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Research Article

COMPARATIVE EFFICACY OF MIFEPRISTONE PLUS MISOPROSTOL VERSUS MISOPROSTOL ALONE IN SECOND TRIMESTER TERMINATION OF PREGNANCY: A RANDOMIZED CONTROLLED STUDY

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ABSTRACT

Background: Termination of pregnancy during the second trimester (13–24 weeks) carries greater clinical risk compared to earlier gestations and demands methods that are both safe and efficient. Misoprostol is commonly used for medical termination; however, pretreatment with mifepristone may improve its effectiveness by enhancing uterine responsiveness.

Objective: To evaluate and compare the effectiveness and safety of a combined mifepristone–misoprostol regimen versus misoprostol alone for second trimester pregnancy termination.

Methods: This randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology at a tertiary care institution in Jaipur. Fifty-four women with singleton pregnancies between 13 and 24 weeks were randomly assigned into two equal groups. The study group received oral mifepristone (200 mg) followed by misoprostol, while the control group received only misoprostol. The primary outcomes assessed were induction-to-abortion interval and length of hospital stay. Secondary outcomes included total misoprostol dose and incidence of side effects.

Results: Participants in both groups were comparable at baseline. The combination regimen resulted in a shorter induction-to-abortion interval, reduced drug requirement, and decreased duration of hospitalization. Although adverse effects such as pain, nausea, vomiting, and fever were observed less frequently in the combination group, the differences were not statistically significant.

Conclusion: Pretreatment with mifepristone enhances the efficiency of misoprostol in second trimester termination without increasing adverse effects. The combined regimen is therefore a preferable option where resources permit.

KEYWORDS: Second Trimester Abortion, Mifepristone, Misoprostol, Induction–abortion Interval, Medical Termination of Pregnancy, Maternal Safety.

Introduction

Pregnancy termination carried out between 13 and 24 weeks of gestation is generally categorized as second trimester termination and is associated with comparatively higher clinical risk than procedures performed earlier in pregnancy[1]. Although fewer cases occur during this

period, they contribute substantially to overall complication rates, making careful selection of management strategies essential[2,3].

The indications for second trimester termination are varied and often medically justified. These commonly include major fetal structural abnormalities identified on ultrasonography, chromosomal anomalies detected through prenatal diagnostic techniques, and intrauterine fetal demise. In addition, certain maternal medical conditions may necessitate termination to preserve the woman's health. Social circumstances, including delayed recognition of pregnancy and pregnancies resulting from sexual violence, also contribute to the need for termination at this stage[4,5]. Regardless of the underlying reason, the primary objective remains the safe and complete evacuation of the uterus with minimal complications and within a reasonable time frame[6].

Approaches to second trimester termination are broadly categorized into surgical and medical methods. Surgical techniques such as dilation and evacuation are effective and widely used in settings where skilled providers and appropriate infrastructure are available[7]. However, medical methods have gained prominence, particularly in low-resource settings, due to their non-invasive nature and wider accessibility[8].

Misoprostol, a synthetic analogue of prostaglandin E1, is frequently used for medical termination because of its uterotonic and cervical ripening effects. Its advantages include low cost, ease of storage, and multiple routes of administration, making it a practical option in diverse healthcare settings[9–11]. Despite its effectiveness, regimens using misoprostol alone may require repeated dosing and are often associated with longer induction-to-abortion intervals and increased incidence of side effects[12].

Mifepristone, an antiprogesterone agent, enhances the effectiveness of prostaglandins by altering the hormonal environment of the uterus. It promotes cervical softening and increases uterine sensitivity to subsequent prostaglandin administration, thereby facilitating the termination process[13,14]. When administered prior to misoprostol, it has been shown to reduce both the duration of induction and the total drug requirement[15].

Recommendations from international organizations such as the World Health Organization and FIGO support the use of a combined mifepristone–misoprostol regimen due to its improved effectiveness and acceptability[16,17]. Evidence from prior clinical studies indicates that administering mifepristone before misoprostol can shorten the duration of the procedure and reduce the total prostaglandin requirement[15,18,19].However, access to mifepristone remains inconsistent in many regions due to regulatory, economic, and logistical constraints[20]. Consequently, misoprostol-only protocols continue to be used in several clinical settings.

Given these considerations, there is a continued need to evaluate and compare available regimens in different populations. The present study was undertaken to assess the effectiveness and safety of a combined mifepristone–misoprostol regimen in comparison with misoprostol alone for second trimester termination of pregnancy.

Aims and Objectives

Aim

To evaluate and compare the clinical effectiveness and safety of a combined regimen of mifepristone followed by misoprostol versus misoprostol alone for termination of pregnancy during the second trimester.

Objectives

- To compare the induction–abortion interval between the two treatment groups.
- To assess the difference in duration of hospital stay among patients receiving the two regimens.
- To evaluate the total dose of misoprostol required to achieve complete abortion in each group.
- To compare the rate of complete abortion between the combination regimen and misoprostol-only regimen.
- To analyze and compare the incidence of adverse effects, including gastrointestinal symptoms and fever, in both groups.
- To determine the need for additional interventions, such as surgical evacuation, if required.

Materials and Methods

Study Design and Setting

This prospective randomized controlled study was conducted in the Department of Obstetrics and Gynaecology at the National Institute of Medical Sciences and Research (NIMS), Jaipur, Rajasthan. The study was carried out over a period of 18 months from June 2024 to November 2025, after obtaining approval from the Institutional Ethics Committee.

Study Population

A total of 54 pregnant women admitted for second trimester termination of pregnancy were included in the study. All participants had singleton pregnancies between 13 and 24 weeks of gestation and fulfilled the criteria for medical termination of pregnancy as per the Medical Termination of Pregnancy (Amendment) Act.

Inclusion Criteria

- Women with gestational age between 13 and 24 weeks
- Singleton pregnancy
- Indications for termination as per legal and clinical guidelines
- Willingness to participate with informed written consent

Exclusion Criteria

- Known hypersensitivity to mifepristone or misoprostol
- Suspected or confirmed ectopic pregnancy

- Severe medical disorders contraindicating medical abortion
- Hemodynamic instability or active severe infection
- Previous uterine scar was evaluated individually and included with caution

Sample Size and Randomization

A total of 54 eligible participants were enrolled and randomly allocated into two equal groups of 27 each using a simple randomization method. Allocation was done to ensure comparable baseline characteristics between the groups.

- **Group A (Combination group):** Received mifepristone followed by misoprostol
- **Group B (Control group):** Received misoprostol alone

Intervention Protocol

Group A (Mifepristone + Misoprostol)

Participants received mifepristone 200 mg orally as a single dose. After an interval of 24–48 hours, misoprostol was administered at a dose of 400 micrograms via vaginal, buccal, or sublingual route at regular intervals until expulsion of the products of conception.

Group B (Misoprostol Alone)

Participants received misoprostol 400 micrograms via vaginal, buccal, or sublingual route at regular intervals until expulsion.

The dosing schedule and route of administration were followed in accordance with standard clinical protocols and FIGO recommendations.

Clinical Assessment and Monitoring

All participants underwent detailed history taking, physical examination, and ultrasonographic confirmation of gestational age prior to initiation of treatment. Vital parameters were monitored regularly throughout the procedure. Patients were observed for onset of uterine contractions, cervical changes, and expulsion of products of conception.

Outcome Measures

Primary Outcomes

- Induction–abortion interval (IAI): Time from first dose of misoprostol to complete expulsion.
- Duration of hospital stay

Secondary Outcomes

- Total dose of misoprostol required
- Incidence of adverse effects (abdominal pain, nausea, vomiting, fever, shivering, diarrhea)
- Need for additional interventions such as surgical evacuation

Definition of Complete Abortion

Complete abortion was defined as expulsion of fetus and placenta without the need for surgical intervention. In cases of retained placenta or incomplete abortion, appropriate surgical management was performed.

Ethical Considerations and Informed Consent

Ethical approval for the study was obtained from the Institutional Ethics Committee prior to commencement. All procedures were conducted in accordance with accepted ethical standards. Participants were informed about the study in detail, and written consent was obtained before enrollment. Confidentiality of patient information was maintained throughout the study by using anonymized data records.

Data Collection

All relevant clinical and demographic data were recorded in a structured proforma. Observations were documented systematically for each participant during the hospital stay.

Statistical Analysis

Data were entered and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as percentages. Comparative analysis between the two groups was performed using appropriate statistical tests, and a p-value of less than 0.05 was considered statistically significant.

Results and Observations

Study Population

A total of 54 women undergoing second trimester termination of pregnancy were included and equally divided into:

- Group A (Mifepristone + Misoprostol): 27 patients
- Group B (Misoprostol alone): 27 patients
- All participants were analyzed.

Table 1: Baseline Characteristics

Variable	Group A (n=27)	Group B (n=27)	p-value
Age (years)	30.44 ± 7.07	29.15 ± 6.65	0.49
Gestational age (weeks)	19.00 ± 3.46	18.07 ± 3.16	0.29

Both groups were comparable at baseline, with no statistically significant difference (Table 1).

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Table 2: Induction - Abortion Interval

Group	Mean ± SD (hours)	Mean Difference	p-value
Group A	21.96 ± 7.33	↓ 11.41 hrs	<0.001
Group B	33.37 ± 9.34	—	

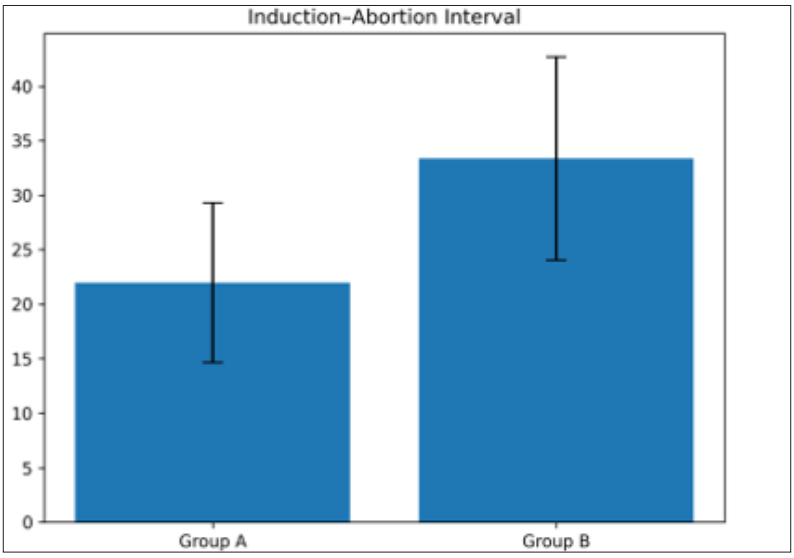

Figure 1. Comparison of induction–abortion interval between the two groups. The mifepristone–misoprostol group demonstrated a significantly shorter interval (p < 0.001). Error bars represent standard deviation

Table 3: Duration of Hospital Stay

Group	Mean ± SD (days)	Mean Difference	p-value
Group A (Mifepristone + Misoprostol)	2.78 ± 0.84	↓ 1.15 days	<0.001
Group B (Misoprostol alone)	3.93 ± 1.02	—	—

Table 4: Total Misoprostol Requirement

Group	Mean ± SD (mcg)	Mean Difference	p-value
Group A	933.33 ± 235.34	↓ 355.56 mcg	<0.001
Group B	1288.89 ± 295.26	—	

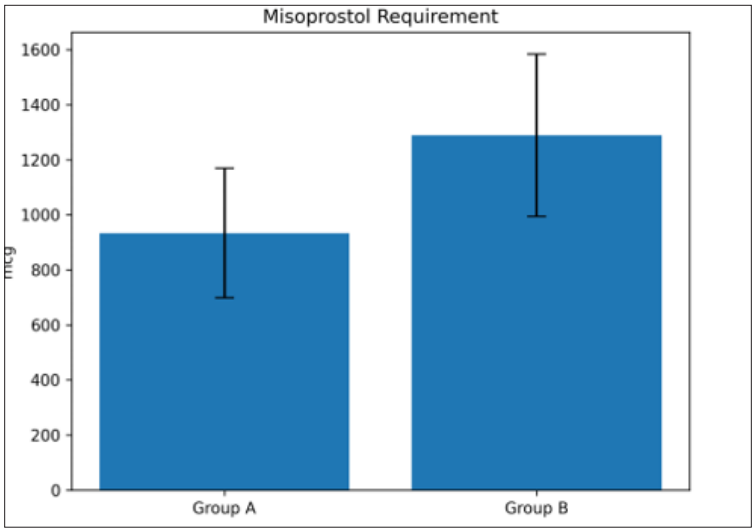

Figure 2.Comparison of total misoprostol requirement between the two groups. The combination regimen required significantly lower doses (p < 0.001). Error bars represent standard deviation

Table 5: Abortion Outcome

Outcome	Group A (n=27)	Group B (n=27)	p-value
Complete abortion	24 (88.9%)	24 (88.9%)	1.00
Incomplete abortion	3 (11.1%)	3 (11.1%)	

Table 6: Adverse effects

Adverse Effect	Group A (n=27)	Group B (n=27)	p-value
Abdominal pain	6 (22.2%)	10 (37.0%)	0.23
Nausea	5 (18.5%)	9 (33.3%)	0.21
Vomiting	4 (14.8%)	7 (25.9%)	0.31
Fever	4 (14.8%)	6 (22.2%)	0.48
Shivering	3 (11.1%)	5 (18.5%)	0.44
Diarrhea	2 (7.4%)	4 (14.8%)	0.39

Table 7: Effect Size and Confidence Intervals

Outcome	Mean Difference / RR	95% Confidence Interval	p-value
Induction–abortion interval	-11.41 hrs	(-15.8 to -7.0)	<0.001
Misoprostol dose	-355.56 mcg	(-515 to -196)	<0.001
Complete abortion	RR = 1.00	(0.86–1.16)	1.00
Side effects	RR = 0.77	(0.44–1.33)	0.41

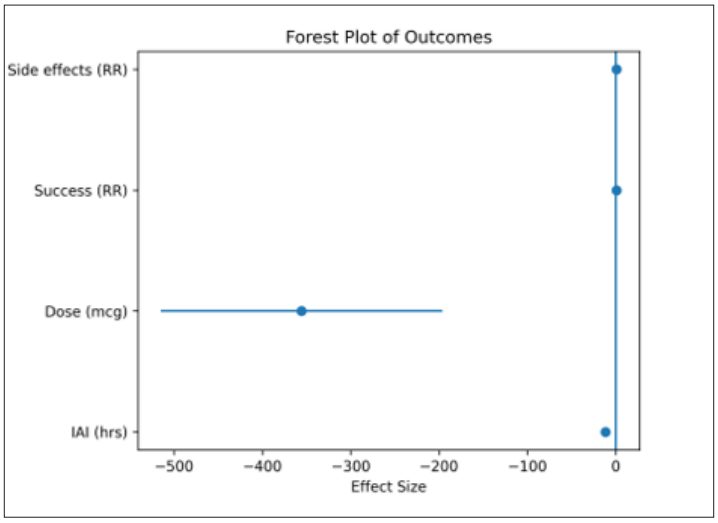

Figure 3.Forest plot comparing effect sizes between the mifepristone–misoprostol group and misoprostol-only group. The combination regimen significantly reduced induction–abortion interval and total misoprostol requirement, while no significant differences were observed in success rate or adverse effects. Error bars represent 95% confidence intervals

Group A showed a significantly shorter induction–abortion interval, indicating superior efficacy (Table 2).

The duration of hospital stay was significantly shorter in the combination group compared to the misoprostol-only group ($p < 0.001$), reflecting improved clinical efficiency and faster completion of the abortion process (Table 3).

The combination regimen required significantly lower misoprostol doses (Table 4).

Both groups had identical success rates, showing no significant difference (Table 5).

Adverse effects were consistently more frequent in the misoprostol-only group (Group B) across all parameters, including abdominal pain, nausea, vomiting, fever, shivering, and diarrhea. However, none of these differences reached statistical significance ($p > 0.05$), indicating comparable safety profiles between the two regimens (Table 6).

Table 7, Strong effect seen in IAI and dose reduction and No significant difference in success or side effects.

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Summary

This study evaluated two medical approaches for second trimester termination of pregnancy. The findings indicate that pre-treatment with mifepristone enhances the overall efficiency of misoprostol by reducing the time required for completion and lowering the total drug dose. Hospital stay was also shorter in the combination group.

Despite these differences in efficiency, both regimens demonstrated similar effectiveness in achieving complete termination. Adverse effects were observed in both groups, with a tendency toward lower frequency in the combination regimen, although this difference was not statistically significant.

Overall, the addition of mifepristone improves procedural convenience without altering safety outcomes.

Discussion

The findings of this study indicate that adding mifepristone prior to misoprostol improves the efficiency of second trimester pregnancy termination without affecting overall success or safety. In the present study, the use of mifepristone prior to misoprostol demonstrated clear advantages in terms of reducing induction time, shortening hospital stay, and lowering total drug requirement, while maintaining comparable safety and success rates.

The baseline comparability of both groups in terms of age and gestational duration indicates that the observed differences in outcomes are unlikely to be influenced by confounding demographic factors. Similar methodological consistency has been emphasized in earlier clinical studies evaluating medical termination regimens, where balanced baseline characteristics are essential for valid comparison[1,2].

One of the most notable findings in this study was the significant reduction in the induction–abortion interval in the combination group. This effect is likely related to the ability of mifepristone to prepare the uterus and cervix, thereby enhancing responsiveness to prostaglandins[3,4]. Earlier studies, including those by Ashok et al. and Tang et al., have reported similar reductions in induction duration with the combined regimen[5,6,21].These results support the concept that combined regimens improve procedural efficiency rather than altering the overall success rate.

A shorter duration of hospitalization was also observed among participants receiving the combined regimen. This has practical implications for both patients and healthcare systems, as reduced hospital stay is associated with improved patient comfort and more efficient utilization of medical resources. Similar trends have been documented in other studies, where faster completion of the abortion process translated into decreased inpatient care requirements.

Another important outcome in this study was the reduced total dose of misoprostol required in the combination group. Lower drug exposure is clinically beneficial, as it may reduce the likelihood of dose-related adverse effects. The lower requirement of misoprostol observed in this study supports the known synergistic interaction between these two agents[6–8,22].The pharmacodynamic interaction between these two agents is well established and contributes to improved treatment efficiency.

Despite these advantages, the rate of complete abortion was identical in both groups. This indicates that while the addition of mifepristone improves the speed and convenience of the procedure, misoprostol alone remains an effective option for achieving termination. Comparable success rates between the two regimens have been reported in multiple studies, where both approaches achieved high rates of complete abortion, typically exceeding 85%[5,9,23].

With regard to safety, the incidence of adverse effects such as nausea, vomiting, and abdominal discomfort was lower in the combination group, although the differences were not statistically significant. This trend may be attributed to the lower cumulative dose of misoprostol required when mifepristone is used. Previous studies have similarly noted that higher prostaglandin doses are associated with increased gastrointestinal side effects, which supports the findings of the present study[7,10,24]. Importantly, no serious complications were encountered in either group, indicating that both regimens are safe when administered under appropriate clinical supervision.

These observations are consistent with current clinical recommendations that favor the combined regimen when available [3,11,25].However, in settings where mifepristone is not readily available, misoprostol alone continues to serve as a practical and effective alternative, despite requiring longer induction times and higher drug doses[10,12,26].

From a clinical standpoint, reducing the induction–abortion interval is particularly important, as prolonged procedures are associated with increased patient discomfort and a higher risk of complications such as infection or excessive bleeding[12,13]. Therefore, regimens that shorten the duration of the process without compromising safety are preferable.

This study has certain limitations that should be considered. The relatively small sample size may limit the ability to detect statistically significant differences in less common outcomes, particularly adverse effects. Additionally, as the study was conducted at a single center, the generalizability of the findings may be limited. The study has certain limitations, including a relatively small sample size and single-center design, which may influence the general applicability of the findings. Further studies involving larger populations would help to confirm these results[14,15].

Conclusion

The present study demonstrates that the combination regimen of mifepristone followed by misoprostol is significantly more efficient than misoprostol alone for second trimester

termination of pregnancy. The addition of mifepristone resulted in a marked reduction in induction–abortion interval and a significant decrease in total misoprostol requirement, thereby improving the overall clinical efficiency of the procedure.

Despite these advantages, the success rates of complete abortion were comparable between the two regimens, indicating that misoprostol alone remains an effective alternative where mifepristone is unavailable. The safety profiles of both regimens were also similar, with no statistically significant increase in adverse effects observed in either group.

From a clinical perspective, the use of mifepristone pretreatment offers important benefits, including shorter duration of hospitalization, reduced patient discomfort, and lower drug exposure, which may contribute to improved patient satisfaction and reduced healthcare burden.

In view of these findings, the combined use of mifepristone and misoprostol may be considered a more efficient option for second trimester termination where available. However, misoprostol alone remains a practical alternative in settings where access to mifepristone is limited.

Conflict of interest

None

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