

Original Article

Use of Combination of Mifepristone and Misoprostol to Terminate Early Pregnancy: Experience at a Tertiary Care Teaching Hospital

Zobaida Sultana Susan¹, Afzallunnesa Chowdhury², Shipra Halder³, Sabarin Ahamed⁴, Helena Afrin⁵, Tahmina Hossain⁶, Raunak Jahan⁷

[Reviewed: 30 July 2016; Accepted on: 1 November 2016; Published on: 1 January 2017]

Abstract

Background: Termination of pregnancy is well prescribed method all over the world to terminate the early pregnancy with the combination of mifepristone and misoprostol tablet orally. **Objective:** The purpose of this present study was to determine the efficacy of mifepristone (200 mg) for medical termination of early pregnancy with oral misoprostol 800 mcg 24 hours later. **Methodology:** This observational study was done in the Department of Gynaecology & Obstetrics at Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh among outdoor patients in 6 months period from July 2014 to December 2014. The patients with intrauterine pregnancy up to 9 weeks and blighted ovum were included. Incomplete abortion and extrauterine pregnancy were excluded. Mifepristone 200 mg followed by misoprostol 800 mg after 24 hours had been given. **Result:** Total 50 patients with 9 weeks of pregnancy were selected over the period of 6 months requesting termination of pregnancy. This study showed termination of early pregnancy up to 9 weeks with tablet mifepristone and tablet misoprostole which was effective as well as the expulsion rate of the product of conception was 92.0% cases and among them 32.0% patients were needed extended dose of misoprostol and 8.0% cases had incomplete abortion who needed surgical evacuation. Some patients had some complications like vomiting, fever, abdominal pain and excessive per vaginal bleeding which were managed accordingly. **Conclusion:** Mifepristone 200 mg followed by misoprostol 800 mcg orally is an effective method for termination early pregnancy with minimum side effects. [*Journal of Science Foundation 2017;15(1):9-13*]

Keywords: Mifepristone; misoprostol; termination of pregnancy; early pregnancy

Introduction

Medical abortion or medication abortion is the termination of pregnancy with the use of medication alone rather than surgery. Over the past two decades, medical methods of abortion have been developed throughout the world. An estimated 26 million pregnancies are terminated legally with more than 78000

¹Junior Consultant, Dept. of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh

²Professor, Department of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh

³Residential Surgeon, Dept. of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh

⁴Medical Officer, Department of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh

⁵Medical Officer, Department of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh

⁶Medical Officer, Department of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh

⁷Junior Consultant, Dept. of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh

Correspondence: Dr. Zobaida Sultana Susan, Junior Consultant, Department of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh; Email: zssusan2014@gmail.com; Cell no.: +8801711009172

deaths (WHO 2012). The availability of acceptable, safe drugs for termination of pregnancy would be of immeasurable value for women and the medical profession.

Implantation of a fertilized ovum involves complex interactions with endometrium. The embryo becomes attached to the endometrial epithelium and invades endometrial stroma on day 6 to 10 after ovulation. These events depend on progesterone which modifies the transcriptions of many genes involved in the implantation process. Progesterone also inhibits myometrial contractions (Chwalisz and Garfield 1997). The drugs used to terminate pregnancy act by inhibiting the synthesis of progesterone inducing myometrial contraction, antagonizing the action of progesterone or inhibiting the development of trophoblast.

The first progesterone antagonist (antiprogestin) to be developed was mifepristone, which binds to the progesterone receptor with an affinity five times as great as that of progesterone. Unlike progesterone, this complex inhibits transcription resulting in the down regulation of progesterone dependent genes with decidual necrosis and detachment of the product of conception (Spitz and Bardin 1993). Anti-progestins also act on endometrial blood vessels causing damage that further compromises the embryo (Johannisson et al., 1989). These agents directly promote uterine contractions by increasing myometrial cell excitability and also cause cervical dilatation (Sakai et al., 1992). Natural prostaglandins, the first agent of this class used for termination of early pregnancy are unstable, lack of specificity and are poorly tolerated (Karim and Filshie 1970). The synthetic prostaglandin E₁ compounds currently used are misoprostol and gemeprost. Misoprostol is inexpensive which can be stored at room temperature and is available in many countries for the treatment and prevention of peptic ulcer disease.

Medical abortion which involves the use of medications to induce an abortion rather than a surgical abortion is an option for women who wish to terminate pregnancy up to 63 days of gestation calculated from 1st day of last menstrual period. In this study, it was focused on the medical termination of pregnancy during the early part of first trimester when the most abortions are performed. The objective of this study was to determine the efficacy of tablet mifepristone followed by tablet misoprostol at 24 hours interval for the termination of early pregnancy.

Methodology

This was an observational study done in the Department of Gynaecology & Obstetrics, Shaheed Suhrawardy Medical College & Hospital (SHSMCH), Dhaka, Bangladesh from July 2014 to December 2014 for a period of six (06) months. This study included women seeking medical termination of pregnancy up to 9 weeks of gestation. All the patients seeking medical termination of pregnancy up to 9 weeks of gestation and blighted ovum were included; however, women with intrauterine pregnancy of more than 9 weeks, incomplete abortion and extrauterine pregnancy were excluded. At the first visit of the patient, a detailed history was taken and a general, systemic and obstetric examination was done. The duration of pregnancy was calculated from the last menstrual period (LMP) and was correlated with a pelvic examination. An ultrasound was carried out to confirm the gestational age and to rule out an ectopic pregnancy. Routine investigations such as blood grouping, a complete blood count, bleeding time and clotting time were carried out. An informed consent was obtained after counseling in regard to the drug dose schedule, hospital visits, the advantages and possible side effects and warning signs so that the patients could call and reach the hospital in time. A patient was given a tablet of mifepristone 200 mg on day 1 after completing the work up and the patient was asked to return in the next day (day 2), 24 hour later, when 4 tablets of misoprostol (800 mcg) were administered buccally.

Anti-ulcerant and anti-emetic were given as required. Patients who did not abort completely after this drug schedule, an extended dose of misoprostol 600 mcg daily in 3 divided doses were given for 5 days. Some information were given to every woman like medical termination of pregnancy, 100.0% sure to terminate the pregnancy, use of these drugs beyond first trimester, didn't do the abortion alone and close attention to the body. These drugs were not used where there was a possibility of extrauterine pregnancy and not be used in IUCD in situ and should not be used where allergic to PG (prostaglandins). Ethical approval was obtained from college ethical committee before the start of the research work. All the patients enrolled for the study was first informed about the drug protocol and informed written consent was obtained prior to medication.

Result

Total 50 patients with 9 weeks pregnancy were selected over the period of 6 month requesting termination of pregnancy. A total number of 42.0% patients were within 26 to 30 years age group. Mean age is 26.2 ± 5.347 years (Table 1).

Table 1: Distribution According to Age (n=50)

Age Group	Frequency	Percentage
20 to 25 Years	16	32.0
26 to 30 Years	21	42.0
31 to 35 Years	13	26.0
Total	50	100.0

Parity ranges from 1 to 5. Among the study population 74.0% were housewives and 26.0% were working ladies; 66.0% were from middle class; 26.0% had previous 1 cesarean section and 2.0% had previous 2 previous section; 46 cases had living pregnancy and 4 cases had blighted ovum. Mifipristone 200 mg followed by misoprostol 800 mg after 24 hours had been given.

Table 2: Type of Termination of Pregnancy among the Study Population (n=50)

Type of Termination	Frequency	Percentage
Complete	46	92.0
Incomplete	4	8.0
Total	50	100.0

Successful termination was done in 92.0% cases (Table 2) and among them 32.0% needed extended dose of misoprostol. Incomplete abortion was occurred in 8.0% who were treated by surgical evacuation. 32% was terminated successfully with extended dose of misoprostol (Table 3).

Table 3: Patients Needed Extended Dose of Misoprostol (n=20)

Type of Termination	Frequency	Percentage
Complete	16	32.0
Incomplete	4	8.0
Total	20	40.0

Table 4: Complications of the Study Population

Complication	Frequency	Percentage
Incomplete abortion	4	8.0
Excessive per vaginal bleeding	8	16.0
Abdominal pain	14	28.0
Vomiting	6	12.0
Fever	7	14.0

Some patients had reported complications like vomiting, fever, abdominal pain and excessive per vaginal bleeding which were managed accordingly (Table 4).

Maximum expulsion occurred in 38.0% cases within 24 hours and the rest were within 1 week and 2 week. After 1 week 30 patients were informed about complete expulsion of product of conception without any complication. After 2 weeks, out of 20 patients, 16 cases showed complete expulsion, and remaining 4 patients required investigation and finally surgical evacuation. Within 24 hours maximum expulsion occurred (38.0%) (Table 5).

Table 5: Time required for medical abortion (n=46)

Time required	Frequency	Percentage
Within 24 hours	19	38.0
Within 1 week	11	22.0
Within 2 week	16	32.0
Total	46	100.0

Discussion

Termination of pregnancy is the most common entity in the practice of obstetrics since antiquity. An estimated 26 million pregnancies are terminated legally each year throughout the world and 20 million are terminated illegally with more than 78000 deaths. A safe medical method would save many lives. Medical termination of early pregnancy means the termination of early pregnancy with medication alone. It is currently a well prescribed method all over the world to terminate the early pregnancy with the combination of mifepristone and misoprostol tablet orally.

The anti-progesterone mifepristone (RU-486) causes abortion by completely blocking progesterone receptors and effect is maximized by adding prostaglandin, especially Misoprostol. Misoprostol which is inexpensive, stable at room temperature and can be administered by different routes, it provides patient compliance. In this study, all women who needed medical termination of early pregnancy up to 9 weeks, were assessed by urine for pregnancy test and USG of lower abdomen to confirm intrauterine living pregnancy or blighted ovum and exclude any medical or surgical conditions like ectopic pregnancy, history of allergy or hypersensitivity to prostaglandin, IUD in place, chronic adrenal failure, hemorrhagic disorder, concurrent anticoagulant therapy or inherited porphyria (ACOG Committee on Obstetric Practice 2002).

If a patient does not have adequate access to medical facilities equipped to provide emergency treatment of incomplete abortion, blood transfusion or emergency resuscitation, medical abortion was not advocated. Though tab misoprostol buccally works as well as vaginally (Burkman 2009), in this study tablet mifepristone 200 mg was given orally followed by tab misoprostol 800 microgm buccally after 24 hours. All the patients were given oral antibiotics and pain killer. Some studies have shown that women have termination of pregnancy within 4 hours of taking 2nd medication (Middleton et al., 2005). Patients were advised to come back after 1 week and 2 weeks for follow up.

According to ACOG, this combination of drugs is effective in 92.0%. Among women with pregnancies of 49 days duration or less, the success rate of these two drugs combination is 92.0 to 98.0%. Complete expulsion occurs in 1 to 6.0% before administration of prostaglandin. In a study, success rate with this two drug combination is about 96.2% which is quite similar to this study (Chen and Creinin 2008). It was observed that patients with less than a 42 day gestational age had a mean bleeding duration after abortion of approximately 6 days, whilst those with more than a 42 day gestational age had a mean bleeding duration of 7-9 days. Peyron et al (1993) had reported a definite positive correlation between the duration of amenorrhea preceding the administration of mifepristone and the duration of bleeding after abortion. It follows that the earliest possible intervention is recommended.

Conclusion

Mifipristone combined with oral Misoprostol is an effective alternative to surgical intervention. Proper counselling about the procedure to be followed as well as information about possible high risk symptoms must be communicated to the patient beforehand. An observation period of 4 to 6 hours after the administration of Misoprostol is a better option as maximum pain and bleeding occurs during that time. But medical termination needs more visits than surgical abortion and it should be provided by only trained clinicians who can provide surgical treatment in the event of failed abortion or excessive bleeding.

Reference

- ACOG Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2002;77(1):67
- Burkman RT. Danforths's Obstetrics and Gynecology. JAMA. 2009;301(6):672

- Chen BA, Creinin MD. Medical management of early pregnancy failure: efficacy. *Seminars in reproductive medicine* 2008;26(5):411-422
- Chwalisz K, Garfield RE. Regulation of the Uterus and Cervix during Pregnancy and Labor Role of Progesterone and Nitric Oxide. *Annals of the New York Academy of Sciences*. 1997;828(1):238-53
- Johannisson E, Oberholzer M, Swahn ML, Bygdeman M. Vascular changes in the human endometrium following the administration of the progesterone antagonist RU 486. *Contraception*. 1989;39(1):103-17.
- Karim SM, Filshie GM. Therapeutic abortion using prostaglandin F_{2α}. *The Lancet*. 1970;295(7639):157-9
- Middleton T, Schaff E, Fielding SL, Scahill M, Shannon C, Westheimer E, Wilkinson T, Winikoff B. Randomized trial of mifepristone and buccal or vaginal misoprostol for abortion through 56 days of last menstrual period. *Contraception*. 2005;72(5):328-32
- Peyron R, Aubeny E, Targosz V, Silvestre L, Renault M, Elkik F, Leclerc P, Ulmann A, Baulieu EE. Early termination of pregnancy with mifepristone (RU 486) and the orally active prostaglandin misoprostol. *New England Journal of Medicine*. 1993;328(21):1509-13
- Sakai N, Tabb T, Garfield RE. Studies of connexin 43 and cell-to-cell coupling in cultured human uterine smooth muscle. *American journal of obstetrics and gynecology*. 1992;167(5):1267-77
- Spitz IM, Bardin CW. Mifepristone (RU 486)--a modulator of progestin and glucocorticoid action. *New England Journal of Medicine*. 1993;329(6):404-12
- World Health Organization. Facts on induced abortion worldwide. World Health Organization, Geneva. http://www.who.int/reproductivehealth/publications/unsafe_abortion/induced_abortion_2012.pdf. 2012