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**Original research article**

# Comparative study of regimen mifepristone and misoprostol with misoprostol alone at first trimester termination of pregnancy

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**Abstract**

A broad array of drugs have been studied for first trimester medical abortion. Studies evaluating different regimens show varying results related to safety, efficacy and other outcomes. Thus, the objectives of this study was to (1) compare the success rates of abortion at First Trimester of Pregnancy, (2) study the side effects of the drugs, and (3) To study the acceptability in the both groups of abortion ≤ 84 days of gestation.

**Methods:** This study was conducted on medical abortion with the given regimen of Mifepristone 200 mg orally and Misoprostol 800 mcg vaginally/orally/sublingually and is compared with only Misoprostol 800 mcg. This study was conducted in the Department of Obstetrics and Gynecology, Katuri Medical College and hospital during the course of years between 2020 November to –2022 October. In total 300 cases were taken for the study and divided into two groups.

**Results:** The combined regimen of Mifepristone and Misoprostol (group A) shown very much efficient as compared with only Misoprostol (group B) with low incidence of side effects (10.32%) and high success rate (97.34%) and acceptability (97.34%) and achieved abortion with in < 4hr induction - abortion (83.34%). The combined regimen comparatively showed least failure rate (2.66%) than group B (33.34%).

**Conclusion:** As per present study that medical methods of abortion are effective, safe and reliable for termination of pregnancy of ≤84 days of gestation. The combined regimen of mifepristone and misoprostol was more effective than the sole administration of Misoprostol and proved its reliability for termination of pregnancy ≤84 days of gestation. More robust studies evaluating both the different combination and misoprostol alone regimens are needed to strengthen existing evidence as well as assess patient perspectives towards a particular regimen.

**Keywords:** First trimester, medical termination of pregnancy, mifepristone, misoprostol

## Introduction

Medical methods emerged as an alternative to surgical abortion dates back since from Egyptian Eber Papyrus in 1550 BC [1, 2] 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 million risk their lives by approaching quacks or untrained abortion providers, and almost from 15,000 to 20,000 women die every year be- cause 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].

With the discovery of prostaglandins in the early 1970s popularized the procedures of MTP [7-9]. The use of prostaglandins has evolved in the last two de- cades and various drugs have been used for first trimester medical abortion. Several studies have explored utilization of mifepristone, methotrexate and various prostaglandins with different doses, routes and intervals of administration [10]. A Cochrane review compared different medical methods for first trimester abortion in 2020 and since that time, there has been growing evidence assessing the effectiveness and safety of medical methods using two specific regimens: the combination regimen (mifepristone and misoprostol) and misoprostol alone [11].

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Nevertheless, individual studies assessing medical management of abortion at ≤84 days have not confirmed superiority of one of these regimens. Not only studies have compared combination of mifepristone and misoprostol (combination mifepristone misoprostol) with their alone use [12-14], other studies have looked at different routes and doses of misoprostol in combined regimens [15,16], besides comparing different intervals between mifepristone and misoprostol doses [17-19]. Similarly, different misoprostol only regimens have been evaluated [20].

The 2012 World Health Organization (WHO) safe abortion guideline had varying regimens for induced abortion at < 12 weeks. With the emergence of new evidence, this systematic review was done as part of the evidence synthesis for the WHO guidance on medical abortion. Options for medical abortion vary globally, and evidence-based guidance is needed to inform clinical care in selecting a regimen. The objectives of this review were to compare the effectiveness, safety and acceptability of different regimens of medical abortion containing mifepristone and/or misoprostol with alone misoprostol at ≤84 days of gestational age.

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.

**Mifepristone**

Mifepristone, also known as RU-486, is a medication typically used to bring about a medical abortion during pregnancy and manage early miscarriage. Common side effects include abdominal pain, feeling tired, and vaginal bleeding. Serious side effects may include heavy vaginal bleeding, bacterial infection, and birth defects if the pregnancy does not end. If used, appropriate follow up care needs to be available. Mifepristone is an anti progestogen. It works by blocking the effects of progesterone, making both the cervix and uterine vessels dilate and causing uterine contraction [21, 22].

**Methods**

This study was conducted in the Department of Obstetrics and Gynecology, Katuri medical college and Hospital, during 2020 to 2022.

**Sample Size**

In total, 300 cases were enrolled and divided into Group-A (150 cases) given regimen of Mifepristone 200 mg orally and Misoprostol 800 mcg vaginally/oral/sublingual. Group-B (150 cases) with only Misoprostol 800 mcg. Guidelines and indications were the same as stipulated under MTP Act, 1971 and modified in 2003.

**Inclusion Criteria**

- Gestational age up to 84 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.

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- Lack of access to emergency services.

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

**Required Investigations**
- CBP
- ABO Rh Typing
- 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:

**Group-A**
**Day 1:** Tab Mifepristone 200 mg orally
**Day 2:** Inj. Anti-D 50 microgram in case of Rh-negative women f/b
**Day 3:** Tab Misoprostol 800 mcg vaginally or orally or sublingually

**Group- B**
**Day 1:** Tab Misoprostol 800 mcg orally or vaginally or sublingually maximum of 3 doses at every 6 hours interval
**Day 2:** Inj. Anti-D 50 microgram in case of Rh-negative women.

Schedule was completed even if woman not aborted alone by Misoprostol at the end of 4 h to 6 hrs, if women do not start bleeding pervaginum, tab Misoprostol was reinstillated. 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.
- Purulent/Foul smelling vaginal discharge.
- Dizziness with syncopal attack.
- Rise of body temperature to over 101.4 °F for more than 4 hr

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
- At woman request

**Side effects of drugs were noted**
- Abdominal pain
- Nausea
- Vomiting
- Diarrhea
- Fever

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- Headache

**Results**

The age group of women in the present study varied from 16 to 40 years. Selected subjects in Group-A maximally 41.04% and 40.30% in Group-B were in the age range of 21–25 years of age, which is the normal range of age for maximum fertility. There were 27 women in Group-A and 25 women in Group-B who belonged to the age group of 16–20 years. The mean age of women was 25.29±4.7 years in Group-A and 27.00 ± 4.4 years in Group-B. *P* value was 0.0335, 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: 83.34% (125 women) in Group-A and 26.66% (40 women) in Group-B and it was more than 4 h in 16.66% (25 women) in Group-A and 73.34% (110 women) in Group-B. The calculated *P* value was 0.001, which was statistically significant. The induction– abortion interval was more in Group-B compared with Group-A. 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 Group-A with 97.34% (148 women) and poor success rate was observed in Group-B with 66.66% (100 women) as compared to Group-A. Failure rates observed were only 2.66% (4 women) in Group-A and 33.34% (50 women) in Group-B and with the P value of 0.0012 (Table 3)

**Table 1:** Distribution of cases according to age group (*n* = 300)

| Age group (in years) | Group-A | | Group-B | |
|---|---|---|---|---|
| | No. | % | | No. |
| 16–20 | 27 | 18 | 25 | 16.70 |
| 21–25 | 55 | 41.04 | 54 | 40.30 |
| 26–30 | 46 | 34.31 | 46 | 34.31 |
| 31–35 | 18 | 12 | 21 | 15.67 |
| 36-40 | 4 | 3.00 | 4 | 3.00 |
| Total | 150 | 100.00 | 150 | 100.00 |

Mean (Group-A) = 25.29 ± 4.7 years
Mean (Group-B) = 27.00 ± 4.4 years
P value = 0.0335 which was not statistically significant

**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 | 125 | 83.34 | 40 | 26.66 |
| > 4 | 25 | 16.66 | 110 | 73.34 |
| Total | 150 | 100 | 150 | 100 |

Mean ± SD (Group-A) = 2.5 ± 1.3 h
Mean ± SD (Group-B) = 3.9 ± 1.5 h
P value = 0.0015 statistically significant

The side effect reported in group-A women after medical abortion in our study was that a 5% (8 cases) of women experienced abdominal pain, which resolved by itself, and no analgesics were required followed by Nausea 4% (6 cases) and 0.66% of Diarrhea and Vomiting (1 case). The side effect reported in group–B women after medical abortion in our study was that a 46.66% (70 cases) experienced abdominal pain followed by Nausea 13.33% (20 cases) and 8% (20 cases) shown Diarrhea and 7.33% (11 cases) shown Vomiting. The overall percentage of side effects was 10.32% (16 cases) in group A and 75.33% (113 cases) in group B. The *P* value was 0.001. The differences between both groups were statistically significant proving the efficiency of the combined regimen of Mifepristone and Misoprostol. 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). We observed that the overall acceptability of the procedure was very high, and it was found acceptable in 98.66% (148) women in Group-A and in Group-B it was 80% (120 women) (Table 5). The medical abortion was found not acceptable in only 1.34% (2) women of Group-A and 20% (30) women of Group-B. The *P* value obtained was 0.0208, which was statistically significant. The reason behind this high acceptance could be the increased gestational age and reduced side effects in Group-A, Hence, the overall satisfaction and acceptability of the method was reduced in Group-B where bleeding duration and the amount increased, which lead to increase in anxiety and discomfort.

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

| Out come | Group A | | Group B | |
|---|---|---|---|---|
| | No | % | No | % |
| Success | 146 | 97.34 | 100 | 66.66 |

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| | | | | |
|---|---|---|---|---|
| Failure | 4 | 2.66 | 50 | 33.34 |
| Total | 150 | 100 | 150 | 100 |

P value = 0.00125

**Table 4:** Distribution of cases according to Adverse effects in both groups

| Adverse effect | Group A | | Group B | |
|---|---|---|---|---|
| | No | % | No | % |
| Abdominal pain | 8 | 5 | 70 | 46.66 |
| Nausea | 6 | 4 | 20 | 13.33 |
| Diarrhoea | 1 | 0.66 | 12 | 8 |
| Vomiting | 1 | 1.11 | 11 | 7.33 |
| Total | 16 | 10.77 | 113 | 75.33 |

Pain abdomen (P value = 0.0016)
Nausea (P value = 0.0014)
Diarrhea (P value = 0.0015)
Vomiting (P value = 0.0010)

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

| Out come | Group A | | Group B | |
|---|---|---|---|---|
| | No | % | No | % |
| Acceptable | 148 | 98.66 | 147 | 98 |
| Not acceptable | 2 | 1.34 | 3 | 2 |
| Total | 150 | 100 | 150 | 100 |

P value = 0.02808

**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 [21] 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.* [23] and in our study the mean ages was 25.29 years in Group-A and 27 years. The side effect reported in group-A women after medical abortion in our study was that a 5% (8 cases) of women experienced abdominal pain, which resolved by itself, and no analgesics were required followed by Nausea 4% (6 cases) and 0.66% of Diarrhea and Vomiting (1 case). The side effect reported in group–B women after medical abortion in our study was that a 46.66% (70 cases) experienced abdominal pain followed by Nausea 13.33% (20 cases) and 8% (20 cases) shown Diarrhea and 7.33% (11 cases) shown Vomiting (*P* value was 0.00006). The differences between both groups were statistically significant proving the efficiency of combined regimen of Mifepristone and Misoprostol. 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

In the study conducted by Deshpande *et al.* [23], 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 [24] study, nausea was noted (86.7% in group A and 87.5% in the group B with 50–63 days of gestation age). Vomiting was noted (52.2% in group A and 62.5% in group B with 50–63 days of gestation age). Therefore, we conclude that medical abortion can be safely performed in cases up to 75 days of gestation, but women should be properly counseled about the increased blood loss and duration of bleeding. In the study conducted by Deshpande *et al.* [23]. The proportion of women with induction abortion interval < 4 hours in the two groups as 83.33% and 72.25% respectively. This difference is statistically not significant (Chi-square=3.47, $p>0.05$). but in our study that the induction–abortion interval was reported as <4 h in majority of women 83.34% (125 women) in Group-A and 26.66% (40 women) in Group-B and it was > 4 h in 16.66% (25 women) in Group-A and 73.34% (110 women) in Group-B. The calculated *P* value was 0.031, which was statistically significant.

in the study conducted by Deshpande *et al.* [23]. The success rate at the end of 14 days in group A and B was 99.16% and 98.75% respectively and this difference is statistically not significant. (Chi-square = 0.19, $p>0.05$). In our study the medical abortion with the given regimen and protocol was observed to be highly successful and complete abortion was achieved in Group-A with 97.34% (148 women) and poor success rate was observed in Group-B with 66.66% (100 women) as compared to Group-A. The calculated *P* value was 0.031, which was statistically significant. Failure rates observed were only 2.66% (4 women) in Group-A and 33.34% (50 women) in Group-B (Table 3). 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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**Conclusion**

As per present study that medical methods of abortion are effective, safe and reliable for termination of pregnancy of ≤84 days of gestation. The combined regimen of mifepristone and misoprostol was more effective than the sole administration of the misoprostol and proved its reliability for termination of pregnancy of ≤84 days of gestation. More robust studies evaluating both the different combination and misoprostol alone regimens are needed to strengthen existing evidence as well as assess patient perspectives towards a particular regimen.

**References**


1. Kurtkoti K. FOGSI focuses on medical abortion; c2010, p. 5, 27, 31.
2. Malacolm P, Campbell M. History of contraception. Gynaecol Obstet. 2008;6(8):9-21. http://big.berkeley.edu.
3. Unsafe Abortion: Global and regional estimates of the incidence of unsafe abortion and associated mortality in 2003. Fifth edition, Word Health Organization Cataloguing in Publication Data. p. 1, 4-6.
4. Megh M. FOGSI. Comprehensive abortion care and post abortion contraception, FOGSI focus; c2012. p. 15.
5. Creinin MD, Schwartz JL, Pymar HC, *et al*. Efficacy of Mifepristone followed on the same day by Misoprostol for early termination of pregnancy: report of a randomised trial. BJOG. 2001;108:469-73.
6. Ashok PW, Penney GC, Flett GMM, *et al*. An effective regimen for early medical abortion: a report of 2000 consecutive cases. Hum Reprod. 1998;13(10):2962-5.
7. Karim SMM. Once-a-month vaginal administration of prostaglandins E2 and F2α for fertility control. Contraception. 1971;3(3):173-83.
8. Karim SMM. Use of prostaglandin $E_2$ in the management of missed abortion, missed labour, and hydatidiform mole. Br Med J. 1970;3(716):196-7.
9. Karim S, Rao B, Ratnam S, Prasad R, Wong Y, Ilancheran A. Termination of early pregnancy (menstrual induction) with 16-phenoxy-ω-tetranor PGE2 methylsulfonylamide. Contraception. 1977;16(4):377-81.
10. Kahn JG, Becker BJ, Maclsaa L, Amory JK, Neuhaus J, Olkin I, *et al*. The efficacy of medical abortion: a meta-analysis. Contraception. 2000;61(1):29-40.
11. Kulier R, Kapp N, Gülmezoglu AM, Hofmeyr GJ, Cheng L, Campana A. Medical methods for first trimester abortion. Cochrane Database of Systematic Reviews. 2011, Issue 11. Art. No.: CD002855. DOI: https://doi.org/10.1002/14651858.CD002855.pub4.
12. Blum J, Raghavan S, Dabash R, Ngoc N, Chelli H, Hajri S, *et al*. A Comparison of misoprostol-only and combined mifepristone-misoprostol regimens for home-based early medical abortion in Tunisia and Vietnam. Int J Gynaecol Obstet. 2012;118(2):166-71.
13. Dahiya K, Ahuja K, Dhingra A, Duhan N, Nanda S. Efficacy and safety of mifepristone and buccal misoprostol versus buccal misoprostol alone for medical abortion. Arch Gynecol Obstet. 2012;285(4):1055-8.
14. Ngoc NT, Blum J, Raghavan S, Nga NT, Dabash R, Diop A, *et al*. Comparing two early medical abortion regimens: mifepristone+misoprostol vs. misoprostol alone. Contraception. 2011;83(5):410-7.
15. Chong E, Tsereteli T, Nguyen NN, Winikoff B. A randomized controlled trial of different buccal misoprostol doses in mifepristone medical abortion. Contraception. 2012;86(3):251-6.
16. Von Hertzen H, Huong NT, Piaggio G, Bayalag M, Cabezas E, Fang AH, *et al*. Misoprostol dose and route after mifepristone for early medical abortion: a randomised controlled noninferiority trial. BJOG. 2010;117(10):1186-96.
17. Guest J, Dog PFW, Thomson MAR, Kosseim ML. Randomized controlled trial of the efficacy of same-day administration of mifepristone and misoprostol for termination of pregnancy with the standard 36 to 48 hour protocol. BJOG Int J Obstet Gynecol. 2007;114:207-15.
18. Creinin MD, Schreiber CA, Bednarek P, Lintu H, Wagner MS, Meyn LA. Mifepristone and misoprostol administered simultaneously versus 24 hours apart for abortion: a randomized controlled trial. Obstet Gynecol. 2007;109(4):885-94.
19. Verma ML, Singh U, Singh N, Shankhwar P, Srivastava D. Efficacy of misoprostol administration 24 hours after mifepristone for termination of early pregnancy. Indian J Med Sci. 2011;65(12):511-7.
20. Blanchard K, Shochet T, Coyaji K, Thi Nhu Ngoc N, Winikoff B. Misoprostol alone for early abortion: an evaluation of seven potential regimens. Contraception. 2005;72(2):91-7.
21. "Mifepristone". The American Society of Health-System Pharmacists. Archived from the original on 22 December 2015. Retrieved 19 December 2015.
22. "Mifepristone Use During Pregnancy". Drugs.com. Archived from the original on 14 March 2018. Retrieved 13 March 2018.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 02, 2023

23. Deshpande S, Yelikar K, Deshmukh A, *et al*. Comparative study of medical abortion by Mifepristone with vaginal Misoprostol in women < 49 days versus 50–63 days of amenorrhoea. J Obstet Gynecol. 2010;60(5):403-7.
24. Kopp Kallner H, Fiala C, Stephansson O, *et al*. Home self- administration of vaginal Misoprostol for medical abortion at 50-63 days compared with gestation of below 50 days. Hum Reprod. 2010;25(5):1153-7.