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**Original Research Article**

# Prospective comparative study of misoprostol alone versus mifepristone plus misoprostol for second-trimester pregnancy termination

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## ABSTRACT

**Background:** Second-trimester medical termination of pregnancy (MTP) is legally permitted in India up to 24 weeks under the MTP Act. Misoprostol is widely used for this purpose, but its efficacy may be enhanced by pre-treatment with mifepristone. This study aimed to compare the efficacy and safety of misoprostol alone versus mifepristone followed by misoprostol for second-trimester pregnancy termination.
**Methods:** A prospective, randomized comparative study was conducted at SKNMC&GH, Pune, involving 61 women between 13-24 weeks gestation. Group I (n=31) received oral mifepristone followed by vaginal misoprostol; Group II (n=30) received misoprostol alone. Primary outcome was induction-to-abortion interval; secondary outcomes included misoprostol dose requirement, need for surgical intervention, and complications.
**Results:** Group I showed a significantly shorter induction-to-abortion interval (7.8±2.3 hrs vs. 11.6±3.1 hrs; p<0.001), required fewer misoprostol doses (3.1±0.9 vs. 4.8±1.2; p<0.001), and had lower curettage rates (6.5% vs. 23.3%; p=0.04). Complete abortion rates were high in both groups (93.5% vs. 86.7%; p=0.37). Stratified analysis confirmed consistent benefits across parity groups and gestational age ranges.
**Conclusions:** Mifepristone pre-treatment significantly improves procedural efficiency and reduces intervention burden in second-trimester medical abortion. The combined regimen is recommended for safer and more predictable outcomes under the MTP framework.

**Keywords:** Mifepristone, Misoprostol, MTP Act, Second-trimester abortion

## INTRODUCTION

Medical termination of pregnancy (MTP) in the second trimester remains a critical component of reproductive healthcare, particularly in cases involving fetal anomalies, maternal health risks, or inevitable abortion. In India, the Medical Termination of Pregnancy Act of 1971 permits legal termination up to 24 weeks of gestation, thereby encompassing the second trimester window for therapeutic intervention.[1] While surgical methods such as dilation and evacuation are effective, medical approaches have gained prominence due to their non-invasive nature and broader applicability in resource-limited settings.[2]

Misoprostol, a synthetic prostaglandin E1 analogue, is widely used for second-trimester termination owing to its uterotonic properties and accessibility.[3] However, its use alone is often associated with prolonged induction-to-abortion intervals, increased dosage requirements, and higher rates of incomplete abortion.[4] To enhance efficacy, mifepristone a progesterone receptor antagonist is frequently administered 48 hours prior to misoprostol, facilitating placental detachment and uterine sensitization.[5]

Several randomized trials and meta-analyses have demonstrated that the combination of mifepristone

followed by misoprostol significantly reduces induction time, improves complete abortion rates, and lowers the need for surgical evacuation compared to misoprostol alone.[6-8] Despite these findings, comparative data from Indian tertiary care settings remain limited, particularly in the context of protocol-driven second-trimester termination under the MTP Act.

This study aims to evaluate and compare the efficacy, safety, and procedural outcomes of two regimens misoprostol alone versus mifepristone followed by misoprostol for second-trimester pregnancy termination. By analyzing induction-abortion intervals, dose requirements, success rates, and complication profiles, the study seeks to identify the optimal medical protocol for safe and effective termination between 13 and 24 weeks of gestation.

This study aims to compare the efficacy and safety of tablet mifepristone 48 hour before vaginal tablet misoprostol in group-I with vaginal tablet misoprostol alone in group-II as a method of second-trimester pregnancy termination. Also, to compare abortifacient efficacy of mifepristone + misoprostol vs. misoprostol alone in second-trimester (13–24 weeks) termination. To evaluate induction-abortion intervals and outcomes to determine the optimal method by comparing the various parameters.

## METHODS

### *Study design and setting*

This was a prospective, randomized, comparative study conducted at the Department of Obstetrics and Gynaecology, Smt. Kashibai Navale Medical College & General Hospital (SKNMC&GH), Pune, Maharashtra, India. The study was carried out between January 2023 and June 2024 and adhered to the provisions of the Medical Termination of Pregnancy (MTP) Act, 1971, which permits termination up to 24 weeks of gestation.[1]

### *Study population*

A total of 61 women aged 18-40 years, presenting for second-trimester pregnancy termination (13-24 weeks gestation), were enrolled after obtaining written informed consent. Participants were selected based on clinical indications including fetal demise, congenital malformations incompatible with life, or inevitable abortion, as defined by the MTP Act.

### *Inclusion criteria*

Pregnant women with gestational age between 13 and 24 weeks with closed cervical os with no active vaginal bleeding, having Singleton pregnancy with fetal demise or structural anomaly and those willing to provide informed consent were enrolled

### *Exclusion criteria*

Cases with hypersensitivity to mifepristone or misoprostol, having active infection, contraindicated to medical abortion, pregnancy with previous scar, Pregnancy with placenta accreta spectrum or unwilling to provide informed consent were excluded.

### *Randomization and intervention*

A computer-generated sequence was used to randomly divide the participants into two groups:

Group I (n=31): Received 200 mg oral mifepristone followed 48 hours later by 400 mcg vaginal misoprostol followed by misoprostol 200 mcg every 4 hrs until delivery.

Group II (n=30): Only misoprostol 400 mcg vaginally followed by 200mcg every 4 hours until delivery.

All patients were monitored in an inpatient setting with continuous vital sign surveillance and ultrasound confirmation of abortion completion.

### *Outcome measures*

Primary and secondary outcomes were recorded as follows:

*Primary outcome*

Induction-to-abortion interval (time from first dose to fetal expulsion).

*Secondary outcomes*

Total number of misoprostol doses required, rate of complete abortion without any surgical intervention, need for additional procedures (e.g., curettage), incidence of complications (e.g., hemorrhage, infection).

### *Data collection and statistical analysis*

Clinical data were recorded using standardized case report forms. Independent t-tests were used to compare continuous variables, which were reported as mean ± standard deviation. When suitable, Fisher's exact test or Chi-square were used to analyse categorical data. A p-value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

The baseline characteristics between the two groups were statistically comparable. Mean age and gestational age did not differ significantly (p=0.62 and p=0.48, respectively), indicating demographic homogeneity. The distribution of

MTP indications fetal anomaly versus inevitable abortion was also similar across groups (p=0.71), ensuring that outcome differences could be attributed to the intervention rather than baseline disparities (Table 1).

**Table 1: Baseline characteristics of study participants (n=61).**

| Parameter | Group I (n=31) (%) | Group II (n=30) (%) | P value |
|---|---|---|---|
| **Mean age (years)** | 27.8±4.2 | 28.3±4.6 | 0.62 |
| **Mean gestational age (weeks)** | 17.2±1.9 | 17.5±2.1 | 0.48 |
| **Indication: fetal anomaly** | 19 (61.3) | 17 (56.7) | 0.71 |
| **Indication: fetal anomaly** | 12 (38.7) | 13 (43.3) | 0.71 |
| **Cervical status: closed os** | 31 (100) | 30 (100) | - |

**Table 2: Induction-to-abortion interval and misoprostol dosing.**

| Parameter | Group I (n=31) (%) | Group II (n=30) (%) | P value |
|---|---|---|---|
| **Mean induction-abortion interval (hours)** | 7.8±2.3 | 11.6±3.1 | <0.001 |
| **Median interval (hours)** | 7.4 | 11.2 | - |
| **Mean misoprostol doses required** | 3.1±0.9 | 4.8±1.2 | <0.001 |

Group I (mifepristone + misoprostol) demonstrated a significantly shorter induction-to-abortion interval compared to Group II (misoprostol alone), with a mean difference of 3.8 hours (p<0.001). Additionally, Group I required fewer misoprostol doses (mean 3.1 vs. 4.8; p<0.001), suggesting enhanced uterotonic synergy with pre-treatment. The need for surgical curettage was significantly lower in Group I (6.5% vs. 23.3%; p=0.04), reinforcing the clinical efficiency of the combined regimen (Table 2).

Both groups achieved high rates of complete abortion, with Group I showing a slightly higher success rate (93.5%) compared to Group II (86.7%), although the difference was not statistically significant (p=0.37). Complication rates were lower in Group I (6.5% vs. 16.7%), but this difference also did not reach statistical significance (p=0.22). These findings suggest that while both regimens are effective, the combined protocol may offer a marginal safety advantage (Table 3).

**Table 3: Abortion outcome and success rate.**

| Outcome parameter | Group I (n=31) (%) | Group II (n=30) (%) | P value |
|---|---|---|---|
| **Complete abortion** | 29 (93.5) | 26 (86.7) | 0.37 |
| **Success rate** | 29/31 (93.5) | 26/30 (86.7) | - |
| **Complications observed** | 2 (6.5) | 4 (13) | 0.22 |

**Table 4: Summary statistics of key outcomes.**

| Metric | Group I (n=31) (%) | Group II (n=30) (%) |
|---|---|---|
| **Mean induction-abortion time** | 7.8 hrs | 11.6 hrs |
| **Mean misoprostol dose count** | 3.1 | 4.8 |
| **Curettage required (%)** | 6.5 | 23.3 |
| **Success rate (%)** | 93.5 | 86.7 |

The summary statistics reinforce the superiority of the mifepristone-augmented protocol in terms of procedural efficiency and reduced intervention burden. The shorter induction-abortion interval and lower misoprostol requirement in Group I suggest a more predictable and resource-efficient termination process. The reduced need for curettage further supports its clinical utility in second-trimester MTP settings (Table 4).

Nulliparous women (parity 0) at 13-14 weeks gestation had the longest induction-to-abortion intervals in both groups. Those in Group I (mifepristone + misoprostol) aborted in 9.2±2.4 hours, whereas Group II (misoprostol alone) required 13.1±2.9 hours, showing a statistically significant reduction of nearly 4 hours (p=0.003). In parity 1 women at 15-16 weeks, the induction interval was 8.4±2.1 hours in Group I compared to 12.0±2.7 hours in Group II (p=0.005), indicating that mifepristone pre-treatment substantially improves procedural efficiency even in early mid-trimester gestations. Among parity 2 women at 17-18 weeks, Group I achieved abortion in 7.5±2.0 hours, while Group II required 10.8±2.5 hours

(p=0.004), reinforcing the time-saving benefit of the combined regimen as gestation advances. In multiparous women (≥3 parity) at 19-20 weeks, Group I completed abortion in 6.8±1.9 hours, compared to 10.5±2.3 hours in Group II (p=0.002), suggesting that mifepristone enhances uterine responsiveness even in physiologically favorable conditions (Table 5).

**Table 5: Induction-to-abortion interval.**

| Parity group | Gestational age range (weeks) | Group I (n=31) | | Group II (n=30) | | P value |
|---|---|---|---|---|---|---|
| | | Number of cases | Mean induction-to-abortion interval (hrs) | Number of cases | Mean induction-to-abortion interval (hrs) | |
| **0** | 13-14 | 7 | 9.2±2.4 | 7 | 13.1±2.9 | 0.003 |
| **1** | 15-16 | 8 | 8.4±2.1 | 8 | 12.0±2.7 | 0.005 |
| **2** | 17-18 | 9 | 7.5±2.0 | 8 | 10.8±2.5 | 0.004 |
| **≥3** | 19-20 | 7 | 6.8±1.9 | 7 | 10.5±2.3 | 0.002 |

## DISCUSSION

This prospective comparative study evaluated the efficacy and safety of mifepristone followed by misoprostol versus misoprostol alone for second-trimester pregnancy termination. The findings demonstrate that pre-treatment with mifepristone significantly reduces the induction-to-abortion interval, lowers the total misoprostol dose requirement, and decreases the need for surgical intervention.

The mean induction-abortion interval in Group I (7.8±2.3 hours) was significantly shorter than in Group II (11.6±3.1 hours), consistent with prior studies. Arora et al reported a mean interval of 7.2 hours in the mifepristone-misoprostol group compared to 12.1 hours in the misoprostol-only group, reinforcing the time-efficiency of the combined regimen.[9] Similarly, Mukhopadhyay et al observed a reduction in induction time from 11.4 to 6.8 hours with mifepristone priming.[10]

The mean number of misoprostol doses required was also significantly lower in Group I (3.1±0.9) compared to Group II (4.8±1.2), aligning with findings from Tang and Ho, who reported enhanced uterine responsiveness and reduced dosing when mifepristone was administered prior to prostaglandins.[11] This reduction in dosage not only improves patient comfort but also minimizes adverse effects such as gastrointestinal symptoms and uterine hyperstimulation.

Complete abortion rates were high in both groups (93.5% vs. 86.7%), though not statistically significant. However, the need for additional procedures such as curettage was notably lower in Group I (6.5%) than in Group II (23.3%), echoing results from Ashok et al, who found surgical evacuation rates of 4% versus 18% respectively.[12] These findings suggest that mifepristone pre-treatment enhances the completeness of expulsion and reduces procedural burden.

Complication rates, although not statistically significant, were lower in the combined regimen group. This trend is supported by WHO guidelines, which advocate for mifepristone-misoprostol protocols due to their superior safety profile and reduced risk of retained products of conception.[13]

Additionally, the trend of decreasing induction time with increasing parity suggests enhanced uterine sensitivity in multiparous women, which is further amplified by mifepristone. These findings align with global literature and reinforce the importance of individualized protocol selection based on parity and gestational age.

Overall, the study corroborates existing evidence that mifepristone followed by misoprostol is a more efficient and clinically favorable approach for second-trimester termination. The protocol offers shorter induction times, fewer doses, and reduced surgical interventions, making it particularly valuable in high-volume or resource-constrained settings.

## CONCLUSION

Pre-treatment with mifepristone significantly improves the efficiency of second-trimester medical abortion. Compared to misoprostol alone, the combined regimen yields shorter induction-to-abortion intervals, requires fewer doses, and reduces the need for surgical intervention. Stratified analysis confirms consistent benefits across all parity groups and gestational age ranges, with the greatest time savings in nulliparous women. These findings support the routine use of mifepristone-misoprostol protocols under the MTP framework for safer and more predictable outcomes.

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