

Result of Combined Mifepriston and Misoprostol in Termination of Early Pregnancy at Different Gestational Age

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Abstract

Introduction: An estimated 56 million induced abortion occurred each year worldwide. Indirect estimates suggest more than 1.2 million annual menstrual regulations (MRs) and induce abortions each year in Bangladesh. Maternal mortality in Bangladesh is 1.76 /1000 live birth, one fourth of these deaths are due to complication of induced abortion. The safety of procedure is therefore of global public health importance. Now medical abortion option have made more available to women in a variety of health care setting and home administration of medical abortion is acceptable.

Objective: To know the outcome and safe use of mifepristone and misoprostol combination up to 9 weeks (<63 days) of missed period to reduce the maternal morbidity, mortality related to complications of menstrual regulation (MR) and induced abortion in Bangladesh.

Materials and Methods: This was a prospective cross sectional study of outdoor patients (100 cases) of Marie Stopes Premium Maternity Hospital, Mirpur-10 who came for menstrual regulation within 9 weeks (63 days) of missed period by MRM (Menstrual Regulation by Medication), using 200mg of oral Mifepristone followed by buccal Misoprostol 800µg. Study period was from July 2014 to December 2014.

Results: Success rates of regimen used in this study that are higher (98%) in case of women <6wks amenorrhoea than that group who have had amenorrhoea up to 9 weeks (94%). There were 4 failures (4%), among them 1(2%) from women <6 weeks and 3 (6%) from women >6 weeks who needed surgical evacuation later on.

Conclusion: MRM with Mifepristone 200mg followed by buccal Misoprostol 800µg is highly effective and safe.

Key-words: Medical abortion, Mifepristone, Misoprostol, Menstrual regulation by medication (MRM).

Introduction

Despite relatively high contraceptive prevalence (61%) compared to other developing countries, Bangladesh continues to have low utilization of long term or permanent contraceptive methods, a high discontinuation rate¹. Menstrual regulation has been part of Bangladesh's national family planning program since 1979. Indirect estimates suggest more than 1.2 million annual menstrual regulations (MRs) and induced abortions each year in Bangladesh². Maternal mortality in Bangladesh is 1.76 /1000 live birth, one fourth of these deaths are due to complication of induce abortion.

An estimated 56 million induced abortion occurred each year worldwide³. The safety of procedure is therefore of global public health importance. Now medical abortion options have made more available to women in a variety of health care setting and home administration of medical abortion is acceptable⁴. In the United States, about one fifth of all out patient abortions are performed medically⁵ and in several countries in Europe⁶, the proportion exceeds 60%.

Medical abortion or MRM is the induction of early abortion by means of medications. It is a non surgical procedure in which drugs are used to induce abortion. Indication of medical abortion are when pregnancy continuation is harmful for maternal life

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or where child would be born with grave physical or mental defect, when women want to avoid surgical procedure for regulation of menstruation, women with uterine malformation or fibroid uterus or had cervical surgery where surgical abortion is technically difficult.

The most effective and safest medical abortion regimen requires the use of two medications: mifepristone and misoprostol. The antiprogestone mifepristone combined with the prostaglandin analogous (misoprostol) is effective for termination of early pregnancy and has a favorable safety profile⁷. Early medical abortion regimens using 200mg oral mifepristone and 800µg misoprostol have been endorsed by Royal College of Obstetricians and Gynecologists (RCOG) as an effective and appropriate method of termination of pregnancy⁸. Although medical abortion regimens approved by most government regulatory agencies specify 600mg mifepristone, in practice, a dose of 200 mg is standard worldwide⁹.

A medical abortion is said to be successful when the medication used, achieves complete expulsion of the products of conception, without the need of any surgical intervention¹⁰. Medical terminations are safe and effective alternative to surgical vacuum aspiration of uterus with high level of patient satisfaction¹¹. Medical abortion allows the women to avoid an invasive procedure and to avoid significant exposure to anesthetic medications. Many women feel medical abortion to be the more "natural" option, like a miscarriage, and prefer being in the comfort of their own home for the process¹².

Mifepristone (RU486) is a potent anti-progestin but when it is administered alone for early pregnancy termination, it results in incomplete expulsion in approximately 20% of women¹³. This relative lack of efficacy may be due to an insufficient increase in prostaglandin concentration in uterus to allow completion of termination¹⁰. Administration of misoprostol after mifepristone, in different dosage schedules, has been found to be effective, feasible and acceptable method of medical termination in early pregnancy¹¹. The regimen we used is similar to those recommended by the World Health Organization (WHO)¹⁴. Research in communities reveals growing

number of women who do not want to undergo invasive procedure such as MVA and seek abortifacient drugs to establish normal menstruation¹⁵. A recent survey of Marie stopes Bangladesh in 62 pharmacies reveals that 51% of drug sellers and pharmacists know of drugs that can be used to induce medical abortion and 30 percent of drug stores and pharmacies sell these drugs to the public¹⁶. This study is to know the efficacy and safe use of medical MR in different gestational age up to 63 days (<9wks) and to reduce the maternal morbidity and mortality for complications of MR and induced abortion by implementation of MRM.

Materials and Methods

Subjects for this prospective randomized cross sectional study were enrolled from outdoor patients (100 cases) of Marie Stopes Premium Maternity Hospital, Mirpur-10, Dhaka-1216, who came for menstrual regulation within 9 weeks (63 days) of missed period by MRM (menstrual regulation by medication), using 200mg of oral mifepristone followed by buccal misoprostol 800µg from July 2014 to December 2014.

All subjects initially received 200 mg of oral mifepristone and then were randomly assigned to receive buccal 800 µg misoprostol at 24-36 hours at health facility or at home. Some client chose self administration of second dose at home, they were given the misoprostol tablet, counsel on proper buccal technique, educated on possible side effects and informed of the safety procedure in case of an emergency. They were then followed up after 14 days with ultrasonography to confirm completion of expulsion. Treatment was considered failed if surgical evacuation was needed for any indication.

Results

Efficacy was analyzed in 100 women. Fifty percent 50% of them were <6 weeks (42 days) and 50% were between 6 weeks (43 days) to 9 weeks (63 days). Twelve patients were at 56 (8 weeks) days to 63 (9 weeks) days. Among women in whom treatment was successful, expulsion starts soon after the administration of misoprostol 70% in four hours and 30% within 24 hours in women <6 weeks of gestation and 62% in four hours and 38% within 24 hours in women >6 weeks of gestation (Table-I).

Table-I: Time of first expulsion after administration of mifepriston and misoprostol (n=100)

Gestational age	Total no of clients	Within 4 hours	(%)	4-24 hours	(%)
<6 weeks	50	35	70%	15	30%
>6-9 weeks	50	31	62%	19	38%

Table-II: Success rate of medical abortion at different gestational age in first trimester (n=100)

Duration	4-5wks	5-6wks	6-7wks	7-8wks	8-9wks
Total no of clients (n=100)	23	27	22	16	12
Failure of medical abortion	0	1	1	1	1
Success rate	100%	96.24%	95.45%	93.75%	91.66%

Table-II shows that there were 4 failures (4%), among them 1(2%) from women <6 weeks and 3(6%) from women >6 weeks, all needs surgical evacuation. Overall success rate of medical abortion is 98% in <6 weeks and 94% in >6-9 weeks.

Table-III: Overall outcome of medical abortion (n=100)

Gestational age	Total no of Clients(n=100)	Failure of medical abortion	Success rate	Failure rate
<6wks	50	1	98%	2%
>6-9wks	50	3	94%	6%

All women had uterine bleeding, whatever the outcome of drug administration. The mean duration of bleeding is 8 ± 2 days in <6 weeks and 10 ± 4 days >6 weeks. No women received transfusion. Only one women (62 days of gestation) had slight vaginal spotting for 28 days. There were correlation between duration of amenorrhea and duration of bleeding. Most of the women 85% had uterine cramp, for which 20% received analgesic drugs. The pain usually started within one hour after taking of misoprostol and it lasted few hours or less. Nausia, diarrhoea and vomiting within four hours of administrating misoprostol in approximately 45%, 12% and 16% of the women respectively. One woman had vasovagal reaction secondary to painful uterine cramps.

Discussion

Medical abortion using mifepristone 200mg followed by 800 µg misoprostol in the first 63 days of gestation is remarkably effective and safe¹⁷. Policy on MRM formulated as a strategic option for expanding safe MR services in Bangladesh¹⁸ in 2011. Mifepristone and misoprostol are the drugs increasingly used by WHO and licensed in about 150 countries¹⁹. These drugs are convenient than MR, because it is given orally with good

good compliances. These drugs are inexpensive and can be stored at room temperature. The regimen used in this study appears to result in success rates that are higher (98%) in case of women <42 days gestation than that group who have had amenorrhea up to 63 days (94%) which is almost similar (95.7%) to a study in Bangladesh²⁰ and a study in Australia²¹ where the success rate is 96.5%. Intensity of uterine cramps after administration of misoprostolis comparatively more in women who had amenorrhea more than 42 days. The apparent decrease in the duration of bleeding in the women <6 weeks of gestation is encouraging.

In this study, no infection was reported. Infection following medical termination of pregnancy is reported to occur in 0.02%-0.92% of cases²³. Death resulting from infection and fatal toxic shock after medical abortion with mifepristone is a known, but very rare²⁴, risk (1.1/1000,000). Although the Royal College of Obstetricians and gynecologists (RCOG) recommends universal prophylactic antibiotics effective against *C. trachomatis* and anaerobes to reduce infection after medical abortion, the WHO¹⁴ does not. The sides effects of two drugs neither more frequent nor more severe but slightly higher in women >6 weeks of amenorrhoea. Regarding side effects mifepristone did not give any serious side effects. Few clients had nausea, vomiting and diarrhoea within of two drugs neither more frequent nor more severe but slightly higher in women >6 weeks of pregnancy.

However, caution should be exercised in using this agent in women at risk for cardiovascular accidents. This study also found higher risk of medical abortion failure rates that had a high proportion in >42 days of gestation (6%) and it is 4% higher than those gestational age <42 days which are almost similar to other studies²⁰⁻²². However higher risk of ongoing pregnancy in these group did not found. Overall risk of medical abortion failure in both groups seems reasonable. Moreover, prompt confirmation of completeness of the abortion by clinical assessment and routine ultrasound may enhance women's satisfaction with the procedure. This study observed no evidence that allowing women to take misoprostol at home increased abortion failure rate or serious complications. Most women preferred this option and

it is presumably substantially more efficient for the health care system than requiring patients to return to the provider for administration of the prostaglandin¹⁷.

Conclusion

In the study reported here that for the termination of pregnancy, in women who had amenorrhea for less than 42 days (<6 weeks) is more successful as well as well tolerated than women had pregnancy between 43 days (>6 weeks) to 63 days (9 weeks). In spite of satisfactory results reported here, we wish to emphasize that the abortion procedure should continue to be medically supervised.

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