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Effect of Intravenous Tranexamic Acid in Reducing Blood Loss during and after Elective Caesarean Section in a Third Level Health Institution: A Randomized Controlled Study

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Abstract

Background: Blood loss during caesarean section (C/S) may lead to postpartum haemorrhage, and is one of the direct causes of maternal mortality and morbidity globally. Tranexamic acid is recommended in the treatment of postpartum haemorrhage (PPH) if oxytocin and other utertonics are ineffective in controlling PPH. In this centre it is not used prophylactically to reduce blood during caesarean section. **Aim:** To assess the effect of prophylactic intravenous tranexamic acid on blood loss during and after elective C/S at the University of Port Harcourt Teaching Hospital (UPTH). **Methods:** This was a prospective, single-blind, randomized, placebo-controlled interventional study conducted at the Obstetric theatre of UPTH from July 2020 to March 2021. Eligible women were randomized into two groups; seventy-two women received intravenous tranexamic acid while seventy-one women received a placebo. Socio-demographic data and the result of the study were collected through a proforma. Data collected was analyzed using Statistical Package for Social Sciences (SPSS) Version 22.0. The results were expressed in tables and charts as frequencies, percentages and mean. Chi-square test, Fisher's exact, and T-test were used to determine the relationship between variables. P-value ≤ 0.05 was considered statistically significant. **Results:** The findings showed that tranexamic acid significantly reduced mean blood loss during and after C/S (p-value < 0.01). The mean total blood loss from C/S to 2 hours post-surgery was significantly lower in the tranexamic acid group (624.88 ± 200.76 ml) in comparison to the placebo group (864.24 ± 229.09 ml), p-value = 0.001. The mean post-C/S packed cell volume (PCV) was significantly higher among the tranexamic acid group (30.68% ± 2.80%) in comparison to the placebo group

(28.07% ± 3.27%), t = 5.131, p-value = 0.0001. The maternal side effects were nausea and vomiting, 9 (12.5%) and 1 (1.4%) participants respectively. **Conclusion:** Tranexamic acid significantly reduced blood loss during and after elective C/S. Maternal side effects were less with tranexamic acid use.

Keywords

Tranexemic Acid, Blood Loss, Elective Caesarean Section, Port Harcourt

1. Introduction

Caesarean section can be defined as the delivery of the fetus, placenta, and membranes through an abdominal and uterine incision after viability. The first documented caesarean section on a living person was performed in 1610 [1]. Maternal mortality and morbidity following a caesarean birth is five times higher than vaginal births, especially the risk of haemorrhage, sepsis, thromboembolism and amniotic fluid embolism [2]. In most countries, the caesarean section rate has exceeded the level of 10% - 15% recommended by the World Health Organisation (WHO) [3]. Maternal morbidity and mortality resulting from bleeding during and after C/S and the resultant post-partum anaemia and associated morbidities from anaemia such as infection, wound breakdown and prolonged hospital stay are becoming increasingly frequent [4].

Post-partum haemorrhage (PPH) accounts for an estimated 25% of global maternal deaths and approximately 12% of survivors after PPH suffer from severe postpartum anaemia, despite considerable scientific advances made at discerning its causes, prevention and effective treatment [5] [6]. At the University of Port Harcourt Teaching Hospital, the prevalence of primary postpartum haemorrhage and anaemia following elective caesarean section in previous studies were 4.82% and 54.8% respectively [7] [8]. The reasons for bleeding during and after caesarean section are due to disorder of one or more of the four processes: uterine atony accounts for 90% of cases, trauma in 7% of cases and haemorrhage resulting from retained placenta tissues and coagulopathies (3%) [1] [6].

The risk factors for bleeding during and after caesarean section include previous PPH, multiparity, obesity, prolonged or augmented labour, multiple pregnancy, previous caesarean section, polyhydramnios, abnormal placentation or morbidly adherent placenta, and macrosomia [1] [9].

To lower the rate of major morbidity and mortality due to uncontrolled blood loss during and after C/S, it is very vital to reduce blood loss during caesarean section and vaginal delivery. Since placental expulsion is a critical window for the reduction of blood loss, various preventive interventions during this stage have been proposed [10]. These interventions can be schematically divided into two categories: a mechanical mechanism involving the active management of the third stage of labour and those involving prohaemostatic agents [11].

The administration of uterotonics, particularly oxytocin, after birth is the

main intervention that has been shown to be effective in reducing blood loss during caesarean section. As part of management and reduction of blood loss during and after caesarean section, haemostatic agents may be administered to aid coagulation [12]. One of these is tranexamic acid (TXA), an antifibrinolytic agent that inhibits the dissolution of the fibrin clots by binding to plasminogen and blocking the interaction of plasminogen with fibrin. Blood loss after caesarean and vaginal births was also found to be reduced by the administration of tranexamic acid in the absence of significant maternal and neonatal complications [13]. Given the hypercoagulable state of pregnancy, possible thromboembolic side effects of TXA administration have been the subject of earlier studies [14]. Reported adverse events were mainly minor side effects such as nausea and vomiting and no clear evidence was found for the increase of thromboembolic events in pregnant women who were administered with low dose tranexamic acid [14].

Recent guidelines by World Health Organization (WHO) recommend administration of TXA for the treatment of PPH if oxytocin and other uterotonics are ineffective in controlling bleeding [5]. It is crucial to identify low-cost and low-risk alternative methods of controlling obstetric haemorrhage during and after caesarean section. Tranexamic acid is a promising agent. It is inexpensive, readily available, easy to administer, has a good safety profile and can be added to uterotonics medications in reducing blood loss during and after caesarean section [13]. Tranexamic acid has been shown to reduce blood loss during C/S, need for surgical intervention from haemorrhage, post-operative anaemia, need for blood transfusion, infection, wound breakdown and increased hospital stay from complications of anaemia [14]. Although obstetric haemorrhages are often an unpredictable event as most women have low-risk pregnancies with no identifiable risk factors, pre-delivery preparation and intervention have reduced the severity of blood loss and decrease the rate of maternal morbidity and perinatal mortality. It is therefore essential to prevent or reduce blood loss during caesarean section [10] [15].

In one of the largest TXA studies to date, the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage (CRASH-2) trial published in Lancet 2010, showed that the use of TXA compared to matching placebo resulted in a significant reduction of overall and haemorrhage-induced mortality in trauma patients receiving early TXA if administered over less than three hours, without increasing the rate of thromboembolism [16]. Also, recent randomized, placebo-controlled trial, called World Maternal Antifibrinolytic (WOMAN) study was conducted on 20,060 women with PPH and with the CRASH-2 trial data findings in mind. The WOMAN trial showed a significant reduction in haemorrhage and the need for surgery to treat severe bleeding [17].

Tranexamic acid is a lysine analogue with a molecular weight of 157 Da that reversibly binds to the lysine-binding sites on plasminogen to inhibit its affinity to bind to multiple proteins including fibrin thereby inhibiting fibrinolysis [18] [19]. It can be administered orally or intravenously. With a plasma protein

binding capacity of 3%, it can completely cross the placenta. Metabolism of tranexamic acid in the liver is low, renal clearance amounts to 95% [20] [21]. Tranexamic acid has a half-life of 2 - 3 hours and adequate therapeutic levels persist for 7 - 8 hours following intravenous administration.

Tranexamic acid is not used prophylactically to minimize blood loss during caesarean section at the University of Port Harcourt Teaching Hospital despite its proven efficacy and safety; which may probably be due to lack of experience and evidence-based study of the medication in this centre, hence this study.

2. Methodology

The study was conducted at the Obstetric theatre of the department of Obstetrics and Gynaecology of the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Rivers State. The labour ward has an annual delivery rate of 2500 - 3000 per year; caesarean section constituting a rate of 47% [22].

This study was a prospective, randomized, controlled interventional study on the effect of tranexamic acid in reducing blood loss during and after elective caesarean section in the UPTH from July 2020 to March 2021; with approval from the UPTH Ethical committee. Eligible participants were assigned to receive either tranexamic acid or placebo via randomization. A detailed history was taken; general and obstetric examinations and pre-operative investigations such as PCV, urinalysis, kidney function test and grouping and cross-matching of blood were done.

The inclusion criteria were those patients aged 20 - 40 years, para 1 to 4, gestational age 37 to 40 weeks, singleton fetus with reassuring fetal rate and patients with indicated elective cesarean section. Patients who did not give consent, known cases of allergy to tranexenamic acid, those with multiple gestation or had antepartum haemorrhage; intrauterine fetal death, pre-eclampsia/eclampsia, co-existing uterine fibroid and macrosomia were excluded.

Also excluded were patients with history of thromboembolic disease, medical conditions such as major liver, heart, kidney, brain and bleeding disorders, anticoagulant therapy, patients requiring blood transfusion due to anaemia and polyhydramnios.

The sample size for this study was calculated using the formula for comparative studies involving quantitative variables [23]. A total of 148 (for the two groups) eligible women were involved in the study.

Collation/analysis of data:

All measurements, investigations and biodata were recorded in the data collection forms. Baseline data included age, weight, height, parity, gestational age, indication for elective C/S, respiratory rate, pulse rate and blood pressure before and after caesarean section, pre and post-caesarean section PCV as well as neonatal parameters (APGAR scores, birth weight).

The anaesthetists who assisted in the study were trained for 5 days (two hours per day) on how to estimate blood loss during and after caesarean section using

the gravimetric method, completion of questionnaires and obtaining data/result for primary and secondary outcomes.

Randomization: The randomization sequence was done by a computer-generated set of random numbers from 1 to 148. Seventy-four random numbers were randomized to GROUP A (Tranexamic acid group) while the remaining 74 numbers were randomized to GROUP B (Placebo or control group). Each participating woman was assigned a number serially according to the time of presentation in such a way that the first patient becomes number 1 automatically while the second patient to present will become number 2 in that order. The study medications were placed in sequentially numbered sealed envelopes and were administered to the patient based on the group that her serial number fell into.

Blinding: Single blinding was employed in this study. The patients were unaware of the medication (TXA or placebo) being allocated to them. Also, the anaesthetists/surgeon assessing the primary outcome of the estimation of blood loss were unaware of the medication assigned to the patient. The packaging process, sealing and numbering were performed by the investigator who was not involved in the surgery.

The tranexamic acid and placebo were identical in appearance. The tranexamic acid used for this study was purchased at the University of Port Harcourt Teaching Hospital Pharmacy and was manufactured by PROTECH Biosystems PVT Ltd., India. Each package contained either tranexamic acid at 1 g (in 10 ml) diluted in 10 ml of water for injection to constitute 20 ml of dilute TXA or 20 ml of water for injection as placebo. Group A (Tranexamic acid group) received 1 gram of intravenous tranexamic acid slowly over 2 minutes, 10 minutes before transverse suprapubic skin incision while the GROUP B (Placebo or control group) received 20 ml of water for injection, 10 minutes before transverse suprapubic skin incision. All patients had lower segment caesarean section under subarachnoid block and the surgery was done by at least a year post-part one senior registrar or a consultant. After delivery, 10 units of oxytocin in 500 ml of normal saline were administered intravenously through an intravenous drip over 15 minutes.

Measurement of blood loss: This was by gravimetric method and the weighing scale used was Spring Scale produced by P.M HANA (HK) Ltd, Hong Kong, China. Measuring blood loss was started after placental expulsion up to the completion of the surgery and from the completion of C/S up to 2 hours after delivery. Pre-weighed drapes, abdominal mops and delivery mats were used during the surgery and precisely counted at the beginning of the caesarean section. To isolate the amniotic fluid from the intra-operative bleeding, the amniotic sac was ruptured with tissue forceps after cutting the uterus and gently drained into a container. After delivery of the placenta, blood was drained into a separate container/receptacle on the drape. The volume of blood in the second container/receptacle on the drape was considered as intra-operative blood loss. Soaked abdominal mops and drapes were weighed after surgery.

The mean blood loss from abdominal mops drapes and delivery mat were calculated using the formula by Gai *et al.* [24]. Blood from mops, drapes and delivery mat = weight of soaked materials – weight of dry materials/1.05; where 1.05 is the specific gravity of blood at 37˚C. To this, the blood drained into the second container after delivery of the placenta was added to get the total intra-operative blood loss. At the end of the operation and when the patient was transferred to the recovery room, all pads were collected and weighed after 2 hours. Two-hour post-operative blood loss was calculated from the soaked pads by the same formula mentioned above. Blood loss above 1000 ml following caesarean section within the first 24 hours of delivery was regarded as PPH.

Packed cell volume was checked pre and 48 hours post-operatively. Patients' one hour and two hours post-operative vital signs (pulse rate, systolic and diastolic blood pressure and respiratory rate) were noted. Patients were also observed during and after surgery for any side effects of the medication, haemodynamic instability and were managed according to need such as the additional need for uterotonic drugs, blood transfusion or surgical interventions such as B Lynch suture or urgent hysterectomy. The newborns were assessed by the neonatologist for fetal birth asphyxia using Apgar scores at 1 and 5 minutes, and babies with birth asphyxia were admitted into the special care baby unit (SCBU).

The data obtained were entered and analyzed using IBM Statistical Package for Social Sciences (SPSS) version 22.0. Data presentations were in tables and charts as appropriate. Descriptive statistics for normally distributed numeric data employed mean ± SD (standard deviation), while median and range were used for numeric data that were not normally distributed. Categorical data were expressed as frequencies and proportions. Inferential analyses for comparison of means between the two groups in the study were done using independent t-test. Inferential analyses were done for qualitative data using Pearson's Chi-square test, Fisher's exact test or Yates' correction as appropriate. $P < 0.05$ was considered statistically significant.

Approval for the study was obtained from the ethical committee of the University of Port Harcourt Teaching Hospital with approval number UPTH/ADM/90/S.11/VOL.XI/904. The trial was also registered with the Pan African Clinical Trial Registry (https://www.pactr.org/) database and the unique identification number for the registry is PACTR202011872201172.

3. Results

After data cleaning, the data for seventy-two participants in the tranexamic acid group and seventy-one participants in the placebo group were analyzed as shown in **Figure 1**.

The mean ages were 33.56 ± 4.25 and 34.35 ± 3.84 for the tranexamic acid and placebo group respectively and the BMI (kg/m^2) were 33.63 ± 4.27 and 31.93 ± 4.85 for the tranexamic acid and placebo group respectively. The difference in

body mass index (BMI) between the 2 groups was statistically significant.

In Figure 2, the main indications for surgery in the tranexamic acid group were previous C/S and/or myomectomy which accounted for 75.0%, malpresentation accounted for 16.7% and maternal request accounted for 5.5% while 69.0% had previous C/S and/or myomectomy, 16.9% had malpresentation, and

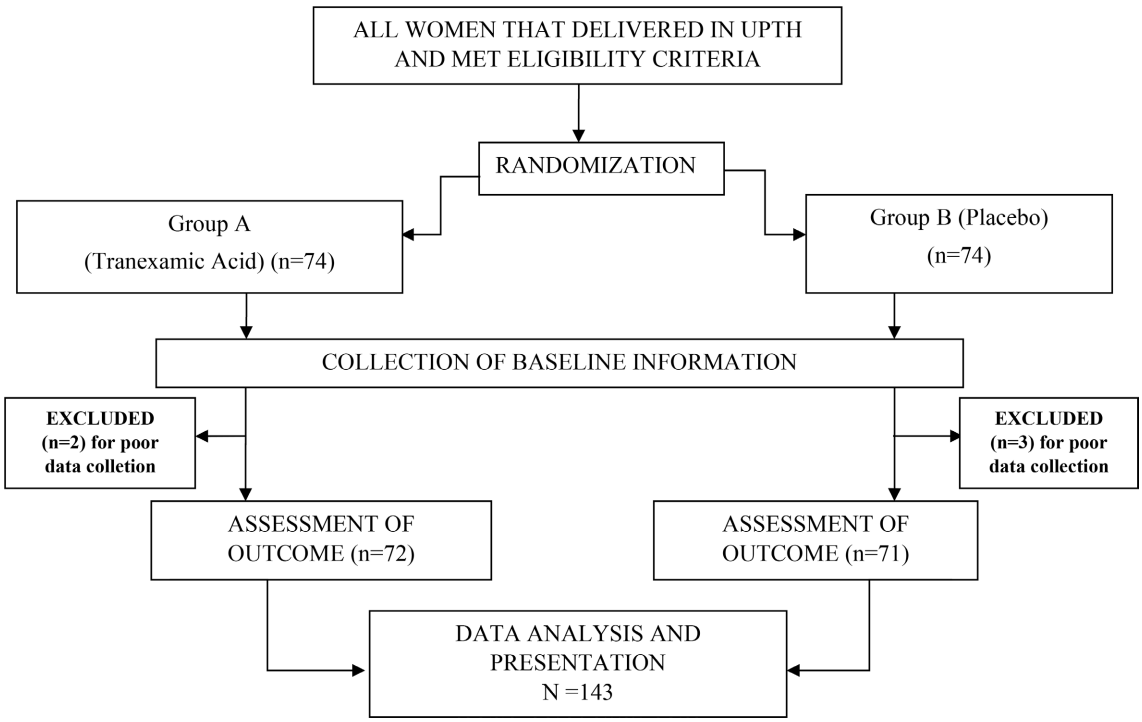

Figure 1. Flow chart of the study protocol showing the number of participants.

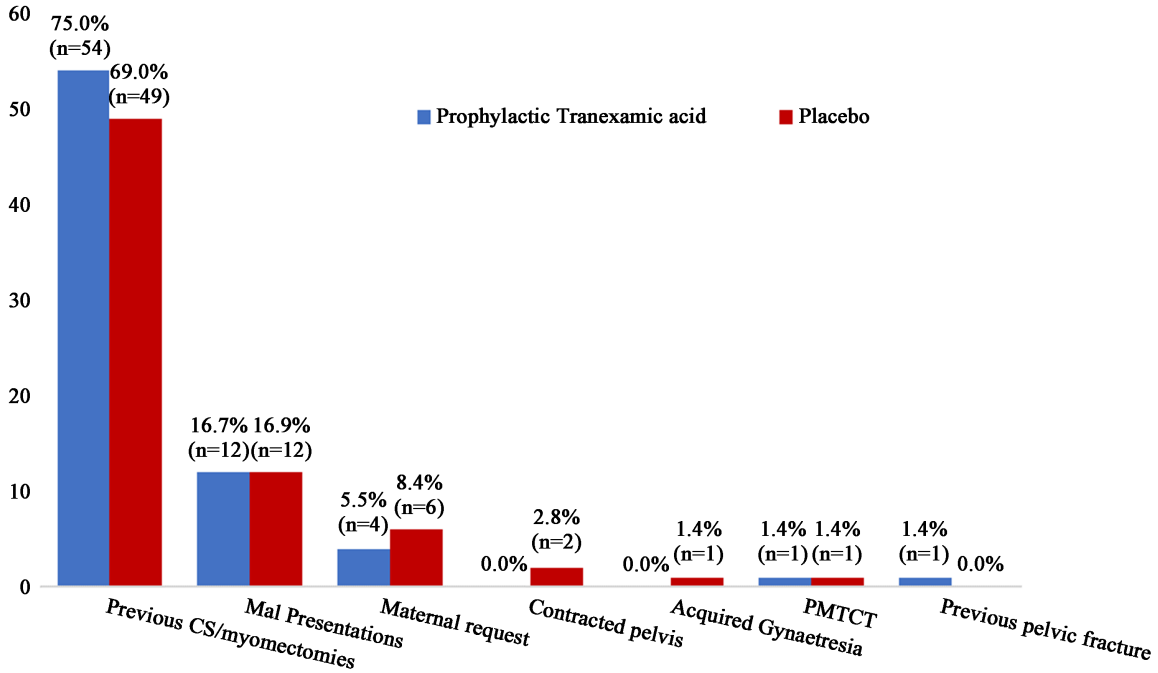

Figure 2. Indications for C/S.

maternal request accounted for 8.4% in the placebo group (Table 1).

The mean pre-C/S systolic BP (mmHg) and diastolic BP (mmHg) in TXA and the mean pre-C/S systolic BP (mmHg) and diastolic BP (mmHg) in the placebo group are as shown in Table 2. The difference in the mean pre-C/S diastolic BP was statistically significant (t = 2.048; p-value = 0.042). Also, the difference in mean post C/S diastolic BP (mmHg) values was also significant (t = 2.335; p-value = 0.021). Post-C/S, the mean pulse rate was significantly higher in the placebo group (88.89 ± 8.03 bpm) in comparison to the tranexemic acid group

Table 1. Demographic characteristics of participants (Comparison of mean demographic and obstetric characteristics between the two groups in the study).

Variable	Study group		t	p-value	CI	
	Tranexamic Acid Mean ± SD	Placebo Mean ± SD			Lower	Upper
Age (years)	33.56 ± 4.25	34.35 ± 3.84	1.146	0.254	−2.161	0.575
BMI (kg/m^2)	33.63 ± 4.27	31.93 ± 4.85	2.185	0.031*	0.161	3.234
Gestational age (wks)	38.15 ± 0.93	38.34 ± 0.91	1.205	0.230	−0.489	0.119
Gravidity	4.06 ± 1.91	3.76 ± 1.84	0.931	0.354	−0.335	0.931
Parity	2.01 ± 0.94	1.74 ± 0.98	1.658	0.100	−0.052	0.595
FHR (bpm)	142.39 ± 7.02	141.27 ± 6.83	0.968	0.335	−1.169	3.412

SD—Standard deviation; *Statistically significant; FHR—Fetal heart rate.

Table 2. Baseline and post-C/S clinical characteristics (Comparison of mean clinical characteristics between the two groups in the study).

Variables	Study group		t	p-value	CI	
	Tranexamic Acid Mean ± SD	Placebo Mean ± SD			Lower	Upper
Baseline clinical characteristics						
Systolic BP (mmHg)	124.76 ± 9.64	119.83 ± 22.53	1.695	0.092	−0.821	10.680
Diastolic BP (mmHg)	79.44 ± 6.87	76.90 ± 7.94	2.048	0.042*	0.089	4.997
Pulse rate (bpm)	83.65 ± 5.06	83.35 ± 5.61	0.337	0.737	−1.465	2.066
Respiratory rate (cpm)	19.82 ± 1.36	19.72 ± 1.39	0.441	0.660	−0.352	0.554
Post C/S clinical characteristics						
Systolic BP (mmHg)	119.44 ± 8.20	122.17 ± 8.62	1.937	0.055	−5.505	0.055
Diastolic BP (mmHg)	72.86 ± 7.72	75.77 ± 7.19	2.335	0.021*	−5.381	−0.446
Pulse rate (bpm)	85.35 ± 6.59	88.89 ± 8.03	2.885	0.005*	−5.966	−1.114
Respiratory rate (cpm)	20.36 ± 1.57	20.38 ± 1.59	0.073	0.942	−0.541	0.503

SD—Standard deviation; *Statistically significant.

(85.35 ± 6.59 bpm), t = 2.885; p-value = 0.005.

The mean blood loss during C/S (mls) in the tranexamic acid group and placebo group showed a significant difference (t = 6.712; p-value = 0.0001). The difference in mean blood loss after C/S to 2 hours post-surgery was also significant (t = 3.798; p-value = 0.001) as shown in Table 3. The difference in the total mean blood loss from C/S to 2 hours post-surgery was significant (t = 6.648; p-value = 0.001). The difference in pre-C/S PCV was not significant (t = 0.605; p-value = 0.546) while the difference in post-C/S PCV was significant (t = 5.131; p-value = 0.0001) between the two groups as shown in Figure 3.

There was need for additional uterotonic medications in 12 participants, (16.7%), need for blood transfusion in 2 (2.8%) participants among the tranexamic acid group while in the placebo group, 36 (50.7%) participants received additional uterotonic medications and 13 (18.3%) had blood transfusion. The differences in

Table 3. Comparison of the primary outcome (Comparison of mean blood loss between the two groups in the study).

Period in study	Study group		t	p-value	CI	
	Tranexamic Acid Mean blood loss ± SD	Placebo Mean blood loss ± SD			Lower	Upper
During CS (mls)	503.67 ± 170.20	704.55 ± 187.39	6.712	0.0001*	−260.05	−141.72
After CS to 2 hours post-surgery (mls)	121.42 ± 49.39	159.69 ± 69.54	3.798	0.001*	−260.09	−141.67
Total blood loss from CS to 2 hours post-surgery (mls)	624.88 ± 200.76	864.24 ± 229.09	6.648	0.001*	−310.55	−168.18

SD—Standard deviation; *Statistically significant.

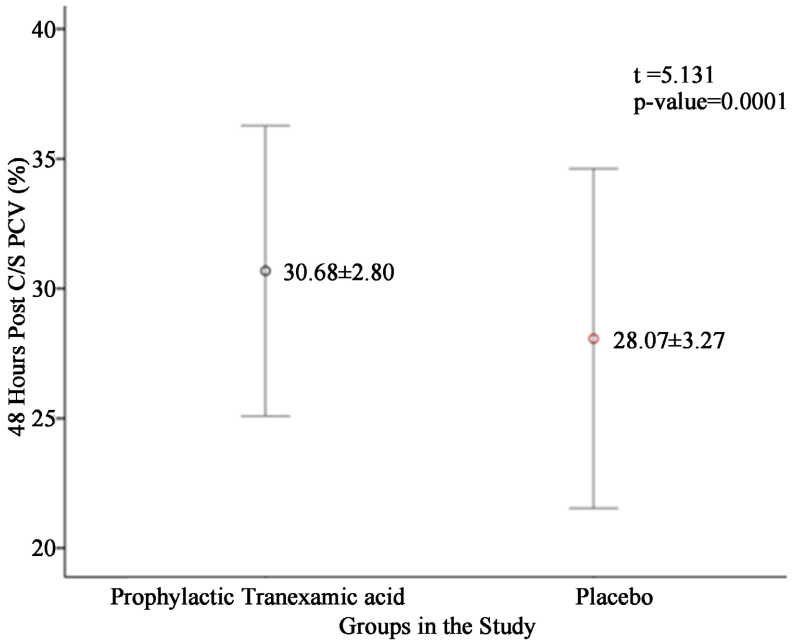

Figure 3. Error bar chart showing the mean and SD 48 hours post-C/S packed cell volume in the two groups.

proportions regarding the need for additional uterotonic medications (Chi Square = 18.573; p-value = 0.0001) and blood transfusion (Chi Square = 9.185; p-value = 0.002) were significant. There was no surgical intervention needed in both groups. These are shown in Table 4.

The maternal side effects in the study participants were only nausea and vomiting which occurred in 9 (12.5%) and 1 (1.4%) participants respectively in the tranexamic acid group. There were no side effects among participants in the placebo group. The differences in proportions for the occurrence of nausea in the two groups were statistically significant (p-value = 0.006). These are shown in Table 5.

The neonatal outcome in the study showed a mean birth weight of 3.27 ± 0.40 kg,

Table 4. Comparison of secondary outcomes (Comparison of secondary outcome variables between the two groups in the study).

Variables	Tranexamic Acid N = 72 n (%)	Placebo N = 71 n (%)	Total N = 143 n (%)	Chi Square	p-value
Additional uterotonic medications					
Yes	12 (16.7)	36 (50.7)	48 (33.6)	18.573	0.0001*
No	60 (83.3)	35 (49.3)	95 (66.4)		
Blood transfusion					
Yes	2 (2.8)	13 (18.3)	15 (10.5)	9.185	0.002*
No	70 (97.2)	58 (81.7)	128 (89.5)		
Surgical intervention					
Yes	0 (0.0)	0 (0.0)	0 (0.0)	0.000	1.000
No	72 (100.0)	71 (100)	143 (100.0)		

*Statistically significant.

Table 5. Maternal side-effects (Comparison of maternal side-effects between the two groups in the study).

Variables***	Tranexamic Acid N = 72 n (%)	Placebo N = 71 n (%)	Total N = 143 n (%)	Chi Square	p-value
Nausea					
Yes	9 (12.5)	0 (0.0)	9 (6.3)	7.470**	0.006*
No	63 (87.5)	71 (100.0)	134 (93.7)		
Vomiting					
Yes	1 (1.4)	0 (0.0)	1 (0.7)	0.000**	1.000
No	71 (98.6)	71 (100.0)	142 (99.3)		

*Statistically significant **Yates' correction; ***None had dizziness, diarrhea, hypotension, allergic skin reaction or thromboembolism.

APGAR score at 1 minute was 7.90 ± 0.30 and APGAR score at 5 minutes was 8.99 ± 0.39 in the tranexamic acid group while in the placebo group, the mean birth weight was 3.36 ± 0.38 kg, APGAR scores at 1 minute was 8.11 ± 0.31, APGAR scores at 5 minutes was 9.01 ± 0.32 as shown in Table 6. There was no significant difference between the two groups. In the tranexamic acid group, 1 (1.4%) baby had low birth weight and there was no special care baby unit (SCBU) admission while in the placebo group, 3 (4.2%) babies had low birth weight and there was 1 (1.4%) SCBU admission. The differences in proportions were not significant (p-value > 0.05) as shown in Table 7.

4. Discussion

In this study, the mean blood loss during C/S in the tranexamic acid group (503.67 ± 170.20 mls) was significantly lower than the mean blood loss in the placebo group (704.55 ± 187.39 mls). After C/S to 2 hours post-surgery, the mean blood loss in the tranexamic acid group (121.42 ± 49.39 mls) was also significantly lower in comparison to the mean blood loss in the placebo group (159.69 ± 69.54 mls).

This present study and that of Roy *et al.* [25], Xu *et al.* [26], Oseni *et al.* [27], Obi *et al.* [28] and Halifa *et al.* [29] among others, have shown that the administration

Table 6. Neonatal outcomes (Comparison of mean neonatal outcomes in the two groups in the study).

Neonatal outcome	Study group		t	p-value	CI	
	Tranexamic Acid Mean ± SD	Placebo Mean ± SD			Lower	Upper
Birth weight (kg)	3.27 ± 0.40	3.36 ± 0.38	1.399	0.164	−0.221	0.037
APGAR score at 1 min	7.90 ± 0.30	8.11 ± 0.31	0.460	0.640	−0.187	0.209
APGAR score at 5 min	8.99 ± 0.39	9.01 ± 0.32	0.468	0.640	−0.146	0.090

SD—Standard deviation.

Table 7. Comparison of neonatal outcomes (Comparison of neonatal outcomes of low birth weight and SCBU admission between the two groups in the study).

Variables	Tranexamic Acid N = 72 n (%)	Placebo N = 71 n (%)	Total N = 143 n (%)	Chi Square	p-value
Low birth weight					
Yes	1 (1.4)	3 (4.2)	4 (2.8)	**	0.366
No	71 (98.6)	68 (95.8)	139 (97.2)		
SCBU admission					
Yes	0 (0.0)	1 (1.4)	1 (0.7)	0.000***	0.994
No	72 (100.0)	70 (98.6)	142 (99.3)		

SCBU—Special Care Baby Unit; **Fisher's Exact; ***Yates' Correction.

of TXA during C/S significantly reduced mean blood loss during and after C/S when compared to a placebo. Compared to our study, Oseni *et al.* study in Northern Nigeria used a higher sample size while Obi *et al.* study in Eastern Nigeria was double blinded. These might make their studies more sensitive. While Halifa *et al.* study was double blinded and both elective and emergency caesarean data was captured, ours was only elective C/S and was single blinded. In all, the outcome the various studies in terms of intra and post-operative blood loss and PCV were similar.

In this study, mean pre-C/S PCV were 32.92% ± 2.36% and 33.18% ± 2.90% among the group that received tranexamic acid and placebo group respectively. This difference in mean values was not significant (t = 0.605; p-value = 0.546). The mean 48 hours post-C/S PCV were 30.68% ± 2.80% and 28.07% ± 3.27% among participants in the tranexamic acid arm and placebo group respectively. This difference in mean values was significant (t = 5.131; p-value = 0.0001). The mean post-operative PCV was higher in the tranexamic acid group when compared to the placebo group even though the mean BMI (kg/m^2) of 33.63 ± 4.27 was higher and significant when compared to the placebo group which had a BMI (kg/m^2) of 31.93 ± 4.85, (p-value = 0.031). The indications for C/S were mainly due to previous C/S and/or myomectomies (75.0%) in the tranexamic acid group when compared to the placebo group (69.0%), and these factors are more associated with intra-operative and post-operative blood loss. The findings of a higher mean post-operative PCV in this study were similar to the findings of Oseni *et al.* [27]. Also, Roy *et al.* [25] revealed that the postoperative fall in haemoglobin was significantly more in the control group.

In this study, there was a need for additional uterotonic medications in 12 (16.7%) participants and need for blood transfusion in 2 (2.8%) participants in the tranexamic acid group while in the placebo group, 36 (50.7%) participants received additional uterotonic medications, 13 (18.3%) had blood transfusion. The proportion of participants requiring additional uterotonic medications and blood transfusion were significantly less among tranexamic acid group in comparison to the placebo group ($p < 0.01$). No surgical intervention was needed in both groups. The findings in this study were similar to the findings by Roy *et al.* [25], in terms of the need for additional uterotonics, in which six mothers in the control group required an extra 10 IU of oxytocin infusion, while only two of the mothers in the TXA group required the same. There was no need for blood transfusion or additional surgical intervention in both groups in the study by Roy *et al.* [25]. In a similar study by Obi *et al.* [28] the need for additional uterotonic (oxytocin) drugs, surgical interventions, blood transfusion was significantly less in the TXA group. The findings from this study and other studies showed that tranexamic acid significantly reduced the need for additional uterotonic medications and blood transfusion.

The maternal side effects were mainly nausea and vomiting which occurred in 9 (12.5%) and 1 (1.4%) participants respectively in the tranexamic acid group in

this study. There were no side effects among participants in the placebo group. The nausea, maternal side effect, was significant (p-value = 0.003). Most other studies referred to in this study did not show significant maternal side effects. In Xu *et al.* [26] study, there was no significant difference in vital signs changes however there were mild, transient side effects more in the tranexamic acid group than the control group.

There was no significant difference in the neonatal outcome in Apgar scores at 1st and 5th minutes or need for SCBU admission in this study. Xu *et al.* [26] study and Halifa *et al.* [29] showed no significant difference in neonatal outcome or complications between the two groups. Also, in the study by Roy *et al.* [25] there was no significant difference in the Apgar scores at 1st and 5th minutes or need for admission into the special care baby unit. The findings on adverse effects on the fetus in this study were similar to the findings by Xu *et al.* [26] and Roy *et al.* [25]. This showed that tranexamic acid has a good safety profile in our study and other previous compared studies.

In summary, this study has shown that tranexamic acid significantly reduced mean total blood loss during and after C/S with minimal maternal side effects and can be comfortably added to uterotonics in reducing blood loss during and after caesarean section. The study has also showed that tranexamic acid reduced post-operative anaemia and need for blood transfusion.

5. Conclusion

The findings from this study showed that tranexamic acid significantly reduces mean blood loss, postoperative anaemia and the need for blood transfusion and use of additional uterotonics, during and after caesarean section. Tranexamic acid medication is easy to administer with a good safety profile and can be added to uterotonics in reducing blood loss during and after caesarean section. Hence, it is an important medication in reducing blood loss during surgery especially in a low resource centre like ours with minimal maternal side effects hence reducing post-partum haemorrhage which is one of the main causes of maternal morbidity and mortality in our environment.

6. Recommendations

Tranexanemic acid is cost-effective, readily available and easy to administer and should be considered as an additional drug to routine oxytocin used to reduce blood loss during C/S. This will greatly reduce maternal morbidity and mortality from postpartum haemorrhage and its sequelae. Multi-center double blind studies are suggested for the future to have a more generalizable conclusion.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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