

Efficacy of Tranexamic Acid in Reducing Blood Loss in Cesarean Section: A Comparative Study

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ABSTRACT

Introduction: Obstetric hemorrhage is one of the major causes of maternal morbidity and mortality. Blood loss during cesarean section is almost twice than that in vaginal delivery. The aim of this study was to evaluate the efficacy of tranexamic acid to reduce blood loss in cesarean section and its side effects. **Methods:** A comparative study was done in 100 women undergoing cesarean section between December 2015 to January 2017. The study group of 50 women received one gram intravenous tranexamic acid and the control group of 50 women did not receive tranexamic acid. Primary outcome measure was blood loss during cesarean section. Secondary outcome measures were drop in post-operative hemoglobin and hematocrit, change in pulse rate and blood pressure, need of additional uterotonics, auxiliary procedures to stop bleeding, blood transfusion rate and maternal and neonatal side effects of the drug. **Results:** Mean intraoperative blood loss in the study group was 443.62 ± 86.73 ml; and in control group, 667.40 ± 131.01 ml ($p < 0.001$). Mean postoperative drop in hemoglobin (g/dl) in the two groups were 0.82 ± 0.27 and 1.86 ± 0.64 respectively ($p < 0.001$). Mean postoperative drop in hematocrit in the two groups were 2.60 ± 0.91 and 5.49 ± 1.97 respectively ($p < 0.001$). Fourteen patients in the control group required additional uterotonics while none in the study group ($p < 0.001$). There was no significant difference in the transfusion requirement ($p = 0.079$). None of the mothers and the newborns had major side effects of drug. **Conclusion:** Tranexamic acid is a safe and effective drug to reduce blood loss in cesarean section.

Keywords: Blood loss, Cesarean section, Tranexamic acid

INTRODUCTION:

Obstetric hemorrhage is one of the major causes of maternal morbidity and mortality in low-income countries. It accounted for more than 27% of maternal deaths in low-income regions and approximately 16% in high-income regions.[1] Postpartum hemorrhage (PPH) can kill a healthy woman within two hours of delivery.[2] Blood loss during cesarean section (CS) is almost twice than that in vaginal delivery and hence there is a need of a drug

that reduces blood loss during CS.

Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its anti-fibrinolytic effect through the reversible blockade of the lysine binding sites on plasminogen molecules.[3] It inhibits conversion of plasminogen to plasmin by tissue plasminogen activators.[4] It has been proved to reduce blood loss in elective surgery, trauma patients, dentistry and menstrual blood loss. Tranexamic acid given within three hours of injury to a large cohort of adults with acute traumatic bleeding significantly reduced death due to bleeding, with no apparent increase in vascular occlusive events.[5] The optimal dosage and the route of administration in obstetric patients is unknown. For general fibrinolysis, a single dose of 1 gm or 10 mg/kg by slow intravenous injection is recommended.

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[6]

The aim of this study was to evaluate the efficacy of tranexamic acid to reduce blood loss after cesarean section and its adverse effects.

METHODS:

This was a comparative study carried out from December 2015 to January 2017 in the Department of Obstetrics and Gynecology, Universal College of Medical Sciences. Ethical clearance was taken from the institutional review committee (UCMS/IRC/114/15). Written informed consents were obtained from the participants.

Sample size was calculated by using the formula,

$$N = \frac{2x [Z (1-\alpha/2) + Z \beta]^2 x \sigma^2}{\Delta^2}$$

where, significance level (α) was taken as 0.05, the desired power (β) as 0.80, standard deviation (σ) as 1 and minimal clinically important difference (Δ) as 0.55. The calculated sample size was 50.36, that is 51 in each group. All patients with singleton pregnancy at term undergoing elective or emergency CS, except those who met exclusion criteria were included in the study. Exclusion criteria were concomitant uterine fibroid, active liver or kidney disease, bleeding disorders, patients on anticoagulants, antepartum hemorrhage, polyhydramnios, macrosomic baby, multiple pregnancy, allergy to tranexamic acid, pre-eclampsia, eclampsia, obstructed labour, previous two or more CS and cesarean under general anesthesia.

Primary outcome measure was blood loss during CS, from incision to the closure of the skin. Secondary outcome measures were change in post-operative hemoglobin and hematocrit at 24 hours, immediate and six hours post CS pulse rate and blood pressure, need of additional uterotonics, need for auxiliary procedures to stop bleeding (B-lynch suture, uterine artery ligation, internal iliac artery ligation and hysterectomy), and blood transfusion rate, and maternal and neonatal side effects of the drug used.

Patients were assessed for selection criteria as soon as the decision for cesarean section was made. Investigations like hemoglobin, hematocrit, platelet, bleeding time (BT), clotting time (CT), prothrombin time/ international normalized ratio (PT/INR) were

sent. Patients were randomized through random number tables into two groups: group one, the study group of 51 women receiving preemptive tranexamic acid and group two, the control group of 51 women without tranexamic acid. However, two patients one in each group were excluded from the final analysis because they underwent CS under general anesthesia due to failed spinal anesthesia. Injection tranexamic acid one gram was given intravenously to the patient in group one just before spinal anesthesia. Two separate suction jars were used to collect the amniotic fluid and the blood. Blood loss after the placental delivery to closure of skin incision was noted from the suction jar. Difference of weight of tetra used before and after surgery was noted and blood loss was calculated. Pulse rate and blood pressure were recorded immediately and at six hours after CS. Hemoglobin and hematocrit were measured 24 hours after the surgery.

All data were collected in the preformed proforma and entered into MS Excel program. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS™) software version 21. Student's t-test and Chi-square test were used for the comparison of quantitative and qualitative variables respectively between the two groups. p value <0.05 was considered statistically significant.

RESULTS:

Both groups were comparable in terms of age, gravidity, parity and period of gestation (Table 1).

Table 1. Comparison of demographic variables between two study groups (N=100)

Variables	Group 1 (n=50) (Mean ± SD)	Group 2 (n = 50) (Mean ± SD)	p value*
Age (years)	25.71±4.6	25.20±4.6	0.82
Gravidity	1.56±0.73	1.6±0.78	0.79
Parity	0.50±0.64	0.48±0.58	0.87
Period of Gestation	39.33±1.40	39.46±1.15	0.61

* p value calculated by Student's t test.

There were 11 cases of elective and 39 cases of emergency cesarean in study group while 13 elective and 37 cases of emergency cesarean in

control group ($\chi^2 = 3.03, df=2 p=0.22$). Fetal distress and previous cesarean were the most common indications in emergency and elective cesareans respectively. Pre-operative laboratory parameters including hemoglobin, hematocrit, platelet, PT/INR, APTT, BT, CT were comparable in both the groups (Table 2).

Mean intraoperative blood loss during CS in the study group was 443.6 ml while in control group was 667.4ml which was significantly less ($t=10.07, df=98, p<0.001$). Similarly, postoperative drop in hemoglobin and hematocrit were significantly less in the study group receiving tranexamic acid compared to the control group (Table 3).

There were no significant differences in the heart rate and blood pressures measured immediately and at sixth postoperative hour between two groups (Table 4).

Fourteen patients in control group required additional uterotonics while none in the study group received additional uterotonics, which was

Table 2. Comparison of preoperative laboratory parameters between the study groups (N=100).

Variables	Group 1 (n=50) Mean ± SD	Group 2 (n=50) Mean ± SD	p value*
Hemoglobin (g/dl)	11.32±1.03	11.58±1.07	0.21
Hematocrit (%)	34.07±3.09	33.79±6.64	0.78
Platelets (X10 ⁹ /L)	2.02±0.41	2.56 ± 2.97	0.20
INR	1.4± 0.09	1.4±0.13	0.72
APTT (seconds)	34.4±1.22	34.15±1.14	0.32
BT (minutes)	1.48±0.34	1.55±0.37	0.28
CT (minutes)	4.14±0.47	4.11±0.77	0.85

* p value calculated by Student's t test.

Table 3. Blood loss and post-operative blood parameters (N=100).

Variables	Group 1 (Mean ± SD)	Group 2 (Mean ± SD)	p value
Intraoperative blood loss(ml)	443.62± 86.73	667.40±131.01	<0.001
Post- operative hemoglobin at 24 hour (g/dl)	10.52±1.05	9.72±1.23	0.001
Postoperative drop in hemoglobin (g/dl)	0.82±0.27	1.86±0.64	<0.001
Post-operative hematocrit at 24 hour (%)	31.21±3.78	28.64±5.88	0.011
Postoperative drop in hematocrit (%)	2.60±0.91	5.49±1.97	<0.001

Table 4. Postoperative vital parameters (N=100).

Variables	Group 1 (Mean ± SD)	Group 2 (Mean ± SD)	p value
Immediate post-operative pulse rate	81.50±6.95	82.8±7.24	0.36
Six hours post-operative pulse rate	77.96±5.1	78.92±5.4	0.36
Immediate post-operative systolic blood pressure	119.48±7.94	118.28±6.84	0.42
Immediate post-operative diastolic blood pressure	72.28±7.2	72.48±6.78	0.88
Six hours post-operative systolic blood pressure	118.64±5.74	116.76±6.73	0.13
Six hours post-operative diastolic blood pressure	72.36±5.07	70.44±5.33	0.40

statistically significant ($p<0.001$). None of the patients in both groups required auxiliary surgical procedures to arrest hemorrhage.

Three patients in control group required blood transfusion while none of them required in study group.

None of the patients had major side effects of tranexamic acid while nausea, vomiting and dizziness were present in 16%, 6% and 2% respectively.

There was no significant difference in Apgar score of neonates in two groups at 5 and 10 minutes with p value of 0.36 and 0.40 respectively. One neonate in the study group developed seizure which was managed with anticonvulsant.

DISCUSSION:

Postpartum hemorrhage is defined as blood loss of more than 500ml in vaginal delivery and 1000ml in CS but can occur even with lesser amount than this in previously compromised patients like in anemia. Most of the maternal deaths occur soon after giving birth and almost all (99%) occur in low-income and middle-income countries.[7,8] One fourth of post partum maternal deaths is due to hemorrhage. Hemorrhage following CS is not uncommon and reducing the amount of CS blood loss carries special sense in countries like Nepal where many pregnant women are already anemic.

Following placental delivery, the level of fibrinogen and fibrin decreases and tissue plasminogen activator activity also increases converting plasminogen to plasmin. This activation can take up to six to ten hours in the postpartum period.[9] Tranexamic acid which is a potent antifibrinolytic drug inhibits this conversion and helps in reducing blood loss following CS. The drug is cheaper, stable at room temperature, a fixed dose can be used without serious maternal and fetal side effects.

The patients in the study group had significantly less amount of intraoperative blood loss (443.62mL) compared to those in the control group (667.40mL) ($p < 0.001$). This observation was similar to the result of other large studies on the subject matter.[10,11] As the amount of blood loss was significantly higher in the control group, the drop in postoperative hemoglobin and hematocrit were also higher compared to the study group, which was statistically significant ($p < 0.001$).

Tranexamic acid can increase the pulse rate especially in elderly women. In this study there was no significant difference in the pulse rate among the two groups of patients taken immediately and at six hours following CS. This study did not show any significant change in post CS systolic and diastolic

blood pressures among the two groups. Our results on the effect of tranexamic acid in postoperative vitals were consistent with other studies.[9,12]

Conventionally uterotonics are the only drugs used to reduce the postpartum blood loss in all modalities of deliveries and are effective as well. However, with the introduction of tranexamic acid which acts through different mechanism their use is declining. Fourteen patients in control group compared to none in the study group required additional uterotonics, which was statistically significant ($p < 0.001$). Interestingly, none of the patients in either group required any auxiliary surgical procedures to arrest hemorrhage. Although tranexamic acid reduced the amount of blood loss significantly it did not have significant impact on the transfusion requirement in large studies like WOMAN trial.[13] In the current study, three patients in control group required blood transfusion while none of them required in study group ($p = 0.079$).

One of the most feared complications of tranexamic acid is the possibility of thromboembolism in the context of higher incidence of thrombosis during pregnancy and postpartum. The incidence of thrombosis during pregnancy and puerperium is five to six times higher than that in the general population and postpartum venous thromboembolism is more common than antepartum venous thromboembolism.[14] Unlike this none of our patients had thromboembolic events. Other large series also failed to demonstrate the increased risk of thromboembolism with the use of tranexamic acid during pregnancy.[13,15,16,17] Minor side effects like nausea, vomiting and dizziness were present in 16%, 8% and 2% of patients respectively who received tranexamic acid. These minor symptoms did not increase the additional morbidity to the patients. In this study there was no maternal death in either group due to postpartum hemorrhage following CS. In a large series the use of tranexamic acid had significantly reduced maternal death due to postpartum hemorrhage without significant adverse effects.[13]

Tranexamic acid given to the mother did not show any adverse effects on neonatal outcome. There was no differences in Apgar score at 5 mins and at 10 mins, seizure and thrombotic events in neonates of both the groups. These observations were similar to the results of another study.[10]

There are certain limitations of this study. Firstly, the sample size is small in the context of increasing CS rate and the extent of the problem of post partum hemorrhage. Secondly, the standard method of estimation of blood loss was not applied due to technical problems.

CONCLUSION:

The preemptive use of tranexamic acid before cesarean section effectively reduces blood loss and need for transfusion without significant adverse effects in the mother and the new born.

Conflict of interest: Authors declare that no competing interest exists.

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REFERENCES:

1. Inter-Agency and Expert Group on Millennium Development Goals Indicators. The millennium development goals report 2015. Department of Economic and Social Affairs of the United Nations Secretariat. 2015. Available from: <https://bit.ly/37KmtJt>
2. WHO. The World Health Report: 2005: Make Every Mother and Child Count. World Health Organization. 2005. Available from: <https://bit.ly/2OqXwLn>
3. Wellington K, Wagstaff AJ. Tranexamic acid: review of its use in management of menorrhagia. *Drugs*. 2003;63(13):1417-33. PMID: 12825966 DOI: [10.2165/00003495-200363130-00008](https://doi.org/10.2165/00003495-200363130-00008)
4. Roberts I. Tranexamic acid in trauma: how should we use it? *J Thromb Haemost*. 2015;13(Suppl 1):S195-9. PMID: 26149023 DOI: <https://doi.org/10.1111/jth.12878>
5. CRASH-2 trial Collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet*. 2010;376(9734):23-32. PMID: 20554319 DOI: [10.1016/S0140-6736\(10\)60835-5](https://doi.org/10.1016/S0140-6736(10)60835-5)
6. Walker G, Association of British Pharmaceutical Industry. ABPI Compendium of data sheets and summaries of product characteristics, 1998-99: with the code of practice for the pharmaceutical industry. London : Datapharm Publication; 1998.
7. Ronsmans C, Graham WJ. Maternal mortality: who, when, where, and why. *Lancet*. 2006;368(9542):P1189-1200. DOI: [10.1016/S0140-6736\(06\)69380-X](https://doi.org/10.1016/S0140-6736(06)69380-X)
8. Say L, Chou D, Gemmill A, Tuncalp O, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health*. 2014;2(6):e323-e33. PMID: 25103301 DOI: [10.1016/S2214-109X\(14\)70227-X](https://doi.org/10.1016/S2214-109X(14)70227-X)
9. Gai MY, Wu LF, Su QF, Tatsumoto K. Clinical observation of blood loss reduced by tranexamic acid during and after cesarean section: a multi-center, randomized trial. *Eur J Obstet Gynecol Reprod Biol*. 2004;112(2):154-7. PMID: 14746950. DOI: [https://doi.org/10.1016/S0301-2115\(03\)00287-2](https://doi.org/10.1016/S0301-2115(03)00287-2)
10. Bhavana G, Abhishek MV, Mittal S. Efficacy of prophylactic tranexamic acid in reducing blood loss during and after cesarean section. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2016;5(6):2011-6. DOI: [10.18203/2320-1770.ijrcog20161708](https://doi.org/10.18203/2320-1770.ijrcog20161708)
11. Yehia AH, Koleib MH, Abdelazim IA, Atik A et al. Tranexamic acid reduces blood loss during and after cesarean section: A double blinded, randomized, controlled trial. *Asian Pacific Journal of Reproduction*. 2014;3(1):53-6. DOI: [10.1016/S2305-0500\(14\)60002-6](https://doi.org/10.1016/S2305-0500(14)60002-6)
12. Gohel M, Patel P, Gupta A, Desai P. Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: a randomized case controlled prospective study. *The Journal of Obstetrics and Gynecology of India*. 2007;57(3):227-30. Available from: <https://bit.ly/37LdDLJ>
13. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet*. 2017;389:2105-16. DOI: [10.1016/S0140-6736\(17\)30638-4](https://doi.org/10.1016/S0140-6736(17)30638-4)
14. Bekassy Z, Astedt B. Treatment with the fibrinolytic inhibitor tranexamic acid-risk for thrombosis? *Acta Obstetrica et Gynecologica Scandinavica*. 1990;69(4):353-4. DOI: [10.3109/00016349009036161](https://doi.org/10.3109/00016349009036161)
15. Gungorduk K, Asıcıoğlu O, Yıldırım G, Ark C, Tekirdağ Aİ, Besimoğlu B. Can intravenous injection of tranexamic acid be used in routine practice with active management of the third stage of labor in vaginal delivery? A randomized controlled study. *Am J Perinatol*. 2013;30(5):407-13. PMID: 23023559 DOI: [10.1055/s-0032-1326986](https://doi.org/10.1055/s-0032-1326986)
16. Svanberg L, Astedt B, Nilsson IM. Abruptio placentae-treatment with the fibrinolytic inhibitor tranexamic acid. *Acta Obstetrica et Gynecologica Scandinavica*. 1980;59(2):127-30. DOI: [10.3109/00016348009154628](https://doi.org/10.3109/00016348009154628)
17. Movafegh A, Eslamian L, Dorabadi A. Effect of intravenous tranexamic acid administration on blood loss during and after cesarean delivery. *International Journal of Gynaecology & Obstetrics*. 2011;115(3):224-26. DOI: <https://doi.org/10.1016/j.ijgo.2011.07.015>