The Egyptian Journal of Hospital Medicine (January 2025) Vol. 98, Page 211- 214

Intravenous Tranexamic Acid for Reducing Blood Loss in Cesarean Myomectomy: A Double-Blind Randomized Controlled Trial

Aly Mohamed Abdel-Bagy, Adham Badawy*,
Nahla W. Shady, Hany F. Sallam, Sherif Salah Eldeen Fahmy, Reham Essam Mohamed
Department of Obstetrics and Gynecology, Faculty of Medicine, Aswan University, Egypt
***Corresponding author:** Adham Badawy, **Mobile: (+20)** 01002416620, **E-mail:** adham_badawy@yahoo.com

ABSTRACT

Background: Cesarean myomectomy is a high-risk surgical procedure associated with significant intraoperative blood loss. Tranexamic acid (TXA), an antifibrinolytic agent, has shown efficacy in reducing perioperative blood loss in various obstetric surgeries. However, its specific effects in Cesarean myomectomy remain underexplored.

Objective: This study aimed to evaluate the efficacy and safety of intravenous TXA in reducing blood loss during Cesarean myomectomy.

Patients and methods: This double-blind, randomized controlled trial was performed in Aswan University Hospital. Pregnant women undergoing Cesarean myomectomy were randomly assigned to receive intravenous TXA or placebo before skin incision, 39 in each group. The primary end point was total intraoperative blood loss. Secondary outcomes assessed were blood transfusion requirement, hemoglobin and hematocrit levels difference, postpartum hemorrhage (PPH) rate and adverse events.

Results: Intraoperative blood loss was significantly lower in the TXA group (medians 700 mL [IQR 101] vs 950 mL [IQR 150] in the placebo group, $p < 0.001$). Similarly, the use of red blood cell transfusion was less in the TXA group (median 0 units [IQR 1]) vs. the placebo group (median 2 units [IQR 2], $p < 0.001$). The TXA group had greater postoperative hemoglobin and hematocrit levels. The incidence of PPH was significantly lower in the TXA group (25.7%) than in the placebo group (51.4%, $p = 0.027$). No thromboembolic events or other significant adverse effects were observed.

Conclusion: Intravenous TXA significantly reduced blood loss and transfusion requirements in women undergoing Cesarean myomectomy, with no increase in adverse events. TXA is a valuable adjunct in managing perioperative blood loss during this complex procedure.

Keywords: Tranexamic acid, Cesarean myomectomy, Blood loss, Postpartum hemorrhage.

INTRODUCTION

Cesarean myomectomy, the surgical removal of uterine fibroids during Cesarean delivery, is a challenging procedure and is associated with substantial intraoperative blood loss [1, 2]. Uterine fibroids, which occur in up to 80% of women of reproductive age and are benign tumors, can be pregnancy adversaries and complicate delivery [3].

Although Cesarean myomectomy provides the dual advantage of both fibroid excision and delivery, it is frequently avoided because of fears of hemorrhage, transfusion dependency, and peripartum morbidity [4, 5]. Identifying strategies to mitigate these risks is essential to improving outcomes in this high-risk population. There is evidence that tranexamic acid (TXA), an antifibrinolytic agent, can help control post-operative bleeding in many surgical procedures. TXA has the effect of stabilizing clots and reducing blood loss by inhibiting the process of fibrinolysis [6].

Previous research has demonstrated the efficacy of TXA in decreasing blood loss during myomectomy and Cesarean section when these procedures are performed separately. However, the use of TXA specifically in the setting of Cesarean myomectomy has not been extensively investigated. While, the isolated impacts of TXA in both myomectomy and Cesarean section have already been documented, relevance of TXA within the combined procedure in the context of Cesarean myomectomy appears to be lacking. Also, the bulk of the studies were concerned with the outcomes of the myomectomy only in non-pregnant women. There is also very little or no evidence about the safety and the outcomes of TXA administration where fibroid removal was done in the course of childbirth [7-11].

This study aimed to assess the effectiveness and the safety of intravenous TXA in women undergoing Cesarean myomectomy in decreasing both intra- and post-operative blood loss.

PATIENTS AND METHODS

Study design and participants: This study was a double-blind, randomized, placebo-controlled trial conducted at Aswan University Hospital. Eligible participants were randomized in a 1:1 ratio to receive either intravenous TXA or placebo (normal saline) prior to Cesarean myomectomy.

The study included 78 pregnant women aged 18-45 years scheduled for Cesarean myomectomy.

Inclusion criteria: Participants were required to have symptomatic uterine fibroids confirmed by preoperative imaging, specifically including at least one fibroid measuring 10 cm or larger, multiple fibroids numbering five or more of any size, or any intramural or broad ligament fibroid measuring 6 cm or larger. The gestational age was required to be 37 weeks or greater.

Received: 23/09/2024
Accepted: 24/11/2024

Exclusion criteria: Participants were excluded if they had known hypersensitivity to TXA, a history of thromboembolic disorders, ischemic heart disease and coagulopathy. Renal or hepatic impairment, and pre-existing conditions requiring anticoagulation therapy.

Sample size calculations: Calculation made by MedCalc V 23, based on a previous study [12]. We estimated a mean intraoperative blood loss of 896.81 mL (SD 519.6 mL) in the placebo group, and a mean intraoperative blood loss of 583.23 mL (SD 379.62 mL) in the TXA administration group, with a two-sided alpha of 0.05 and 80% power, a total of 70 participants (35 per group) is required. Accounting to 10% dropout rate, the total sample size for the study was 78 participants (39 per group).

Randomization and blinding: The research team employed computer-generated permuted blocks for randomization, stratifying participants by fibroid size. The pharmacy department prepared blinded study drugs, ensuring that only pharmacy staff knew the group assignments.

Intervention: Participants in the TXA group received a 1 g bolus dose of intravenous TXA over 10 minutes before the skin incision, followed by a continuous infusion of 1 g over the next 8 hours. The placebo group was given a similar volume of 0.9% saline solution following the same protocol.

Surgical procedure: The surgical procedure was consistent for all participants. General anesthesia was administered by the anesthesiologist. A standard Cesarean section was performed, followed by myomectomy. Blood loss was carefully measured by adding the volume from suction canisters and the weight of surgical sponges.

Ethical approval: The study proposal was approved by the Institutional Review Board (IRB) of Aswan University Hospital. Prior to enrollment, all individuals provided written informed consents. The study adhered to the principles outlined in the Declaration of Helsinki.

Statistical analysis

Data analysis was performed using SPSS version 29.0, with statistical significance set at $p \leq 0.05$. Various statistical tests were used, including the Shapiro-Wilk test, the independent sample t-test, the Chi-square test, and the Mann-Whitney U test. P values that were ≤ 0.05 were supposed to be statistically significant.

RESULTS

The study found no significant differences between the groups regarding age or gestational age (Table 1).

Table (1): Comparison between TXA group and control group according to age & gestational age

		TXA Group	Control Group	Stat test	P-value
Age	Mean ±SD	32(5.28)	31.45(5.39)	t = 0.425	0.672
	Median (IQR)	32(8)	31(7)		
Gestational age	Mean ±SD	38.057(0.72)	38.057(0.72)	MW= 612	1
	Median (IQR)	38(1)	38(1)		

TXA: Tranexamic Acid, SD: Standard Deviation, IQR: Interquartile Range

Women who received TRX had lower blood loss (710 ml) than the placebo group (891 ml, $p < 0.005$) and required fewer RBC units ($p < 0.005$). Additionally, the difference between preoperative and 24-hours postoperative hemoglobin and hematocrit levels was significantly smaller in the TRX acid group than in the control group ($p < 0.005$) (Table 2).

Table (2): Comparison between TXA group and control group clinical outcome

		TXA Group	Control Group	Stat test	P-value
RBC (unit) transfusion	Mean ±SD	0.428±0.104	1.97±0.44	MW= 169	<0.001
Blood loss	Mean ±SD	710±110	891±124	MW= 183.5	<0.001
	Median (IQR)	700 (101)	950 (150)		
Hb difference	Mean ±SD	0.697±0.19	1.69±0.41	MW= 58.5	<0.001
HCT difference	Mean ±SD	1.65±0.400	4.65± 1.15	MW= 74	<0.001
PPH	Yes	9 (25.7%)	18 (51.4%)	X^2= 4.884	0.027
	No	26 (74.3%)	17 (48.6%)		

RBC: Red Blood Cells, Hb: Hemoglobin, HCT: Hematocrit, PPH: Postpartum Hemorrhage, MW: Mann-Whitney Test, X^2: Chi-square Test

DISCUSSION

This study revealed that intravenous TXA during Cesarean myomectomy decreased intraoperative blood loss, the need for blood transfusions, and the incidence of PPH. These findings align with previous research highlighting the hemostatic benefits of TXA in various obstetric settings, including Cesarean deliveries and standalone myomectomies.

Ortuanya *et al.* [13] demonstrated that prophylactic TXA reduces postpartum blood loss, enhances postpartum hemoglobin levels, decreases the use of uterotonics, and protects against PPH in high-risk pregnant women during Cesarean section. Our findings extend these observations specifically to the complex scenario of concurrent myomectomy, where the surgical complexity and hemorrhagic risk are substantially elevated. **Sentilhes *et al.*** [14] found in a multicenter, double-blind trial that TXA reduced blood loss over 1000 mL and the need for RBC transfusion by day 2 postpartum. These findings align with the hemostatic benefits of TXA observed in our study.

Likewise, a randomized controlled trial conducted by **Olaleye *et al.*** [8] showed that TXA reduced blood loss associated with myomectomy.

The study's secondary outcomes further underscore TXA's clinical utility. Patients in the TXA group demonstrated significantly lower red blood cell transfusion requirements and reduced hemoglobin and hematocrit level variations. In the TXA group, the rate of PPH was significantly lower, with only 25.7% of patients experiencing blood loss exceeding 1L compared to 51.4% in the control group. Similarly, these findings corroborate **Cheema *et al.*'s** [10] recent meta-analysis, which highlighted the potential TXA's function in limiting excessive blood loss during Cesarean deliveries. In terms of safety, **Pacheco *et al.*** [15] found no difference in thromboembolic events between the TXA and placebo groups, suggesting that TXA has a favorable safety profile. This is consistent with our findings, where TXA administration was not associated with any significant adverse events.

We have confirmed other studies on the possible usefulness of TXA in surgical procedures that need blood loss control. The cited mechanisms (clot stabilization, and inhibition of fibrinolysis) appear to be especially effective in the context of Cesarean myomectomy. TXA stabilizes the clot and minimizes continuous blood loss by interfering with the fibrinolytic process, potentially reducing maternal morbidity [6].

LIMITATIONS

Our single-center study may limit the generalizability of the results. Additionally, while short-term benefits of TXA were evident, long-term maternal outcomes require further investigations. Future research should focus on multicenter trials and extended follow-up periods to confirm TXA's efficacy and safety in Cesarean myomectomy.

CONCLUSION

Our study provided great evidence to recommend the use of intravenous TXA during Cesarean myomectomy procedure to minimize blood loss during surgery as well as to reduce the number of women who may need to be transfused, and who will develop PPH. These findings confirmed the existing literature on the use of TXA in surgical procedures. Also, there is certainly a need for blood management medications in complicated surgeries that include TXA in their management.

No funding.
No conflict of interest.

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