

Effect of Tranexamic Acid on Blood Loss in Elective Cesarean Delivery

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Abstract

Background: tranexamic acid as an agent given before surgical procedures reduces the blood transfusion risk, mean volume lost, and the requirement for reintervention due to bleeding issues, without raising thrombotic risks.

Aim: to evaluate Tranexamic acid agent infusion as regards its efficacy in blood volume loss reduction in practice of elective lower segment cesarean section delivery.

Patients and Methods: A double blinded, randomized, controlled research clinical trial. All study subjects have been recruited from the cases scheduled for elective cesarean delivery in the labor ward of Mokattam Insurance Hospital. The study subjects were totally 200 cases allocated in by randomization into 2 research groups. The study research group have been composed of 100 cases that were administered a mixture of tranexamic acid 25mg/kg in 200 ml of normal saline by intravenous drip for 20 minutes before incision, while the control research group contained 100 cases administered a volume of normal saline in accordance to patient's weight (25 mg/kg) by intravenous drip for 20 minutes before time of incision.

Results: Blood loss volume was statistically significantly lower among Tranexamic research group than among placebo research group (p value <0.001). Postoperative hematocrit was statistically significantly higher among Tranexamic research group than among placebo research group (p value =0.020). Hematocrit reduction was statistically significantly lower among Tranexamic research group than among placebo research group (p value <0.001). PPH and blood transfusion were statistically significantly less frequent among Tranexamic research group (p values=0.010, 0.005 consecutively).

Conclusions and Recommendation: The administration of tranexamic acid before starting a cesarean section is valuable as a prophylaxis against intra-operative and post-partum bleeding issues.

Future research studies are required to consider various variables such as racial and ethnic differences and consider various clinical case scenarios e.g. previous cesarean delivery and categorization of more possible critical indications of cesarean such as second stage cesarean, emergency cesarean section and time interval of decision to incision as those variables could influence blood volume loss indices.

Introduction

Postpartum hemorrhage is defined clinically as blood loss of 500 cc or more within 24 hours after delivery. Statistical estimates of its incidence in the research studies differ widely, from 3 % to 15 % of deliveries⁽¹⁾. About one in five of these hemorrhages progress to severe form that could jeopardize maternal life or future fertility and causes hazardous risks exposure to issues transfusion, surgical intervention, and intensive care admission⁽²⁾. Post partum hemorrhage is considered a leading cause for maternal mortality and accounting for around 25% of all maternal mortalities globally⁽³⁾. Its clinically expected risk factors involve prior history of post partum hemorrhage, multi parity, obesity, prolonged or augmented course of labor, multifetal gestation, prior cesarean mode of delivery, polyhydramnios, and macrosomia⁽⁴⁾. Tranexamic acid is a synthetic derivative of the

amino acid lysine that has an antifibrinolytic pharmacological impact via the reversible blockage of the lysine binding sites on plasminogen molecules⁽⁵⁾. Intravenous administration of Tranexamic acid have been routinely implemented for management and prevention of bleeding with satisfactory results research findings from previous research trials have displayed that Tranexamic acid in elective surgical procedure decreases the blood transfusion risk, mean volume transformed, and the requirement for re-operation due to active bleeding, without raising thrombotic events⁽⁶⁻¹⁰⁾.

Aim

The current research main goal is to assess and evaluates Tranexamic Acid infusion as regards the efficiency in blood loss reduction during elective lower segment cesarean section delivery.

Patients and Methods

The current research study is a double blinded, randomized, controlled research trial. All study subjects have been recruited from the cases admitted for elective cesarean delivery in the labor ward of Mokattam Insurance Hospital. The research study performance was started after approval of research study protocol by Research and Ethical Committee of the department of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University. A cohort of 200 cases have been recruited in the research study after clarifying the procedure and taking a written consent from every case that is going to participate in the research study. The cases have been randomized into 2 research groups. Study research group composed of 100 cases that will be administered a mixture of tranexamic acid 25mg/kg in 200 ml of normal saline intravenous drip 20 minutes before making the skin incision, control research group composed of 100 cases received a volume of normal saline according to patient's weight (25 mg/kg) intravenous drip 20 minutes before making the skin incision. Inclusive research criteria involved the following, case age from 25-40 years, BMI (20-28) Kg/m², Gestational age > 37 weeks, Singleton pregnancy. Exclusive research criteria, medical disorders: e.g. Hypertension, Diabetes mellitus, liver, kidney, Cardiac diseases, Pregnancy-induced disorders e.g. pre-eclampsia, eclampsia. Over distended uterus e.g. polyhydramnios, fetal macrosomia, accidental hemorrhage, Placenta previa,

Previous atonic postpartum hemorrhage, cases on medications: e.g. anticoagulants and antiplatelets, Multifetal gestations, pregnancy less than 37 weeks gestation, contraindications to tranexamic acid: e.g. Allergy, blood diseases. Estimation of blood loss by observation of blood loss by suction, towels and pads were placed under women buttocks then weighting the pads.

Primary research outcome:

The primary research outcome of this study is to investigate the reduction of blood loss ≤ 500 cc as assessed by suction, towels, pads placed under women buttocks then weighting the pads to allow objective measurement of blood loss just after delivery of the baby.

Secondary research outcome:

Investigating and observing severe PPH (>1000 cc), the incidence of women requiring supplementary uterotonic agents, blood transfusion, or emergency surgery for treatment of PPH.

Only three patients needed blood transfusion, two patients had attack of PPH, no mortality and four patients were excluded.

Written informed consent was obtained from all study subjects before recruitment in the study after explanation of the purpose and procedures of the study.

Results

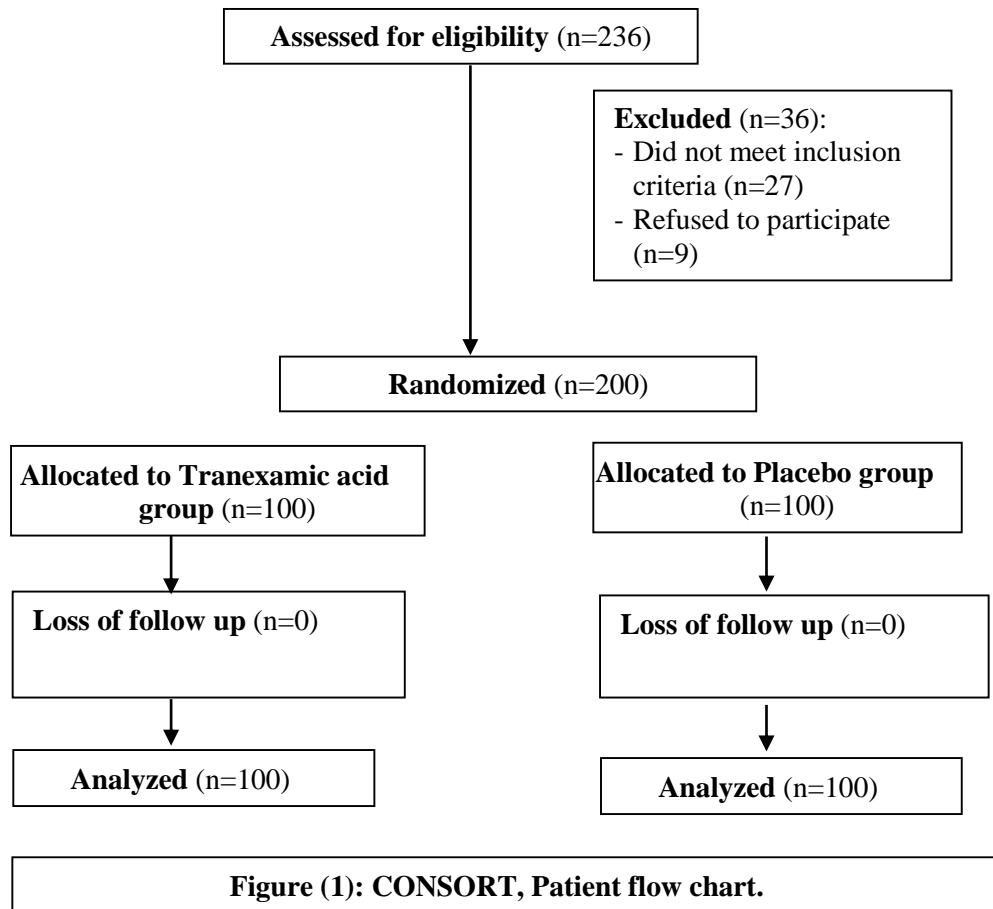


Table (1): Demographic characteristics among the studied groups

Items	Measure	Tranexamic (N=100)	Placebo (N=100)	P
Age (years)	Mean±SD	31.8±3.8	32.5±3.4	^0.174
	Range	25.0–40.0	26.0–40.0	
BMI (kg/m ²)	Mean±SD	24.2±1.2	24.1±1.2	^0.658
	Range	20.6–27.3	20.4–26.8	
GA (weeks)	Mean±SD	39.3±1.0	39.2±1.2	^0.424
	Range	37.0–42.0	37.0–42.0	
Indications (n, %)	Dystocia	36 (36.0%)	39 (39.0%)	#0.893
	Fetal distress	26 (26.0%)	27 (27.0%)	
	Malpresentation	20 (20.0%)	14 (14.0%)	
	Prolonged labor	10 (10.0%)	12 (12.0%)	
	CPD	6 (6.0%)	5 (5.0%)	
	Others	2 (2.0%)	3 (3.0%)	

^Independent t-test, #Chi square test

No significant statistical difference between the studied groups regarding demographic characteristics (age, BMI, Gestational age, indications for cesarean section p values =0.174, 0.658, 0.424, 0.893, consecutively).

Table (2): Hemoglobin (gm/dL) among the studied groups

Variable	Measure	Tranexamic (N=100)	Placebo (N=100)	^P
Pre operative	Mean±SD	12.5±0.8	12.6±0.9	0.258
	Range	10.6–14.3	10.3–14.4	
Post operative	Mean±SD	11.7±0.8	11.4±0.9	0.027*
	Range	9.9–13.4	9.2–13.2	
Reduction	Mean±SD	0.8±0.1	1.2±0.1	<0.001*
	Range	0.5–1.1	0.9–1.5	
Value of Tranexamic acid				
Value		Mean±SE		95% CI
Reduction difference		0.41±0.02		0.37–0.44

^Independent t-test, CI: Confidence interval, *Significant

Table (2) and figure (2) show that: No significant difference between the studied groups regarding preoperative hemoglobin. Postoperative hemoglobin was significantly higher among Tranexamic group than among placebo group (p value 0.027) Hemoglobin reduction was significantly lower among Tranexamic group than among placebo group (p value <0.001).

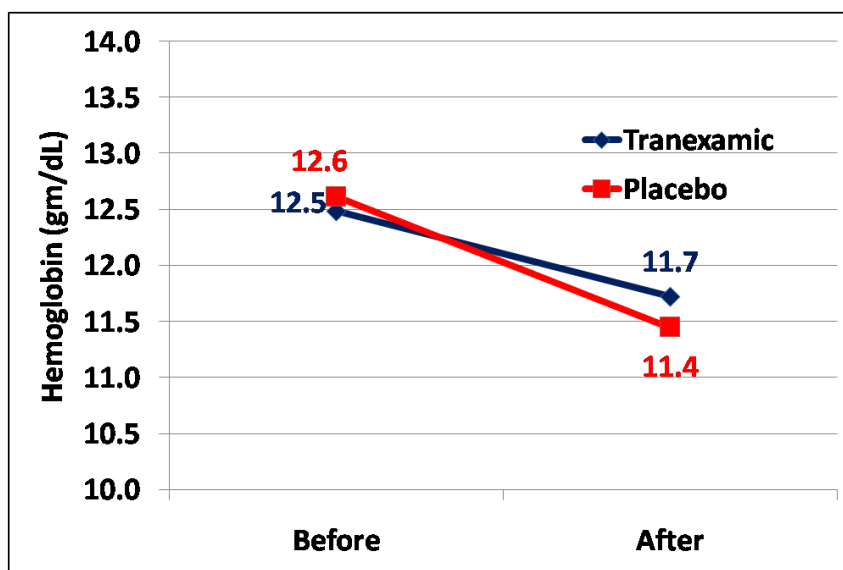


Figure (2): Hemoglobin among the studied groups

Table (2): Hematocrit (%) among the studied groups

Variable	Measure	Tranexamic (N=100)	Placebo (N=100)	^P
Pre operative	Mean±SD	41.3±3.2	41.9±4.1	0.247
	Range	31.2–49.3	31.0–51.0	
Post operative	Mean±SD	38.8±3.2	37.5±4.1	0.020*
	Range	28.7–46.8	27.2–46.6	
Reduction	Mean±SD	2.5±0.4	4.3±0.3	<0.001*
	Range	1.7–3.7	3.0–4.9	
Value of Tranexamic acid				
		Mean±SE	95% CI	
Reduction difference		1.83±0.05	1.74–1.92	

^Independent t-test, CI: Confidence interval, *Significant

Table (2) and figure (3) show that: No statistical significant difference between the research study groups as regards preoperative hematocrit (p value =0.247). Postoperative hematocrit was statistically significantly higher among Tranexamic research group than among placebo research group (p value =0.020). Hematocrit reduction was statistically significantly lower among Tranexamic research group than among placebo research group (p value <0.001).

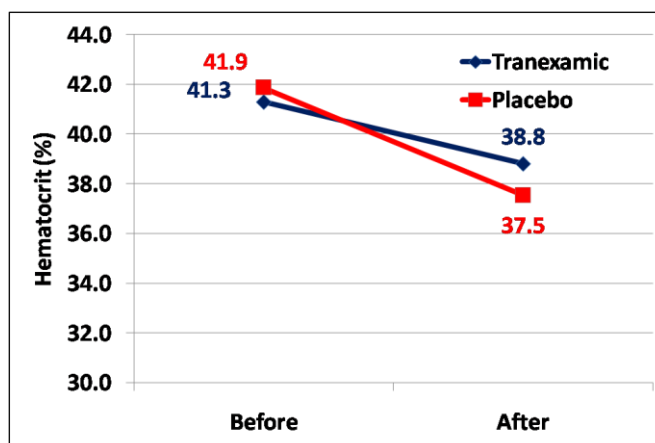


Figure (3): Hematocrit among the studied groups

Table (3): Blood loss volume (mL) among the studied groups

Measure	Tranexamic (N=100)	Placebo (N=100)	^P
Mean±SD	257.6±42.7	441.9±65.2	<0.001*
Range	161.3–384.9	307.7–631.5	
Value of Tranexamic acid			
Value	Mean±SE	95% CI	
Blood loss reduction	184.3±7.8	168.9–199.7	

^Independent t-test, CI: Confidence interval, *Significant

Table (3) shows that: Blood loss volume was statistically significantly lower among Tranexamic research group than among placebo research group (p value <0.001).

Table (4): Maternal complications and side effects among the studied groups

Conditions	Tranexamic (N=100)	Placebo (N=100)	P	RR (95% CI)
PPH	2 (2.0%)	11 (11.0%)	#0.010*	0.29 (0.08–1.06)
Blood transfusion	1 (1.0%)	10 (10.0%)	#0.005*	0.17 (0.03–1.13)
Others	0 (0.0%)	0 (0.0%)	--	--

#Chi square test, *Significant, RR: Relative risk, CI: Confidence interval

Table (4) show that: PPH and blood transfusion were statistically significantly less frequent among Tranexamic research group (p values=0.010, 0.005 consecutively).

Table (5): Comparison between the studied groups regarding neonatal condition

Scores		Tranexamic (N=100)	Placebo (N=100)	P	RR (95% CI)
APGAR 1	Mean±SD	7.9±1.3	8.0±1.6	^0.496	--
	Range	3.0–10.0	3.0–10.0		
APGAR 5	Mean±SD	8.9±1.0	8.9±1.3	^0.673	--
	Range	4.0–11.0	4.0–11.0		
RDS		1 (1.0%)	2 (2.0%)	&1.000	0.66 (0.13–3.31)
NICU		2 (2.0%)	4 (4.0%)	&0.683	0.66 (0.21–2.06)
Death		1 (1.0%)	1 (1.0%)	&1.000	1.00 (0.25–4.03)

^Independent t-test, &Fisher's Exact test, *Significant

Table (5) show that: No significant statistical difference between the studied groups regarding neonatal condition (APGAR 1min, 5min, RDS, NICU, Death, p values =0.496, 0.673, 1.00, 0.683, 1.00, consecutively).

Discussion

The current research study was conducted to evaluate efficacy of usage of tranexamic acid to decrease blood loss intra-operative in cases undergoing cesarean section deliveries ⁽¹¹⁾.

Intra-operative blood loss and post partum hemorrhage could be avoided through the use of prophylactic utero-tonics by timely and appropriate management. Nevertheless, it has been clearly shown that the administration of

uterotonics, and in particular oxytocin is effective in preventing PPH. On the other hand enhancement of chemical hemostasis, a complementary biochemical hemostatic impact could be predictable from the complementary usage of prohemostatic agents e.g Tranexamic acid in its chemical nature a synthetic derivative of the lysine amino acid that have an antifibrinolytic pharmacological impact via

reversible blockage of the lysine binding sites on plasminogen molecules. Intravenous administration of Tranexamic acid have been classically applied in practice for management and prevention of bleeding issues with encouraging clinical results⁽¹²⁾.

As regards the current research study results no statistically significant difference between the studied groups regarding demographic characteristics. (age, BMI, Gestational age, indications for cesarean section p values =0.174,0.658,0.424,0.893,consecutively). No significant difference between the studied groups regarding preoperative hemoglobin. Postoperative hemoglobin was statistically significantly higher among Tranexamic research group than among placebo research group (p value 0.027) Hemoglobin reduction was statistically significantly lower among Tranexamic group than among placebo research group (**p value <0.001**).

In addition blood loss volume was statistically significantly lower among Tranexamic research group than among placebo research group (p value <0.001). PPH and blood transfusion were statistically significantly less frequent among Tranexamic research group (p values=0.010, 0.005 consecutively).

Finally no statistical significant difference between the studied research groups as regards neonatal condition (APGAR 1min, 5min, RDS, NICU, Death, p values= 0.496, 0.673, 1.00, 0.683, 1.00, consecutively).

In the research study of **Jianjun et al.**⁽¹³⁾ the cases' clinical features and parameters in the two research groups were similar, with no statistical significant difference between the two research groups. The study research group (88 women) was administered Tranexamic acid, whereas the control group 86 women who did not received. In the results the research team of investigators revealed that Tranexamic acid administration statistically significantly decreased the amount of blood volume loss from the end of cesarean section till 2 hours postpartum: (46.6 ± 42.7 ml) in the study research group versus (84.7 ± 80.2 ml) in the control research group (p <0.01), It furthermore statistically significantly decreased the amount of total blood volume from placental delivery to 2 hours postpartum: (379.2 ± 160.1 ml) in the research study group, (441.7 ± 189.5 ml) in the control research group (p value = 0.02). Finally post partum hemorrhage was arrested in

65 cases (75.6%) in the control research group and in 81 cases (92.0%) in the tranexamic acid research group (p<0.01). No statistically significant abnormal vital signs have been noted after TXA administration. Mild temporary side effects existed more often in the tranexamic acid research group than in the control research group⁽¹⁴⁾.

In another research study similar to the current research study in approach and aim of **Sekhvat et al.**⁽¹⁵⁾ research team of investigators, the cases' clinical characteristics in the two research groups were similar, in which there was no statistically significant difference between the two research groups. The study research group involved 45 cases that have been administered tranexamic acid, while the control research group was composed of 45 study subjects that didn't receive tranexamic acid. The findings of the research study revealed that Tranexamic acid statistically significantly decreased the blood volume loss from the end of cesarean delivery till 2 hours postpartum: (28.02 ± 5.53 ml) in the study research group (37.12 ± 8.97 ml) versus in the control research group (p value =0.001), Hb 24 h after cesarean delivery was statistically significantly more in tranexamic research group than control research group (12.57 ± 1.33g/dl in the tranexamic group and 11.74 ± 1.14g/dl in the control research group, p value =0.002). The research team concluded that tranexamic acid as a pharmacological agent could be implemented safely and efficiently to decrease bleeding occurring during cesarean section performance. Another research study conducted similar to the current research study Tranexamic acid statistically significantly decreased amount of total blood volume loss from placental delivery: (241.61 ± 6.77ml) in the study research group, (510.66 ± 7.72 ml) in the control group (p value = 0.0001)⁽¹⁶⁾.

Conclusion and Recommendations:

The usage of tranexamic acid before starting a cesarean section is valuable as a prophylaxis against intra-operative and post-partum bleeding issues as displayed by the current research study results. Further research studies are required by integrating greater number of patients and putting in consideration various variables such as racial and ethnic differences. Another issue that is recommended in future research efforts is to consider various case

scenarios such as previous cesarean and categorization of more possible critical indications of cesarean such as second stage cesarean and emergency cesarean section and time interval of decision to incision as those variables could affect blood volume loss indices. Future research efforts could aid in clinical practice protocols application as regards tranexamic acid usage and safety profiles to be followed on an international levels .

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