Original Article

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# Is Misoprostol Alone, Administered 24 h a Valid Option for Medical Abortion?

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## Abstract

**Background:** Medical abortion with misoprostol alone has been established as a safe and effective alternative to combined therapy with mifepristone with misoprostol.

**Aims and Objectives:** The objective of this study was to evaluate the safety and efficacy of three doses of 1000 μg misoprostol administered at 24 h interval, for medical abortion.

**Materials and Methods:** A total of 60 prospective patients are attending our outpatient department for termination of pregnancy who fulfilled the inclusion criteria were included in this study after informed consent. Outcomes measured were: (1) Successful abortion (complete abortion without requiring additional procedure), (2) side-effects, (3) mean time of onset of cramping, (4) mean time of onset of bleeding, (5) mean duration of bleeding, (6) mean decrease in hemoglobin and, (7) mean time of menstruation returning. Medical abortion was successful in 54 of 60 (90%) patients.

**Results:** The mean change in hemoglobin was 0.7 ± 0.4 g/dl. Cramping began at 5.1 ± 3.4 h and lasted 3.7 ± 1.9 h. Vaginal bleeding started at 6.46 ± 1.6 h and lasted 7.0 ± 4.6 days. Time to return of menstruation was 37 ± 7.1 days.

**Conclusions:** The present study suggests that 1000 μg misoprostol administered vaginally at 24 h intervals could be a more economical and viable option in situations where financial constraints restrict the use of mifepristone. Moreover, the 24 h interval improves patient compliance and allows outpatient management.

**Key words:** First trimester pregnancy, Medical abortion,Termination, Vaginal misoprostol

## INTRODUCTION

Medical abortion has become the method of choice for termination of pregnancy and has superseded surgical evacuation due to ease, convenience and decreased complication rates.[1] Mifepristone followed by misoprostol has a high success rate and is the pharmacological agent of choice for the procedure.[2,3] Though Asian manufacturers have provided the drug at comparative low cost, non-availability of the drug in some countries and economic constraint of the large populations in developing countries is a major concern when it comes to providing affordable medical termination of pregnancy (MTP) to the needful leading to an increase in unsafe abortions.[4] A growing body of evidence has now shown that misoprostol can be used as a single agent to induce an early abortion.[5-7] Multiple modifications of the dose and interval in which misoprostol may be administered have provided additional options while improving acceptability and efficacy.[3,5,8,9]

The objective of this study was to confirm the effectiveness and safety to achieve a complete abortion by giving misoprostol 1000 μg at 24 h intervals. This is more economical, and the interval between doses ensures better compliance by not interfering in the day to day activities. Not hospitalizing patients would allow better acceptability, increase confidentiality and lower the burden on health care facilities.

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## MATERIALS AND METHODS

This study was conducted in a teaching institution where 60 consecutive patients fulfilling the inclusion criteria were enrolled after written informed consent (Table 1). The protocol was approved by the local ethics committee.

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The inclusion criteria were: (1) Women seeking MTP up to 49 days gestation as counted from the 1st day of the last menstrual period; (2) informed consent; (3) access to a telephone; (4) residence within 1 h distance from the hospital; (5) voluntary permission for surgical intervention if medically advised or in cases of failure.

Women were excluded from the study if they had, (1) A known allergy to prostaglandins; (2) a history of cardiac, respiratory renal, hepatic or adrenal disease; (3) a history of thromboembolism, hypertension, coagulopathy and diabetes mellitus; (4) history or sonographic evidence of uterine pathology; (5) active genital infection; (6) previous uterine surgery; and (7) prior uterine bleeding.

The patients were informed of the nature of the study, risks benefits, visiting schedule and the possible requirement of suction and evacuation if incomplete abortion or failure occurred. The patient was instructed to report to the hospital immediately in case of excessive bleeding, cramps or any other side effects. The patient was advised to keep a diary of the symptoms experienced.

### Drug Protocol

At the first visit, the patient was given a tablet of paracetamol. After ½ h five tablets of misoprostol (200 μg each) were inserted in the posterior fornix. The patient was instructed to lie in the lateral position for ½ h and then allowed to go home. On day 2, the patient was asked about bleeding and side-effects experienced. Pulse and blood pressure were noted, and a p/s and p/v were done. The same dose of misoprostol was repeated. On day 3, the same procedure was carried out as on day 2.

Patients were called for follow-up on day 7 or earlier in case of excessive bleeding or severe side effects experienced. On day 7, an ultrasound examination was conducted for the presence of the gestation sac, retained products of conception or increased endometrial thickness (>16 mm significant).

The next follow-up was scheduled on day 14 for assessment of amount and duration of bleeding, pelvic examination, repeat hemoglobin and for surgical evacuation in case of incomplete abortion or failure. The patient was then advised to report back after the next menses or earlier in case she experienced bleeding, fever or abdominal pain.

The principal outcomes assessed were successful abortion, side effects, mean expulsion time and mean decrease in hemoglobin. Secondary outcomes assessed were mean duration of bleeding, mean time of onset of cramping, mean time of onset of bleeding and mean time of menstruation returning. Side effects assessed included chills, nausea, dizziness, fever, vomiting, diarrhea and pelvic pain.

Success was defined as complete evacuation of the products of conception without the need for surgical intervention. Failure was defined as recourse to surgical abortion for decision to drop out, doctors decision as a result of complications (such as excessive bleeding, pain, retained products or infection) or failure due to inefficiency of the method itself that is when the gestational sac was not expelled.

Statistical analysis was performed using SPSS software. A paired *t*-test was used for comparisons and a probability (*P*) level of <0.05 was considered as significant.

## RESULTS

The trial included 60 women who requested a pregnancy termination and who complied with the inclusion criteria. The patient characteristics are mentioned in Table 1. It was observed that 86.7% patients who underwent medical abortion were of urban residence and 100% were educated. Also, 70% of patients undergoing abortion were of parity 2 and more.

Cramping began at 5.1 ± 3.4 h and lasted 3.7 ± 1.9 h. The duration of cramping pain was <5 h in 90% of patients, and 70% did not require any analgesics. Vaginal bleeding started at 6.46 ± 1.6 h and lasted 7.0 ± 4.6 days. The most common side-effects noted (Table 2) were cramping pain (100%), nausea (70%), diarrhea

**Table 1: Characteristics of the patients (*n*=60)***

| | *N* (%) |
|---|---|
| Age | |
| <30 | 38 (63.3) |
| 31-40 | 20 (33.3) |
| >40 | 2 (3.3) |
| Marital status | |
| Married | 58 (96.7) |
| Single | 2 (3.3) |
| Education | |
| Uneducated | 0 (0) |
| Educated | 60 (100) |
| Parity | |
| 0 | 2 (3.3) |
| 1 | 16 (26.7) |
| 2 | 30 (50) |
| 3 | 12 (20) |
| Previous abortions | |
| 0 | 36 (60) |
| 1 | 18 (30) |
| 2 | 6 (10) |
| Residence | |
| Urban | 52 (86.7) |
| Rural | 8 (3.3) |

(46.7%), chills (46.7%) and fever (23.3%). Onset of bleeding was after the first dose of misoprostol in 95% and after the second dose in 5% (Table 3). The duration of bleeding was <5 days in 46.7% of patients. The mean change in hemoglobin was 0.7 ± 0.4 g/dl. Time to return of menstruation was 37 ± 7.1 days. The success rate was 90%. Six women were classified as failure (Table 4), according to protocol criteria. Of these, four patients (66.7% of failures) had excessive bleeding, and two (33.3% of failures) had retained products of conception on ultrasound. There was no case of failure due to the continuation of pregnancy.

## DISCUSSION

MTP was liberalized in India through the MTP Act 1971.[10] Initially, surgical procedures were the mainstay of termination of pregnancy, however, there was need for better methods since complications such as perforation, synechiae formation, cervical injury and infections associated with surgical methods were unacceptable.

**Table 2: Side-effects**

| Symptom | Number of cases | Percentage |
|---|---|---|
| Chills | 28 | 46.7 |
| Dizziness | 12 | 20.0 |
| Nausea | 42 | 70.0 |
| Vomiting | 12 | 20.0 |
| Abdominal cramps | 60 | 100.0 |
| Diarrhea | 28 | 46.7 |
| Fever | 14 | 23.3 |
| Flushing | 12 | 20.0 |
| Headache | 12 | 20.0 |
| Rash | 0 | 0.0 |
| Itching | 0 | 0.0 |
| Redness | 0 | 0.0 |

**Table 3: Bleeding after each dose of misoprostol**

| Dose | Number of cases | Percentage |
|---|---|---|
| 1st | 57 | 95 |
| 2nd | 3 | 5 |
| 3rd | 0 | 0 |
| No bleeding | 0 | 0 |
| Total | 60 | 100 |

**Table 4: Outcome of treatment by gestation**

| Outcome | *N* (%) | | |
|---|---|---|---|
| | <35 days | 36-42 days | 43-49 days |
| Success | 20 (100) | 24 (88.9) | 10 (76.9) |
| Incomplete | 0 (0) | 1 (3.7) | 1 (7.7) |
| Excessive bleeding | 0 (0) | 2 (7.4) | 2 (15.4) |
| Missed | 0 (0) | 0 (0) | 0 (0) |
| Continuing pregnancy | 0 (0) | 0 (0) | 0 (0) |
| Total | 20 | 27 | 13 |

The rate of major morbidity was 1%, and that of minor morbidities was 10%.[11] The 2003 amendment to the MTP act permitted medical abortions up to a gestation of 49 days.[10] Medical abortions are more acceptable to women since it provides a natural way of termination of pregnancy that is safe, effective and non-invasive, and does not require hospitalization thus minimizes inference with day to day activities.[12]

Mifepristone followed by misoprostol has become standard regime for MTP,[3,8,9,13] however the non-availability of mifepristone in number of countries and high cost has limited its scope. Misoprostol alone is a valid alternative to this regime which is reported to be safe and effective.[1,4,5,7] Various dosage schedules from 600, 800, 1000 μg administered at 3 h, 6 h and 12 h interval[6,7] have been documented. Though outcomes improved at 3 h intervals from 6 h interval of misoprostol, no difference was noticed between 6 h and 12 h intervals.

Success rate in the present study was 90%. Pre-treatment with mifepristone before the administration of misoprostol has efficacy rates of 97-98%.[3,8,9] Medical abortion with the use of misoprostol as a single agent has success rates of 88.7-93%. Increasing the dose of misoprostol from 800 μg to 1000 μg was shown to improve the success rate.[7] Success rates were higher with less when the patients presented earlier (Table 4), which is consistent with previous studies.[3-9]

Bleeding lasted 7.0 ± 4.6 days, which was less than that observed in previous studies. Side-effects noted were similar to those of various studies using misoprostol in repeated doses.[3-6]

In the present study, we increased the dosage interval to 24 h with aim to make it an outpatient department regime thus eliminating the need of hospitalization for induction of abortion. Administration of doses at home by either self administration or by mid-level health providers can improve compliance and acceptability.[13-18]

The reduction in cost of treatment by more than 50% compared to the present recommendations has a major impact in an economically constrained setting. Onset of bleeding was after the first dose of misoprostol in 95% which suggests that possibly many patients would not require repeated doses thus further cutting the price by more than 80%.

The reduction of economic burden of unwanted pregnancies, improved accessibility of safe abortion methods in remote areas, regimens that are acceptable to the patients by complying with their need for discretion and

convenience will have a major impact in reducing morbidity and mortality rates. It could, in most cases, dispense with the need for a surgical procedure for MTP and at the same time make termination of pregnancy at a very early stage of embryogenesis possible thus minimizing, if not eliminating, the ethical reservations on the issue. Medical abortion thus provides women with a choice in method and saves lives.

## CONCLUSION

The drug amount of 1000 μg misoprostol administered vaginally at 24 h intervals could be a more economical and viable option in situations where financial constraints restrict the use of mifepristone. Moreover, the 24 h interval improves patient compliance and allows out patient management.

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