Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(5):1121-1124

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Simultaneous administration of mifepristone and misoprostol for medical abortion up to 7 weeks gestation-a pilot study

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ABSTRACT

Most widely used regimen for first trimester medical abortion is 200mg of oral mifepristone followed by 800 mcg misoprostol intravaginally 48 hrs apart. However this interval regimen is associated with lot of apprehension in the waiting period which adversely affects the choice regarding the method termination of pregnancy. The aim of this study was to find out a regimen that is convenient and improves the patient compliance without compromising efficacy. This prospective pilot study was carried out after obtaining ethical clearance. 50 eligible women with gestational age ≤7 weeks who visited family planning unit for medical termination of pregnancy were included in the study. After taking written informed consent, women received 800 mcg misoprostol intravaginally within 15 minutes of oral administration of 200mg mifepristone. Women were then asked to come for follow up visits on 2nd day, 7th day and 14th day of drug administration. Primary outcome measure was the rate of complete abortion at 2 weeks without the need for suction evacuation. The complete abortion rate with simultaneous regimen was 92% at 2 weeks. The mean induction to abortion interval was 6.8 hours. Mean duration of bleeding was 7.5 days. The overall acceptability rate was 90%.Our study concludes that simultaneous administration is a promising regimen with equal efficacy and higher acceptability as compared to the standard interval regimen for early first trimester medical abortion.

Key words: medical abortion, mifepristone, misoprostol, mifepristone- misoprostol interval

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INTRODUCTION

Hemorrhage, sepsis and unsafe abortions are the leading causes of maternal mortality; the latter being responsible for 13% of maternal deaths [1, 2]. To overcome the complications associated with surgical abortion, FDA in 2000 approved mifepristone and misoprostol for medical abortion in first trimester abortion. India approved this combination for clinical usage in 2001 [3]. For medical abortion up to 63 days gestation, there are various regimens available as per WHO guidelines. They include 200mg of oral mifepristone followed by either 800 mcg misoprostol vaginally 1-3 days later or 800 mcg misoprostol sublingually 2 days later or 400 mcg misoprostol orally or vaginally 2 days later up to 49 days gestation.

These regimens are though highly effective, the only drawback being the interval between two drugs. During this interval the patient can have bleeding, pain and other side effects associated with misoprostol along with increased apprehension in the waiting period. Also the patient has to visit the hospital again for misoprostol administration. This interval has eventually adversely affected the preference of patients regarding choice for method of abortion. Surgical abortion that completes in one day still has an edge over the medical abortion. This study was conducted

with the aim to find out whether simultaneous administration of two drugs can prove to be an effective alternative that improves patient's acceptability and quality of care without compromising the efficacy.

EXPERIMENTAL SECTION

This prospective pilot study was conducted at a tertiary hospital in India. Ethical clearance was taken from ethical committee of the hospital (approval number-HRH/16925) before starting the study. Women eligible for medical termination as per MTP act India with gestational age ≤7 weeks, , who were intelligent enough to understand the instructions and the need for follow up visits, have easy access to health care facility and who were ready to undergo surgical abortion if needed were included in the study. Women with contraindications to mifepristone (chronic steroid administration, known adrenal disease) and misoprostol (glaucoma, sickle cell anemia, mitral stenosis, poorly controlled seizure disorders, allergy to prostaglandins), liver, kidney , lung or heart disease, smoker, hemoglobin less than 8gm%, ectopic pregnancy, undiagnosed adnexal mass, breast feeding , active cervicits, lack of access to emergency services and who want concurrent sterilization were excluded. 50 women attending the family planning unit who fulfill the above criteria were enrolled in the study after detailed history, thorough examination and pre abortive counseling. Written informed consent was taken from them. Each patient underwent minimum investigations like hemoglobin, blood grouping, urine examination and ultrasonography. Patients received 200 mg mifepristone orally followed by 800mcg misoprostol vaginally within 15 minutes. Women were made to lie down for half an hour and were allowed to go home after four hours of observation with the advice to come for follow up visits. Anti D was administered to Rh negative patients. Patients were advised to take analgesics and antiemetics when needed.

First follow up visit was made at 24hours of drug administration. History was taken regarding the time of start of bleeding, amount of bleeding, expulsion of products of conception and any side effects. Transvaginal ultrasonography was done to find out whether the sac has been expelled or not. All patients were then advised to come for second follow up visit at one week of drug administration. Detailed history was taken and transvaginal ultrasonography was done to confirm complete abortion. Those with incomplete abortion were asked to come for third follow-up visit at two weeks of drug administration: Women who have not aborted completely till now will be considered to have treatment failure. Women were asked to rate individual adverse effects as none at all, present but not worse, worse but not troublesome, worse and troublesome but without the need for additional treatment, worse and severe enough requiring additional treatment. They were also asked to use Likert scale (strongly agree, agree, neither agree nor disagree, disagree, strongly disagree) to rate the acceptability of medical abortion regarding time taken for abortion, vaginal bleeding, abdominal pain, adverse effects, overall acceptability and whether they would recommend this regimen to a friend or choose similar regimen again if required . Selection of any of the first three options on Likert scale by the patient was considered as an acceptable response.

Statistical analysis

Statistical analysis was performed with SPSS 12.0 for windows. Data was presented as mean ± SD. The regimen was considered successful if there was complete abortion in ≤ 2weeks without the need for suction evacuation. Primary outcome measure was the rate of complete abortion at 2 weeks without the need for suction evacuation whereas secondary outcome measures included induction to abortion interval, incidence of adverse effects, acceptability and need for emergency surgical evacuation.

RESULTS

The mean age of patients in this study was 28.5 years; 40% patients being < 30 years of age. 16% women were nulliparous, 50% were primiparous and 34% were multiparous. There was previous history of abortion in 32% women. 44% belonged to the lower socioeconomic strata, 50% middle socioeconomic strata and 6% belonged to upper socioeconomic strata. Gestational age as confirmed by ultrasound was < 5weeks in 22% patients, >5 weeks to 6 weeks in 58% and >6 weeks to 7 weeks in 20%patients. 52% and 48% patients had hemoglobin > 10 gms and between 8-10 gms respectively. Mean time of onset of bleeding after misoprostol administration was 3.2 hours. Mean duration of bleeding was 7.5 days. Blood loss was comparable to normal menses in 76% patients. Among 24% patients with more than normal flow, one patient got admitted and underwent surgical evacuation. Mean induction to abortion interval was 6.8 hours. Chills, nausea, vomiting and diarrhea were present in 4%, 20%, 12% and 4% patients respectively. 80% patients had mild abdominal pain while 20% experienced moderate pain. 8% patients had to take analgesics for pain. Rate of complete abortion was 68% at 24 hours and 84% at one week.

Complete abortion rate at two weeks was 92%. Among the patients with regimen failure 4% had incomplete abortion, 2% had missed abortion and emergency suction evacuation was needed in another 2% of patients. Overall acceptability of the regimen was 90%. Time taken for treatment was acceptable to 92% patients, pattern of vaginal bleeding was acceptable to 84% patients, and associated abdominal cramps were acceptable to 90% patients. 80% patients accepted that they would like to recommend this regimen to others or would like to use it again if required in future.

DISCUSSION

This study shows that simultaneous administration of mifepristone and misoprostol for first trimester abortion has results comparable to standard interval regimens. Initial regimen for medical abortion was recommended only upto 7 weeks gestation and included 600 mg of mifepristone orally followed by 400 mcg of oral misoprostol 48 hrs later. After that the research work was conducted focusing on the dose of mifepristone, route of administration of misoprostol and gestational age upto when medical abortion can be conducted safely. The different regimens which we use presently are the result of hard and sincere research work. Since the standard interval regimen is associated with decreased acceptability and increased dropout rates, now the focus of research has shifted towards decreasing the time interval between the two drugs.

The rationale for using two drugs simultaneously is based on scientific evidence. Mifepristone blocks progesterone receptors causing trophoblast separation, cervical ripening, increases release of prostaglandins and increases the sensitivity of myometrium to prostaglandins- all these actions requiring at least 18 hrs [4]. Misoprostol, prostaglandin E1 analogue causes myometrial contractions and cervical ripening [5]. Pharmacokinetics studies have shown that peak levels in serum are reached in 1-2 hours of oral mifepristone intake which is then metabolized slowly by liver and is excreted in bile with elimination half life of 20 hrs [4]. After vaginal administration of misoprostol the peak levels are reached in serum in 70-80 min and significant serum levels are present 4-6 hours later leading to abdominal pain in 2 hours and bleeding in about 3 hours; hence supporting the simultaneous usage of two drugs [5, 6, 7, 8]. Efficacy of mifepristone alone for medical abortion is 3-4% and that of single dose of misoprostol is 70-75%. Combination of two drugs simultaneously has improved the results. This again emphasizes the need for further research focusing on pharmacokinetics of two drugs.

Standard interval regimens using mifepristone and misoprostol have efficacy varying between 95-100%. Rate of complete abortion in our study is comparable to other studies in the literature that varied from 89-100% [6, 7, 8, 9], the efficacy being comparable to interval regimens. Some studies have however shown less encouraging results with simultaneous regimen [10].

As far as the incidence of side effects is concerned there are varied results in the literature. Some studies have shown less incidence of nausea, vomiting and bleeding pattern abnormalities with simultaneous regimens as compared to interval regimen [6, 9] while others have shown similar incidence in two groups [11]. Incidence of chills and diarrhea was found to be more in simultaneous usage of two drugs according to some studies [9, 10].

Almost all the studies in the literature have shown higher acceptability with simultaneous regimen varying from 86-97% [10, 11, 12].

The meta analysis of pooled data of 5 RCT's (1999-2008) regarding use of two types of interval regimens for first trimester medical abortion, shows no statistically significant difference in efficacy between shorter and longer dosing intervals. However gestational age, parity, previous abortions, state of cervix and route of misoprostol administration are some of the factors upon which the success rate of a regimen depends [13].

CONCLUSION

Simultaneous regimen being equally efficacious as the standard interval regimen with the additional advantage of reduced apprehension, decreased cost burden, increased compliance and higher acceptability is a suitable alternative to the interval regimen for first trimester medical abortion upto 7weeks; however flexible approach should be applied taking into consideration gestational age, parity and other factors.

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