e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(11); 729-734

Original Research Article

Effect of Intravenous Tranexamic Acid on Blood Loss during and After Caeserean Delivery: A Prospective Randomised Study

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Received: 20-05-2023 Revised: 13-06-2023 / Accepted: 22-07-2023
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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to document the efficacy of intravenous (IV) tranexamic acid in reducing blood loss during and after caesarean section (CS)

Material & methods: The present study was conducted in the Department of Obstetrics and Gynaecology for one year. 100 women were included in the study. Patients were divided into two groups: Control group A: (n=50) IV placebo i.e.10 ml of Ringer Lactate and Study Group (B):(n=50) IV intravenous tranexamic acid 1g (10 ml).

Results: The mean age, weight and height of both the groups were not statistical significant. Majority of the respondents were parity 0, 33 (66%), followed by gravida 1, 28 (56%), and gravida 2, 20 (40%). The most common indication for LSCS was CPD 27 (27%), followed by Post-dated pregnancy with high floating head 25 (25%), Previous one/two caesarean section 20 (20%). The mean total blood loss was 499.75 ± 111.20 ml and 690.85 ± 198.41 ml in TXA and the control group respectively. The result was found to be significant (p=0.001). Tranexamic acid significantly reduces bleeding from the time of delivery of placenta to 2 hours postpartum. According to post-operative vitals, the mean pulse rate showed statistical significant difference. APGAR scores did not show any significant difference in both the groups. The most common side effect was nausea followed by vomiting in both the groups which was non significant

Conclusion: Pre-operative IV tranexamic acid significantly reduced blood loss during & after elective CS without any significant adverse effects.

Keywords: Tranexamic acid, Anti-fibrinolytics, Blood loss, Caesarean delivery, Post-partum haemorrhage

Introduction

Cesarean section (CS) rates have increased to as high as 25 to 30 % in many areas of the world. [1] Delivery by CS can cause more complications than normal vaginal delivery and one of the most common complications is primary or secondary postpartum hemorrhage (20%). PPH is generally defined as blood loss greater than or equal to 500 ml within 24 hours after birth, while severe PPH is blood loss greater than or equal to 1000 ml within 24 hours.

PPH is the most common cause of maternal death worldwide. Most cases of morbidity and mortality due to PPH occur in the first 24 hours following delivery and these are regarded as primary PPH whereas any abnormal or excessive bleeding from the birth canal occurring between 24 hours and 12 weeks postnatally is regarded as secondary PPH. [2]

There are four causes of PPH: uterine atony, trauma to the birth passage, retained placental tissue or membranes and coagulopathies such as DIC. [3] It is responsible for approximately 27% of maternal deaths worldwide, [4] and this number may be up to 60% in some countries, [5] making it the single most important leading cause of pregnancy-related deaths. In order to reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the amount of bleeding during and after lower segment cesarean section (LSCS). PPH can reach disastrous proportions during caesarean section. Management of haemorrhage after CS may range from administration of oxytocic's and blood transfusion to more radical measures such as hysterectomy. [6,7]

Use of antifibrinolytic agent such as tranexamic acid (TXA), inhibit fibrinolysis and the stabilization of

existing blood clots by preventing the activation of the proenzyme plasminogen to plasmin, thereby preventing the proteolytic action of plasmin on fibrin threads. [8] The mechanism of action of TXA is the reversible blockage of lysine binding sites on plasminogen molecules. [9] to block plasmin from binding and degradation linked fibrin. TA may enhance the effectiveness of endogenous hemostatic mechanism. [10,11,12] Early use of intravenous TXA (as early as possible after clinical diagnosis of PPH, and only within 3 hours of birth) in addition to standard care is recommended for women with clinically diagnosed PPH following vaginal birth or caesarean section.

Hence the aim this study was to assess the effect of tranexamic acid on blood loss during and after CS.

Material & methods

The present study was conducted in the Department of Obstetrics and Gynaecology, Yashoda Multi-speciality Hospital,Somajiguda, Hyderabad, India for one year. 100 women were included in the study. Patients were divided into two groups: Control group A: (n=50) IV placebo i.e.10 ml of Ringer Lactate and Study Group (B):(n=50) IV intravenous tranexamic acid 1g (10 ml).

Inclusion Criteria:

Elective caesarean section in women aged 20-40 years with a singleton pregnancy at term (37 completed weeks)
Regular antenatal care
Informed consent obtained

Exclusion Criteria:

1) Pregnancy complications like pre-eclampsia, polyhydramnios, macrosomia, multiple pregnancies, preterm labour.

2) Abnormal placenta such as placenta praevia and abruptio placentae

3) Severe medical and surgical complications involving the heart, liver or kidney, brain disease, blood dyscrasias, coagulation disorders and severe anaemia.
4) History of thromboembolic disorders
5) Allergy to tranexamic acid
The primary outcome was to estimate the blood loss. Blood loss was measured by weighing pads, mops, drapes before and after surgery and blood in the suction container after surgery. Two separate suction containers were used to avoid mixing of blood and amniotic fluid. Total blood loss was calculated as the difference in the weight of the pads, mops and drapes before and after surgery and the sum of the amount of blood in the suction container. The difference between the pre- operative and post-operative haemoglobin was compared. The pre-operative, intra- operative and post-operative vitals were also compared.

Statistical analysis was done using IBM SPSS version 21.0 for Windows. Descriptive statistics like mean, standard deviation, and percentages were used. Analytical statistics like Chi-Square Test, t-test were used for seeing association. In our study, there was a significant decrease in intraoperative and postoperative blood loss in women receiving tranexamic acid. There was significant fall in post-operative haemoglobin in control group as compared to study group. Also, women who received tranexamic acid did not develop any significant complications. Consent was obtained from the participating individuals. A unique code number was given but no name was mentioned to maintain confidentiality.

Results

Table 1: Distribution of patient characteristics in study and control groups

Parameters	Study group (mean ± sd) [range (min-max)]	Control group (mean ± sd) [range (min-max)]	p value
Age (years)	25.00±4.71 (18-36)	25.88±5.39 (18-38)	0.387
Weight (kgs.)	65.22±5.58 (53-75)	64.86±8.476 (49-83)	0.803
Height (mts.)	1.55±0.04 (1.48-1.63)	1.55±0.04 (1.48-1.65)	0.889

The mean age, weight and height of both the groups were not statistically significant.

Table 2: Distribution of patient characteristics in study and control groups

Parameters		Study group (n=50) n (%)	Control group (n=50) n (%)	p value
Gravida	1	28 (56)	31 (62)	0.450
	2	20 (40)	19 (38)	
	3	2 (4)	0 (0)	
Parity	0	33 (66)	36 (72)	0.481
	1	16 (32)	14 (28)	
	2	1 (2)	0 (0)	

Majority of the respondents were parity 0, 33 (66%), followed by gravida 1, 28 (56%), and gravida 2, 20 (40%).

Table 3: Distribution of patients based on indications for LSCS

Indication for caesarean section	Study group (n=50) n (%)	Control group (n=50) n (%)	p value
Postdated pregnancy with high floating head	14 (28)	11 (22)	0.945
CPD	13 (26)	14 (28)	
Previous one/two caesarean section	9 (18)	11 (22)	
Primigravida with breech	9 (18)	8 (16)	
Elderly primigravida	5 (10)	6 (12)	

The most common indication for LSCS was CPD 27 (27%), followed by Post-dated pregnancy with high floating head 25 (25%), Previous one/two caesarean section 20 (20%).

Table 4: Distribution of patients based on intra-operative blood loss

Parameters	Study group (n=50) (mean ± sd) [range (min-max)]	Control group (n=50) (mean ± sd) [range (min-max)]	p value
Blood vol. in suction (ml)	98.64 ± 28.89 (44-150)	220.80 ± 64.48 (100-320)	0.001
Blood vol. in mops+sheets (ml)	401.11 ± 112.43 (180.40-611.32)	470.05 ± 141.07 (210.4-700.80)	0.008
Total intra-op blood loss (ml)	499.75 ± 111.20 (260.40-691.32)	690.85 ± 198.41 (319.10-1020.8)	0.001

The mean total blood loss was 499.75 ± 111.20 ml and 690.85 ± 198.41 ml in TXA and the control group respectively. The result was found to be significant (p=0.001).

Table 5: Distribution of patients based on post-operative vitals

Parameters	Study group (n=50) (mean ± sd) [range (min-max)]	Control group (n=50) (mean ± sd) [range (min-max)]	p value
Pulse (per min.)	83.76 ± 7.52 (70-98)	91.6 ± 5.07 (80-100)	0.001
SBP (mm of Hg)	110.96 ± 4.59 (94-134)	109.92 ± 7.89 (90-130)	0.124
DBP (mm of Hg)	68.44 ± 6.011 (60-80)	69.32 ± 7.22 (60-80)	0.753
Respiratory rate (per min.)	14.38 ±1.22 (12-16)	14.00 ± 1.71 (12-18)	0.493

According to post-operative vitals, the mean pulse rate showed statistical significant difference.

Table 6: Distribution of patients based on total (intra + post-operative) blood loss - from delivery of placenta till 2 hours after caesarean section

Parameters	Study group (n=50) (mean ± sd) [range (min-max)]	Control group (n=50) (mean ± sd) [range (min-max)]	p value
Total blood loss	559.68 ± 113.80 (319.40-745.32)	800.91 ± 200.26 (413.90-1167.60)	0.001

Tranexamic acid significantly reduces bleeding from the time of delivery of placenta to 2 hours postpartum.

Table 7: Distribution of patients based on APGAR scores of newborn

Parameters	Study group (n=50) (mean ± sd)	Control group (n=50) (mean ± sd)	p value
1 minute APGAR score	7.06 ± 1.25 (5-9)	7.18 ± 1.35 (4-9)	0.559
5 minutes APGAR score	8.66 ± 1.00 (6-10)	8.64 ± 0.98 (6-10)	0.910

APGAR scores did not show any significant difference in both the groups.

Table 8: Distribution of patients based on side effect profile

Side effect	Study group	Control group	p value
Nausea	16	13	0.508
Vomiting	09	08	1.135
Diarrhoea	01	00	0.312
Signs of thrombosis	0	0	

The most common side effect was nausea followed by vomiting in both the groups.

Discussion

PPH is generally defined as blood loss greater than or equal to 500 ml within 24 hours after birth, while severe PPH is blood loss greater than or equal to 1000 ml within 24 hours. PPH is the most common cause of maternal death worldwide. Most cases of morbidity and mortality due to PPH occur in the first 24 hours following delivery and these are regarded as primary PPH whereas any abnormal or excessive bleeding from the birth canal occurring between 24 hours and 12 weeks postnatally is regarded as secondary PPH. [13] Risk factors for PPH include grand multiparity and multiple gestation. However, PPH may occur in women without identifiable clinical or historical risk factors. It is therefore recommended that active management of the third stage of labour be offered to all women during childbirth, whenever a skilled provider is assisting with the delivery. [14] The incidence of PPH is greatest in low/middle-income nations, particularly in sub-Saharan Africa where it can be larger than 30%. [15-17] The worldwide incidence of PPH is estimated to be between 6% and 11% with substantial regional variability. [16,17] Tranexamic acid acts by competitively blocking the lysine binding sites on plasminogen, thereby prevents the lysis of the formed clot. Its onset of action is 5-15 minutes with duration of action of 3 hours. Tranexamic acid binds more avidly with to the plasminogen molecule than amino-caproic acid. It is used to treat or prevent excessive blood loss from major trauma, postpartum bleeding, surgery, tooth removal, epitaxis and heavy menstrual bleeding. After delivery of the baby, there is transient activation of fibrinolytic cascade for 6-10 hours. [18]

The mean age, weight and height of both the groups were not statistical significant. Majority of the respondents were parity 0, 33 (66%), followed by gravida 1, 28 (56%), and gravida 2, 20 (40%). The most common indication for LSCS was CPD 27 (27%), followed by Post-dated pregnancy with high floating head 25 (25%), Previous one/two caesarean section 20 (20%). The mean total blood loss was 499.75 ± 111.20 ml and 690.85 ± 198.41 ml in TXA and the control group respectively. The result was found to be significant (p=0.001). Tranexamic acid significantly reduces bleeding from the time of delivery of placenta to 2 hours postpartum. Patients in the study group had mean total blood loss (intra-operative + post-operative blood loss) of 559.68 ± 113.80 ml, while patients in control group had mean blood loss of 800.91 ± 200.26 ml. Reduction in blood loss by about 30% (p value= 0.001; highly significant). Similar results were observed by Mayur et al with the total blood loss in CS from placental delivery to 2 hours post-delivery of 372.71 in the TXA group, versus 469.70 ml in the control group (p=0.003). [19] Mirghafourv and et al conducted a double-blind randomized controlled trial on 120 women with a singleton pregnancy. [20] The total blood loss [519 (320) vs. 659 (402) ml, P=0.036] was significantly lower in the TXA group compared to the control group. Sekhavat et al conducted a prospective randomized study on 90 primipara mothers which showed that tranexamic acid significantly reduced blood loss from end of CS to 2-hour post-partum; 28.02±5.53 ml blood loss in the tranexamic group vs. 37.12±8.97 ml in the control group (p=0.000). [21]

In our study there was also significant increase in pulse rate in both the groups. Similarly, in a study conducted by Ray et al there was also significant increase in pulse rate, mean 84/min in the study group versus 92/min in the control group (p=0.000). [22,23] Other parameters such as systolic blood pressure, diastolic blood pressure and respiratory rate did not have any significant difference in the two groups. Side effect profile of tranexamic acid such as nausea, vomiting and diarrhoea was similar in both groups. These results were similar to

previous studies. The incidence of thrombosis during pregnancy and puerperium is 5-6 times higher than in the general population. When the antifibrinolytic drug, tranexamic acid is administered, the increased risk of thrombosis should be considered during C-section and postpartum period. In our study, none of the mothers developed thrombosis. In the current study, there is no significant difference between APGAR score of the baby at 1 min and 5 min following delivery. None of the babies required NICU admission. The similar result was found in a study conducted by Gai et al. [18] Thus tranexamic acid has no effect on the APGAR score of the baby.

Limitation of Study

- Blood volume collected was only approximate
- The blood collected over the drape sheets could not be accounted for.
- The blood loss did not include the amount collected in suction bottle before the placental delivery & hence the volume calculated would definitely be slightly less than the actual loss.
- Long term effect of drug was not taken into account.

Conclusion

Administration of intravenous tranexamic acid 20 minutes before spinal anaesthesia significantly reduces the amount of blood loss during and after caesarean section. It is not associated with side effects and or complications like thrombosis. Also, it doesn't not have adverse neonatal outcome and can safely be used during CS and postpartum period.

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