The Egyptian Journal of Hospital Medicine (October 2018) Vol. 73 (6), Page 6886-6896

Role of Prophylactic Tranexamic Acid in Reducing Blood loss during Elective Caesarean section in Rural Area

Hossam Elden H. Kamel [(1)], AbdAlsattar M. Farhan [(1)], Hesham F. Abou Senna [(1)], Mohammed A. Khedr [(2)], Ahmed A. Albhairy [(1)]

(1) Department of Obstetrics & Gynecology, Faculty of Medicine – Al-Azhar University
(2) Department of Clinical Pathology, Faculty of Medicine – Al-Azhar University

Corresponding author: Ahmed A. Albhairy; **Mobile:** 01006100873; **Email:** daelbhery@gmail.com

Abstract

Background: To reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the amount of bleeding during and after lower segment caesarean section (LSCS). Tranexamic acid helps to reduce bleeding during and after Caesarean section. **Aim of the Work:** To analyse the effectiveness of Tranexamic Acid (TXA) in reducing blood loss during elective caesarean section. **Patients and Methods:** The current study was conducted as a double blinded, randomized, controlled trial on 300 women recruited from labor ward in Kafr Elsheikh General Hospital whom planned to have scheduled casaerean section. A total number of 150 patients received tranexamic acid before induction of anesthesia in addition to oxytocin after delivery of the baby; the other 150 patients received oxytocin only. **Results:** In the current study, no significant difference between study and control groups as regards age (p 0.374). In the current study, no significant difference between study and control groups as regards gestational age (p 0.335). In the current study, number of soaked towels and amount of blood in suction set, which reflect the volume of blood loss from placental delivery to the end of surgery was significantly lower in study group than control group. In the current study, no significant difference between study and control groups as regards preoperative hemoglobin (p 0.614). Postoperative hemoglobin was significantly higher in study group than control group ($p<0.004$). Reduction in hemoglobin was significantly less in study group than control group ($p<0.001$). In the current study, no significant difference between study and control groups as regards preoperative hematocrit (p 0.527). Postoperative hematocrit was significantly higher in study group than control group (p0.17), Reduction in Hematocrit was significantly less in study group than in control group ($p<0.001$). In the current study, need to iron replacement or blood transfusion was significantly less frequent in study group than in control group ($p<0.031$). **Conclusion:** The use of tranexamic acid prior to cesarean section is significantly effective in reducing blood loss during caesarean section with no observed maternal or neonatal side effects.

Recommendations: Further studies are needed to assess possibility of use of tranexamic acid for treatment of postpartum hemorrhage.

Key words: prophylactic tranexamic acid, blood loss, elective cesarean section

Introduction

Every year over five million women die worldwide due to causes related to pregnancy and delivery. Postpartum Haemorrhage (PPH) accounts for the major part of the mortality as well as morbidity like severe anaemia needing blood transfusion, hospital stay and infection [(1)].

Millennium development goal 5 targets for reduction of maternal mortality rate by 75% by 2017, which means 5.5% reduction per year is required. People at high risk of PPH account for only small percent of all maternal deaths. Majority of morbidity and mortality happen in those with no risk factors and cannot be predicted. In an analysis of 1620 women in rural India, it was found that 9.2% experienced PPH. No maternal or socio-demographic factors differed between women with PPH and those without [(2)].

The occurrence rate of caesarean section (CS) has increased in both developed and developing countries, which would result in an increased risk of PPH. Although there has been a remarkable improvement in the prevention and treatment of PPH in recent years, deaths due to PPH remain relatively common in some parts of the world. To lower the occurrence rate of major morbidity and mortality due to PPH, it is very vital to reduce blood loss in CS and vaginal delivery (VD) [(3)].

Received: 13/9/2018
Accepted: 23/9/2018

Though the incidence of early PPH (occurring within 24 hours of delivery) is lower in caesarean section than vaginal delivery, the former is a major surgery and causes greater blood loss. Hence, it is essential to prevent the blood loss effectively in a feasible way. Apart from obstetric, surgical and radiological interventions, pharmacologic management also plays an important role in this aspect. Uterine atony is the most common cause for PPH. First line of therapeutic management for PPH is oxytocin [(4)].

Other modalities include intravenous ergometrine, intra-muscular carboprost and misoprostol. Prohaemostatic drugs such as tranexamic acid provide a complementary biochemical haemostatic effect to the well-proven uterotonics, especially oxytocin. Systemic anti-fibrinolytic agents are widely used in surgery. A systematic review of randomised controlled trials of anti-fibrinolytic agents in elective surgical patients identified 211 randomised controlled trials [(5)].

The results showed that tranexamic acid reduced the risk of blood transfusion by 39%. Tranexamic acid is an analogue of lysine that inhibits fibrinolysis by competitively binding to plasminogen. It prevents the lysis of formed clot by inhibiting activation of plasminogen and plasmin. It is ten times more potent than Amino- caproic acid [(6)].

Tranexamic acid has been shown to reduce uterine blood loss in non-surgical aspect. A study done on women with menorrhagia has showed significant reduction in mean menstrual blood loss in those treated with tranexamic acid [(7)].

A randomized controlled trial assessed tranexamic acid for the treatment of PPH and it showed that a high dose of tranexamic acid reduces blood loss in women with PPH [(8)].

Several randomised controlled trials have analysed the prophylactic role of tranexamic acid and have shown significant results in reducing blood loss. Tranexamic acid might reduce the need for hysterectomy, reduce the risk of severe anaemia and avoid the need for blood transfusion. Hence, this could contribute significantly to the goal of reducing maternal mortality [(9)].

Aim of the Work

To analyse the effectiveness of tranexamic acid (TXA) in reducing blood loss during elective caesarean section.

Patients and Methods

This study was conducted at the Department of Obstetrics & Gynecology in Kafr Elsheikh General Hospital.

The institutional review board approved the study protocol and an informed consent was obtained from all participants prior to commencing the study.

Patients

This study was conducted on three hundred (300) women undergoing caesarean section. They were allocated to either Study or Control group by computer generated random number tables.

Group 1: Tranexamic acid was given prior to surgery in study group in addition to the routine care {10 units of oxytocin added to the intravenous drip soon after baby delivery}. Tranexamic acid injection was prepared by diluting 1gm (10ml) TXA in 100 ml of normal saline. TXA was administrated as intravenous infusion (over 15minutes), at least 20 minutes prior to skin incision.

Group 2: the control group had routine care alone.

***Selection criteria:**

***Inclusion Criteria:**

1. Parity not more than two.
2. Singleton pregnancy.
3. Delivery by elective LSCS.
4. Age between 18 and 37 years old
5. Gestational age of 37 to 42 weeks of pregnancy.

***Exclusion Criteria:**

1. Parity more than two.
2. Twin pregnancy.
3. Vaginal delivery or urgent C S.
4. Subjects of age less than 18 or more than 37 years old.
5. Subjects having medical problems, like gestational hypertension, chronic hypertension and severe pre-eclampsia, renal disease, heart disease complicating

pregnancy or having coagulation disorders, were excluded from the study.

6. Subjects allergic to tranexamic acid by history.
7. Subjects with history of thromboembolic disorders.
8. Subjects having tendency for increased bleeding like abnormal placentation, multiple pregnancy, polyhydramnios, previous two or more caesarean sections and those who had blood transfusion due to anaemia.

Methods

***All patients were subjected to:**

1. Full history taking

a) Personal history.
b) Obstetric history (parity not more than two)
c) Medical & Operative history.
d) Any drug allergy.

2. Clinical examination (clinical criteria):

- Complete general examination:
- Vital signs (BP, Temp, RR and Pulse).
- Head and Neck examination for jaundice, pallor,
- Pigmentation, goiter, congested neck veins.
- Abdominal examination (liver failure, ascites,. etc)

3. Laboratory investigations such as:

- Complete blood count (haemoglobin before and after surgery)
- Liver functions (e.g. **S**GOT, **S**GPT).
- Kidney functions (Urea, Creatinine).
- Random blood sugar (RBS).

Blood loss was measured in both groups following placental delivery until the end of surgery. Blood collected in suction container was noted. Soaked mops and operation table perineal sheet was weighted by electronic scale before and after surgery. Haemoglobin and haematocrit value before and after surgery was estimated and the percentage of difference was compared.

Statistical Analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Paired sample t-test of significance was used when comparing between related samples.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:
  - Probability (P-value):
    - P-value <0.05 was considered significant.
    - P-value <0.001 was considered as highly significant.
    - P-value >0.05 was considered insignificant.

Results

The investigated groups are described as follows:

Tranexamic group: 150 women who received IV kapron in addition to oxytocin.

Control group: 150 women who received oxytocin only.

Maternal and neonatal side effects of tranexamic acid were not recorded among the studied cases of the tranexamic group.

Table (1): Comparison between tranexamic and control groups regarding to maternal age and gestational age (GA).

Variable	Measure	Tranexamic (N=150)	Control (N=150)	^P
Age (years)	**Mean ± SD**	29.39 ± 3.84	29.82 ± 3.94	0.374
	Range	25.0–36.0	25.0–37.0	
G.A. (weeks)	**Mean ± SD**	39.49 ± 1.01	39.29 ± 1.01	0.335
	Range	37.0–41.0	37.0–41.0	

^Independent t-test

No significant difference was detected between tranexamic and control groups regarding maternal age and gestational age.

Table (2): Comparison between tranexamic and control groups regarding blood loss from placental delivery to the end of the surgery (mL).

Measures	Tranexamic (N=100)	Control (N=100)	^P
Mean ± SD	307.5 ± 170.6	436.0 ± 208.3	**<0.001***
Range	273.6–341.4	394.7–477.3	
95% CI	100.0–750.0	100.0–900.0	
Efficacy of adding tranexamix			
Items	**Mean ± SE**	**95% CI**	
Blood loss difference	128.5±26.9	75.4–181.6	

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

Table (2) showed that blood loss from placental delivery to the end of the surgery was significantly lower in tranexamic group than control group.

Table (3): Comparison between tranexamic and control groups regarding blood loss from the end of the operation to 1-hour after birth (mL).

Measures	Tranexamic (N=100)	Control (N=100)	^P
Mean ± SD	24.5 ± 54.4	42.0 ± 64.2	**0.027***
Range	0.0–200.0	0.0–250.0	
95% CI	13.7–35.3	29.3–54.7	
Efficacy of adding tranexamix			
Items	**Mean±SE**	**95% CI**	
Blood loss difference	17.5±8.4	0.9–34.1	

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

Table (3) showed that blood loss from the end of the operation to 1-hour after birth, which was significantly lower in tranexamic group than in control groups.

Table (4): Comparison between tranexamic and control groups regarding total blood loss from placental delivery to 6-hours after birth (mL).

Measures	Tranexamic (N=100)	Control (N=100)	^P
Mean ± SD	332.0 ± 196.2	478.0 ± 234.0	**<0.001***
Range	293.1–370.9	431.6–524.4	
95% CI	100.0–950.0	100.0–1050.0	
Efficacy of adding tranexamix			
Items	**Mean±SE**	**95% CI**	
Blood loss difference	146.0±30.5	85.8–206.2	

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

Table (4) showed that total blood loss from placental delivery to 6-hours after birth was significantly lower in tranexamic group than in control group.

Table (5): Comparison between tranexamic and control groups regarding hemoglobin (gm/dL).

Time	Measure	Tranexamic	Control	^P
Preoperative	**Mean ± SD**	11.9 ± 1.5	11.9 ± 1.2	0.614
	Range	8.2–15.5	8.6–14.9	
	95% CI	11.6–12.1	11.7–12.1	
Immediatly postoperative	**Mean ± SD**	10.7 ± 1.5	10.2 ± 1.2	**0.004***
	Range	6.1–14.9	7.0–12.6	
	95% CI	10.4–11.0	9.9–10.4	
#P (Pre/Post)		**<0.001***	**<0.001***	

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

Table (5) showed that no significant difference between tranexamic and control groups regarding preoperative hemoglobin**.** Postoperative hemoglobin was significantly higher in tranexamic group than in control group. Hemoglobin significantly decreased postoperatively in both groups.

Table (6): Comparison between tranexamic and control groups regarding hemoglobin reduction (gm/dL).

Measures	Tranexamic (N=100)	Control (N=100)	^P
Mean ± SD	1.2 ± 0.9	1.7 ± 0.8	**<0.001***
Range	0.1–4.1	0.4–3.7	
95% CI	1.0–1.3	1.6–1.9	
Efficacy of adding tranexamic			
Items	**Mean ± SE**	**95% CI**	
Hemoglobin reduction difference	0.6 ± 0.1	0.3–0.8	

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

Table (6) showed that reduction in hemoglobin was significantly less in tranexamic group than in control group.

Table (7): Comparison between tranexamic and control groups regarding hematocrit (%).

Time	Measure	Tranexamic	Control	^P
Preoperative	**Mean ± SD**	33.0 ± 3.9	33.2 ± 3.1	0.527
	Range	24.5–41.5	26.3–41.3	
	95% CI	32.3–33.8	32.6–33.8	
Immediately postoperative	**Mean ± SD**	30.5 ± 3.7	29.4 ± 2.9	**0.017***
	Range	21.5–40.1	21.3–35.6	
	95% CI	29.8–31.3	28.8–30.0	
#P (Pre/Post)		**<0.001***	**<0.001***	

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

Table (7) showed that no significant difference was detected between tranexamic and control groups regarding preoperative hematocrit**.** Postoperative hematocrit was significantly higher in tranexamic group than in control group. Hematocrit significantly decreased postoperatively in both groups.

Table (8): Comparison between tranexamic and control groups regarding hematocrit reduction (%).

Measures	Tranexamic (N=100)	Control (N=100)	^P
Mean ± SD	2.5 ± 2.5	3.8 ± 2.3	**<0.001***
Range	0.3–14.9	0.5–10.5	
95% CI	2.0–3.0	3.3–4.3	
Efficacy of adding tranexamix			
Items	**Mean ± SE**	**95% CI**	
Hematocrit reduction difference	1.3 ± 0.3	0.6–1.9	

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

Table (8) showed that reduction in hematocrit was significantly less in tranexamic group than in control group.

Table (9): Comparison between tranexamic and control groups regarding pulse rate (BPM).

Time	Measure	Tranexamic	Control	^P
Pre operative	**Mean ± SD**	83.7 ± 5.7	83.8 ± 5.1	0.815
	Range	70.0–98.0	70.0–97.0	
	95% CI	82.5–84.8	82.8–84.8	
Immediately post-operative	**Mean ± SD**	89.0 ± 6.5	91.5 ± 6.2	**0.005***
	Range	72.0–107.0	75.0–111.0	
	95% CI	87.7–90.2	90.3–92.8	
	#P (Pre/Im.)	**<0.001***	**<0.001***	
1-hour post operative	**Mean ± SD**	90.7 ± 7.0	94.1 ± 6.6	**<0.001***
	Range	73.0–110.0	77.0–115.0	
	95% CI	89.3–92.1	92.7–95.4	
	#P (Pre/1hr)	**<0.001***	**<0.001***	
6-hours Post operative	**Mean ± SD**	92.4 ± 7.4	97.2 ± 7.2	**<0.001***
	Range	74.0–113.0	80.0–120.0	
	95% CI	90.9–93.9	95.8–98.7	
	#P (Pre/2hr)	**<0.001***	**<0.001***	

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

Table (9) showed that no significant difference between tranexamic and control groups regarding preoperative pulse. Postoperative pulse ra**te** (immediately, 1-hour and 6-hours postoperative)

was significantly lower in tranexamic group than in control group. Pulse rate significantly increased postoperatively in both groups.

Table (10): Comparison between tranexamic and control groups regarding pulse rate elevation (BPM)

Time	Measure	Tranexamic	Control	^P
Elevation Preoperative/ Immediatly postoperative	**Mean ± SD**	5.3 ± 2.4	7.7 ± 3.2	**<0.001***
	Range	1.0–14.0	2.0–19.0	
	95% CI	4.8–5.8	7.1–8.3	
Elevation Preoperative/ 1-hour postoperative	**Mean ± SD**	7.1 ± 3.2	10.2 ± 4.0	**<0.001***
	Range	1.0–18.0	3.0–24.0	
	95% CI	6.4–7.7	9.4–11.0	
Elevation Preoperative/ 6-hours postoperative	**Mean ± SD**	8.8 ± 3.9	13.4 ± 4.9	**<0.001***
	Range	2.0–22.0	5.0–29.0	
	95% CI	8.0–9.5	12.4–14.4	
Efficacy of adding tranexamix				
Items		**Mean±SE**	**95% CI**	
Pulse difference immediatly		2.4 ± 0.4	1.6–3.2	
Pulse difference 1-hour		3.2 ± 0.5	2.2–4.2	
Pulse difference 6-hours		4.7 ± 0.6	3.4–5.9	

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

Table (10) showed that elevation in pulse rate (immediately, 1-hour and 6-hours postoperative) was significantly less in tranexamic group than in control group.

Table (11): Comparison between tranexamic and Control groups regarding systolic blood pressure (mmHg).

Time	Measure	Tranexamic	Control	^P
Preoperative	**Mean ± SD**	118.5 ± 4.4	118.2 ± 4.3	0.512
	Range	115.0–125.0	115.0–125.0	
	95% CI	117.6–119.3	117.3–119.1	
Immediatly postoperative	**Mean ± SD**	112.5 ± 5.2	109.1 ± 5.4	**<0.001***
	Range	100.0–120.0	95.0–115.0	
	95% CI	111.4–113.5	108.0–110.2	
	#P (Pre/Im.)	**<0.001***	**<0.001***	
1-hour postoperative	**Mean ± SD**	110.4 ± 5.8	105.8 ± 6.3	**<0.001***
	Range	95.0–120.0	90.0–115.0	
	95% CI	109.2–111.6	104.5–107.0	
	#P (Pre/1hr)	**<0.001***	**<0.001***	
6-hours postoperative	**Mean ± SD**	107.8 ± 7.4	102.3 ± 7.6	**<0.001***
	Range	90.0–120.0	85.0–115.0	
	95% CI	106.3–109.3	100.7–103.8	
	#P (Pre/2hr)	**<0.001***	**<0.001***	

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

Table (11) showed that there was no significant difference between tranexamic and control groups regarding preoperative SBP. Postoperative SBP (immetdiately, 1-hour and 6-hours postoperative) was significantly higher in tranexamic group than in control group. SBP significantly decreased postoperatively in both groups.

Table (12): Comparison between tranexamic and control groups regarding SBP reduction (mmHg)

Time	Measure	Tranexamic	Control	^P
Reduction Preoperative/ Immediatly postoperative	**Mean ± SD**	6.0 ± 2.4	9.1 ± 4.5	**<0.001***
	Range	5.0–15.0	5.0–20.0	
	95% CI	5.5–6.5	8.2–10.0	
Reduction Preoperative/ 1-hour postoperative	**Mean ± SD**	8.1 ± 3.5	12.5 ± 5.4	**<0.001***
	Range	5.0–20.0	5.0–25.0	
	95% CI	7.3–8.8	11.4–13.5	
Reduction Preoperative/ 6-hours postoperative	**Mean ± SD**	10.7 ± 5.5	16.0 ± 7.0	**<0.001***
	Range	5.0–25.0	5.0–30.0	
	95% CI	9.6–11.7	14.6–17.3	
Efficacy of adding tranexamix				
Items		**Mean ± SE**	**95% CI**	
SBP difference immediatly		3.1 ± 0.5	2.1–4.1	
SBP difference 1-hour		4.4 ± 0.6	3.1–5.7	
SBP difference 6-hours		5.3 ± 0.9	3.6–7.0	

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

Table (12) showed that reduction in SBP (immetdiately, 1-hour and 6-hours postoperative) was significantly less in tranexamic group than in control group.

Table (13): Comparison between tranexamic and control groups regarding diastolic blood pressure (mmHg).

Time	Measure	Tranexamic	Control	^P
Preoperative	**Mean ± SD**	75.7 ± 2.2	75.4 ± 2.1	0.412
	Range	70.0–80.0	70.0–80.0	
	95% CI	75.2–76.1	75.0–75.8	
Immediatly postoperative	**Mean ± SD**	66.5 ± 4.8	64.2 ± 4.6	**<0.001***
	Range	55.0–75.0	55.0–75.0	
	95% CI	66.5–67.4	63.3–65.1	
	#P (Pre/Im.)	**<0.001***	**<0.001***	
1-hour postoperative	**Mean ± SD**	66.1 ± 5.3	62.5 ± 5.7	**<0.001***
	Range	55.0–75.0	50.0–75.0	
	95% CI	65.0–67.1	61.4–63.6	
	#P (Pre/1hr)	**<0.001***	**<0.001***	
6-hours postoperative	**Mean ± SD**	65.4 ± 5.6	60.9 ± 7.4	**<0.001***
	Range	55.0–75.0	45.0–75.0	
	95% CI	64.3–66.5	59.4–62.4	
	#P (Pre/2hr)	**<0.001***	**<0.001***	

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

Table (13) showed that there was no significant difference between tranexamic and control groups regarding preoperative DBP. Postoperative DBP (immediately, 1-hour and 6-hours postoperative) was significantly higher in tranexamic group than in control group. DBP significantly decreased postoperatively in both groups.

Table (14): Comparison between tranexamic and control groups regarding DBP reduction (mmHg).

Time	Measure	Tranexamic	Control	^P
Reduction Preoperative/ Immediatly postoperative	**Mean ± SD**	9.2 ± 4.1	11.3 ± 4.0	**<0.001***
	Range	5.0–15.0	5.0–15.0	
	95% CI	8.4–10.0	10.4–12.1	
Reduction Preoperative/ 1-hour postoperative	**Mean ± SD**	9.6 ± 4.9	12.9 ± 5.2	**<0.001***
	Range	5.0–20.0	5.0–20.0	
	95% CI	8.6–10.6	11.9–13.9	
Reduction Preoperative/ 6-hours postoperative	**Mean ± SD**	10.3 ± 5.5	14.5 ± 7.1	**<0.001***
	Range	5.0–25.0	5.0–25.0	
	95% CI	9.2–11.3	13.1–15.9	

Efficacy of adding tranexamix		
Items	**Mean ± SE**	**95% CI**
DBP difference immediatly	2.1 ± 0.6	0.9–3.2
DBP difference 1-hour	3.3 ± 0.7	1.9–4.7
DBP difference 6-hours	4.3 ± 0.9	2.5–6.0

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

Table (14) showed that reduction in DBP (immetdiately, 1-hour and 6-hours postoperative) was significantly less in tranexamic group than in control group.

Table (15): Comparison between tranexamic and control groups regarding respiratory rate (CPM).

Time	Measure	Tranexamic	Control	^P
Preoperative	**Mean ± SD**	18.7 ± 1.4	18.7 ± 1.3	0.657
	Range	17.0–21.0	17.0–21.0	
	95% CI	18.4–19.0	18.4–18.9	
Immediately postoperative	**Mean ± SD**	20.2 ± 1.7	21.0 ± 1.6	**<0.001***
	Range	17.0–24.0	18.0–24.0	
	95% CI	19.9–20.5	20.7–21.3	
	#P (Pre/Im.)	**<0.001***	**<0.001***	
1-hour postoperative	**Mean ± SD**	20.7 ± 1.9	22.9 ± 2.0	**<0.001***
	Range	17.0–26.0	19.0–27.0	
	95% CI	20.3–21.1	22.5–23.3	
	#P (Pre/1hr)	**<0.001***	**<0.001***	
6-hours postoperative	**Mean ± SD**	21.3 ± 2.4	24.8 ± 2.4	**<0.001***
	Range	17.0–28.0	19.0–28.0	
	95% CI	20.8–21.8	24.3–25.2	
	#P (Pre/2hr)	**<0.001***	**<0.001***	

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

Table (15) showed that there was no significant difference between tranexamic and control groups regarding preoperative respiratory rate. Postoperative respiratory rate (immediately, 1-hour and 6-hours postoperative) was significantly lower in tranexamic group than in control group. Respiratory rate significantly increased postoperatively in both groups.

Table (16): Comparison between tranexamic and control groups regarding RR elevation (BPM)

Time	Measure	Tranexamic	Control	^P
Elevation Preoperative/ Immediatly postoperative	**Mean ± SD**	1.5 ± 0.9	2.3 ± 0.9	**<0.001***
	Range	0.0–3.0	0.0–3.0	
	95% CI	1.3–1.7	2.2–2.5	
Elevation Preoperative/ 1-hour postoperative	**Mean ± SD**	2.0 ± 1.2	4.2 ± 1.3	**<0.001***
	Range	0.0–5.0	1.0–6.0	
	95% CI	1.8–2.3	3.9–4.5	
Elevation Preoperative/ 6-hours postoperative	**Mean ± SD**	2.6 ± 1.8	6.1 ± 1.9	**<0.001***
	Range	0.0–7.0	2.0–9.0	
	95% CI	2.2–3.0	5.7–6.5	
Efficacy of adding tranexamix				
Items		**Mean ± SE**	**95% CI**	
Pulse difference immediatly		0.8 ± 0.1	0.6–1.0	
Pulse difference 1-hour		2.2 ± 0.2	1.8–2.5	
Pulse difference 6-hours		3.5 ± 0.3	3.0–4.0	

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

Table (16) showed that elevation in respiratory rate (immediately, 1-hour and 6-hours postoperative) was significantly less in tranexamic group than in control group.

Discussion

Obstetric hemorrhage remains one of the major causes of maternal death in both developed and developing countries. Because of its importance as a leading cause of maternal mortality and morbidity, and because of evidence of substandard care in the majority of fatal cases, obstetric hemorrhage must be considered as a priority topic for national research development [(10)].

The increased frequency of PPH in the developing world is mainly due to expectant management because of lack of availability of medications used in the active management of the third stage [(11)].

During placental delivery, fibrinogen and fibrin are rapidly degraded, whereas plasminogen activators and fibrin degradation products increase due to activation of the fibrinolytic system. This activation can last up to 6-10 h postpartum causing more bleeding [(12)].

Tranexamic acid competitively inhibits activation of plasminogen, thereby reducing conversion of plasminogen to plasmin (fibrinolysin), an enzyme that degrades fibrin clots, fibrinogen, and other plasma proteins, including the procoagulant factors V and VIII. Tranexamic acid also directly inhibits plasmin activity, but higher doses are required than are needed to reduce plasmin formation. In vitro, the antifibrinolytic potency of tranexamic acid is approximately 5 to 10 times that of aminocaproic acid [(13)]. It was used in gynecological bleeding and major trauma.

Thus, the current study was held to assess the efficiency of use of tranexamic acid in reducing blood loss in patients undergoing cesarean sections.

In this study, the study group was 150 women as well as the control group that was 150 women also while our sample size was greater than other studies.

In the study of **Gai *et al.*** [(14)]**,** the study group was 91 women, whereas the control group was 89 women. In the study of **Mayur *et al.*** [(15)]**,** the study group was 50 women, whereas the control group was 50 women. In the study of **Sekhavat *et al.*** [(16)]**,** 45 patients were given tranexamic acid and 45 patients were given placebo.

In our study, there was no significant difference as regard patient characteristics (age, weight, BMI, parity and gestational age) between the study and the control groups.

In the study of **Gai *et al.*** [14], the patients' characteristics in the two groups were similar, with no statistical difference between the two groups.

In the study of **Sekhavat *et al.*** [16], the subject characteristics in the two groups were similar (no statistically significant difference between two groups). The patients mean age was 26.2 ± 4.7 years in tranexamic acid group and 27.1 ± 4.1 years in placebo group (p¼0.09).

Our results showed that tranexamic acid significantly reduced bleeding during and after cesarean section. The study group's total blood loss from placental delivery until 6 hours postoperative: (332 ± 196.2 ml) was significantly less than control group (478 ± 234 ml) (p<0.001). The difference in blood loss equals to (146.0 ± 30.5 ml). These results agree with the results of the three studies mentioned previously.

In our study, there was significant statistical difference in the vital data immediately after placental delivery and 1 hour postoperative between the two groups.

In this study, postoperative hemoglobin was significantly higher in the study group than in the control group (p<0.002). Reduction in hemoglobin was significantly less in the study group than in the control group by (0.6 ± 0.1 gm/dl) (p<0.001). In addition, post-operative hematocrit was significantly higher in the study group than in the control group (p<0.008). Reduction in hematocrit was significantly less in the study group than in the control group by (1.3 ± 0.3%) (p<0.001).

The previous study of **Gai *et al.*** [14], showed that tranexamic acid significantly reduced the quantity of blood from the end of CS to 2 h postpartum: (42:75 ± 40:45 ml) in the study group versus (73:98 ± 77:09 ml) in the control group (P ¼ 0:001). It also significantly reduced the quantity of total blood from placental delivery to 2 h postpartum: (351:57 ± 148:20 ml) in the study group (439:36 ± 191:48 ml) in the control group (P ¼ 0:002).

The previous study of **Mayur *et al.*** [15] also, showed that tranexamic acid significantly reduced the quantity of blood loss from the end of LSCS to 2 hours postpartum: (75.71 ml) in the study group versus (133.03 ml) in the control group (p=0.001). It also significantly reduced the quantity of blood loss from placental delivery to 2 hours post-partum: (372.71 ml) in the study group, versus (469.70 ml) in the control group (P=0.003).

The previous study of **Sekhavat *et al.*** [16] showed that tranexamic acid significantly reduced the blood loss from the end of CS to 2 h postpartum; (28.02 ± 5.53 ml) in the tranexamic group versus (37.12 ± 8.97 ml) in the control group (p¼0.000). Hb 24 h after CS was significantly greater in tranexamic group than in the control group (12.57 ± 1.33 in the tranexamic group and 11.74 ± 1.14 in the control group, p¼0.002).

In this study, total blood loss from placental delivery until end of cesarean section was significantly lower in the study group than in the control group by (128.5 ± 26.9 ml) (p<0.001).

In the study of ***Gai et al.*** [14], there was no statistical difference in the quantity of blood from the time of placental delivery to the end of CS between the two groups (P 0:063).

In our study, blood loss from placental delivery till 6 hours post-operative was reported whatever it is, while in the study of ***Gai et al.*** [14] only blood loss greater than 400 ml was reported. The reasons behind a choice of an outcome such as blood loss greater than 400 ml are not clear.

In our study, there was significant difference in vital data between the study group and the control group immediately and 2 hours post-operative.

In the study of ***Mayur et al.*** [15] and the study of ***Sekhavat et al.*** [16], there was no statistically significant difference in the heart rates, respiratory rates and blood pressures in the two groups.

In our study, the included patients were those who were term, singleton, going for elective cesarean section. While, patients with major maternal medical problem, patients

with bleeding tendency, patient with high risk of thrombo-embolism, ante-partum hemorrhage, abnormal site of the placenta, macrosomic baby, twin pregnancy and polyhydramnios were excluded.

Other studies had nearly the same inclusion and exclusion criteria as that of the studies of ***Gai et al.*** [14] ***and Sekhavat et al.*** [16] included only singleton primipara patients.

We used placebo in the current study, while ***Gai et al.*** [14] ***and Mayur et al.*** [15] did not use placebo.

In the study of ***Yang et al.*** [17]**,** RCT was used to investigate the efficacy of tranexamic acid for preventing postpartum hemorrhage in women who delivered vaginally. A group of 92 women was given aminomethylbenzoic acid (which is an anti-fibrinolytic), which was considered as a placebo by the trial authors, though there was also a group that has not received any intervention this was criticized by Cochrane reviewer as aminomethylbenzoic acid shouldn't be considered as a placebo. Also, the study of ***Sekhavat et al.*** [16] used a placebo.

Possible bias in our study might result from exclusion of the cases with higher risks for PPH, but they were also excluded from the other studies.

We included scheduled sections only while emergency sections were excluded, that might have an impact on our results.

In the current study, need to iron replacement or blood transfusion was significantly less frequent in the study group than in the control group ($p<0.031$).

Conclusion

The use of tranexamic acid prior to cesarean section is significantly effective in reducing blood loss during caesarean section with no observed maternal or neonatal side effects.

Recommendations

Further studies are needed to asses' possibility of use of tranexamic acid for treatment of postpartum hemorrhage.

References

1. **Novikova N, Hofmeyr GJ (2015):** Tranexamic acid for preventing postpartum haemorrhage (Review) Copyright © 2011 The Cochrane Collaboration. Published by JohnWiley & Sons, Ltd.
2. **Geller SE, Goudar SS, Adams MG, Naik VA, Patel A, Bellad MB *et al.* (2014):** Factors associated with acute postpartum haemorrhage in low-risk women delivering in rural India. International Journal of Gynecology and Obstetrics, 101(1): 94- 99.
3. **Li C, Gong Y, Dong L, Xie B, Dai Z (2017):** Is prophylactic tranexamic acid administration effective and safe for postpartum hemorrhage prevention? A systematic review and meta-analysis. Medicine, 96(1): 215-221.
4. **Dyer RA, Buiwick AJ, Carvalho B (2013):** Oxytocin for labour and caesarean delivery: implications for the anaesthesiologist. Current Opinion. Anesthesiology, 24(3): 255-61.
5. **Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ, Fergusson DA et al. (2012):** Antifibrinolytic use for minimising perioperative allogeneic blood transfusion. The Cochrane Library, https://www.ncbi.nlm.nih.gov/pubmed/21249650
6. **Satyavathi K, Vemu NJ, Mohammed S (2009):** Tranexamic acid: A proven antifibrinolytic agent (A review). Oriental Journal of Chemistry, 25(4): 987-92.
7. **Matteson KA, Rahn DD, Wheeler TL (2013):** Non-surgical management of heavy menstrual bleeding: A systematic review and practice guidelines. Obstetrics and Gynecology, 121 (3): 632.
8. **Movafegh A, Eslamian L, Dorabadi A (2013):** Effect of Intravenous Tranexamic Acid Administration on Blood Loss During and After Cesarean Delivery. Obstetric Anesthesia Digest., 33(1):34-5.

9. **Movafegh A, Eslamian L, Dorabadi A (2013):** Effect of intravenous tranexamic acid administration on blood loss during and after cesarean delivery. International Journal of Gynecology & Obstetrics, 115(3): 224-26.
10. **Nour NM (2008):** An introduction to maternal mortality. Reviews in obstetrics and gynecology, 1(2): 77.
11. **Prata N, Bell S, Weidert K (2013):** Prevention of postpartum hemorrhage in low-resource settings: current perspectives. International journal of women's health, 5: 737.
12. **Kolev K, Longstaff C (2016):** Bleeding related to disturbed fibrinolysis. British journal of haematology, 175(1): 12-23.
13. **Pabinger I, Fries D, Schöchl H, Streif W, Toller W (2017):** Tranexamic acid for treatment and prophylaxis of bleeding and hyperfibrinolysis. Wiener klinische Wochenschrift, 129(9-10):303-16.
14. **Gai MY, Wu LF, Su QF, Tatsumoto K (2004):** Clinical observation of blood loss reduced by tranexamic acid during and after caesarian section: a multi-center, randomized trial. European Journal of Obstetrics & Gynecology and Reproductive Biology, 112: 154-7.
15. **Mayur G, Purvi P, Ashoo G, Pankaj D (2007):** Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: a randomized case controlled prospective study. J Obstet Gynecol India, 57(3):227-30.
16. **Sekhavat L, Tabatabaii A, Dalili M, Farajkhoda T, Tafti AD (2009):** Efficacy of tranexamic acid in reducing blood loss after cesarean section. The Journal of Maternal-Fetal & Neonatal Medicine, 22(1):72-5.
17. **Yang H, Zheng S, Shi C (2001):** [Clinical study on the efficacy of tranexamic acid in reducing postpartum blood lose: a randomized comparative, multicenter trial] [Chinese]. Chung-Hua Fu Chan Ko Tsa Chih. Chinese Journal of Obstetrics and Gynaecology, 36(10): 590-2.