

Comparative Study of Mifepristone with Vaginal Misoprostol for First Trimester Termination of Pregnancy at Different Gestational Ages

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About the Author



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Abstract

Methods This study for medical abortion was conducted in the Department of Obstetrics and Gynaecology, Zenana Hospital, SMS Medical College, Jaipur during 2011–2012. In total 280 cases were taken for the study and divided into two groups, among whom there were six defaulters in each group who failed to present for follow-up.

Objectives The objectives of this study were to (1) compare the success rates of abortion at different gestational ages, (2) study the side effects of the drugs, and (3) study the acceptability in both the groups.

Results The medical abortion with the given regimen and protocol was observed to be highly successful, and complete abortion was achieved in 98.51 and 97.76 % of the patients in Group-A and Group-B, respectively. Failure

rates observed were only 1.49 % in Group-A and 2.24 % in Group-B.

Conclusions Medical abortion can be safely performed in cases up to 63 days of gestation, but women should be counseled about the increased blood loss and duration of bleeding.

Keywords Termination of pregnancy · Mifepristone · MTP

Introduction

The first recorded evidence of induced abortion was from Egyptian Eber Papyrus in 1550 BC [1, 2].

Over 5000 years ago, the Chinese Emperor Shen Nung described the use of mercury for inducing abortion [3].

Each year, throughout the world, approximately 210 million women become pregnant, and around 130 million of them go on to deliver live-born infants. The remaining

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80 million pregnancies end in stillbirth, or spontaneous, or induced abortion. Approximately 46 million pregnancies are voluntarily terminated each year, and around 19 million unsafe abortions are performed [3, 4].

Unsafe abortion nonetheless remains a neglected health care problem in developing countries. Unsafe abortion is characterized by the inadequacy of the provider's skills and use of hazardous techniques and unsanitary facilities. Women who resort to clandestine facilities or unqualified providers put their health and life at risk [3].

In India, nearly 15 million abortions are estimated to be taking place each year; of these, 10 millions risk their lives by approaching quacks or untrained abortion providers, and almost from 15,000 to 20,000 women die every year because of complications of unsafe abortions [5].

In order to reduce the number of unsafe abortions, the Govt. of India passed MTP Act in 1971 which came into force from April 2, 1972, and rules were modified in 2003 to strengthen the MTP ACT [6].

Hence, high-quality safe abortion services should be made available even at grass root levels to avoid the need of women turning to unauthorized personnel for abortion.

Misoprostol

It is a synthetic Prostaglandin E1 analog discovered in 1967 by Robert et al. and marketed for the first time in 1985 for the prevention of NSAID-induced gastric ulcers [1].

Misoprostol binds to myometrial cells causing strong myometrial contractions and causes cervical softening and dilatation and then expulsion of products of conception. It is stable at room temperature and well absorbed from the gastrointestinal tract and vaginal mucosa. By virtue of being selective for PGE1 receptors, Misoprostol has no significant effects on bronchi and blood vessels, with minimal effects compared to other prostaglandins.

The advantages of medical abortion are that there is no need for anesthesia and surgery, it affords better privacy, since only the woman and her gynecologist need to know about her pregnancy, and it does not cause surgical trauma leading to life-threatening complications like uterine perforation and bowel injuries.

MOHFW, GOL Comprehensive Abortion Care

Guidelines, 2010 reiterates the safety and efficacy of medical method of abortion and makes recommendations for medical methods for early abortions. The DCGI recently approved a combipack of one 200 mg tablet of Mifepristone and four 200 mcg tablets of Misoprostol for MMA up to 63 days [4].

Methods

This study was conducted in the Department of Obstetrics and Gynaecology, Zenana Hospital, SMS Medical College, Jaipur during 2011–2012.

Sample Size

In total, 280 cases were enrolled:

- Group-A (140 cases)—Gestational age up to 49 days.
- Group-B (140 cases)—Gestational age 50–63 days.

Guidelines and indications were the same as stipulated under MTP Act, 1971 and modified in 2003.

Inclusion Criteria

- Gestational age up to 63 days.
- Commitment to complete the process, adhering to the protocol.
- Emergency preparedness.
- Willing to undergo for surgical abortion in case of failure or excess bleeding.

Exclusion Criteria

- Confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass.
- Pregnancy with intrauterine device in situ.
- Hb < 10 gm %.
- Coagulopathy or anticoagulant therapy.
- Hypersensitivity to Mifepristone or Misoprostol.
- Systemic disorders of cardiovascular system, renal disease, liver disease, respiratory disease.
- Inherited porphyrias.
- Glaucoma.
- Uncontrolled seizure disorders.
- Vaginal infections.
- Lack of access to emergency services.

Detailed clinical history was recorded, and bimanual pelvis examination was done.

Required Investigations

- Hb
- ABORh
- Urine
 - Albumin
 - Sugar
- Ultrasonography was done in doubtful cases:

1. Women with discrepancy between history and clinical findings.
2. Women having irregular cycle.
3. Women with suspected ectopic pregnancy.

After confirming the gestational age and after obtaining written consent as per Forms C and F1, the following medical regimen was given:

Day1 Tab Mifepristone 200 mg orally
 Day3 Inj. Anti-D 50 microgram in case of Rh-negative women f/b
 Day3 Tab Misoprostol 400 µg vaginally

Schedule was completed even if woman aborted alone by Mifepristone.

At the end of 4 h, if women do not start bleeding per-vaginum, tab Misoprostol 400 µg was reinstilled.

The women were instructed to note the following:

- Time of onset of bleeding.
- Timing of passage of products of conception.
- Duration of bleeding.
- Side effects.

Patients were informed about the warning signs:

- Prolonged and excessive bleeding (>2 pads/hr for >2 h) [1].
- Purulent/Foul smelling vaginal discharge.
- Dizziness with syncopal attack.
- Rise of body temperature to over 101.4 °F for more than 4 h.

She was asked to avoid alcohol, anti-inflammatory medications, and aspirin for this duration.

Women were called for follow-up after 14 days, and clinical and ultrasound evaluations were done for confirmation of completion of abortion. During that visit, all the side effects or complications reported by the subjects were recorded.

Outcome

1. Success was defined as expulsion of products of conception with no need for surgical intervention.
2. Failure was considered in case of suction curettage done for any reasons including
 - Incomplete abortion
 - Ongoing pregnancy
 - Prolonged and excessive bleeding (>2 pads/hr for >2 h)
 - At woman request

Side effects of drugs were noted:

- Abdominal pain

- Nausea
- Vomiting
- Diarrhea
- Fever
- Headache

Results

The age group of women in the present study varied from 16 to 40 years. The maximum number of women (41.04 and 40.30 % in Group-A and Group-B, respectively) belonged to 21–25 years of age, which is the normal range of age for maximum fertility. There were 17 women in Group-A and 9 women in Group-B who belonged to the age group of 16–20 years. The mean age of women was 25.29 years in Group-A and 27 years in Group-B. *P* value was 0.0535, which was not statistically significant, and both groups were comparable (Table 1).

Observations made from Table 2 were that the induction–abortion interval was ≤4 h in majority of women: 81.34 and 70.15 % in Group-A and Group-B, respectively, and it was more than 4 h in 18.66 % in Group-A and 29.85 % in Group-B. The calculated *P* value was 0.2610, which was statistically not significant. The induction–abortion interval was more in Group-B compared with Group-A, because of the increased gestational age and more time being required for expulsion of bigger gestational sac or products of conception (Table 2).

The medical abortion with the given regimen and protocol was observed to be highly successful, and complete abortion was achieved in 98.51 and 97.76 % in Group-A and Group-B, respectively. Failure rates observed were only 1.49 % in Group-A and 2.24 % in Group-B (Table 3).

Two women underwent surgical evacuation in Group-A and three women in Group-B.

Table 1 Distribution of cases according to age group (*n* = 268)

Age group (in years)	Group-A		Group-B	
	No.	%	No.	%
16–20	17	12.69	9	6.72
21–25	55	41.04	54	40.30
26–30	46	34.31	46	34.31
31–35	12	8.96	21	15.67
≥36	4	3.00	4	3.00
Total	134	100.00	134	100.00

Mean (Group-A) = 25.29 ± 4.7 years

Mean (Group-B) = 27.00 ± 4.5 years

P value = 0.0535 which was not statistically significant was comparable

Table 2 Distribution of cases according to induction–abortion interval in two groups

Induction-abortion interval (in hrs)	Group-A		Group-B	
	No.	%	No.	%
≤4	109	81.34	94	70.15
>4	25	18.66	40	29.85
Total	134	100.00	134	100.00

Mean ± SD (Group-A) = 3.5 ± 1.3 h
 Mean ± SD (Group-B) = 3.7 ± 1.5 h
 P value = 0.2610

Table 3 Distribution of cases according to success rates in both groups

Outcome	Group-A		Group-B	
	No.	%	No.	%
Success	132	98.51	131	97.76
Failure	2	1.49	3	2.24
Total	134	100.00	134	100.00

P value = 0.0325

In Group-A, two evacuations were done—one for retained products of conception and one for heavy bleeding.

In Group-B, three evacuations were done—one for heavy bleeding, one for missed abortion, and one for retained products of conception which was diagnosed by ultrasonography on the 14th day.

The side effect reported by the women after medical abortion in our study was that a majority of women experienced abdominal pain (15.67 and 37.31 % in Group-A and Group-B, respectively), which resolved by itself, and no analgesics were required. Nausea was reported by 10.45 % in group-A and 30.60 % in group-B. P value was 0.00006 for abdominal pain and 0.00004 for nausea. The differences between both groups were statistically significant. These differences could be attributed to the fact that as the gestational age increases, abdominal pain also increases due to expulsion of larger gestational sac and increased dose of Misoprostol required (Table 4).

Diarrhea and vomiting were reported by only 0.00, 3.73 % in Group-A and 2.00, 5.22 % in Group-B, respectively, and the differences were not statistically significant in both the groups.

We observed that the overall acceptability of the procedure was very high, and it was found acceptable in 97.76 % women in Group-A and in Group-B it was 91.79 % (Table 5).

The medical abortion was found not acceptable in only 2.24 % women of Group-A and 8.21 % women of Group-B. The P value obtained was 0.02808, which was statistically

Table 4 Distribution of cases according to adverse effects (n = 268)

Adverse effects	Group-A		Group-B	
	No.	%	No.	%
Pain abdomen	21	15.67	50	37.31
Nausea	14	10.45	41	30.60
Diarrhea	0	0.00	2	1.49
Vomiting	5	3.73	7	5.22

Pain abdomen (P value = 0.00006)
 Nausea (P value = 0.00004)
 Diarrhea (P value = 0.15575)
 Vomiting (P value = 0.55470)

Table 5 Distribution of cases according to acceptability of the procedure in both groups

Outcome	Group-A		Group-B	
	No.	%	No.	%
Acceptable	131	97.76	123	91.79
Not acceptable	3	2.24	11	8.21
Total	134	100.00	134	100.00

P value = 0.02808

significant. The reason behind this difference could be the increased gestational age in Group-B, where bleeding duration and the amount increased, which lead to increase in anxiety and discomfort. Hence, the overall satisfaction and acceptability of the method was reduced in Group-B.

Discussion

In a similar study by Creinin et al. [5], the mean ages were 26 years in Group-1 and 25 years in Group-2.

In Ashok et al.’s [6] study, the mean age of women was 26.0 years.

In Agarwal et al.’s [7] study, the maximum number of women were between 26 and 30 years of age, i.e., 53.4 %.

The mean ages were 26.53 years in Group-A and 26.93 years in Group-B in the study conducted by Deshpande et al. [8].

The side effects reported by the women after medical abortion in our study were that a majority of women experienced abdominal pain (15.67 and 37.31 % in Group-A and Group-B, respectively), which resolved by itself, and no analgesics were required; nausea was reported by 10.45 % in group-A and 30.60 % in group-B. P values were 0.00006 for abdominal pain and 0.00004 for nausea. The differences between both groups were statistically significant. These differences could be attributed to the fact that as the gestational age increases, abdominal pain also increases due to

expulsion of larger gestational sac and increased dose of Misoprostol required. Diarrhea and vomiting were reported by only 0.00, 3.73 % in Group-A and 2.00, 5.22 % in Group-B, respectively, and the differences were not statistically significant in both the groups.

In the study conducted by Deshpande et al. [8], abdominal pain was seen in 15 % and 37.50 % of women in Group-A and Group-B respectively; nausea was reported in 10 % in Group-A and 31.11 % in Group-B, and these results were comparable to those of our study.

In Kallner et al.'s [9] study, nausea was noted (86.7 % in group with <50 days of gestation age and 87.5 % in the group with 50–63 days of gestation age). Vomiting was noted (52.2 % in group with <50 days of gestation age and 62.5 % in group with 50–63 days of gestation age).

Conclusions

Termination of an early unwanted pregnancy is a basic concern of a woman; for this purpose, she has been using several traditional methods and remedies since very ancient times. After legalization of medical termination of pregnancy, surgical methods were the only available option.

Previously medical abortion was approved only for cases up to 49 days of gestational age, but now it has recently been approved by WHO and FOGSI for cases up to 63 days or 9 weeks of gestational age.

From our study, we conclude that medical abortion is an effective, safe, and acceptable method for termination of early pregnancy up to 63 days of gestational age. The duration of bleeding and amount of blood loss increased with the increase in the gestational age, but it was not highly significant in both groups; very high complete abortion rates were observed; and the acceptability of the procedure was also very high.

Therefore, we conclude that medical abortion can be safely performed in cases up to 63 days of gestation, but women should be properly counseled about the increased blood loss and duration of bleeding.

Compliance with Ethical Requirements and Conflict of Interest After confirming the gestational age and after obtaining the written consent as per Forms C and F1, medical regimen was given. The author has no conflict of interest.

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