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## Original Research Article

# Efficacy of combination of tablet mifepristone and misoprostol for first trimester pregnancy termination at different gestational age

Poonam Bhojwani, Pragati Meena\*, Gajendra Singh Verma

Department of Obstetrics and Gynecology, NIMS Medical College, Jaipur, Rajasthan, India

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**\*Correspondence:**

Dr. Pragati Meena,

E-mail: [drpragati02@gmail.com](mailto:drpragati02@gmail.com)

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### ABSTRACT

**Background:** Medical method of abortion is a safe, effective and affordable method for first trimester termination. However, nausea, vomiting, diarrhoea, excess bleeding and incomplete abortion are known side effects. The aim of study was to compare the success rate of abortions in both groups, to compare the induction-abortion interval in both groups and to study the side effects of the drugs.

**Methods:** This study was conducted in department of obstetrics and gynecology, NIMS Medical College, Jaipur, India during June 2017-August 2017. Total hundred cases were taken and divided into two groups. Group A was gestational age upto 49 days, Group B was gestational age 50-63 days. Both groups were given tab. mifepristone 200mg. followed by 48 hrs. by 4 tablets of tab misoprostol.

**Results:** The results of the given regimen were highly successful and complete abortion was achieved in 96% and 94% in group A and group B respectively. The difference between two groups was statistically not significant (p value =0.64). Failure rates were seen in only 4% of group A and 6% of group B. Pain abdomen was seen in 16% of group A and 38% of group B patients. The difference between both groups was statistically significant (p value=0.02). Nausea was seen in 10% of group A and 30% of group B patients. The difference between both groups is statistically significant(p value=0.018).

**Conclusions:** First trimester pregnancy can be successfully terminated with combination of mifepristone and misoprostol upto 63 days (9 weeks) of pregnancy.

**Keywords:** Mifepristone, Misoprostol, Termination of pregnancy

### INTRODUCTION

Abortion is willful termination of pregnancy before period of viability. In most cases it is an unwanted pregnancy.<sup>1</sup> Each year throughout world approx. 210 million women become pregnant and around 130 million of them deliver live born infants.

Approx. 46 million pregnancy are voluntarily terminated each year and around 19 million unsafe abortions are performed.<sup>2,3</sup> In India almost 15000-20000 women die each year because of complication of unsafe abortion.<sup>4</sup>

Unsafe abortions are a cause of maternal morbidity, so Gov. of India passed MTP act in 1971 which came in force from April 2, 1972.

WHO recommendations on medical abortion are restricted to early first trimester (upto 63 days since the first day of last menstrual period).<sup>5</sup>

Tab mifepristone (RU486) is antiprogesterone drug and misoprostol is a synthetic prostaglandin analog which was marketed for first time in 1985 for the prevention of NSAIDS induced gastric ulcer.<sup>6</sup>

Both drugs are USFDA approved for medical abortion.

DCGI (drug controller general of India) has approved a combipack of one 200mg. tablet of mifepristone and four 200mcg. of misoprostol for medical method of abortion up to 63 days.<sup>3</sup>

Vacuum aspiration (mechanical or electrical) was the most popular method of doing first trimester abortions till recently when abortifacient agents such as antiprogesterone (Mifepristone) and prostaglandins (Misoprostol) were approved by United States Food and Drug Administration in 2000 for first trimester pregnancy termination

Mifepristone acts in several ways but its main action is to block the action of progesterone, a hormone necessary to sustain pregnancy and misoprostol causes uterine contractions, which expels the foetus and other products of conception.<sup>7</sup>

There are certain advantages and disadvantages of surgical and medical methods of inducing abortion. The main advantages of medical abortions are that surgical and anaesthetic risks are avoided and the procedure is less painful than surgical abortion under local anaesthesia. The disadvantages of medical abortion are that it requires longer period for completion, multiple visits and it is not available after certain period of amenorrhea.<sup>8</sup>

Initially when mifepristone was approved for first trimester abortions, a higher dose of 600mg was recommended. However, similar results have been achieved with a much lower dose of 200mg.<sup>9,10</sup> In this study we have used a lower dose of 200mg mifepristone.

Initially there were concerns about the use of this method in India as the cost of mifepristone was high but now with the lower dose being used and each tablet costing approximately Rs 320/- this method is found to be cost effective. Indeed, medical abortion can be done safely, effectively and acceptably in the outpatient family planning department of urban and rural hospital of India.<sup>11</sup>

The aim of study was to compare the success rate of abortions in both groups, to compare the induction-abortion interval in both groups and to study the side effects of the drugs.

## METHODS

This study was conducted in department of obstetrics and gynecology, NIMS Medical College, Jaipur, India from June 2017-August 2017.

Total 100 cases were enrolled. they were divided in two groups:

- Group A- (50 cases) -gestational age upto 49 days
- Group B- (50 cases) -gestation age upto 63 days

Study was initiated after obtaining Ethics committee permission. Study duration was three month from 1-6-2017 to 31-8-2017.

### Inclusion criteria

- Patient who were compliant with the protocol, who were ready to undergo surgical abortion in case of failure or excess bleeding
- Gestation age upto 63 days
- Patients who have early access to emergency services.

### Exclusion criteria

- HB<10 gm%
- Suspected ectopic, adenexal mass
- Hypersensitivity to mifepristone or misoprostol
- Patient on anticoagulant or having coagulopathy
- Any systemic disorder –liver, renal or cardiovascular disease.

Thorough clinical examination was done, and proper history was also taken. Blood group and HB was done as routine investigation. Sonography was done only in cases suspected to be ectopic pregnancy.

Written consent was taken as per form C.

Patients were given tablet mifepristone 200mg. on first day then after 48 hrs. tablet misoprostol 400ugm. was given vaginally. If no bleeding occurs after 48 hrs., then tablet misoprostol 400mcg was repeated.

Women were called after 14 days and Ultrasound was done for confirmation of abortion. Women were asked to report immediately if they develop any of the following problem-

- Excessive and prolonged bleeding
- Fainting or syncopal attack
- Fever>101OF
- Foul smelling purulent discharge

Side effects of drugs were also asked

- Nausea
- Vomiting, diarrhea
- Pain abdomen
- Fever.

## RESULTS

The age group of women in present study varied from 18 to 40 years. The maximum number of women (40% in Group A and 38% in Group B belonged to 21-25 years of

age. There were 34% in Group A and 36% in Group B belonging to 26-30 years of age. P value was 0.157 which was statistically not significant. In present study p value <0.05 was statistically significant.

**Table 1: Distribution of cases according to age group (n=100).**

Age group (in years)	Group-A		Group-B	
	No.	%	No.	%
18-20	6	12	3	6
21-25	20	40	19	38
26-30	17	34	18	36
31-35	4	8	10	20
>36	3	6	0	0
Total	50		50	

P value=0.157

**Table 2: Distribution of cases according to duration of amenorrhea.**

Group A		Group B	
No. of patients	Duration of amenorrhea (in days)	No. of patients	Duration of amenorrhea (in days)
30	<40 days	18	50-55 days
15	41-45 days	28	56-59 days
5	46-49 days	4	60-63 days

In present study in Group A 30 patients had amenorrhea of less than 40 days, 15 patients had amenorrhea between 41-45 days while only 5 patients had amenorrhea between 46-49 days.

In Group B 28 patients had amenorrhea between 56-59 days, 18 patients had amenorrhea 50-55 days, while only 4 patients had amenorrhea 60-63 days.

**Table 3: Distribution of cases according to days of bleeding.**

Days of bleeding	No. of patients in Group A	No. of patients in Group B
<5 days	2	5
5-10 days	36	12
11-13 days	10	31
> 14 days	2	2

In Group A 36 patients had bleeding per vagina for only 5-10 days, 10 patients had bleeding for 11-13 days, 2 patients had bleeding for <5 days and 2 patients had bleeding for >14 days.

In Group B 31 patients had bleeding for 11-13 days, 12 patients had bleeding for 5-10 days, 5 patients had bleeding for <5 days while only 2 patients had bleeding for >14 days.

As period of amenorrhea is more in Group B patients so maximum patients had prolonged bleeding for 11-13 days while in Group A patient's period of amenorrhea is less so maximum patients had bleeding only for 5-10 days. This can be explained by the fact that bigger product of conception need more time for expulsion.

In present study 2 patient in Group A and 2 patients in Group B had bleeding for more than 14 days although the amount of bleeding was minimal in both groups and sonography done on day 14 showed retained product of conception for which suction and evacuation was done under general anaesthesia. Only 1 patient of group B had severe bleeding for which suction evacuation was done immediately and blood was transfused.

**Table 4: Distribution of cases according to induction abortion interval.**

Induction abortion interval (in hours)	Group A		Group B	
	No.	%	No.	%
<4 hrs.	40	80	35	70
>4hrs.	10	20	15	30
Total	50	100	50	100

P value=0.24

In majority of women the induction abortion interval was <4hrs: 80% in Group A and 70% in Group B respectively. Induction abortion interval was >4 hrs. in 20% of Group A and 30% of group B. The calculated P value was 0.24 which was statistically not significant. Time taken for abortion was more in Group B then Group A as can be explained by the fact that period of gestation was more in group B patients, so they took more time for abortion.

**Table 5: Distribution of cases according to side effects.**

Side effects	Group A		Group B	
	No.	%	No.	%
Pain abdomen	8	16	19	38
Nausea	5	10	15	30
Diarrhoea	0	0	1	2
Vomiting	2	4	3	6

Pain abdomen (p value=0.02), Nausea (p value=0.018), Diarrhoea (p value=0.31), Vomiting (p value=0.65)

Major side effect reported by women in our study was pain abdomen 16% in Group A and 38% in Group B. Nausea was second major adverse effect of medical abortion, found in 10% and 30% in Group A and Group B respectively. P value was for pain abdomen was (0.02) and P value for nausea was 0.018. The difference between both groups were statistically significant. In group B the gestation age is more so there is more pain abdomen for expulsion of products of conception.

Diarrhoea and vomiting was reported in 0% and 2% in Group A and 2% and 6% of Group B respectively. The difference was statistically not significant in both groups.

**Table 6: Distribution of case according to success rate in both groups.**

Outcome	Group A		Group B	
	No.	%	No.	%
Success	48	96	47	94
Failure	2	4	3	6
Total	50		50	

The Mifepristone and Misoprostol combination regimen given for first trimester abortion was found to be highly successful in both groups. 96% patients in Group A aborted easily while 94% in group B patient aborted. In group A 2 patient had incomplete abortion for which evacuation was done while in group B failure was seen in 3 patients. One patient had heavy bleeding for which evacuation had been done and two patients had retained products of conception which was diagnosed in USG done after 14 days.

P value is more than 0.05 so the difference between both groups is statistically not significant.

## DISCUSSION

The patients enrolled in present study belonged to 18-40 years of age. Maximum patients 40% in Group A and 38% in Group B were of 21-25 years of age.

The mean age was 26. 53 years in Group A and 26. 93 years in Group B in study conducted by Deshpande et al.<sup>12</sup>

In Ashok et al study the mean age of women was 26 years.<sup>13</sup>

In present study maximum patients had amenorrhea <40 days in group A and maximum patients had amenorrhea 56-59 days in group B.

In group A maximum patients had bleeding for 5-10 days while in group B maximum patient had bleeding for 11-13 days.

80% of patients in group A aborted quickly within 4 hours of taking of tablet misoprostol while in group B 70% patients aborted within 4 hours of taking of tablet misoprostol.

In present study the side effects reported by the women were that majority of women had pain abdomen 16% in Group A and 38% in Group B, but the pain resolved on it's own, no analgesic was required. Nausea was reported in 10% of Group A and 30% of Group B patients. P values were 0.02 for abdominal pain and 0.018 for nausea. The differences between both groups were statistically significant. As in Group B the gestation age is more so bigger size gestation sac when expelled causes more pain abdomen and nausea.

Diarrhea and vomiting were reported in 0% and 4% of Group A and 2% and 6% in Group B respectively. The differences between both groups were statistically not significant.

In the study conducted by Deshpande et al abdominal pain was seen in 15% and 37. 50% in women of Group A and Group B respectively.<sup>12</sup>

In a study conducted by Kallner et al nausea was noted in 86. 7% in group with <50 days of gestation age and 87. 5% in the group with 50-63 days of gestation age.<sup>14</sup> Vomiting was reported in 52. 2% in group with <50 days of gestation and 62. 5% in group with 50-63 days of gestation age.

The combination of mifepristone and misoprostol was found to be successful in inducing abortion in 96% of Group A and 94% in Group B patients. This shows that mifepristone and misoprostol combination can be used for medical termination upto 63 days of gestation.

## CONCLUSION

From present study we conclude that medical abortion is safe, affordable, effective and easily acceptable method for first trimester termination.

Medical abortion of pregnancy has recently been approved by WHO and FOGSI upt 63 days (9 weeks). Previously it was approved only upto 49 days (7 weeks).

If proper counselling of patients is done, then medical abortion can be successfully performed thus we can avoid all the complications of surgical abortion.

However, we should explain the patient the risk of increased blood loss as the gestation age increase and also the chance of retained products of conception in advance gestation age.

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