ORIGINAL RESEARCH PAPER

Obstetrics & Gynecology

KEY WORDS:mifepristone, pregnancy termination, misoprostol.

EARLY PREGNANCY TERMINATION WITH ORAL MIFEPRITONE AND VAGINAL MISOPROSTAL

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ABSTRACT

Objective: To determine the efficacy, side effect and acceptability of medical abortion using mifepristone 200mg orally and misoprostol 800µg vaginally in patients less than 49 days of gestation.

Materials and methods: Seventy six women who requested termination of pregnancy up to 49 days of gestation were administered 200mg mifepristone orally followed 48 hours later by 800µg of misoprostol per vaginally.

Results: Ninety six percent (96%) women had complete abortion with this regimen. There was no ongoing pregnancy. The average duration of per vaginal bleeding was 12-13 days. There were some side effects, which include abdominal pain, vomiting, fever etc.

Conclusion: This mifepristone-misoprostol regimen is highly effective in terminating pregnancy in women up to 49 days duration with minimum side effects and this medical method may be advisable to practice as an alternative to surgical procedure where adequate skilled attendance is lacking.

Introduction:

It is estimated that 46 million pregnancies are terminated voluntarily each year, 27 million carried under safe condition and 19 million falling into the category of 'unsafe' abortion[1]. Until the second half of twentieth century, dilatation and curettage was the most common method of termination followed by vacuum aspiration, which gained greater acceptance and became the standard care. But unsafe abortion conducted by unskilled personals in unsterile environment is still a great global issue, where safe medical method could save many of these lives[2]. As a result the regimen of mifepristone followed by a suitable uterotonic (usually misoprostol) has become increasingly available and is now the gold standard for this indication[3].

Medical abortion using mifepristone and misoprostol are safe, highly effective and well accepted by women who wish to avoid invasive procedure[4-6]. Millions of women worldwide have safely terminated their pregnancies with medication mifepristone—or RU 486

Since it was first introduced in the late 1980s. Research in the past two decades has identified several highly effective regimens for early medical abortion with a success rate of 95 to 98 percent, consisting of 200 mg of mifepristone followed by 400 or 800 mcg of misoprostol[7]. Mifepristone is an antiprogestine and acts by antagonizing progesterone's effect at the receptor level in the endometrium; it causes decidual breakdown and detachment of the embryo[8]. It also increases myometrial response to exogenous prostaglandins[9]. Misoprostol is a synthetic prostaglandin E1 analog that is well absorbed from the vaginal mucosa[10]. Misoprostol softens the cervix and stimulate uterine contra ction[11]. These actions ultimately cause sloughing of the uterine lining and expulsion of any tissue in the uterus[10,11].

Materials and Methods:

We enrolled 76 healthy women who requested termination of pregnancies in Apollo hospital since May 2005 till June 2007. These women were offeredThe medical termination of pregnancy with proper counselling, and they accepted the method. The duration of gestation was less than 49 days from the 1st day of last menstrual period.

Entry criteria included age at least 18 years, singleton uterine pregnancy not exceeding 49 days gestation, acceptance for medical termination, willingness to comply with the visit schedule and willingness to have a surgical evacuation if required.

Potential subjects were excluded if they had any contraindication to mifepristone and misoprostol including chronic systemic steroid administration or adrenal disease, glaucoma, mitral stenosis, sickle cell anaemia, seizure disorder and cardio-vascular disease.

In all cases, first the pregnancies were confirmed by pregnancy test. Those who had regular menstrual period, their gestational age as well as intra uterine singleton pregnancy were confirmed by abdominal ultrasound in the gynaecological out-patient department. However, those who had irregular periods, their gestational age were confirmed by transvaginal sonogram in the ultrasound department of same hospital.

On day one, a detailed history was taken, a physical examination was performed and baseline haemoglobin level, blood grouping, Rh typing and random blood sugar were advised. All women were prescribed 200mg of mifepristone to be taken orally at home. Forty-eight hours after mifepristone administration, the women were asked to get admitted to the gynaecology department of Apollo hospital for short period, when 800µg tablet of misoprostol were introduced per vaginally by the duty doctor. These patients stayed in the hospital for about 4 to 6 hours and their vital signs including pulse, B.P and temperature were monitored hourly. Any complain made by the patient were recorded and treatment given accordingly, for example analgesic for pain relief, paracetamol for fever and antiemetic for vomiting. If the patient's blood type was Rh negative, she also received 50µg Rh immunoglobulin intramuscularly.

The patients were asked to record the number of days of vaginal bleeding for next 14 days. They were scheduled to return for a follow up examination after

14 days when a transvaginal ultrasound was done in women who complained persisting vaginal bleeding to exclude the possibility of incomplete abortion. No further follow up was scheduled for those women who had stopped bleeding at this point. However a second follow-up visit was scheduled one week later for those who continued to bleed.

The side effects and duration of per vaginal bleeding was recorded and checked. If emergency or elective curettage was not required during the interval up to 21 days, the outcome was classified as complete abortion. All women were asked to use barrier method for contraception.

The primary outcome was complete abortion rate. The duration of vaginal bleeding and side effects of the treatment were also studied. Patient with incomplete abortion, defined as pregnancy termination with partial expulsion of the products of conception were given the option of either to wait for another week for the process to complete, or having a vacuum aspiration.

Complete medical abortion with no surgery and no additional misoprostol administration was classified as treatment success. All outcomes that resulted in a surgical intervention were classified as treatment failure. Reason for surgery was coded as ongoing pregnancy, incomplete abortion, medically necessary (i.e. for bleeding or pain that warranted surgery) or patient request.

Primary end point of the study was expulsion of the conception with no need for surgical intervention. Secondary end points were the rate of continued pregnancy and the incidence of side effects.

Results:

Table I summarizes baseline and demographic variables of the patients included in the study. The majority of the patient had gestational age between 43 and 49 days. There were 24 women whose gestational age was less than 42 days and 8 women had less than 35days. Age range of the patients was between 20-40 years. More than 50% of the patients were gravida 2nd and 3rd. Most of the patients were Bangladeshi origin, one was American, two were Chinese and one was European. History of previous termination of pregnancies was present among 40% of patients.

Table-I Baseline & Demographic variable of women

Characteristics	Number of	%(n)	
		patient (N)	
Gestational age (N=76)			
	35days or less	8	10.5
	36-42days	24	31.5
	43-49days	44	57.8
Age group (N=76)			
	<20	4	5.2
	20-24	14	18.4
	25-29	18	23.6
	30-34	16	21.0
	>35	24	31.5
Gravidity			
	1	14	18.4
	2	20	26.3
	3	20	26.3
	4 or more	22	28.9
Number of previous abortion			
	0	46	60.5
	1	16	21.0
	2	8	10.5
	3 or more	6	7.8
Blood group·	Rh-ve	2	
2.6			
·	Rh+ve	74	97.3
Race			
	Bangladeshi	72	94.7
	Chinese	2	2.6
	American black	1	1.3
	European	1	1.3

The rate of incomplete abortion was 3.9%.One patient had complete abortion before taking misoprostol. There was no failure representing ongoing pregnancy in any patient. All surgical evacuation was done for persisting vaginal bleeding due to incomplete abortion.

Table II shows the number and percentage of the patients who had side effects. Vaginal bleeding is a natural consequence of abortion process, and occurred in all patients those had terminated medically. But quite heavy per vaginal bleeding occurred in 23.9%of patients during hospital stay. Another 13% complained of maximum pervaginal bleeding on the following day of misoprostol administration. However no patient received any emergency hospitalization or blood transfusion for excessive pervaginal bleeding. Hospitalization was Needed for surgical evacuation in 3.9% of the women. Among other side effects 60% complained mild to moderate pain. Only one patient complained severe pain. Other complaints included nausea and vomiting 40.9%, 5.2% fever and 3.9% diarrhea.

The patients those complained of pain were managed with hyoscine N butyl bromide and diclofenac sodium. Narcotic analgesics were not required by any patients for pain relief. Other patients received antiemetic for vomiting, antipyretic for rise of temperature and or saline for diarrhea.

Table-II Incidence of side effects reported by the patients

Side Effects	Number of patients	%
Pain or cramps	46	60
Nausea	23	30.2
Fever/chill	4	5.2
Vomiting	8	10.5
Dizziness	3	3.9
Diarrhea	3	3.9

Discussion:

This study of 76 women represents the report of a method for early first trimester medical abortion undertaken in Apollo Hospital, Dhaka. The mifepristone–misoprostol regime used was found to be a highly effective method for termination of pregnancy, had acceptable side effect and generally well tolerated[12]. This method is recommended in many parts of world specially USA, China, and parts of European countries where this regime is considered as national guidelines for patients who wants termination in early pregnancy[13]. Moreover in developing countries where surgical termination conducted by the unskilled attendants leading to severe maternal morbidity and mortality, can be prevented by this medical termination method using the mifepristone and misoprostol regime.

The combined results for the treatment in our study are similar to those reported in general[14]and more specifically in a French[15] and a Scottish[16] study, even though the gestational age in our study was 49 days, compared to 50 and 56 days in the French[15] and the Scottish[16]series, respectively.

Consistent with other studies, the side effects profile of most of the patient in this study reported some combination of pain, gastrointestinal complains and Bleeding. However severity of those complaints did not require emergency hospitalization or blood transfusion for any patient. Nausea and vomiting were not severe enough to warrant intervention with intravenous fluid. Two percent women received Rh immunoglobulin as they were Rh negative. In case of Rh negative patients standard dose of immunoglobulin must be given after a medical or surgical termination regardless of the gestational age[17.] Bleeding is an expected consequence of the treatment. Twenty-three point nine percent of the patients reported that the bleeding was heavy, while only 13.0% reported heavy bleeding the first days after their ward stay. Most published studies report similar results[17, 18]. However, none of our patients were treated for bleeding, either with curettage or blood transfusions, as has been described regularly by others[18, 19], and [20]. Also, the median duration of bleeding of 14 days is in line with other studies[19,20.]

Continuing pregnancy after attempts at medical induction of abortion is a major concern because of the risk of congenital malformation. Although there are no confirmed reports of congenital anomalies after the administration of mifepristone, there are reports of congenital malformation after the use of misoprostol alone[21, 22], and [23]. This malformation includes scalp or skull defects, cranial nerve palsies and limb defect[24, 25]. In our study there was no case leading to continuation of pregnancy following medical termination. However in a multicenter trial conducted by WHO the incidence of continuation of pregnancy rate was 0.4%[26].

In general, 5% of women required surgical curettage following medical termination of pregnancy27. In our study the incidence of incomplete abortion was 3.9%.

Complete expulsion before the administration of misoprostol is between 1-6% of the women; the larger rates within these ranges are associated with earlier gestation[18]. In our study only one patient had complete termination before administration of misoprostol.

The advantages of medical treatment are termination can be conducted as soon as the pregnancy has been confirmed; it is a non-invasive procedure, does not require anaesthesia and well accepted by the women[28]. Recent studies have confirmed high acceptability rates showing 84-96% women requesting terminat ion of pregnancy for a subsequent abortion[29]. Moreover misoprostol is cheap, easily available, and stable at room temperature. However the disadvantages are, it requires more clinic visits than surgical procedure and per vaginal bleeding continues for 10-12 days on average.

Recently, large number of studies is conducted to evaluate the efficacy of mifepristone and misoprostol regime, using different routes in different doses and in different interval for medical termination of early pregnancy. For example, instead of 200mg mifepristone orally, 100mg is used in different studies, and misoprostol is used orally, sublingually, buccally in different doses of 200, 400 and 600µg The interval between the drugs are also shortened from 48 hours to 24 hours to 12 hours or even given simultaneously31. The results from some clinical trials showed the efficacy is not statistically different but has lower success rate if the interval between the drugs is shorten to less than 8 hours[31].

In conclusion, now-a-days medical termination is considered the method of choice in most developed as well as developing parts of the world. As the medical termination is safe and effective, it may be justified to practice the procedure in Bangladesh to save many maternal lives and prevent complications associated with the surgical procedure carried out by unskilled attendants.

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