ORIGINAL ARTICLE

Role of Tranexamic Acid in Reducing Blood Loss during and after Caesarean Section"

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ABSTRACT

Aim: To find out the efficacy and safety of tranexamic acid (TXA) in reducing blood loss during and after lower segment caesarean section (LSCS).
Study Design: A concurrent parallel study
Place and Duration of Study: The study was conducted in gynecology and obstetrics department of Kishwar Fazal Teaching Hospital of Amna Inayat Medical College Lahore from April 2019 to January 2020.
Methodology: After taking ethical approval from institutional Ethical committee, 84 women undergoing lower segment caesarean section (LSCS) were included in the study. All mothers included in the study were between the age of 20 to 28 years having a body weight in range of 55 to 65 Kg and 145 cm to 160 cm height. Their duration of pregnancy was between38 to 41+6 weeks. Patients were divided into two groups. Each group consisted of 42 women. The injection Tranexamic acid (TXA) was given to one group (TXA group) while other group did not receive any drug (control group). TXA injection was given just before the start of surgery. Blood loss was collected and measured from the time of placental delivery to the end of lower segment cesarean section (LSCS) and then from the end of LSCS to the two hours postpartum. Hemoglobin, haematocrit, urine analysis, liver function tests, renal function were tested in both the groups before and after surgery.
Results: Tranexamic acid significantly reduced the quantity of the blood loss from placental delivery to the end of LSCS which was 412.44 ± 199.2 ml in the TXA group versus 800.22 ± 306.72 ml in the control group ($p<0.001$). It also decreased the quantity of blood loss from the end of LSCS to 2 hours postpartum which was 55.7 ± 43.3 ml in the TXA group versus 63.6 ± 48.0 ml in the control group ($p = 0.188$), was not significant. No complications or side effects were noted in either group.
Conclusion: Tranexamic acid significantly reduced the amount of blood loss during the LSCS as compare to control group but it did not reduce the blood loss significantly after the caesarean section. Its use was not associated with any side effects or complication like thrombosis. So, TXA can be used safely and effectively in women undergoing LSCS to reduce intra-operative blood loss.
Key words: Tranexamic acid (TXA), Lower segment caesarean section (LSCS). Control group

INTRODUCTION

PPH (Postpartum hemorrhage) is considered to be the main cause of the maternal mortality the world over[1,2]. 4-0.23 to 3% of obstetric patients suffer severe delayed or secondary postpartum hemorrhage[3]. Japanese wife and husband researchers introduced anti-fibrinolytic, Episilon Aminocarpoic acid for the first time to reduce maternal mortality due to postpartum hemorrhage. Later on researchers reached to a more potent substance named Tranexamic acid[4]. Intravenous administration of TXA showed comparable results to prostaglandins in reducing post partum hemorrhage in patients having atony after vaginal delivery and c. section[5]. For improvement in drug safety during lactation and pregnancy the data available in clinical practice should be collected which needs to be validated[6]. Lower section Caesarean section (LSCS) rates have been increased to as high as 25 – 30% in many areas of the world[7,8]. Delivery by c. section can cause more complications than normal vaginal delivery and one of the most common complications is intra-operative loss and primary or secondary postpartum hemorrhage (20%)[9] which leads to increased maternal morbidity and mortality. Almost 125000 women die from obstetric hemorrhage every year despite significant improvement in obstetric care[10] therefore, it is very important to take proper steps to reduce the amount of bleeding during and after LSCS[11]. Finding from MATTERs study reveal that the use of TXA in conjunction with a blood component- based resuscitation following massive blood loss results in improvement of coagulopathy and survival[11].Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine that exerts its anti-fibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules. TXA has been shown to be very useful in reducing blood loss and incidence of blood transfusion in different types of surgeries but there are few studies showing its effect on reducing

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blood loss during and after LSCS. The objective of this study was to determine the efficacy and safety of TXA in reducing the blood loss during and after LSCS.

METERIAL AND METHOD

It was a concurrent parallel study carried out in gynecology and obstetric department of Kishwar Fazal teaching hospital/ Amna Inayat Medical College Lahore from April 2019 to January 2020. The study was carried out on 84 full term pregnancies. Full term primigravida and gravid-2 with singleton pregnancy being delivered by LSCS were included in the study. Females with medical problems, bleeding disorder, Diabetes, hypertension, Preeclampsia, Eclampsia, Placental abnormalities, abnormalities of amniotic fluid, multiple gestations, Anemia and previous history of thromboembolism are not included in the study.

The TXA was administered at least 10 minutes prior to skin incision. After delivery of the baby, 5 IU IV bolus of pre-prepared oxytocin and 0.4 mg methylergometrine was given by the anesthetist. Heart rate, respiratory rate and blood pressure were checked and noted before the surgery, immediately after placental delivery and 2 hours after birth respectively. The blood loss was measured following placental delivery within the 2 hours after postpartum. Uterine contractility, placental separation, any neonatal problem, and side effects caused by TXA were noted. Blood collected from the suction container (the volume was measured in ml as marked on the container) was noted and soaked mops, pads, and operation table sheet were weighed by electronic scale before and after the surgery. Blood loss was measured as intraoperative amount of blood loss (ml) = weight of sponges and soaked sheets used during surgery – weight of sponges and sheets prior to surgery + volume of blood sucked in suction container after placental delivery. In addition, pads used after surgery upto2 hours postpartum also weighed to find out the blood loss. However, blood loss before placental delivery and amniotic fluid was not included in measuring blood loss. Hemoglobin and Haematocrit were carried out before and after surgery. Statistical analysis has been done by SPSS 16.0 mean and standard deviations were calculated for continuous variable like age, weight, height in meters and gestational age for both control and TXA group. Independent sample t-test was used to find the significant difference. Two sample paired t-test was also used to find the difference between hemoglobin (pre and post-operatively) and haematocrit (pre and postoperatively) variables, Level of significance in terms of p-value was considered as $p \leq 0.05$ is significant.

RESULTS

The patient characteristics in the two groups were similar with no statistically significant difference between age, weight and gestational age (Table I). All LSCS were done under spinal anesthesia. The duration of surgery was 45-50 minutes in 50% of the cases. There was no statistically significant difference in the heart rates (HR) (p=0.78), respiratory rate (RR) (p=0.64) and Systolic blood pressures (SBP), Diastolic blood pressure (DBP) between the two groups, after 2 hours of delivery (Table II).

The difference in drop of hemoglobin and haematocrit was also not statistically significant in both groups (Table III). In the control group, 12 patients required blood transfusions (33%), while in TXA group only 3 patients required the transfusion (8%). There was statistically significant difference in the quantity of the blood loss from the time of placental delivery to the end of CS ($p < 0.001$). There was statistically no significant difference in the quantity of the blood loss from end of LSCS to 2 hours postpartum (p=0.188), Table IV). Thromboembolism was not noted in any patient.

Table I: Demographic features of participants

Group	Age (Years)	Height (meter)	Weight (Kilograms)	Gestational age (weeks)
Tranexamic acid (42 cases)	24.18 ± 3.93	1.5625 ± 0.038	66.58 ± 7.02	38.32 ± 0.80
Control gp(42 cases)	24.89 ± 4.16	1.5435 ± 0.040	64.50 ± 9.22	38.47 ± 0.910
p-value	0.45	0.043	0.27	0.43

*p value < 0.05 considered as significance

Table II: Vital signs after placental delivery:

	Immediately after placental delivery			One hour after placental delivery			Two hours after CS		
	TXA gp	Control gp	p-value	TXA gp	Control gp Gp	p-value	TXA	Control gp	p-value
HR (beats/min)	92.31±21.96	91.50±7.40	0.834	92.31±21.96	91.50±7.40	0.833	87.71±10.51	88.33±3.77	0.78
RR(breaths/min)	18.05±0.517	18.72±0.81	<0.001	18.42±0.79	18.05±0.23	0.0086	18.18±0.60	18.11±0.74	0.645
SBP (mmHg)	122.15±10.18	126.6±9.25	0.05	119.57±8.24	123.33±12.87	0.137	116.60±7.85	117.50±9.96	0.677
DBP (Hg)	71.31±18.76	78.75±8.97	0.035	77.50±7.00	65.94±23.31	0.005	75.21±6.28	72.25±11.58	0.173

TXA= Tranexamic acid; HR = Heart rate; RR= Respiratory rate; SBP= Systolic blood pressure; DBP = Diastolic blood pressure.

Table III: Comparison of hemoglobin and haematocrit among study groups

	Preop. Hb %	Postop. Hb%	Preop. HCT	Postop. HCT
Tranexamic acid gp (n=42)	9.76± 0.85	8.67 ± 0.715	34.97 ± 2.42	33.08 ± 1.80
p-value	< 0.001		< 0.001	
Control gp (n=42)	9.88 ± 1.26	8.0 ± 0.94	34.83 ± 3.0	30.53 ± 3.28
p-value	< 0.001		< 0.001	

Preop = Preoperative; Postop=Postoperative; Hb%=Hemoglobin (gm %); HCT=Haematocrit.

Table IV: Comparison of blood loss among the study groups.

Group	Placental delivery to the end of CS (ml)	The end of CS to 2 hours postpartum (ml)
Tranexamic acid	356.44 ± 143.2	35.68 ± 23.29
Control gp	710.22 ± 216.72	43.63 ± 28.04
p-value	< 0.001	0.188

DISCUSSION

Tranexamic acid exerts its Antifibrinolytic effect by blocking the lysine-binding locus of the plasminogen and plasmin molecules, thereby preventing the binding of plasminogen and plasmin to the fibrin substrate. TXA also inhibits the conversion of plasminogen to plasmin by the plasminogen activators. TXA is a potent inhibitor of fibrinolysis, was first reported by Okamoto in 1962[7,8,9,10,11]. Since then, TXA has been widely used to treat heavy menstrual bleeding[12] and to reduce blood loss in elective surgery where it reduces blood transfusion by about one-third[13,14]. Maternal hemorrhage accounts for over a quarter of maternal deaths, an effective treatment of intraoperative blood loss and postpartum hemorrhage contribute importantly in decreasing maternal mortality[7,10,13]. Postpartum hemorrhage is defined as blood loss of > 500 ml after vaginal delivery of baby and > 1000 ml after CS. Continuous and constant efforts are made to take measures in reducing bleeding following delivery by CS or vaginal delivery. The WOMEN Trial (World Maternal Antifibrinolytic Trial) is done to determine the effect of early administration of TXA on mortality, hysterectomy and other morbidities. Results showed significant reduction in blood loss and morbidity[13]. More recently, the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage (CRASH-2) trial has shown that the early administration of TXA significantly reduces mortality in bleeding trauma patients[9,10,11]. Indeed, on the basis of the results of the CRASH-2 trial, TXA has been included in the WHO list of essential medicines[17]. It has been used for the treatment of various types of bleeding for many years e.g., menorrhagia during surgeries intra-operatively and postoperatively[18,19].

During placental delivery, fibrinogen and fibrin are rapidly degraded, whereas plasminogen activators and fibrin degradation products (FDP) increase due to activation of the fibrinolytic system. This activation can last up to 6 – 10 hours postpartum, causing more bleeding, which can be taken care of by anti-fibrinolytic agents. Therefore, the use of TXA appears to reduce the blood loss. Severe anemia following postpartum bleeding is an important cause of maternal morbidity and is likely to make more women vulnerable to fatal postpartum hemorrhage (PPH). Reducing operative blood loss would also reduce the risks and costs associated with blood transfusion. Blood is a scarce resource but even when it is available, it can transmit potentially fatal viral infections. Economic evaluation has shown that giving TXA to reduce bleeding in elective surgery would be life saving in the circumstances when there is a shortage of blood, because more blood will be available for those who need it[20]. In those countries where blood is readily available, the use of TXA will decrease the risk of transfusion-transmitted viral infections because fewer units of blood would be transfused.

This study was a concurrent parallel which showed that TXA significantly reduced bleeding from the time of placental delivery to two hours postpartum in LSCS. This study shows significant decrease in the blood loss volume in TXA group as compared with the control group. Similar study carried out in India by Mayuret et al[14] showed comparable results in reducing the blood loss. Another study carried out by Ming-Ying et al., in China showed that TXA significantly reduces bleeding from the time of placental delivery to the end of caesarean section, which was 351 ml in the study group while 440 ml in the control group[12,15]. Zhen et al. showed similar results after vaginal delivery; there was significantly less blood loss in the TXA group (243 ml) when compared to those who received no treatment (390 ml)[13,16].

Ferrer et al. identified three randomized controlled trials involving 461 participants. Out of 3, 2 were those who had cesarean section and 1 having normal delivery. Combining the effect of the three trials, use of TXA significantly reduced the mean blood loss by 92ml compared to no treatment. There was no mortality and thromboembolic event was noted.

This study also showed reduction in the incidence of postpartum hemorrhaging from 13% to 30% in TXA group as compared to control. In this study, 12 patients from the control group required the blood transfusions while 3 patients in the TXA group required transfusion. There was no significant alteration in the vital signs of subjects following TXA administration. There were no abnormalities in liver and renal function tests and urine analysis. All the neonates had good Apgar score at birth. Administration of TXA in pregnant women may raise concerns about thromboembolism. However, previous studies have shown the safety of this drug for use in both pregnant and non-pregnant patients[13,18]. In the present study, thromboembolic events were not evaluated because the time period and sample size was too small for adequate power; however, none of the women showed any signs or symptoms of immediate thromboembolic events and other side effects like nausea, vomiting and diarrhea were not statistically significant by difference in the two groups.

Limitations of study: A small sample size and duration of study period are limitations of this study. Blood loss was measured after placental delivery, and consequently. Skin, muscle, and uterine hemorrhage were not considered. Long-term effects of TXA on the patients and the neonates were not taken into account. There is need to undertake multicenter randomized controlled trials to study its long term effects and risk of thromboembolism.

CONCLUSION

Tranexamic acid significantly reduced the amount of blood loss during the lower segment caesarean section, but it did not significantly reduce the blood loss after the caesarean section. Its use was not associated with any side effects and complications like nausea, vomiting, diarrhea and thromboembolism. Thus TXA can be used safely and effectively in subject undergoing LSCS.

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