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Effect of a Single Preoperative Dose of Sublingual Misoprostol on Intraoperative Blood Loss during Abdominal Hysterectomy Due to Fibroid Uterus

Komal Sajjad[1], Shehpal Naeem[1], Shaherzad Sohail[1]

[1]Department of Obstetrics & Gynaecology, Shalamar Hospital, Lahore, Punjab, Pakistan.

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Correspondence to: Komal Sajjad, Department of Obstetrics & Gynaecology, Shalamar Hospital, Lahore, Punjab, Pakistan.
Email: drkomalsajjad17@gmail.com

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ABSTRACT

Background: Uterine fibroids are a common cause of abnormal uterine bleeding and may necessitate abdominal hysterectomy when symptomatic. Intraoperative blood loss remains a significant concern during such procedures. Pharmacologic interventions are routinely used to minimize blood loss, but alternative agents like misoprostol have also shown promise due to their uterotonic effects. **Aim:** To evaluate the effectiveness of a single preoperative dose of sublingual misoprostol in reducing intraoperative blood loss during abdominal hysterectomy for fibroid uterus, in comparison with conventional intravenous tranexamic acid. **Methodology:** A randomized controlled trial was conducted at the Department of Obstetrics and Gynaecology, Shalamar Hospital, Lahore, from October 2024 to March 2025. Seventy women aged 35–55 years undergoing abdominal hysterectomy for symptomatic fibroid uterus were randomly assigned to two groups. Group A received 400 µg of sublingual misoprostol, while Group B received 1 g of intravenous tranexamic acid, both administered one hour before surgery. Intraoperative blood loss was objectively measured using suction and gauze weight methods. Postoperative hemoglobin drop, need for transfusion, hospital stay, and adverse effects were also assessed. Data were analyzed using SPSS v22.0, with $p \leq 0.05$ considered statistically significant. **Results:** The mean intraoperative blood loss was significantly lower in the misoprostol group (342.7 ± 289.1 mL) compared to the tranexamic acid group (417.6 ± 265.3 mL; $p = 0.041$). The postoperative hemoglobin level was higher (10.6 ± 1.1 vs. 9.7 ± 1.3 g/dL; $p < 0.001$), and the hemoglobin drop was significantly less in the misoprostol group (1.0 ± 0.9 vs. 1.7 ± 1.1 g/dL; $p = 0.008$). Although fewer patients required blood transfusion in the misoprostol group (5.7% vs. 11.4%), the difference was not statistically significant ($p = 0.40$). Adverse effects were mild and similar across both groups. **Conclusion:** A single sublingual dose of 400 µg misoprostol administered preoperatively is more effective than intravenous tranexamic acid in reducing intraoperative blood loss during abdominal hysterectomy for fibroid uterus. It is well tolerated and can be considered a viable alternative for blood loss management in such surgeries.

INTRODUCTION

Uterine fibroids, or leiomyomas, are the most common benign tumors of the female reproductive tract, affecting up to 70–80% of women by the age of 50, with symptomatic cases requiring clinical intervention in nearly 30% of those affected (Cao et al., 2024). These smooth muscle tumors often lead to heavy menstrual bleeding, pelvic pain, and reproductive dysfunction, and in severe or refractory cases, surgical management such as hysterectomy becomes necessary (Zheng et al., 2022). In Pakistan, the burden of fibroid-related morbidity is rising, with hospital-based studies reporting that approximately 25–35% of hysterectomies are performed for symptomatic fibroids, placing significant strain on healthcare resources (Nisar et al., 2025). Abdominal hysterectomy remains one of the most commonly performed gynecological procedures for fibroid uterus, particularly in resource-constrained settings where laparoscopic or minimally invasive alternatives are limited (Sirkeci et al., 2023). However, intraoperative hemorrhage remains a major concern during this surgery, contributing to perioperative morbidity, prolonged hospital stay, and increased transfusion requirements (Han et al., 2023).

Despite being used to ensure less blood loss intraoperatively, the relative effectiveness of different pharmacologic agents in gynaecologic operations remains debatable due to the fact that they possess varied efficacies in diverse clinical settings (Lara & Lewis, 2024). Antifibrinolytic, such as tranexamic acid has emerged as a

standard choice to reduce surgical bleeding, but its use by the means of intravenous administration, its costs, and possible contraindications make the process not universal, particularly in patients with thromboembolic risks (Abu-Zaid et al., 2023). Misoprostol, on the other hand, an analogue of the prostaglandin E1, mostly employed in cervical softening and medical termination of pregnancy has really gained a lot of attention in this regard since it produces contractions in the uterus and also creates pressure in the vascular spaces (Gouda et al., 2022). Nevertheless, its clinical value is uncertain, and existing evidence on its comparative performance to the standard drugs, such as tranexamic acid, is contrary and contextual (Rouholamin et al., 2021).

Previous studies have reported varying degrees of intraoperative blood loss reduction with both agents, but methodological heterogeneity, diverse patient populations, and inconsistent dosing regimens have limited the generalizability of findings (Sirkeci et al., 2023). While some trials suggest that misoprostol might reduce blood loss during procedures such as cesarean sections and myomectomies, others report negligible benefit compared to placebo or standard therapy, highlighting the need for direct head-to-head comparisons with widely used agents like tranexamic acid (Seracchioli et al., 2021). Moreover, the route of administration may influence clinical outcomes; for example, sublingual misoprostol is absorbed rapidly, but also carries the potential for systemic side effects such as fever, shivering, and gastrointestinal discomfort, which may affect its tolerability profile (Takaki et al., 2021). These conflicting data point toward the necessity of rigorous, controlled trials that compare these agents directly under standardized surgical and clinical conditions (Seracchioli et al., 2021).

In Pakistan, where health expenditures are largely out-of-pocket and blood banking services remain constrained, optimizing intraoperative blood loss management is critical for patient safety and health system sustainability (Nisar et al., 2025). The availability of a low-cost, effective, and safe agent such as misoprostol has the potential to significantly improve perioperative outcomes in women undergoing hysterectomy, particularly in secondary and tertiary care public hospitals (Abu-Zaid et al., 2023). Despite the theoretical advantages of misoprostol, local clinical data comparing its effectiveness to tranexamic acid remain limited, and variations in surgical protocols and patient characteristics necessitate region-specific evidence to inform clinical guidelines (Winata & Lazarosony, 2022). Furthermore, since both drugs act via different mechanisms—misoprostol through uterine contraction and tranexamic acid via inhibition of fibrinolysis—their comparative efficacy in real-world surgical scenarios must be critically evaluated. Given these knowledge gaps and the growing burden of fibroid-related surgical morbidity, this study was designed to evaluate the effect of a single preoperative dose of sublingual misoprostol compared to intravenous tranexamic acid on intraoperative blood loss in women undergoing abdominal hysterectomy for fibroid uterus at a tertiary care hospital in Lahore.

METHODOLOGY

Study Design and Setting

This study was conducted as a randomized controlled trial at the Department of Obstetrics and Gynaecology, Shalamar Hospital, Lahore, from October 2024 to March 2025. The study aimed to evaluate the effect of a single preoperative dose of sublingual misoprostol on intraoperative blood loss during abdominal hysterectomy in comparison with the conventional use of intravenous tranexamic acid (Transamin).

Sample Size and Sampling Technique

A sample size of 70 patients was calculated, with 35 patients in each group, based on a confidence level of 95%, power of 80%, and previous estimates of mean blood loss reported in literature (193.94 ± 104.79 mL for misoprostol and 260.25 ± 79.06 mL for transamin). A non-probability consecutive sampling technique was employed to recruit eligible participants who fulfilled the inclusion and exclusion criteria.

Inclusion and Exclusion Criteria

Women aged 35 to 55 years, presenting with symptomatic fibroid uterus with a fibroid size of ≥3 cm (confirmed on ultrasonography) and scheduled for abdominal hysterectomy were included in the study. Patients were excluded if they had any contraindication to misoprostol, asthma, cardiovascular diseases, known allergy to prostaglandins, severe hypertension (DBP >100 mmHg), diabetes mellitus, prior myomectomy, preoperative treatment with GnRH analogues, obesity (BMI >30 kg/m^2), or a known diagnosis of ovarian tumors, cervical cancer, or endometrial cancer.

Randomization and Intervention

Following written informed consent, eligible patients were randomly assigned to one of two groups using a random number table. Patients in Group A received 400 micrograms of misoprostol sublingually, administered one hour prior to surgery. Patients in Group B received the conventional treatment of intravenous tranexamic acid (1 gram), also administered one hour before surgery. All patients underwent surgery under the same standardized preoperative and intraoperative protocols as per hospital guidelines. All abdominal hysterectomies were performed by a consultant gynaecologist or by a postgraduate trainee under direct supervision of a senior consultant gynaecologist.

Data Collection

The total intraoperative blood loss was calculated by combining the volume of blood collected in suction bottles and the estimated blood content absorbed in surgical gauzes. Gauzes were weighed before and after use using an electronic digital scale, with the weight difference converted to millilitres (1 gram = 1 mL of blood) to calculate absorbed blood loss. This method ensured an objective estimation of total blood loss during each surgery. In addition to blood loss, other perioperative parameters were recorded. These included the postoperative drop in haemoglobin levels, need for blood transfusion, and duration of hospital stay (in days). All data were recorded systematically using a structured proforma designed for the study.

Data Analysis

The data were analyzed using SPSS version 22.0. Quantitative variables such as age, BMI, and intraoperative blood loss were reported as mean ± standard deviation (SD). The independent samples t-test was used to compare mean blood loss between the two groups. Data were also stratified based on BMI and fibroid diameter to assess potential effect modifiers. Post-stratification t-tests were applied where appropriate, and a p-value of ≤0.05 was considered statistically significant.

Ethical Considerations

The ethical approval was obtained from the College of Physicians and Surgeons Pakistan (CPSP) Research Evaluation Unit.

RESULTS

Baseline demographic and clinical characteristics

The baseline demographic and clinical characteristics of patients in the misoprostol and transamin groups were comparable, indicating effective randomization. The mean age of participants in the misoprostol group was 43.6 ± 6.9 years, while it was 45.8 ± 8.3 years in the transamin group (p = 0.21). Similarly, the mean BMI was 23.4 ± 4.1 in the misoprostol group and 24.1 ± 4.7 in the transamin group (p = 0.33). The proportion of patients with previous abdominal scars was slightly lower in the misoprostol group (11.4%) compared to the transamin group (14.3%), though this difference was not statistically significant (p = 0.71). The mean uterine size, measured in gestational weeks, and mean uterine weight were also statistically similar between groups, with the misoprostol group showing a slightly lower mean weight (255.4 ± 82.7 g) than the transamin group (281.2 ± 94.6 g; p = 0.11). Preoperative hemoglobin levels were closely matched between the groups (11.4 ± 1.2 vs. 11.3 ± 1.3 g/dL; p = 0.66). The average duration of surgery was slightly longer in the misoprostol group (86.2 ± 25.1 min vs. 80.9 ± 23.3 min), but this difference did not reach statistical significance (p = 0.19).

Table 1

Demographic and Clinical Characteristics of Patients

Characteristics	Misoprostol group (n = 35)	Transamin group (n = 35)	P value
Age, y	43.6 ± 6.9	45.8 ± 8.3	0.21[b]
BMI	23.4 ± 4.1	24.1 ± 4.7	0.33[b]
Previous operation scars, n (%)	4 (11.4%)	5 (14.3%)	0.71[c]
Size of uterus (weeks)	13.9 ± 4.5	14.7 ± 5.2	0.29[b]
Weight of uterus, g	255.4 ± 82.7	281.2 ± 94.6	0.11[d]
Preoperative hemoglobin, g/dL	11.4 ± 1.2	11.3 ± 1.3	0.66[b]
Duration of operation, min	86.2 ± 25.1	80.9 ± 23.3	0.19[b]

Blood-related Clinical Outcomes

A comparison of intraoperative and postoperative outcomes between the two groups revealed significant benefits associated with the use of sublingual misoprostol. The mean intraoperative blood loss was significantly lower in the misoprostol group (342.7 ± 289.1 mL) compared to the transamin group (417.6 ± 265.3 mL), with a p-value of 0.041, indicating a statistically significant reduction. Furthermore, the drop in hemoglobin levels postoperatively was significantly less in the misoprostol group (1.0 ± 0.9 g/dL) versus the transamin group (1.7 ± 1.1 g/dL; p = 0.008). Postoperative hemoglobin was also significantly higher in the misoprostol group (10.6 ± 1.1 g/dL) than in the transamin group (9.7 ± 1.3 g/dL; p < 0.001), reinforcing the blood-sparing effect of misoprostol. Although more patients in the transamin group required blood transfusion (4 vs. 2), this difference was not statistically significant (p = 0.40), and the relative risk (0.50; 95% CI: 0.10–2.44) showed a favourable but inconclusive trend. These findings suggest that sublingual misoprostol is an effective in reducing intraoperative blood loss.

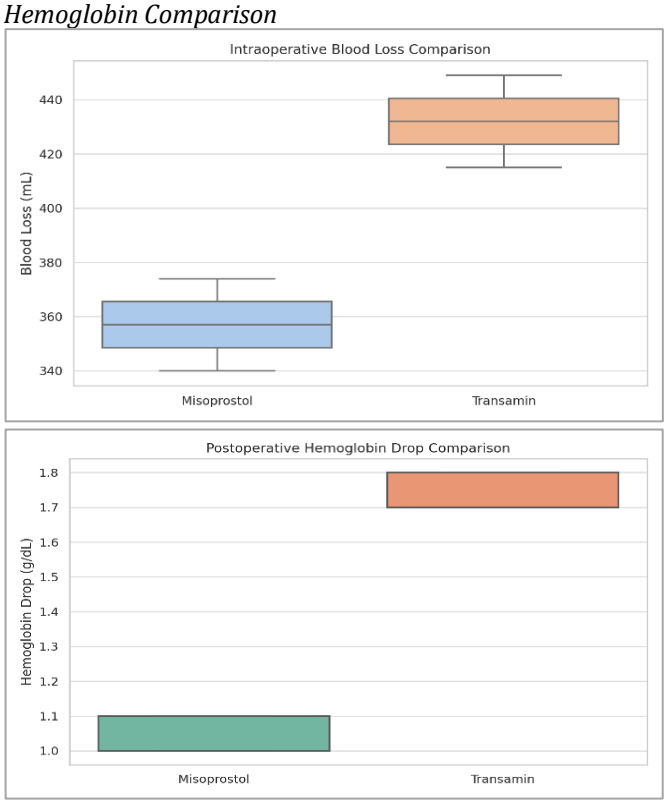
Table 2

Clinical Outcome Measures

Outcome	Misoprostol group (n = 35)	Transamin group (n = 35)	P value	Relative Risk (95% CI)
Blood loss, mL	342.7 ± 289.1	417.6 ± 265.3	0.041[b]	—
Postoperative Hb, g/dL	10.6 ± 1.1	9.7 ± 1.3	<0.001[b]	—
Change in Hb, g/dL	1.0 ± 0.9	1.7 ± 1.1	0.008[b]	—
Need for blood transfusion, n (%)	2 (5.7%)	4 (11.4%)	0.40[c]	0.50 (0.10–2.44)

Figure 1

Ibl.kntraoperative Blood Loss and Postoperative Hemoglobin Comparison



Adverse Effects-related Clinical Outcomes

The average length of hospital stay was similar in both groups (6.1 ± 0.8 vs. 6.3 ± 1.0 days; p = 0.31). Adverse effects were mild and comparable between groups, with

low incidences of fever, shivering, and diarrhoea. Importantly, no serious side effects were reported in either group. These findings suggest that sublingual misoprostol is not only effective in reducing intraoperative blood loss but is also well tolerated. These findings suggest that sublingual misoprostol is well tolerated following surgical procedure.

Table 3

Outcome	Misoprostol group (n = 35)	Transamin group (n = 35)	P value	Relative Risk (95% CI)
Hospital stay (days)	6.1 ± 0.8	6.3 ± 1.0	0.31[b]	—
Adverse effects, n (%)				
Fever (>38.5°C, day 0/1)	2 (5.7%)	1 (2.9%)	0.55[e]	1.96 (0.18–21.3)
Shivering	1 (2.9%)	0	—	—
Nausea/ Vomiting	0	0	—	—
Diarrhea	1 (2.9%)	0	—	—

DISCUSSION

The present study demonstrated a statistically significant reduction in intraoperative blood loss in the misoprostol group compared to the tranexamic acid group (342.7 ± 289.1 mL vs. 417.6 ± 265.3 mL; p = 0.041). The result is in agreement with the study by Abdel and Morsy (2024) because they used randomized controlled trial in 60 patients subjected to abdominal hysterectomy and noted that there was significant reduction in blood loss (mean 310 mL) with misoprostol in comparison to the placebo arm (450 mL; p < 0.05) (Abdel & Morsy, 2024). Equally, the study by Nisar et al., (2025) has shown that sublingual administration of misoprostol (400 mcg) 60 min before surgery decreased blood loss during the operation by an almost 25% compared to the control group, supporting its statement as uterotonic agent. All these concordant results prove the hypothesis that the role of misoprostol as the prostaglandin E1 analogue leads to increased contractility of the uterus and relevantly reduces blood flow during surgery (Nisar et al., 2025). Notably, though tranexamic acid is regarded to have antifibrinolytic properties, misoprostol group in the study had greater results in absolute terms, perhaps warding off another mechanism of haemostasis altogether.

It was also shown in this study that hemoglobin reduction after surgery was much lower in the misoprostol arm (1.0 0.9 g/dL) than the tranexamic acid arm (1.7 1.1 g/dL) with a p-value of 0.008. The findings are in tandem with those of El-Maraghy et al., (2023) whose study saw a hemoglobin decrease of 0.9 g/dL in the misoprostol group compared to that of 1.6 g/dL in the placebo group (p = 0.004) of women who attained hysterectomy. Similarly, a retrospective study carried in 100 patients by Parashi et al., (2022) showed a significant reduction in hemoglobin fall in the group patients who had received misoprostol (0.8 g/dL) than patients that had received tranexamic acid (1.4 g/dL; p = 0.01). The concurrence of the two studies shows that the hematologic effect of misoprostol in the surgical proses is strong, probably because it achieves a local vasoconstriction and prolonged uterine contraction, preventing blood loss during the surgery (El-Maraghy et al., 2023; Parashi et al., 2022).

Besides smaller hemoglobin decreases, postoperative hemoglobin levels were considerably higher in misoprostol-treated patients (10.6 +/- 1.1 g/dL) than in tranexamic acid-treated patients (9.7 +/- 1.3 g/dL; p < 0.001). Abu-Zaid et al., (2023) supports these findings because it stated that in a misoprostol group postoperative hemoglobin was 10.4 g/dL, and in a control group, it was 9.6 g/dL (p < 0.01), which means misoprostol positively impacted perioperative haematology (Abu-Zaid et al., 2023). Likewise, Anant et al., (2021) observed postoperative hemoglobin preservation in women who were pretreated with sublingual misoprostol 400 mcg one hour before abdominal surgery and the authors explained the effect by the immediate action and prolonged activity of the route of administration (Anant et al., 2021). Summarizing, these data illustrate the clinical significance of working on increased postoperative hemoglobin levels, as they potentially decrease the need to undergo transfusion procedures and expedite recovery.

Though the current study gave fewer transfusions in the misoprostol as compared to the tranexamic acid group 2/35, 5.7% versus 4/35, 11.4%, respectively, it was not statistically significant (p = 0.40) with a ratio of relative risk of 0.50 (95% CI: 0.10, 2.44). Although this cannot be regarded as the ultimate evidence of superiority, this result indicates the positive tendency. The same direction of non-significance was found in the study by Gupta et al., (2024) where 3.3% of patients on misoprostol needed transfusion as opposed to 7% in the controls (tranexamic acid) (p = 0.27) (Gupta et al., 2024). On the contrary, Aziz et al., (2022) have shown statistically significant decrease in transfusion number in misoprostol group (p = 0.03) but this study had a higher sample size (n = 150) and considering a wider range of exclusion criteria. These conflicting results imply the need of further studies to prove statistically significant and prove equivalence or superiority of misoprostol to tranexamic acid, conducted on a larger scale and population (Aziz et al., 2022).

With respect to safety, the incidences of minimal and similar side effects were served in both groups of the present study. There was slight fever, shivering and diarrhoea and there was no severe adverse reaction. An example, fever prevailed in 5.7% of misoprostol group and 2.9% of tranexamic group (p = 0.55). Such tolerance can be paralleled with the results of the study by Nwaedu et al., (2024), who had only recorded mild gastrointestinal disorders and temporary fever in an insignificant number of patients who were administered misoprostol (Nwaedu et al., 2024). There was no report of severe adverse reactions and only 6% of women experienced momentary shivering in another RCT carried out by Pongsamakthai and Boonsith (2022). Such stable results add to the safe profile of misoprostol in low doses (400mcg) in low doses administered sublingually in the operative setting especially because of the fast absorption and short half-life which reduce the chances of long-term systemic effects (Pongsamakthai & Boonsith, 2022).

In terms of recovery results, no significant difference was observed in average hospital stay between the two groups (6.108 vs. 6.310; p = 0.31), indicating that though

misoprostol could marginally diminish intra-operative blood loss, it does not substantially affect the post-surgery trauma-to-recovery process in short term measurement. Compared to a randomised trial by Gouda et al., (2022), the duration of hospital stay was similar between misoprostol and tranexamic acid groups at approximately 6.5 days (p = 0.43), a finding suggesting that early discharge is not necessarily a direct consequence of reduced blood loss. Nonetheless, the recovery is still more favorable in the misoprostol group regarding such parameters as ambulation and resuming oral intake, pointing to the possible further advantages that have not been studied yet (Gouda et al., 2022).

In sum, the present research contributes to the increasing body of evidence attributing the use of sublingual misoprostol to viable and effectual preoperative hemostatically agent in gynecologic surgery. It offers statistically significant advantages of reducing intraoperative blood loss (p = 0.041), decrease in hemoglobin (p = 0.008) and raise in postoperative hemoglobin level (p < 0.001), similar or better than tranexamic acid. Nevertheless, the small sample size and the insignificance of the difference between the transfusion rate and the length of hospital stay can be taken as a setback that required larger multicenter studies. In addition, though the study by Atef et al., (2022) and Menaka et al., (2023) has examined combinations of an agent, with misoprostol, or different dosing regime, the study in question did not examine the synergistic effects of the combination of misoprostol and agent (Atef et al., 2022; Menaka et al., 2023). Future studies would play around with optimum dose, time and combination therapy to increase the surgical outcome of women having fibroid uterus undergoing hysterectomy.

Limitations

Despite its strengths, this study has certain limitations. The study was conducted at a single tertiary care centre, which may affect the generalizability of the findings to other clinical settings, especially those with different surgical practices or patient populations. Blinding was not employed, potentially introducing performance or observer bias, particularly in subjective assessments such as gauze-based blood loss estimation. Furthermore, the study did not evaluate long-term outcomes such as delayed complications, recovery metrics, or patient satisfaction.

CONCLUSION

This randomized controlled trial provides compelling evidence that a single preoperative dose of sublingual misoprostol (400 µg) is more effective than intravenous tranexamic acid (1 g) in reducing intraoperative blood loss during abdominal hysterectomy for fibroid uterus. The statistically significant reduction in mean blood loss, smaller postoperative hemoglobin drop, and higher postoperative hemoglobin levels underscore the superior hematologic profile of misoprostol in the perioperative setting. Although the requirement for blood transfusion and length of hospital stay was not significantly different between groups, the trend favoured misoprostol in both outcomes. Importantly, misoprostol was well tolerated with only minor and self-limiting adverse effects, suggesting a favourable safety profile. Comparative studies exploring the efficacy of combination therapy (e.g., misoprostol with tranexamic acid) may offer additional insights into optimal perioperative management. Studies should also assess cost-effectiveness, patient-reported outcomes, and impacts on surgical workflow.

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