Advances in Social Sciences Research Journal – Vol.7, No.3
Publication Date: Mar. 25, 2020
DoI:10.14738/assrj.73.7914.
Emarah, M. S. A. (2020). Safety And Efficacy Of Vaginal Misoprostol In Treatment Of First Trimester Miscarriage. *Advances in Social Sciences Research Journal,* 7*(3)* 138-144.

Safety And Efficacy Of Vaginal Misoprostol In Treatment Of First Trimester Miscarriage

Mohamed S. A. Emarah (MD)
Department of Obstetrics and Gynaecology,
Benha Teaching Hospital, Egypt.

ABSTRACT

Objective: This study was conducted to determine the outcome of medical treatment with vaginal misoprostol in missed miscarriage. Methods: A randomized controlled study was performed in Benha Teaching Hospital between April 2016 and June 2017. Eighty patients diagnosed with miscarriage before 13 weeks of gestation and wanted to try medical treatment were included. A detailed ultrasound scan was performed to confirm the diagnosis. Patients took 400 microgram (mcg) of misoprostol vaginal as an initial dose, and repeated the same dose 4-6 hours apart. Successful medical abortion was defined as spontaneous expulsion of gestational products (including gestational sac, embryo, fetus, and placenta). Ultrasonography at least 24 hours later from the initial dose to assess the uterine cavity if gestational products were not expelled, surgical evacuation was performed. Results: About two-thirds of patients (77.5%) had a successful outcome. The median interval time from pill to expulsion was 18 hours in the successful medical treatment group. Conclusion: Medical treatment with vaginal misoprostol should be a proper option for the first trimester miscarriage, especially for the patient who want to avoid surgical procedure. We can reduce the unnecessary sedation or surgical intervention in the patients with the first trimester miscarriage.

INTRODUCTION

Miscarriage, also known as missed abortion, is generally defined as spontaneous loss of a pre-viable pregnancy[1]. It complicates 15% to 20% of all pregnancies, 75% of miscarriages occur during the first trimester[2-4]. So long as ectopic pregnancy is ruled out, almost half of miscarriage get to be expelled spontaneously within two to six weeks[5,6]. However, anxiety of the women diagnosed with miscarriage and symptoms such as vaginal bleeding and abdominal pain usually require prompt interventions for termination of miscarriage[7].

Surgical evacuation using vacuum aspiration or curettage is the most common method for termination of miscarriages[6]. It is widely used because it can achieve complete removal of products of conception in a short time. A kind of anesthesia or sedation is usually necessary during surgical evacuation. However, there are some patients who want to avoid any surgical intervention and prefer non-invasive medical treatment to surgical evacuation.

In the western, the combined regimen of mifepristone followed 36 – 48 hours later by the prostaglandin E1 analgoue misoprostol is generally used for the medical treatment of the first trimester abortion with high efficacy and good patient acceptability[8-10]. Medical abortion using the anti-progesterone mifepristone and prostaglandin analogue was approved in France, UK, and Sweden in 1988, 1991 and 1992, respectively. In the USA, mifepristone was approved for medical abortion in 2000[11].

Misoprostol, a synthetic analogue of natural prostaglandin E1, was first marketed in the 1980s to prevent gastric or duodenal ulcer. Misoprostol has been used for long time, also it is inexpensive, easy to be kept at room temperature. Misoprostol has additional effect on uterine

contractility and cervical ripening, so World Health Organization (WHO) recommended misoprostol for obstetric and gynaecologic indications[12].

In obstetric or gynecologic use, misoprostol can be administrated widely via vaginal as well as oral or sublingual routes. The pharmacokinetics of misoprostol showed that serum concentrations of vaginally administrated misoprostol were higher than those of orally administrated misoprostol[13]. However, the efficacy between vaginal route and oral or sublingual route was known to be equivalent and oral or sublingual route is much easier to be taken than vaginal route. Previous studies reported the effectiveness of vaginal misoprostol[14-23].

Diagnosis of missed miscarriage is considered when we met one of the following criteria:

- Crown – rump length (CRL) of at least 7 mm and no heartbeat;
- Mean gestational sac diameter of at least 25 mm and no embryo;
- No embryo with heartbeat on a follow-up scan at least 2 weeks after an initial ultrasound scan that showed a gestational sac without a yolk sac;
- No embryo with heartbeat on a follow-up scan at least 11 days after an initial ultrasound scan that showed a gestational sac with a yolk sac[4].

Aim of the work:

In this study, we tried to determine the outcome of medical treatment with vaginal misoprostol in the first trimester miscarriage, and the need for surgical abortion.

MATERIALS AND METHODS

Eighty cases with first trimester missed miscarriage, diagnosed either clinically by presentation of mild vaginal bleeding or during follow up by ultrasound, are included in our study.

The study population was consisted of patients who were 18 to 42 years old, primigravida to para 4 wheather vaginal delivery (V.D.) or cesarean section (C.S), diagnosed with miscarriage before 14 weeks of gestation in Department of Obstetrics and Gynaecology, Benha Teaching Hospital, from April 2016 to June 2017.

Those who wanted to avoid surgical intervention and waited until the next day after taking misoprostol as a medical treatment for termination of first trimester missed miscarriage, were enrolled in this study.

Complete history taking, complete physical examination and routine laboratory investigations included complete urine analysis complete blood count, blood sugar level and coagulation profile were done.

The corrected gestational sac was determined by measurement of the size of gestational sac or CRL at the point of diagnosis of miscarriage by ultrasound.

Patients not suitable for medical abortion with misoprostal were excluded, such as presence of considerable vaginal bleeding, suspected molar pregnancy, suspected ectopic pregnancy or contra-indication to prostaglandin.

Participants received 400 microgram (mcg) of misoprostol vaginal at the level of external cervical os as initial dose, and repeated the same dose 4 – 5 hours apart. At least 24 hours later after the first dose, patients were examined by ultrasound scan to verify whether gestational products were remained in the uterine cavity or not.

Successful medical abortion was defined as spontaneous expulsion of gestational products at least 24 hours later from the initial dose.

If gestational products were not expelled spontaneously, surgical evacuation was performed.

We defined the successful medical treatment group as patients with spontaneous expulsion of gestational products by vaginal misoprostol and the failed medical treatment group as those with remained gestational products despite medications whether incomplete abortion or no response to vaginal misoprostol or those with severe vaginal bleeding needed immediate surgical interference. We evaluated the side effects of misoprostol, such as fever chilling sense, nausea, vomiting abdominal pain or diarrhea.

The statistical analysis was performed using SPSS version 20.0 for windows (SPSS Inc., Chincago IL, USA). Comparison of the continuous variables was carried out using the Mann-Whitney U test, and proportions were compared using pear – son's X^2 test. A probability value of < 0.05 was considered statistically significant.

RESULTS

Eighty cases with first trimester miscarriage diagnosed clinically by presentation of mild vaginal bleeding, or during follow up, where diagnosis was confirmed by ultrasonography.

All cases were hospitalized for trial of medical abortion. Sixty two patients (77.5%) had successful outcome until the next day, after taking vaginal misoprostol, where they were classified as the successful medical treatment group. The other eighteen patients (22.5%), underwent surgical evacuation, and were classified as the failed medical treatment group with statistically significant difference ($P < 0.05$) (Table 1).

Table (1): Success rate in the study group.

Characteristic	Number (n)	Percent (%)	P –value
Successful medical treatment group	62	77.5	
Failed medical treatment group	18	22.5	
Total	**80**	**100**	**< 0.05**

As regarding, the age, in the successful medical treatment group, the age in years ranged from 18 to 42 years with a median of (32) years, and ranged from 18 to 40 years with a median of (30.5) years in the failed medical treatment group, with no statistically significant difference ($P = 0.253$) (Table 2).

Table (2): Clinical characteristics of study population as regarding the age and parity.

Characteristic	Successful medial treatment group (n = 62)	Failed medical treatment group (n = 18)	P – value
Age (yers)	32 (18 – 42)	30.5 (18 – 40)	0.253
Nulliparity	13 (20.96%)	4 (22.22%)	0.383
Para one	14 (22.58%)	4 (22.22%)	0.480
Para two	12 (19.35%)	4 (22.22%)	0.370
Para three	12 (19.35%)	3 (16.66%)	0.256
Para four	11 (17.74%)	3 (16.66%)	0.246

As regarding to parity, the successful medical treatment group were nulliparas 13 cases (20.96%), para one, 14 cases (22.58%), para two, 12 cases (19.35%), para three 12 cases (19.35%) and para four, 11 cases (17.74%) and the failed medical treatment group were nulliparas, 4 cases (22.22%), para one, 4 cases (22.22%), para two, 4 cases (22.22%), para three, 3 cases (16.66%) and para four, 3 cases (16.66%), with no statistically significant difference, as regarding the parity in both groups (Table 2).

As regarding the mode of delivery wither through vaginal delivery (V.D), or through cesarean section (C.S), the successful medical treatment group were nulliparas, 13 cases, para one, 14 cases (8 cases through V.D and 6 cases through C.S), para two, 12 cases, (6 cases through V.D and 6 cases through C.S), para three, 12 cases, (7 cases through V.D and 5 cases, through C.S), para four, 11 cases (6 cases through V.D and 5 cases through C.S) and the failed medical treatment group were nulliparas, 4 cases, para one, 4 cases (2 cases through V.D and 2 cases through CS) para three, 3 cases (2 cases through V.D and one case through C.S) para four, 3 cases, 2 cases through V.D and one case through C.S).

With no statistically significant difference between the two groups as regarding the mode of previous delivery (Table 3).

Table (3): Clinical characteristics of study population, as regarding the mode of previous delivery whether through vaginal delivery (V.D) or through cesarean section (C.S.).

Characteristics	Successful group (no = 62)			Failed group (n = 18)			P
	Number Percent	V.D	C.S	Number Percent	V.D	C.S	
Nullipara	13 cases 22.96%	-	-	4 cases 22.22%	-	-	0.383
Para one	14 cases 22.58%	8	6	4 cases 22.22%	2	2	0.480
Para two	12 cases 19.35%	6	6	4 cases 22.22%	2	2	0.370
Para three	12 cases 19.25%	7	5	3 cases 16.66%	2	1	0.256
Para four	11 cases 17.74%	6	5	3 cases 16.66%	2	1	0.246

As regarding the failed medical treatment group, where surgical evacuation was done, they were, 8 cases (10%) had incomplete miscarriage, 5 cases (6.25%) due to severe bleeding, and 5 cases (6.25%), due to failed response to vaginal misoprostal, Table (4).

Table (4): As regarding the failed medical treatment group (n = 18 cases 22.5%), where surgical evacuation was done.

Characteristics	Number of cases	Percent
Incomplete miscarriage	8	10%
Severe bleeding	5	6.25%
No response	5	6.25%
Total	**18**	**22.5%**

DISCUSSION

The principal findings of this study were following: 1) gestational products were spontaneously expelled in about two-thirds of patients with only vaginal misoprostol until the

next day; 2) the median interval time from pill to expulsion of gestational products was 18 hours in the successful medical treatment group.

Vaginal miscoprostal in the first trimester miscarriage can be a proper option to the patients who have fear about surgery and anesthesia, and want to avoid any surgical intervention. Although we conducted surgical evacuation the next day for the remained gestational products in this study, it is also possible to observe more without surgical intervention. If the patients in the failed medical treatment group took additional misoprostol and waited a few more days, the rate of successful medical treatment would have increased.

A pharmacokinetics – related study addressed that the plasma concentrations of misoprostol was higher in vaginal insertion than in oral administration, but several serious complications were associated with vaginal misoprostol such as premature separation of placenta, postpartum hemorrhage, uterine rupture and amniotic fluid embolism in patients with fetal demise[24,25]. There was 5 cases of severe bleeding.

In spite of recent advances in surgical techniques and perioperative care, surgical curettage of the gravid uterus is a risk factor for intrauterine adhesions and abnormally invasive placenta in subsequent pregnancy[26,27]. Spontaneous expulsion of gestational products induced by misoprostol dose not hurt uterus.

According to the 2006 WHO frequently asked clinical questions about medical abortion, several factors should be taken into account when counseling a woman about her choice between medical and surgical abortion[28]. Besides of patients who want to avoid surgical intervention and anaesthesia, there are several favorable conditions for medical abortion as follows: 1) very early gestation; up to 49 days of gestation, medical abortion is considered to be more effective than surgical abortion; 2) severe obesity body mass index (BMI), greater than 30); 3) uterine malformations or a fibroid uterus, or previous cervical surgery. Maternal severe obesity or uterine malformation make surgical intervention difficult[28].

Although not included in this study, there was a case transferred from local clinic to our hospital because of failed surgical treatment of miscarriage. She had a bicornuate uterus, and gestational products were located in the right uterus. We tried to evacuate the gestational products surgically, but eventually failed to access to the right uterus with gestational products. She took 400 mcg of misoprostol and repeated the same dose 4 hours later. After 14 hours later since the initial pill, the gestational products came down to the external os of cervix, on examination, we easily removed the gestational products.

There are several strengths and limits of this study. Despite, the limitations of our study are attributable to the inherent weakness of a retrospective study and small sample size. If further prospective studies with a large population identify some contributing factors associated with successful medical treatment, it will be helpful in the counseling of patients.

CONCLUSION

In conclusion, medical treatment with vaginal misoprostol (MS) can be a proper option for the first trimester miscarriage without any serious complications, especially for the patients who want to avoid surgical procedure. We can reduce the unnecessary sedation or surgical intervention in the patients with the first trimester miscarriage.

ACKNOWLEDGEMENTS

This research was supported by General Organization of Teaching Hospitals and Institutes (GOTHI), Ministry of health.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

References

Hurt KJ, Guile MW, Bienstock JL, Fox HE and Wallach EE. The Johns Hopkins manual of gynecology and obstetrics. 4th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2011.

National Collaborating Centre for Women's and Child-dren's Health (GB); National Institute for Health and Clinical Excellence (GB); Royal College of Obstetricians and Gynaecologists (GB).Ectopic pregnancy and miscarriage: diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage. London (GB): Royal College of Obstetricians and Gynaecologists; 2012.

Francis O. An analysis of 1150 cases of abortions from the government R.S.R.M. Lying – in Hospital, Madras. J Obstet Gynaecol. India 1959, 10 : 62 – 70.

Cuningham FG. Williams Obstetrics. 24th ed. New York (NY): McGraw-Hill; 2014.

Olvier A, Overton C. Diagnosis and management of miscarriage. Practitioner 2014; 258 : 25 – 8, 23.

Kripke C. Expectant management vs. surgical treatment for miscarriage. Am Fam Physician 2006; 74 : 1125 – 6.

Tuncalp O, Gulmezoglu AM and Souza JP. Surgical procedures for evacuating incomplete miscarriage. Cochrane Database Syst Rev 2010: CD001993.

Schaff EA, Stadalius LS, Eisinger SH, Franks P. Vaginal misoprostol administered at home after mifepristone (RU486) for abortion. J Fam Pract 1997; 44 : 353 – 60.

Westhoffa C, Dasmahapatra R, Schaff E. Analgesica during at home use of misoprostol as part of a medical abortion regimen. Contraception 2000; 62 : 311-4.

Creinin MD, Schreiber CA, Bednarek P, Lintu H, Wanger MS, Meyn LA, et al. mifepristone and misoprostol administered simultaneously versus 24 hours apart for abortion : randomized controlled trial. Obstet Gynecol. 2007; 109 : 885 – 94.

Kopp Kallner H, Fiala C, Gemzell – Danielsson K. Assessment of significant factors affecting acceptability of home administration of misoprostol for medical abortion. Contraception 2012; 85 : 394 – 7.

Tang J, Kapp N, Dragoman M, de Souza JP. WHO recommendations for misoprostol use for obstetric and gynecologic indications. Int J Gynaecol Obstet 2013; 121 : 186-9.

Zieman M, Fong SK, Benowitz NL, Banskter D, Darney PD. Absorption kinetics of misoprostol with oral or vaginal administration. Obstet Gynecol. 1997; 90 : 88 – 92.

Bracken H, Dabash R, Tsertsvadze G, Posohova S, Shah M, Hajri S, et al. A two – pill sublingual misoprostol out – patient regimen following mifepristone for medical abortion through 70 days' LMP : a prospective comparative open – label trial. Contraception 2014; 89 : 181 – 6.

Chong E, Tsereteli T, Nguyen NN, Winikoff B. A randomized controlled trial of different buccal misoprostol doses in mifepristone medical abortion. Contraception 2012; 86 : 251 – 6.

Tang OS, Lau WN, Ng EH, Lee SW and Ho PC. A prospective randomized study to compare the use of repeated doses of vaginal with sublingual misoprostol in the management of first trimester silent miscarriages. Hum Reprod 2003; 18 : 176 – 81.

Schaff EA, Fielding SL, Westhoff C. Randomized trial of oral versus vaginal misoprostol at one day after mifepristone for early medial abortion. Contraception 2001; 64 : 81 – 5.

Aronsson A, Bygdeman M, Gemzell-Danielsson K. Effects of misoprostol on uterine contractility following different routes of administration. Hum Reprod 2004; 19 : 81 – 4.

Tang OS, Lau WN, Chan CC and Ho PC (2004): A prospective randomized comparison of sublingual and vaginal misoprostol in second trimester termination of pregnancy. BJOG 2004; 111 : 1001–5.

Kulier R, Kapp N, Gulmezoglu AM, Hofmeyr GJ, Cheng L, Campana A. Medical methods for first trimester abortion. Cochrane Database Syst Rev 2011: CD002855.

Cunningham FG. Williams obstetrics. 23rd ed. New York (NY): McGraw-Hill; 2010.

Bracken H; Family Planning Association of India (FPAI)/Gynuity Health Projects Research Group for Simplifying Medical Abortion in India. Home administration of miso-prostol for early medical abortion in India. Int J Gynaecol. Obstet 2010; 108 : 228 – 32.

Kopp Kallner H, Fiala C, Stephansson O, Gemzell-Dan-ielsson K. Home self-administration of vaginal misoprostol for medical abortion at 50-63 days compared with gestation of below 50 days. Hum Reprod 2010; 25 : 1153-7.24. Hofmyr GJ, Gulmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database Syst Rev 2010 : CD000941.

Hofmeyr GJ, Gulmezoglu AM, Pileggi C. Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database Syst Rev 2010 : CD000941.

Gomez Ponce de Leon R, Wing D, Fiala C. Misoprostol for intrauterine fetal death. Int J Gynaecol Obstet 2007; 99 Suppl 2 : S190-3.

Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome – one century later. Fertil Steril 2008; 89 : 759 – 79.

Engelbrechtsen L, Langhoff – Roos J, Kjer JJ, Istre O. Placenta accreta : adherent placenta due to Asherman syndrome. Clin Case Rep 2015; 3 : 175 – 8.

von Hertzen H, Baird D. Bellagio study and conference center. Frequently asked questions about medical abortion. Contraception 2006; 74 : 3 – 10.