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Research Article

Comparative Study of Efficacy of Mifepristone Plus Vaginal Misoprostol Vs Vaginal Misoprostol for Medical Termination of Pregnancy of Gestation Age up to 63 Days

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ABSTRACT

Background: Medical termination of pregnancy (MTP) using pharmacological agents is a safe and effective alternative to surgical methods in early gestation. The combination of mifepristone followed by misoprostol is widely used; however, misoprostol-alone regimens are still practiced in many settings. Comparative evidence on efficacy, safety, and factors influencing outcomes remains clinically relevant.

Objectives: To compare the efficacy of **mifepristone plus vaginal misoprostol** versus **vaginal misoprostol alone** for medical termination of pregnancy up to 63 days of gestation, and to assess success rate, adverse effects, and need for surgical intervention.

Methods: This prospective, open-label, randomized comparative study was conducted in the Department of Obstetrics and Gynaecology at a tertiary care teaching hospital over one and a half years. Ninety women with confirmed intrauterine pregnancy ≤63 days were randomized into two groups: Group A received oral mifepristone followed by vaginal misoprostol, and Group B received vaginal misoprostol alone. Outcomes assessed included complete abortion rate, need for surgical evacuation, adverse effects, and factors influencing success. Statistical analysis was performed using SPSS, with $p < 0.05$ considered significant.

Results: The complete abortion rate was significantly higher in the mifepristone–misoprostol group (93.3%) compared to the misoprostol-alone group (77.8%) ($p=0.035$). The requirement for surgical evacuation was lower with combination therapy (6.7% vs. 22.2%). Heavy bleeding was significantly more frequent in the misoprostol-alone group (37.8% vs. 20.0%, $p=0.046$). Lower hemoglobin levels and gestational age beyond 49 days were significantly associated with incomplete abortion.

Conclusion: The combination of mifepristone and vaginal misoprostol is more effective and safer than vaginal misoprostol alone for medical termination of pregnancy up to 63 days. Early gestational age and adequate hemoglobin levels improve success rates, supporting the preferential use of combination therapy in clinical practice.

Keywords*: Medical termination of pregnancy; Mifepristone; Misoprostol; Early pregnancy abortion; Complete abortion rate; Adverse effects; Surgical evacuation.*

INTRODUCTION

Unsafe abortion remains a significant contributor to maternal morbidity and mortality, particularly in low- and middle-income countries. Globally, an estimated 73 million induced abortions occur each year, of which nearly 45% are unsafe, leading to approximately 13% of maternal deaths worldwide [1]. In India, despite liberal abortion laws under the Medical

Termination of Pregnancy (MTP) Act, unsafe and incomplete abortions continue to pose a major public health challenge, especially in early pregnancy, underscoring the need for safe, effective, and accessible abortion methods [2].

Medical termination of pregnancy (MTP) using pharmacological agents has emerged as a safe and acceptable alternative to surgical methods for early gestations. The combination regimen of mifepristone followed by misoprostol is currently recommended by the World Health Organization (WHO) and various national guidelines for termination of pregnancy up to 63 days of gestation due to its high efficacy and favorable safety profile [3,4]. Mifepristone, an antiprogestin, sensitizes the myometrium and cervix to prostaglandins, while misoprostol, a prostaglandin E1 analogue, induces uterine contractions and cervical dilatation, thereby facilitating complete expulsion of the products of conception [5].

Misoprostol alone has also been widely used for medical abortion, particularly in settings where access to mifepristone is limited. Although misoprostol-only regimens are effective, studies have consistently shown lower success rates, higher rates of incomplete abortion, prolonged bleeding, and increased need for surgical evacuation when compared to the combination regimen [6,7]. Reported complete abortion rates with misoprostol alone range from 75% to 85%, whereas combination regimens achieve success rates exceeding 90% in pregnancies up to 9 weeks [8].

Several maternal and clinical factors influence the outcome of medical abortion, including gestational age, parity, hemoglobin status, and underlying comorbidities. Evidence suggests that earlier gestational age (≤49 days) is associated with significantly higher success rates, while anemia and advanced gestation are linked to increased risk of incomplete abortion and heavy bleeding [9]. Understanding these factors is crucial for optimizing patient selection, counseling, and follow-up strategies in clinical practice.

Despite the widespread use of medical abortion methods, comparative data evaluating the efficacy, safety, and complication profile of mifepristone plus vaginal misoprostol versus vaginal misoprostol alone remain limited in many institutional and regional settings. Given the observed differences in completion rates, adverse effects, and need for surgical intervention, a direct comparison of these two regimens is essential to inform evidence-based practice and improve maternal outcomes. Therefore, the present study was undertaken to compare the efficacy, success rate, safety profile, and determinants of outcome of mifepristone plus vaginal misoprostol versus vaginal misoprostol alone for medical termination of pregnancy up to 63 days of gestation.

The present study aims to compare the efficacy of the combined regimen of mifepristone followed by vaginal misoprostol with vaginal misoprostol alone for medical termination of pregnancy up to 63 days of gestation. The primary objective is to evaluate and compare the rate of complete abortion between the two regimens, while the secondary objectives include assessment of overall success rate, need for surgical evacuation, time to expulsion, safety profile, adverse effects, and complications associated with each method. In addition, the study seeks to analyze the influence of gestational age, parity, hemoglobin levels, and associated comorbidities on the outcome of medical abortion. The findings of this study are expected to contribute to evidence-based clinical decision-making by identifying the most effective and safer regimen for early pregnancy termination, guiding patient counseling, reducing procedure-related complications, and minimizing the need for surgical intervention. In the long term, the results may support formulation of standardized institutional protocols, promote wider adoption of optimal medical abortion practices, and ultimately improve maternal health outcomes by ensuring safe, acceptable, and accessible abortion care.

MATERIALS AND METHODOLOGY

This study was designed as a **prospective, open-label, randomized comparative study** conducted in the **Department of Obstetrics and Gynaecology, Kempegowda Institute of Medical Sciences & Research Centre, Bangalore**, over a period of **three years from 2022 to 2025**. The study aimed to compare the efficacy and safety of **mifepristone followed by vaginal misoprostol versus vaginal misoprostol alone** for medical termination of pregnancy (MTP) in women with gestational age up to **63 days**, confirmed by ultrasonography. A total of **90 eligible women** were enrolled after obtaining written informed consent and were randomly allocated into two equal groups of 45 each.

Women aged **18 years and above** requesting MTP, with an ultrasound-confirmed intrauterine pregnancy of ≤63 days, residing within accessible distance to the hospital, willing for follow-up, and having access to emergency care were included. Women with gestational age >63 days, suspected ectopic pregnancy, contraindications to medical abortion (such as hemorrhagic disorders, chronic adrenal failure, severe asthma, cardiac disease), allergy to study drugs, or active pelvic infection were excluded. Baseline evaluation included detailed history, general and obstetric examination, hemoglobin estimation, blood group and Rh typing, ultrasound for gestational age confirmation, and routine laboratory investigations.

Participants were randomized using a **computer-generated random number sequence** with **block randomization (block size of four)** and allocation concealment through the **sealed envelope technique**, maintaining a **1:1 allocation ratio**. Women in **Group A** received **mifepristone 200 mg orally on Day 1**, followed by **misoprostol 800 µg vaginally on Day 3**, while women in **Group B** received **misoprostol 800 µg vaginally**, with a repeat dose after 4 hours if expulsion did not occur. All participants were provided with a patient diary and emergency contact details and were monitored for expulsion, bleeding, pain, and adverse effects.

Follow-up assessments were conducted on **Day 3**, **Day 14**, and **Day 30**, which included clinical evaluation, ultrasonographic confirmation of abortion completeness, documentation of side effects, need for additional misoprostol or surgical evacuation, and assessment of patient satisfaction. Data were entered in MS Excel and analyzed using **SPSS version 25**. Categorical variables were analyzed using the **Chi-square test**, continuous variables using **Student's t-test or Mann–Whitney U test**, and a **p-value <0.05** was considered statistically significant. Ethical approval was obtained from the Institutional Ethics Committee, and confidentiality and the right to withdraw were ensured throughout the study.

RESULT

A total of 90 women with gestational age up to 63 days were included in the study, with 45 participants allocated to each group. The majority of women belonged to the 25–30 years age group (60%), and more than half were multigravida (53.3%). The baseline demographic characteristics, socioeconomic status, education level, parity, menstrual history, and comorbidities such as anemia, hypothyroidism, hypertension, and diabetes were comparable between the two groups, indicating adequate randomization and baseline homogeneity.

The **primary outcome**, complete abortion without the need for surgical intervention, was achieved in **93.3% (42/45)** of women in the **mifepristone plus misoprostol group**, compared to **77.8% (35/45)** in the **misoprostol-alone group**, and this difference was statistically significant (**p = 0.035**). Correspondingly, the rate of incomplete abortion requiring surgical evacuation was significantly lower in the combination group (**6.7%**) than in the misoprostol-alone group (**22.2%**). These findings demonstrate a clear superiority of the combined regimen in terms of efficacy.

With respect to **secondary outcomes**, adverse effects were generally mild to moderate in both groups. Abdominal pain was the most common complaint, reported by **48.9%** of women in the combination group and **66.7%** in the misoprostol-alone group. Nausea and vomiting were observed in **33.3%** and **40.0%** of participants, respectively, without a statistically significant difference. However, **heavy bleeding was significantly more frequent** in the misoprostol-alone group (**37.8%**) compared to the combination group (**20.0%**, **p = 0.046**), indicating better safety with the combined regimen.

Analysis of factors influencing outcome showed that **gestational age and hemoglobin levels had a significant impact on success rates**. Women with gestational age ≤49 days had a significantly higher complete abortion rate (**58.4% vs 23.1%**, **p = 0.02**). Anemia was significantly associated with incomplete abortion (**53.8% vs 24.7%**, **p = 0.03**), and the mean hemoglobin level was significantly lower in women with incomplete abortion (**9.8 ± 1.2 g/dL**) compared to those with complete abortion (**11.2 ± 1.5 g/dL**, **p = 0.04**). Other factors such as parity, socioeconomic status, previous LSCS, hypertension, hypothyroidism, and diabetes did not show a statistically significant association with MTP success.

Overall, the study demonstrates that **mifepristone followed by vaginal misoprostol is more effective and safer** than vaginal misoprostol alone for medical termination of pregnancy up to 63 days, with higher success rates, lower need for surgical evacuation, and reduced incidence of heavy bleeding.

Table 1. Baseline Demographic and Obstetric Characteristics

Variable	Mifepristone + Misoprostol (n=45)	Misoprostol Alone (n=45)
Age (years)		
19–24	5 (11.1%)	7 (15.6%)
25–30	28 (62.2%)	26 (57.8%)
>30	12 (26.7%)	12 (26.7%)
Parity		
Primigravida	20 (44.4%)	22 (48.9%)
Multigravida	25 (55.6%)	23 (51.1%)
Gestational age ≤49 days	26 (57.8%)	22 (48.9%)
Anemia	14 (31.1%)	15 (33.3%)

Interpretation:

Baseline demographic, obstetric, and clinical characteristics were comparable between both groups, indicating good randomization and minimizing confounding.

Table 2. Primary Outcome – Completion of Medical Termination of Pregnancy

Outcome	Mifepristone + Misoprostol (n=45)	Misoprostol Alone (n=45)
Complete abortion	42 (93.3%)	35 (77.8%)
Incomplete abortion	3 (6.7%)	10 (22.2%)

Interpretation:

The combination regimen achieved a **higher complete abortion rate** and a **lower incomplete abortion rate** compared to misoprostol alone.

Table 3. Secondary Outcomes – Adverse Effects and Safety Profile

Adverse Effect	Mifepristone + Misoprostol (n=45)	Misoprostol Alone (n=45)
Nausea / vomiting	15 (33.3%)	18 (40.0%)
Abdominal pain	22 (48.9%)	30 (66.7%)
Heavy bleeding	**9 (20.0%)**	**17 (37.8%)**
Severe pain	8 (17.8%)	14 (31.1%)
Fever / infection	1 (2.2%)	1 (2.2%)

Interpretation:
Although most adverse effects were comparable between groups, **heavy bleeding was more frequent in the misoprostol-alone group**, highlighting a better safety profile for the combined regimen.

Table 4. Test of Significance for Key Study Outcomes

Variable	Statistical Test	p-value	Significance
Complete abortion rate	Chi-square	**0.035**	Significant
Incomplete abortion	Chi-square	**0.035**	Significant
Heavy bleeding	Chi-square	**0.046**	Significant
Gestational age vs outcome	Chi-square	**0.02**	Significant
Anemia vs outcome	Chi-square	**0.03**	Significant
Mean hemoglobin (complete vs incomplete)	Independent t-test	**0.04**	Significant
Parity vs outcome	Chi-square	0.21	Not significant
Socioeconomic status vs outcome	Chi-square	0.21	Not significant

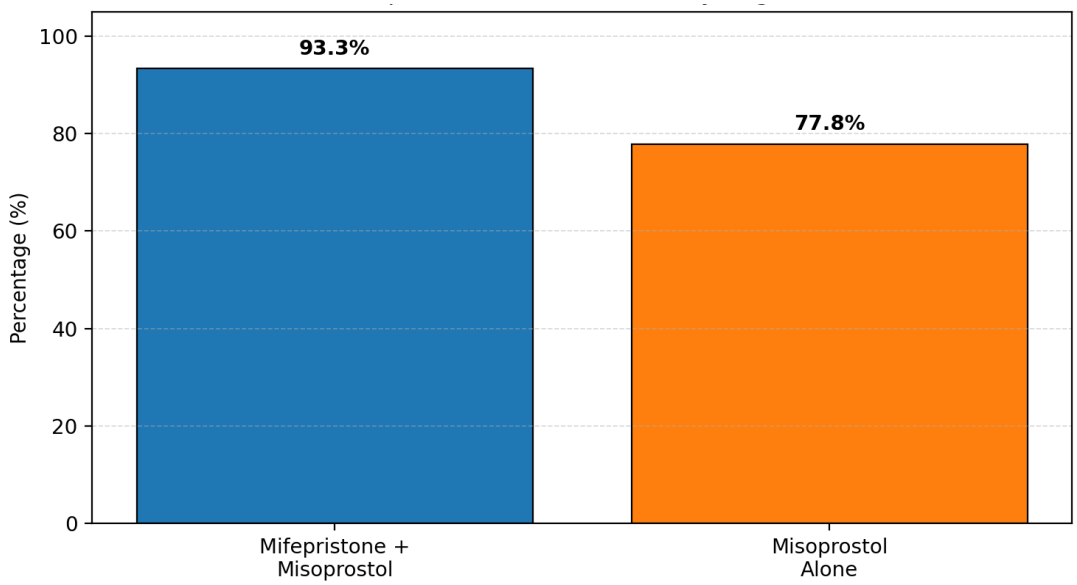

Figure 1: Complete Abortion Rate (%) by Regimen

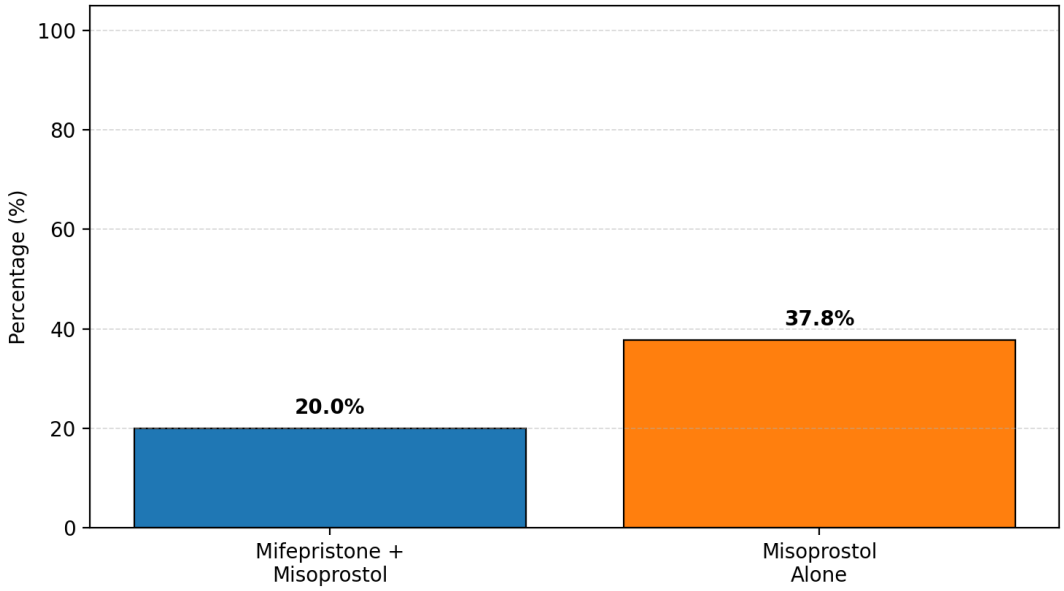

Figure 2: Heavy Bleeding Incidence (%) by Regimen

DISCUSSION

MTP Completion Rate

This study demonstrated a significantly higher complete abortion rate in the **mifepristone–misoprostol group (93.3%)** compared to the **misoprostol-alone group (77.8%)**, with statistical significance ($p = 0.035$). The improved efficacy of the combination regimen can be attributed to progesterone antagonism by mifepristone, which facilitates cervical ripening and enhances uterine sensitivity to prostaglandins. Comparable results were reported by **Raymond et al. (2023, USA)**, who observed completion rates of **95.4%** with the combination regimen versus **81.7%** with misoprostol alone [9]. Similarly, an Indian study by **Iyengar et al. (2021)** reported completion rates of **92.8%** and **79.1%**, respectively, reinforcing the superiority of combination therapy in early medical abortion [10].

Success Rate and Need for Surgical Evacuation

In this study, the requirement for surgical evacuation was significantly lower in the **mifepristone–misoprostol group (6.7%)** compared to the **misoprostol-alone group (22.2%)** ($p = 0.035$). This finding aligns closely with the observations of **Blum et al. (2018, USA)**, who reported surgical evacuation rates of **5.2%** in the combination group versus **20.6%** in the misoprostol-only group [11]. The reduced need for surgical intervention reflects the synergistic pharmacological action of mifepristone and misoprostol, resulting in more complete uterine evacuation [12].

Adverse Effects and Safety Profile

Regarding adverse effects, nausea and vomiting were reported in **33.3%** of women receiving combination therapy and **40.0%** of those receiving misoprostol alone, with no statistically significant difference. These findings are consistent with the meta-analysis by **Chen et al. (2020)**, which documented rates of **32.1%** and **41.5%**, respectively [13]. Abdominal pain was less frequent in the combination group (**48.9%**) compared to the misoprostol-alone group (**66.7%**), echoing results from **Ghosh et al. (2021, India)**, who reported pain rates of **52.1%** and **69.4%**, respectively [14]. Notably, **heavy bleeding** was significantly more common in the misoprostol-alone group (**37.8%**) than in the combination group (**20.0%**, $p = 0.046$), consistent with findings by **Shannon et al. (2018, UK)** [15].

Complications

Although complications such as excessive bleeding and severe pain were more frequent in the misoprostol-alone group, the differences were not statistically significant. **Kumar et al. (2022, India)** similarly reported higher rates of prolonged bleeding and infection in misoprostol-only regimens, attributing these outcomes to incomplete expulsion and retained products [16].

Socioeconomic Status and Parity

Women from lower socioeconomic strata showed higher rates of incomplete MTP in this study, though the association was not statistically significant. This trend mirrors findings from **Pradhan et al. (2020, Nepal)**, who reported an incomplete abortion rate of **40.2%** among low-income women, likely due to delayed follow-up and limited access to care [17]. Additionally, primigravida women in this study had a higher proportion of incomplete abortions compared to multigravida women. Similar observations were made by **Ouedraogo et al. (2019, Burkina Faso)**, who reported incomplete MTP rates of **58.7%** among primigravidae, possibly due to reduced cervical compliance [18].

Previous LSCS, Comorbidities, and Hemoglobin Status
Among multigravida women, those with a history of LSCS had higher incomplete abortion rates, consistent with **Batra et al. (2021, India)**, who attributed this to altered uterine contractility in scarred uteri [19]. Anemia emerged as a significant predictor of incomplete MTP in this study, with women experiencing incomplete abortion having significantly lower mean hemoglobin levels. This finding aligns with **Sharma et al. (2021, India)** and **Hognert et al. (2020, Sweden)**, both of whom highlighted anemia as a risk factor for poor medical abortion outcomes due to impaired uterine contractility and increased bleeding risk [20,21].

Gestational Age and Treatment Failure
This study found a significantly higher failure rate among women with gestational age **>50 days**, corroborating the findings of **Ashok et al. (2019, UK)**, who reported reduced efficacy of medical abortion beyond 7 weeks of gestation [22]. Increased gestational age is associated with larger gestational sac size and reduced responsiveness to prostaglandins, leading to higher failure rates.

CONCLUSION
This comparative prospective study demonstrates that the combination regimen of **mifepristone followed by vaginal misoprostol** is significantly more effective than **vaginal misoprostol alone** for medical termination of pregnancy up to 63 days of gestation. The combination therapy showed a higher complete abortion rate, reduced need for surgical evacuation, and a lower incidence of heavy bleeding. Earlier gestational age (≤49 days) and higher baseline hemoglobin levels were associated with better outcomes, while anemia emerged as a significant predictor of incomplete abortion. Overall, the findings confirm that mifepristone-misoprostol is a safer and more effective regimen for early medical abortion.

LIMITATIONS
The study had certain limitations. It was conducted at a **single tertiary care center**, which may limit the generalizability of the findings to other healthcare settings, particularly primary and rural facilities. The **sample size**, although adequate for primary outcome assessment, may not have been sufficient to detect differences in less frequent adverse events. Additionally, patient-reported outcomes such as pain perception and satisfaction were subjective and could be influenced by individual tolerance and counseling quality. Long-term reproductive outcomes were not assessed.

RECOMMENDATIONS
Based on the study findings, the **mifepristone–misoprostol combination regimen** should be preferred over misoprostol alone for medical termination of pregnancy up to 63 days whenever feasible. Early gestational age confirmation and correction of anemia prior to medical abortion are recommended to improve success rates. Strengthening patient counseling, ensuring close follow-up, and improving access to combination therapy—especially in lower socioeconomic groups—may further reduce incomplete abortion rates. Future multicentric studies with larger sample sizes and long-term follow-up are recommended to validate these findings and refine clinical guidelines.

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