

Role of intravenous tranexamic acid on cesarean blood loss: a prospective randomized study

Abstract

Background: Postpartum hemorrhage (PPH) is a major cause of maternal mortality globally. Tranexamic acid (an anti-fibrinolytic agent) is a novel approach to prevent this dreadful complication.

Aim of the work: The aim was to study the efficacy and safety of intravenous tranexamic acid in reducing blood loss during and after the lower segment cesarean section.

Patients and methods: In this prospective randomized clinical study, 200 mothers scheduled for elective CS were randomly selected and divided into two groups (study and control) of 100 each. The study group received 1 g IV tranexamic acid immediately before LSCS. And the control group received 30 ml of 5% glucose, all mothers received 10 units of oxytocin in 500 ml of normal saline.

Results: The mean intraoperative and postpartum blood loss was significantly lower in the study group than the control group.

Conclusion: Preoperative IV tranexamic acid significantly reduced blood loss during elective CS without any significant adverse effects.

Keywords: postpartum hemorrhage, tranexamic acid, cesarean section

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Introduction

Cesarean section (CS) rates nowadays is about 25 to 30 % all over the world and has many complications if compared with vaginal delivery, primary and secondary postpartum hemorrhage constitute about (20%) of these complications. It also associated with increased rate of maternal mortality and morbidity, so it is important to reduce bleeding during and after Cesarean section (CS) delivery.¹ Postpartum hemorrhage (PPH) is blood loss of ≥ 500 mL after vaginal delivery, or ≥ 1000 mL after caesarean section. However, if pre-existing bad health condition as cardiac disease or severe anemia, blood loss of as little as 200 mL is considered life-threatening.² In Cesarean delivery, there is 10% decrease in hematocrit value with 6% incidence of blood transfusion compared with 4% only in vaginal delivery. Multiple medications, such as methylergonovine, oxytocin, prostaglandin F₂ α , and misoprostol, are life-saving to control bleeding in CS.³⁻⁵ TXA is a synthetic derivative of lysine High affinity for lysine binding sites on plasminogen to block plasmin from binding and degrading linked fibrin. TA may enhance the effectiveness of endogenous hemostatic mechanism.^{6,7} TA can be used by intravenous rout to reduce hemorrhage in many surgical operations.^{8,9} In gynecology, especially idiopathic menorrhagia, tranexamic acid was considered well-tolerated and effective oral treatment. In obstetrics, it also can be used in different bleeding conditions (placenta previa and placental abruption).¹⁰

Patients and methods

A randomized, placebo-controlled, clinical study, during the period from June 2018 till March 2019, and after Institutional Ethical Committee approved the protocol. The study carried out on clinically free singleton antenatal women (20–35 years old),

Primary, 2nd or 3rd gravida, more than or equal 38 weeks gestation planed for elective CS with normal range of platelet count. If the pregnant women have allergy to tranexamic acid or with any risk factor for postpartum hemorrhage (PPH) (sever pre-eclampsia, polyhydramnios, fetal macrosomia, multiple gestation, preterm labor, antepartum hemorrhage (placenta previa or accidental hemorrhage), abnormal placentation, fibroid uterus, history of uterine atony or postpartum hemorrhage, and emergency CS, were excluded from the study along with women suffering from any blood disease, anemia (hemoglobin < 10 g %) and any medical or surgical complain. Initially we recruited 220 women admitted for elective CS, 16 were excluded due to different causes (vaginal delivery 7 cases, emergency LSCS 4 cases, fetal distress 2 cases, scar tenderness 3 cases) 4 patients refused to give consent for the study, finally 200 women were allocated for the study and randomly divided into two equal groups (Figure 1).

Patients involved in this study were subdivided into two groups

Group A (Study Group): Included one hundred (100) patients. They were given tranexamic acid (1g/ 10 mL) diluted in 20 mL of 5% glucose and administrated slowly intravenous in a period of 5-minute at least 10 minutes before skin incision.

Group 2 (placebo Group): Included one hundred (100) patients, received 30 mL of 5% glucose. After CS both groups were taken bolus intra venous 5 IU of oxytocin, followed by oxytocin infusion (30 IU in 500 ml lactated Ringer's solution in a period of four hours, also 1 g cefazoline antibiotic diluted in 20 mL normal saline was given slowly intravenous. Vital signs (pulse, blood pressure and respiratory rate) were recorded before operation, after placental delivery, 1 and 2 hour post-partum. Prothrombine time (PT), activated partial

thromboplastine time (aPTT), and blood picture (CBC) were recorded before CS operation and 24 hours later. Volume of blood loss was estimated by the difference in hematocrit values before and one day after cesarean delivery by these two formulas.

- a) Estimated blood volume (EBV) in mL= the woman’s weight in kg × 85.¹¹
- b) Estimated blood loss = (EBV) × $\frac{\text{preop hematocrit} - \text{postop hematocrit}}{\text{preop hematocrit}}$.¹¹

Liver function tests (serum ALT, AST and bilirubin) and renal function tests (serum creatinine and urea) was evaluated day before and day after CS to assess TA side effects. After delivery, 500 mL normal saline with 10 IU were infused intravenous during 30 minutes duration, followed by three bottles of IV fluid with 5 IU in each, one bottle every four hours. After that, further oxytocin was given if required.

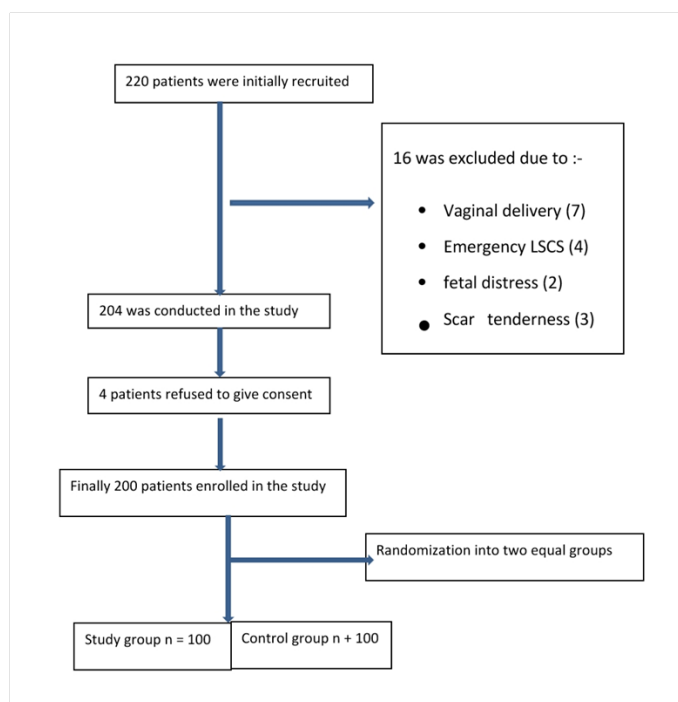


Figure 1 Summary of study design.

Results

The results of this study are summarized in 6 tables.

Table 1 Shows that the study and placebo groups were equally matched with respect to demographic characteristics (age, weight, gravidity), period of gestation at which CS was done, preoperative hemoglobin % with no statistically significant difference between both groups.

Table 1 Clinical data of the tranexamic acid (study) and placebo groups

	Study Group (n100)	Placebo Group (n=100)	P value
Age	29.71±4.18	29.75±4.01	0.961 (NS)
Weight	82.67±9.21	81.33±8.75	0.457(NS)
Gravida I	80 (80%)	76 (76%)	0.759 (NS)
2 nd	112 (112%)	124 (124%)	0.579 (NS)
3 rd	8 (8%)	0 (0%)	0.511(NS)
Gestation (weeks)	38.92 +/- 1.38	39.02 +/- 1.42	0.722 (NS)
Hb (g %)	10.33 +/- 1.26	10.80 +/- 1.34	0.05 (NS)

Table 2 shows vital signs (pulse, respiratory rate (RR), or blood pressure (SBP and DBP) before, immediately after placental delivery, 1 hour and 2 hours after CS between the study and placebo groups with no statistically significant difference between study and control groups.

Table 3 Demonstrates comparison between Pre-operative and postoperative PT(s), A PTT(s), ALT (IU/L), AST (IU/L), serum Creatinine (mg/dl), serum Urea (mg/dl) and Platelet count in study and control group. a comparison between study-placebo preoperative (p1), study-placebo postoperative (p2), comparison between pre and post-operative study group (p3), comparison between pre and post-operative placebo group (p4). There was no statistically significant difference in all previous parameters between both groups.

Table 4 Exhibits Comparison between Pre-operative and postoperative HCV% P1= a comparison between study-placebo preoperative, (p2) study-placebo postoperative, (p3) pre and post-operative study group and (p4) pre and post-operative placebo group The mean postoperative hematocrit level (HCT%) in the TA group was (31.8±1.5) which was higher than those of the placebo group (29.1±1) with statistically significant difference p value <0.001, on the other hand in comparing the mean hematocrit level HCT% in the

study group pre and post- operative, it was (33±3.7) & (31.8±1.5) respectively with no statistically significant difference P value 0.02 (599.9±206.4 mL) in the study group which is markedly lower than the placebo group (780.7±215.7mL) with statistically significant difference. P value ≤0.001

Table 5 Reveals that the mean estimated blood loss was

Table 2 Vital signs before and immediately after placental delivery and 1 and 2 Hours after CS in the Study (Tranexamic) and Placebo Groups

	Before placental delivery			Immediately after placental delivery			One hour after placental delivery			Two hours after placental delivery		
	Study	Placebo	p	Study	Placebo	P	Study	Placebo	p	Study	Placebo	p
Pulse (beat/min)	90.12 ±11.16	92.4 ±9.34	0.44 (NS)	91.6 ±13.3	90.4 ±12	0.546 (NS)	81.2 ±7.93	80.2 ±8.15	0.39 (NS)	79.4 ±10.3	79.7 ±10.3	0.83 (NS)
RR (breaths/min)	19.04 ±4.86	21.48 ±2.99	0.35 (NS)	19.8 ±2.14	19 ±2.1	0.755 (NS)	20.2 ±6.7	19.6 ±2.3	0.38 (NS)	19.3 ±1.9	19.3 ±2	0.87 (NS)
SBP (mmHg)	120.6 ±11.04	125.2 ±12.02	0.75 (NS)	117.5 ±11.97	117 ±12.1	0.836 (NS)	116.3 ±15.5	113.3 ±16.5	0.22 (NS)	114.8 ±11.92	113.2 ±15.4	0.45 (NS)
DBP (mmHg)	76.04 ±10.12	81.28 ±9.73	0.68 (NS)	65.4 ±11.3	67.4 ±11.3	0.216 (NS)	72.3 ±11.2	72 ±9.7	0.83 (NS)	72.2 ±10.2	72.6 ±7.7	0.75 (NS)

Table 3 Comparison between Pre-operative and postoperative PT(s), A PTT(s), ALT (IU/L), AST (IU/L), serum Creatinine (mg/dl), serum Urea (mg/dl) and Platelet count in study and control group

	Pre-operative		P1	postoperative		P2	P3	P4
	Study Group (n=100)	Placebo Group (n=100)		Study Group (n=100)	Placebo Group (n=100)			
PT(s)	Mean ± SD	11.9±0.3	0.94	11.8±0.4	11.8±0.4	1	0.21	0.16
		11.9±0.4	(NS)			(NS)	(NS)	(NS)
A PTT(s)	Mean ± SD	31.7±2.6	0.27 (NS)	32.4±2	32.7±2.6	0.52 (NS)	0.13 (NS)	0.46 (NS)
ALT (IU/L)	Mean ± SD	17±6.58	0.22 (NS)	18.47±6.7	20.75±8.32	0.13	0.27 (NS)	0.28 (NS)
AST (IU/L)	Mean ± SD	18.5±8.6	0.27 (NS)	18.23±7.9	21.23±9.23	0.08 (NS)	0.87 (NS)	0.69 (NS)
serum Creatinine (mg/dl)	Mean ± SD	0.84±0.17	0.36 (NS)	0.88±0.19	0.87±0.18	0.59 (NS)	0.26 (NS)	0.08 (NS)
serum Urea (mg/dl)	Mean ± SD	28.3±5.14	0.09 (NS)	29.9±5.25	31.33±5.76	0.24 (NS)	0.12 (NS)	0.39 (NS)
Platelet count	Mean ± SD	210,000±0.62	0.59 (NS)	205000±0.48	204000±0.46	0.70 (NS)	0.65 (NS)	0.89 (NS)

N.B: P1= comparison between study-placebo preoperative, P2= comparison between study-placebo postoperative, P3= comparison between pre and post-operative study group, P4= comparison between pre and post-operative placebo group.

Table 4 Comparison between Pre-operative and postoperative HCT (%)

	Pre-operative		P1	Postoperative HCT		P2	P3	P4
	Study Group (n=100)	Placebo Group (n=100)		Study Group (n=100)	Placebo Group (n=100)			
Mean ± SD	33±3.7	32.9±1.6	0.54 (NS)	31.8±1.5	29.1±1	≤0.001*	0.02(NS)	≤0.001*

P ≤0.001 is statistically significant.

Table 5 Estimated blood loss (mL)

	Study Group (n=50)	Placebo Group (n=50)	p
Mean ± SD	599.9±206.4	780.7±215.7	≤0.001*

P ≤0.001 is statistically significant.

Table 6 tranexamic acid adverse reactions Nausea, vomiting & diarrhea occurred in 18, 8, 2 cases respectively in the study group & 5, 3, 0 cases respectively in the placebo group. None of the subjects had any evidence of thrombosis. No statistically significant difference.

Table 6 Comparison of adverse drug reaction in both groups

	Study Group (n=010)	Placebo Group (n=010)	P
Nausea	18	5	0.55(NS)
Vomiting	8	3	1(NS)
Diarrhea	2	0	1(NS)
Signs of thrombosis	0	0	-

Discussion

The most important finding of this study is that, blood loss was 599.9±206.4 mL in the study group in comparison to 780.7±215.7 ml in the control group. Which means reduction in blood loss by approximately 23% (P=0.001). As regard extra need of 10 IU oxytocin, only three women in the study group compared to twelve in control group. In consistent with the present study, Movafegh. used 10 mg/kg of TA before skin incision by 20 minutes. Mean blood loss was (329.5±39.6 versus 545.7 ± 94.4 mL) in study and control groups respectively with statistically significant difference P < 0.001), also with statistically significant smaller doses of oxytocin (29±5.8 vs. 43±5.4 units P= 0.001.¹² Comparable study carried out by Gai.¹³ in China showed that tranexamic acid significantly reduced bleeding during and two hours after delivery by 30% in comparison to control group also postpartum hemorrhage was markedly decreased by 25.7% as it occurred only in 22 cases versus 35 cases in control group. P value =0.029 these findings correlated well with the current study and also in Leila Sekhavat,¹⁴ Baird EJ¹⁵ & Bresnoc.¹⁶ In the current study, no statistically significant difference was found in vital signs either before or immediately after delivery of the placenta, 1 or 2 hours after CS, between the two studied groups, which is consistent with Movafegh et al.,¹² and Gai et al.,¹³ Also there was no statistically

significant changes in CBC, PT, aPTT, liver or renal function tests after TA administration, this is inconsistent with Baird EJ¹⁵ Bresnoc et al.,¹⁶ Gai,¹³ Gohel et al.,¹⁷ Sekhavat et al.,¹⁴ and Yang et al.,¹⁸ Pregnant women have about five to six folds risk of thrombotic complications than non-pregnant women,¹⁹ especially in post-partum period after CS in women with TA administration. TA appears in cord blood nearly at the same level of maternal blood as it crosses the placenta; also it appears in breast milk but in very low amount, 1/100 of that in maternal blood.²⁰ In spite of that, patients under antifibrinolytic agents treatment, have an increased incidence of thrombotic events, there is no statistically significant increase risk in those with TA treatment.²¹ Svanberg et al.,²² treated 67 cases t by tranexamic acid due to abruptio placenta, no thrombosis occurred or any side effect in form of nausea, vomiting, diarrhea was observed in any patient. Bekassy and Astedt²³ included 3014 women including 45 pregnant women & gave tranexamic acid to prevent bleeding at conization of cervix, thromboembolic episodes were absent and no side effects reported. Baird EJ¹⁵ A study of 400 pregnant women with normal vaginal deliveries who received tranexamic acid during labor; no thrombosis nor significant adverse effects occurred. Similar results were found in the study of Gohel et al.,¹⁷ Sekhavat et al.,¹⁴ and Gai et al.,¹³ At the same time, the current results were similar with previous studies of Bresnoc,¹⁶ Svanberg et al.,²² Bekassy and Astedt,²³ Baird EJ,¹⁵ Gai et al.,¹³ Gohel et al.,¹⁷ and Sekhavat et al.,¹⁴.

Conclusion

Intravenous Tranexamic Acid was associated with a reduction in intraoperative blood loss among pregnant women undergoing cesarean section and can be safely used without any evident risk of thrombosis. The main limitation of the current study, that we excluded all high risk patients for post-partum hemorrhage.

Acknowledgments

None.

Conflict of Interest

The author declares there no conflict of interest here.

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