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Comparison of Tranexamic Acid and Misoprostol in Reducing Blood Loss During Cesarean Section

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ABSTRACT

Excessive blood loss during cesarean section remains a major contributor to maternal morbidity and mortality. Various uterotonic and antifibrinolytic agents are used to reduce perioperative hemorrhage, with Tranexamic Acid and Misoprostol being commonly utilized options. However, evidence comparing their effectiveness in reducing intraoperative blood loss is limited. **Objectives:** To determine whether tranexamic acid or misoprostol is more effective in reducing blood loss during cesarean section. **Methods:** Between January 2025 and June 2025, this quasi-experimental study was conducted at the Department of Obstetrics and Gynecology, Shahida Islam Medical College, Lodhran. A total of 126 obstetric patients undergoing C-section were allocated into two groups, i.e. Tranexamic Acid group and the Misoprostol group, at the time of anesthesia. Baseline data regarding age, gravida, parity, and abortion history were recorded. Intraoperative mean blood loss was compared by using an independent samples t-test, and $p \leq 0.050$ was considered significant. **Results:** In the Tranexamic Acid group, mean intraoperative blood loss was lower as compared to the Misoprostol group (282.97 ± 82.80 mL vs. 366.68 ± 116.01 mL; $p<0.001$). Similar results were noted after stratification of gravida, parity, and abortion history. Postoperative hemoglobin and hematocrit decline were also less in the Tranexamic Acid group. **Conclusions:** Our results suggest that tranexamic acid provides superior control of blood loss during cesarean section when compared with misoprostol. Based on these outcomes, tranexamic acid may be a better choice for prophylactic use to limit intraoperative bleeding in cesarean deliveries.

INTRODUCTION

Cesarean section (C-section) has become one of the most commonly performed surgical procedures worldwide and is associated with a higher risk of postpartum hemorrhage (PPH) than vaginal delivery [1]. PPH is also a significant cause of postpartum morbidity, and uterine atony is the most common cause [2]. Consequently, intraoperative and postoperative blood loss during C-section is a clinical priority that needs to be optimized. An antifibrinolytic agent, tranexamic acid (TXA), has become prominent due to the ability to reduce the blood loss during obstetric procedures by preventing fibrinolysis [3]. Several meta-analyses and clinical trials have proved its safety and efficacy when used before skin incision in obstetric patients during C-section [4, 5]. Another agent that is used by many obstetricians because of its uterotonic effects is misoprostol, which is an analog of prostaglandin E1, especially in low-resource settings [6]. The two drugs possess different modes of action, and their administration as single or in combination has demonstrated potential in enhancing the outcomes of the mother. There have been mixed results on comparative studies of TXA and misoprostol. Other studies have

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documented that TXA is a much more effective agent in reducing the total blood loss as compared to misoprostol, with fewer side effects [7, 8]. Other trials, on the other hand, discovered that misoprostol was also just as effective or better in some environments, especially in the management of bleeding after operation [9]. Further, there are synergistic effects when both drugs are administered together to achieve the reduction of intraoperative bleeding and the unnecessary use of further uterotonics [10, 11].

Although both tranexamic acid (TXA) and misoprostol are widely used to reduce blood loss during cesarean section, existing studies show variable results due to differences in clinical protocols, patient populations, and routes of administration. This inconsistency creates uncertainty regarding the most effective, safe, and practical option, particularly in resource-limited settings. The study aimed to directly compare intraoperative blood loss between tranexamic acid and misoprostol during cesarean section to determine the more effective intervention for preventing obstetric hemorrhage and guiding evidence-based clinical practice.

METHODS

This quasi-experimental study was conducted in the Department of Obstetrics and Gynecology, Shahida Islam Medical College, Lodhran, from 03 May 2024 to 02 November 2024, after obtaining ethical approval from the institutional review committee (Approval No. SIMC/ET.C./0041/24). Given the quasi-experimental design, formal randomization and allocation concealment were not implemented. Eligible participants were allocated sequentially into two groups using an alternate allocation method at the time of enrollment. This allocation approach was applied uniformly throughout the study period to minimize selection bias, and baseline demographic and obstetric characteristics were assessed and found to be comparable between the two groups. The sample size was calculated using the WHO-recommended formula for comparison of two independent group means as described by Lwanga and Lemeshow [12]. The formula used was $n = 2(Z\alpha/2 + Z\beta)^2 \sigma^2 / (\mu_1 - \mu_2)^2$, where n represents the required sample size per group, $Z\alpha/2 = 1.96$ for a 95% confidence level, $Z\beta = 0.84$ corresponding to 80% study power, σ denotes the pooled standard deviation, and $(\mu_1 - \mu_2)$ represents the expected difference in mean blood loss. A previously published study by Bose and Beegum reported mean blood loss of 416.0 ± 135.77 mL in the tranexamic acid group and 505.83 ± 214.94 mL in the misoprostol group. Using these values, the pooled standard deviation was calculated as 179.17 mL and the expected mean difference as 89.83 mL. The calculated sample size was 63 participants per group, resulting in a total sample size of 126 patients [13]. A non-probability consecutive sampling technique was employed. Women aged 20–40 years with singleton pregnancies at or beyond 37 weeks of gestation undergoing elective lower segment cesarean section under spinal anesthesia were included after obtaining written informed consent. Patients with multiple pregnancies, placenta previa or placenta accreta spectrum, antepartum hemorrhage, known coagulopathy or thromboembolic disease, hypersensitivity to the study drugs, or preoperative hemoglobin levels below 10 g/dL were excluded. Baseline demographic and obstetric data, including age, gravida, parity, and history of abortion, were obtained from patients' medical records and obstetric charts at the time of admission. Participants were allocated into two treatment groups. In the tranexamic acid group, patients received 1 g of tranexamic acid administered intravenously over 10 minutes immediately after delivery of the neonate and clamping of the umbilical cord. This dose and route were selected based on previously published randomized controlled trials demonstrating efficacy in reducing blood loss during cesarean section. In the misoprostol group, patients received 800 µg of misoprostol administered rectally after delivery of the neonate. The rectal route was chosen due to its sustained uterotonic effect, improved bioavailability, and reduced gastrointestinal adverse effects. The selected dose is consistent with standardized obstetric protocols for hemorrhage prevention. All patients in both groups received 10 IU of oxytocin following placental delivery as part of routine uterotonic management. Due to the different routes of administration of tranexamic acid and misoprostol, blinding of surgeons and operating room staff was not feasible. To minimize observer bias, standardized methods for blood loss estimation were applied uniformly in all cases. Postoperative hemoglobin assessment and data recording were performed by personnel who were not involved in group allocation or intraoperative management. Intraoperative blood loss was estimated using a standardized method for all participants. Blood collected in suction bottles was measured directly at the end of surgery after exclusion of amniotic fluid. Blood loss from surgical mops was estimated using the gravimetric method, assuming that a 1 g increase in mop weight corresponded to 1 mL of blood. The same estimation technique was applied consistently across both study groups to ensure accuracy and uniformity of measurement. Hemoglobin and hematocrit levels were measured preoperatively and 24 hours postoperatively using automated hematology analyzers in the hospital laboratory following routine quality-controlled procedures. The estimated blood volume for each patient was calculated using the standard formula of 85 mL per kilogram of body weight. The primary outcome measure of

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the study was intraoperative blood loss during cesarean section. Secondary outcome measures included postoperative changes in hemoglobin levels and the requirement for additional uterotonic agents during the immediate postoperative period. Blood transfusion requirements were monitored; however, no patient in either group required transfusion during the study period, and therefore this outcome was not subjected to comparative analysis. Data on operative time, surgeon experience, and specific indications for cesarean section were not collected and were therefore not included in the analysis. All procedures were conducted at the same institution following standardized operative protocols to minimize procedural variability. Adverse effects or side effects related to tranexamic acid or misoprostol were not predefined outcome measures and were not systematically recorded. Patients were observed clinically during and after surgery as part of routine postoperative care; however, no structured documentation of adverse events was undertaken. Consequently, side-effect profiles such as nausea, vomiting, or shivering were not formally compared between the two groups. The collected data were entered and analyzed using SPSS version 26.0. Continuous variables, including age, intraoperative and postoperative blood loss, hemoglobin, hematocrit, and estimated blood volume, were assessed for normality using the Shapiro–Wilk test and visual inspection of histograms. As the data demonstrated approximate normal distribution, continuous variables were expressed as mean ± standard deviation. Categorical variables such as gravida, parity, and history of abortion were presented as frequencies and percentages. The mean intraoperative blood loss between the tranexamic acid and misoprostol groups was compared using the independent samples t-test. Stratified analyses were performed according to gravida, parity, and abortion history to assess their potential influence on outcomes. A p-value of 0.005 or less was considered statistically significant.

RESULTS

A total of 126 women were analyzed (63 received tranexamic acid and 63 received misoprostol). Intraoperative blood loss averaged 282.97 ± 82.80 mL with tranexamic acid and 366.68 ± 116.01 mL with misoprostol. Postoperative loss was 125.83 ± 55.99 mL and 176.29 ± 63.23 mL, respectively. Pre-operative hemoglobin was 11.67 ± 1.23 g/dL in the tranexamic acid group versus 11.50 ± 1.14 g/dL in the misoprostol group; 24-hour values were 10.92 ± 1.28 g/dL and 10.24 ± 1.07 g/dL. Pre-operative hematocrit measured 34.88 ± 3.76% and 34.37 ± 3.43%, falling to 32.49 ± 3.94% and 30.44 ± 3.49% at 24 hours. Estimated blood volume was 6132.62 ± 616.67 mL with tranexamic acid and 5974.33 ± 630.28 mL with misoprostol (Table 1).

Table 1: Descriptive Statistics of Blood Loss and Hematological Parameters in Both Study Groups

Variables	Tranexamic Acid Group	Misoprostol Group
Intraoperative blood loss (mL)	282.97 ± 82.80	366.68 ± 116.01
Postoperative blood loss (mL)	125.83 ± 55.99	176.29 ± 63.23
Hemoglobin (pre-op) (g/dL)	11.67 ± 1.23	11.50 ± 1.14
Hemoglobin (24 hr post-op) (g/dL)	10.92 ± 1.28	10.24 ± 1.07
Hematocrit (pre-op) (%)	34.88 ± 3.76	34.37 ± 3.43
Hematocrit (24 hr post-op) (%)	32.49 ± 3.94	30.44 ± 3.49
Estimated Blood Volume (mL)	6132.62 ± 616.67	5974.33 ± 630.28

For intraoperative blood loss, the between-group difference was −83.71 mL (tranexamic acid minus misoprostol), with a 95% CI of −119.29 to −48.14 mL and p<0.001, indicating lower blood loss with tranexamic acid during surgery (Table 2).

Table 2: Comparison of Intraoperative Blood Loss in the Two Study Groups

Group	n	Mean ± SD (mL)	Mean Difference (TXA–Miso)	95% Confidence Interval	p-value
Tranexamic Acid Group	63	282.97 ± 82.80	—	—	—
Misoprostol Group	63	366.68 ± 116.01	—	—	—
Independent t-Test	—	—	−83.71 mL	−119.29 to −48.14	<0.001*

(*) indicates a statistically significant difference at p≤0.005*

Among primigravida, intraoperative loss was 312.24 ± 91.55 mL (tranexamic acid) vs 394.25 ± 133.68 mL (misoprostol); mean difference −82.01 mL, 95% CI −151.92 to −12.11, p = 0.023. For multigravida, values were 268.88 ± 75.82 mL vs 342.50 ± 108.41 mL; difference −73.62 mL, 95% CI −119.40 to −27.84, p=0.002. In grand multipara, results were 266.00 ± 76.24 mL vs 382.71 ± 58.19 mL; difference −116.71 mL, 95% CI −193.31 to −40.12, p=0.006 (Table 3).

Table 3: Stratified Analysis of Intraoperative Blood Loss According to Gravida

Gravida Category	Group	n	Mean ± SD (mL)	Mean Difference (TXA–Miso)	95% CI	p-value
Primigravida	Tranexamic Acid	22	312.24 ± 91.55	−82.01	−151.92 to −12.11	0.023*
	Misoprostol	25	394.25 ± 133.68			
Multigravida	Tranexamic Acid	36	268.88 ± 75.82	−73.62	−119.40 to −27.84	0.002*
	Misoprostol	32	342.50 ± 108.41			
Grand Multipara	Tranexamic Acid	5	266.00 ± 76.24	−116.71	−193.31 to −40.12	0.006*
	Misoprostol	6	382.71 ± 58.19			

(*) indicates a statistically significant difference at p ≤ 0.005*

Among primipara, losses were 279.86±69.12 mL vs 351.72 ± 73.22 mL; difference −71.86 mL, 95% CI −113.86 to −29.86, p=0.001. For multipara, 289.00 ± 86.00 mL vs 380.28±137.57 mL; difference −91.28 mL, 95% CI −146.19 to −36.38, p=0.001. In grand multipara, 253.20±122.33 mL vs 356.50 ± 146.22 mL; difference −103.30 mL, 95% CI −289.76 to 83.16,

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p=0.242 (Table 4).

Table 4: Stratified Analysis of Intraoperative Blood Loss According to Parity

Parity Category	Group	n	Mean ± SD (mL)	Mean Difference (TXA–Miso)	95% CI	p-value
Primipara	Tranexamic Acid	22	279.86 ± 69.12	−71.86	−113.86 to −29.86	0.001*
	Misoprostol	25	351.72 ± 73.22			
Multipara	Tranexamic Acid	36	289.00 ± 86.00	−91.28	−146.19 to −36.38	0.001*
	Misoprostol	32	380.28 ± 137.57			
Grand Multipara	Tranexamic Acid	5	253.20 ± 122.33	−103.30	−289.76 to 83.16	0.242
	Misoprostol	6	356.50 ± 146.22			

Asterisk (*) indicates statistically significant difference at p≤0.005*

Among women without prior abortion, intraoperative loss was 287.22 ± 84.32 mL (tranexamic acid) vs 388.03 ± 122.70 mL (misoprostol); difference −100.80 mL, 95% CI −143.21 to −58.39, p<0.001. In those with prior abortion, values were 257.44 ± 71.89 mL vs 329.57 ± 94.70 mL; difference −72.12 mL, 95% CI −143.74 to −0.50, p=0.049 (Table 5).

Table 5: Stratified Analysis of Intraoperative Blood Loss According to Abortion History

Abortion History	Group	n	Mean ± SD (mL)	Mean Difference (TXA–Miso)	95% CI	p-value
No History of Abortion	Tranexamic Acid	54	287.22 ± 84.32	−100.80	−143.21 to −58.39	<0.001*
	Misoprostol	40	388.03 ± 122.70			
History of Abortion	Tranexamic Acid	9	257.44 ± 71.89	−72.12	−143.74 to −0.50	0.049*
	Misoprostol	23	329.57 ± 94.70			

Asterisk (*) indicates statistically significant difference at p ≤ 0.005*

DISCUSSION

The present quasi-experimental study demonstrates that tranexamic acid was more effective than misoprostol in reducing intraoperative blood loss during elective cesarean section. This finding is consistent with the randomized controlled study by Bose and Beegum, who reported that tranexamic acid significantly reduced intraoperative blood loss, perioperative hemoglobin decline, and the need for additional uterotonic agents compared with misoprostol, particularly in women without high baseline risk for hemorrhage [13]. The observed superiority of tranexamic acid in the current study may be attributed to its antifibrinolytic mechanism, whereby it inhibits plasminogen activation and stabilizes fibrin clot formation, thereby reducing surgical bleeding. In contrast, misoprostol primarily exerts its effect through uterine contraction, which may be less effective in controlling intraoperative blood loss where vascular disruption and tissue trauma coexist with uterine atony [14]. Contrasting findings have been reported in the literature. Hussein *et al.* observed that intrauterine misoprostol resulted in lower calculated blood loss compared with preoperative tranexamic acid in women undergoing cesarean section [14]. Similarly, Pakniat *et al.* reported reduced total blood loss, suction volume, and postoperative hemoglobin decline in patients receiving misoprostol compared with tranexamic acid [15]. These discrepancies may be explained by variations in drug dosage, route of administration, timing relative to skin incision or placental delivery, differences in baseline hemorrhage risk, and variability in surgical technique and blood loss estimation methods. Other studies have reported comparable efficacy between tranexamic acid and misoprostol. Dawoud *et al.* demonstrated that both agents were effective in reducing intraoperative and postoperative blood loss compared with oxytocin alone, with no statistically significant difference between the two interventions [16]. Similar findings were reported by Deeksha *et al.* who observed equivalent efficacy of tranexamic acid and misoprostol, with a slight advantage to tranexamic acid in terms of blood conservation and fewer side effects in low-risk cases [17]. Ogah *et al.* also reported no significant difference in mean intraoperative blood loss between tranexamic acid and misoprostol, although shivering was more frequently observed in the misoprostol group [18]. Evidence from recent meta-analyses further highlights this variability. Cheema *et al.* reported that tranexamic acid significantly reduced mean blood loss, hemoglobin decline, and transfusion requirements, particularly when administered before skin incision [19]. In contrast, Abu-Zaid *et al.* found no meaningful difference between tranexamic acid and misoprostol with respect to blood loss, hemoglobin change, uterotonic requirement, or transfusion rates, suggesting therapeutic equivalence [20]. Collectively, these findings indicate that both agents are effective in reducing blood loss during cesarean delivery, with relative efficacy influenced by study design and clinical context. Although tranexamic acid and misoprostol act through different pharmacological mechanisms, the present study evaluated these agents as individual interventions and did not assess their combined use. Therefore, no recommendation can be made regarding routine combination therapy based on the current findings. Given the complementary mechanisms of action, future well-designed randomized controlled trials may explore the efficacy and safety of combined tranexamic acid and misoprostol administration for improved hemostatic control during cesarean section.

This study has several limitations. Operative time, surgeon experience, and specific indications for cesarean section were not recorded and therefore could not be controlled for, which may have influenced intraoperative blood loss. Additionally, blinding of surgeons and operating room staff was not feasible due to the differing routes of drug

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administration, which may have introduced observer bias during intraoperative blood loss estimation. Adverse effects related to tranexamic acid and misoprostol were not systematically monitored or documented, and side-effect profiles such as nausea, vomiting, and shivering were not formally assessed, limiting comparison of safety outcomes between the two interventions. Furthermore, estimation of blood loss using gravimetric and visual assessment methods may be subject to inter-observer variability. Despite these limitations, the study provides clinically relevant comparative data using standardized operative protocols in a uniform institutional setting.

CONCLUSIONS

Results of this study showed that preoperative use of Tranexamic Acid is associated with significantly lower intraoperative blood loss as compared to Misoprostol in obstetric patients undergoing C-section. This effect remained consistent after stratification of gravida, parity groups, and history of abortion. These findings suggest that Tranexamic Acid is a more effective uterotonic adjunct for reducing intraoperative blood loss during C-section. Incorporating Tranexamic Acid into perioperative management protocols may help minimize maternal blood loss and reduce the need for blood transfusion, thereby improving postoperative outcomes

Authors' Contribution

Conceptualization: TP
Methodology: Q, S
Formal analysis: Q, TT, MKJ, SUN, S
Writing and Drafting: TT, MKJ
Review and Editing: TP, Q, TT, MKJ, SUN, S

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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