useful for elective medical abortions, cervical ripening before surgical abortions, evacuation of uterus in case of embryonic or fetal death and induction of labour[10]. Misoprostol is widely available of low cost, stable at room temperature and easy to use for both patient and clinician make this an excellent treatment in low source setting[11,12].

The objective of performing this study was to evaluate the efficacy, acceptability and dose of sublingually in the management of first trimester pregnancy termination.

PATIENTS AND METHODS

This is observational study conducted in Obstetrics & Gynaecological Department at Peoples Medical College Hospital Nawabshah. A total of 150 patients with the diagnosis of missed and incomplete miscarriage up to 13 weeks were invited to participate into the study after taking informed consent. Diagnosis of missed miscarriage was made when Os was closed, nil or mild vaginal bleeding, an embryonic or no fetal cardiac activity seen on ultrasound. Incomplete miscarriage was diagnosed when there was history of passage of tissue

and or blood, Os was opened mild or moderate bleeding or an ultrasound showing fetal remnants.

Exclusion criteria, women with fever, haemoglobin less than 9 g/dl, heavy vaginal bleeding regarding emergency surgical evacuation, contraindication to prostaglandin therapy (Asthma, Uncontrolled blood pressure, Hypertension, Glaucoma, Cardiac and Renal disease).

All eligible women who consented were counseled and given detailed information about protocol. For incomplete abortion single dose of 600 µg was given sublingually. For missed miscarriage 600 µg of misoprostol was given sublingually and repeated after 3 hours and waited for 7 – 14 days until complete miscarriage. The patients were explained about side effects and were instructed to report if they have heavy bleeding. They were told that bleeding may start anytime and complete abortion take one to two weeks. In case of profuse bleeding explained us soaking more than 2 extra large sanitary pads an hour for more than 2 consecutive hours or bleeding continuously for two weeks, they were instructed to report back to hospital. In case of retained placenta of conception third dose of 600 µg is repeated sublingually and left to ward for a total of 14 days from the first dose. All women were followed up till complete abortion or 14 days. Acceptability was allowed by verbally asking the patient if they were satisfied with this treatment or unsatisfied.

RESULTS

A total of 150 patients with missed miscarriage 119 (79.33 %) and incomplete miscarriage 31 (20.66 %) uptil 13 weeks gestation were included in the study. Demographic characteristic of women with miscarriage (Table-I). The mean age is 28.34 years, mean gestational age is 8.61 weeks, mean parity is 4.79 and 139 women completely evacuated, remaining 11 underwent surgical evacuation of uterus thus the efficacy of sublingual misoprostol in our study is 92 %. 127 (84.66 %) women had complete miscarriage by the end of 7th day with two doses of 600 µg sublingual misoprostol 3 hours apart. 23 (15.33 %) patients were given third dose sublingual misoprostol as they came with retained products of conception at the 7th day.

Single dose misoprostol was given to all incomplete miscarriage and all of them had complete miscarriage in first 24 hours. Total 11 women underwent surgical evacuation and 2 due to heavy bleeding and remaining 9 were unsatisfied and could not wait larger and efficacy of sublingual misoprostol is 48.66 % in 24 hours of administration of drug and 30.66 % in 48 hours although majority of patients were from miscarriage. Total 2 women had heavy bleeding remaining had mild and moderate bleeding.

We also included women with history of previous cesarean section. We had 21 patients with previous one cesarean section and 7 patients with 2 cesarean sections who were given same dose of misoprostol another with no added complication.

Regarding side effects, only 18.66 % observed shivering, 11.33 % nausea, 4 % unpleasant taste and 3.33 % diarrhea.

Patients satisfaction was 94 % (141 patients) and only 9 (6 %) were unsatisfied who refused to wait larger for spontaneous complete miscarriage and opted for surgical evacuation on 3rd of treatment. Acceptability was 92.67 %, whereas 7.33 % does not like to choose method again.

Table No.1: Demographic Characteristic of Women With Miscarriage (n = 150)

Parity				
Parity	Frequency	Percent	Valid Percent	Cumulative Percent
1-3	19	12.7	12.7	12.7
4-6	41	27.3	27.3	40.0
>6	90	60.0	60.0	100.0
Total	150	100.0	100.0	

Gestational Age				
Gestational Age	Frequency	Percent	Valid Percent	Cumulative Percent
<2 weeks	36	24.0	24.0	24.0
7_13 weeks	114	76.0	76.0	100.0
Total	150	100.0	100.0	

Statistics (n = 150)			
Statistics	age	party	Gestational Age
Mean	28.3400	4.7933	8.6133
Median	28.0000	5.0000	9.5000
Mode	30.00	6.00	10.00
Std. Deviation	5.65190	2.68052	3.58930

Type of Abortion	No of Cases	Percentage
Missed abortion	119	79.33 %
Incomplete abortion	31	20.67 %

Table No.2: Frequency of women requiring different dose regimen (n = 150)

Outcome Measures	No. of Cases	Percentage
Induction to Delivery Time		
24 hours	73	49.67 %
48 hours	46	30.66 %
72 hours	21	14.00 %
96 hours	03	2.00 %
07 days	07	4.67 %
Dosage		
Single dose	31	20.67 %
Two doses	96	64 %
Three doses	23	15.33 %

Table No.3: Side Effects (n = 150)

Side Effects	No. of Cases	Percentage
Blood Loss		
Mild	87	58 %
Moderate	61	40.67 %
Heavy	02	10.33 %
Shivering	28	18.66 %
Nausea	17	11.33 %
Unpleasant Taste	06	4 %
Diarrhoea	05	3.33 %
Satisfaction		
Satisfied	141	94 %
Unsatisfied	09	6 %
Acceptability		
Yes	139	92.67 %
No	11	7.33 %

DISCUSSION

Misoprostol, a prostaglandin PGE1 analogue has cervical ripening and uterotonic properties thus making it is useful drug in obstetrics[3,13]. Misoprostol is widely available. It is of low cost and stable at room temperature. There are varieties of medical and surgical techniques for termination of pregnancy[14].

It is easy to use of both for the patient and clinician. It is thus excellent choice of treatment for use in low resources setting[9]. Uterine evacuation by medical methods reduces the morbidity associated with surgical intervention[1,15].

This study demonstrates the efficacy and safety of outpatient medical management of first trimester miscarriage. The use of two doses of 600 µg, misoprostol sublingually with followup for 7 – 14 days reduce the need of surgical evacuation by 94 %. In addition, this dose and route achieved 73 (49.67 %). Complete miscarriage in the first 24 hours and 30.66 % in 48 hours following therapy. We also found that women with spontaneous incomplete miscarriage were more likely to have complete expulsion after one dose of 600 µg sublingually than women with missed miscarriage. The higher patient satisfaction in our study also reflect successfully outcome which highlights the importance of counseling women before opting for medical management regarding side effects, waiting time of 7 – 14 days and needs surgical intervention in those who failed to successfully evacuate the uterus within this time frame.

The overall success rate for complete miscarriage in our study is 94 % which is comparable to similar studies reported from China and India. They used 600 µg of sublingually and vaginal misoprostol and reported an overall success rate of 87.5 % and 86 respectively[13,16], whereas Khatija et al[17] from Pakistan reported 92 % success rate single dose of sublingually misoprostol. Higher success in our study may be due to waiting time of 7 – 14 days as its is well recommended that waiting period of 7 days should be allowed to maximize the chance of success and reduce the number of unnecessary surgical interventions[13].

Two studies comparing a single dose of oral misoprostol 600 µg versus 600 µg two doses with a 4 hours interval showed no difference in efficacy between the two regimen[18,19] weeks et al used 600 µg of oral misoprostol and showed success rate of 96.3 %[19]. Different misoprostol alone regimen have been reported in literature for medical management of first trimester miscarriage. These studies are difficult to compare on different regimen and waiting time was used. WHO clinical guidelines 2007 clearly recommends 600 µg of g/L misoprostol only 2 doses 3 hours apart for the management of first trimester missed miscarriage with waiting periods of 7 – 14 days[20].

In our study, sublingual administration found side effects shivering 18.66 %, nausea 11.33 %, unpleasant taste 4 % and Diarrhoea 3.33 %. In another study, JS Bagrate[21] from South Africa reported 21 % whereas Tang OS et al[13] found 70 % incidence of diarrhea and 20 % found another study in Pakistan[22]. The unpleasant taste found 63 % in one study in UK[23], whereas one study in Pakistan found only 15 % cases[22]. Blood loss on reported by patient in our study was moderate 40.67 %, heavy loss was observed in only 10.33 % (2 cases). They were hospitalize and underwent surgical evacuation, remaining 58 % had mild bleeding reflect the safety of misoprostol in another study at Pakistan found heavy loss 6 cases and moderate in 75 %, 20 % cases had mild bleeding[22].

It appears that one regimen of 600 µg sublingually upto two doses has well tolerated by in patient which is not much increase in side effect. We have found that our medical regimen is associated with high degree satisfaction and acceptability. Wards and Grazin et al[24,25] also found high satisfaction in their study on medical management. The introduction of any new management intervention must also convince health providers that in addition to safety and tolerability, it might be acceptable to patient. We have found that our medical regimen is associated with high degree satisfaction and acceptability.

Medical management using misoprostol could revolutionize the existing treatment option of abortion. This method greatly improve access and service by enabling women to seek effective appropriate care at secondary and primary healthcare facilities with non surgical trend, providing it could be clean the burden on tertiary healthcare facilities economic resources because of its low costs as well as reducing the need to surgical supplies, stabilization and altering.

CONCLUSION

Misoprostol prove with benefit of efficacy, safety and acceptability in first trimester pregnancy failure. In low resources countries achieve infection haemorrhage and uterine damage can for two commonly reported on

consequences of post surgical care. Misoprostol treatment can prove to be a rewarding step towards reducing morbidity and mortality.

REFERENCES

1. Chia KV, Oqbo VI. Medical termination of missed abortion. J Obstet Gynaecol 2002; 19: 266-71.
2. Bhattacharjee N, Ganguly RP, Saha SP. Misoprostol for termination of mid-trimester post-caesarean pregnancy. Aust NZ J Obstet Gynecol 2007;47:23-5..
3. Tang OS, Miao BY, Lee SWH, Ho PC. Pilot study on the use of repeated doses of sublingual misoprostol in termination of pregnancy up to 12 weeks gestation: efficacy and acceptability; Hum Reproduction 2002; 17: 654-8.
4. Aronson A, Helstrom L, Gemzell-Danielson K. Sublingual compared with oral misoprostol for cervical dilatation prior to vaccum aspiration: a randomized comparison. Contraception 2004; 69(2):165-9.
5. Von Hertzen H, piaggio G, Huong NTM et al. Misoprostol for termination of early pregnancy—a randomized multicentre equivalence trial on two routes and two intervals. Geneva: WHO; 2007.
6. Nielsen S, Hahlin M. Expectant management of first trimester spontaneous abortion. Lancet 1995; 345: 84-6.
7. World Health Organization, United Nations Children's Funds, United Nations Population Funds, Maternal mortality in 1995. Geneva: World Health organization; 2001
8. Dao B, Blum J, Th eiba B, Rhagavan S, et al. Is misoprostol safe, effective and acceptable alternative to manual vacuum aspiration for post abortion care? Results from a randomized trial Burkina Fasco, West Africa. Br J Obstet Gynaecol 2007; 114:1368-75.
9. Bique C, Usta M, Debora B, chong E, et al. Comparison of misoprostol and manual vacuum aspiration for the treatment of incomplete abortion. Int J Gynecol Obstet 2007; 98(3):222-6.
10. Chawla S. A study of efficacy of misoprostol in missed abortion. Med J Af 2007;63:241-2.
11. Coughlin LB, Roberts D, Haddad NG, Long A. Medical management of first trimester miscarriage (blighted ovum and missed abortion): Is it effective? J Obstet Gynecol 2004;24:69-71.
12. Al-Bbour AN, Akashek H, Al-Jayousi T. Missed abortion: Termination using single dose versus two doses of vaginal misoprostol tablets. Pak J Med Sci 2007;23:920-3.
13. Tang OS, Lau WN, Ng EH, Lee SW, Ho PC. A prospective randomized study to compare the use of repeated doses of vaginal with sublingual misoprostol in management of first trimester silent miscarriage. Hum Repro 2003; 18: 176-81.
14. Petrous S, Trinder J, Broklehurst P, Smith L. Economic evaluation of alternative management methods of first trimester miscarriage based on results of MIST trial. BJOG 2006; 113:879-89.
15. Tango OS, Schweer H, Seyberth HW, Lee SWH, HO PC. Pharmacokinetics of diff erent routes of administration of misoprostol. Hum Reprod 2002;17: 332-6.
16. Sharma D, Singhal SR. Rani XX. Sublingual misoprostol in management of missed abortion in India. Trop Doc 2007;37: 39-40.
17. Bano K, Talat, Iqbal S. Alternatives to surgical evacuation of uterus: misoprostol for post-abortion care. J Surg Pak 2009;14(2):53-57.
18. Blanchard K, Taneepanichskul, Kiriwat O, et al. Two regimen of misoprostol for treatment of incomplete abortion. Obstet Gynecol 2004; 103: 860-5.
19. Weeks A, Alia G, Blum J, et al. A randomized trial of oral misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion in Kampala, Uganda. Obstet Gynecol 2005;106: 540-7.
20. WHO Clinical Guidelines Bellagio, Italy in Feb 2007 Gemzell- Danielsson et al., Int J Gynecol Obstet(2007) 99, S182–S185 FIGO October 2009.
21. Bagratee JS, Khullar V, Regan L. A randomized controlled trial comparing medical and expectant management of first trimester miscarriage. Hum Repro 2004;19:2; 266-271.
22. Sadia J, Sidrah N, Asif ZA. Sublingual misoprostol in the management of first trimester miscarriage. Pak J Surg 2010; 26 (2): 169 – 73.
23. Hamoda H, Ashok PW, Flett GMM. A randomized trial of mifepristone in combination with misoprostol administered sublingually or vaginally for medical abortion at 13- 20 weeks gestation. Hum Repro 2005; 20: 23.
24. Wood SL, Brain PH. Medical Management of Missed Abortion: a randomized clinical trial. Obstet Gynecol 2002; 99: 563-6.
25. Graziosi GC, Van der Steeg JW, Reuwer PH, Drogtrop AP, Bruinse HW, Mol BW. Economic evaluation of misoprostol in the treatment of early pregnancy failure compared to curettage aft er an expectant management. Hum Reproduct 2005; 20: 1067-71.

Address for Corresponding Author:
Dr. Farida Wagan
Associate Professor Obs & Gynae,
Peoples University of Medical & Health Sciences
Nawabshah.
Phone No: 0301-3817416