Original Research Article

Safety profile of tranexamic acid during and after caesarean section

Agrawal U[1], Shrivastava P[2]

[1]Dr Usha Agrawal, Assistant Professor, Department of Obstetrics and Gynecology, [2]Dr Preshant Shrivastava, Associate Professor, Department of Medicine, People's College of Medical Sciences & Research Centre, Bhopal, MP, India.

Address for Correspondence: Dr Preshant Shrivastava, MD (Medicine), E-8/16, Basant Kunj, Arera Colony, Bhopal (M.P.). E mail: dr_dada1@yahoo.com

Abstract

Introduction: Delivery by caesarean section can cause many complications. The most common complications documented are primary and secondary postpartum hemorrhage. Tranexamic acid is a synthetic analogue of the amino acid lysine and its action is to reduce blood loss. Both antepartum and PPH are being treated by TXA extensively. The present study was undertaken to evaluate the efficacy and safety of tranexamic acid in reducing the blood loss during and after LSCS. **Material & Methods:** Hundred pregnant women undergoing LSCS were included in the study. Subject were allocated in two groups–1) Study group–50 Subject who received tranexamic acid. 2) Control group–50 Subject who did not received tranexamic acid. **Results:** There was no significant alteration in the vital signs of subjects following tranexamic acid administration at time of delivery & at 1 hr & 2 hr postpartum. In our study, not a single patient developed signs of thrombosis. The side effects of tranexamic acid as nausea, vomiting & diarrhea were not statistically significant in both the groups in our study. In our study, there was no statistical difference in APGAR score at 1 & 5 minutes of the baby in both the groups. **Conclusion:** Data analysis of our study suggests that tranexamic acid can be used safely in LSCS with no serious side effects, and without increasing the occurrence of thrombosis.

Key words: Caesarean section, Tranexamic acid, postpartum hemorrhage

Introduction

Reducing blood loss and the need for blood transfusions in LSCS remains a major concern. Many interventions have been developed over the past decades to achieve this goal. In order to reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the amount of bleeding during and after LSCS [1].

A popular approach is to minimize peri-operative bleeding through the prophylactic use of the antifibrinolytic agents aprotinin, tranexamic acid (TXA), and epsilon aminocaproic acid (EACA) [2]. Especially, tranexamic acid has seen a renaissance among patients undergoing surgery, with many studies showing clinical efficacy. Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible blockade of the lysine binding sites on plasminogen molecules [3,4]. Intravenous administration of tranexamic acid has been routinely used for many years to reduce haemorrhage during and after various surgical procedures like coronary artery bypass, oral surgery, orthotopic liver transplantation, total hip or knee arthroplasty, and urinary tract surgery. Tranexamic acid has been shown to be very useful in reducing blood loss and incidence of blood transfusion in these surgeries. Despite these promising results, valid data on safety are lacking, as large sample sizes are needed to determine this outcome. The present study was undertaken to evaluate the efficacy and safety of tranexamic acid in reducing the blood loss during and after LSCS.

Adverse Drug Reaction: Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur, they may need medical attention. The same effect that makes tranexamic acid help prevent or stop bleeding also may cause blood clots that could be dangerous. The following possible signs & symptoms of blood clots may occur:

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Headache (severe & sudden); loss of coordination (sudden); pain in chest, groin or legs, especially the calves; shortness of breath (sudden); slurred speech (sudden); vision changes (sudden); weakness or numbness in arm or leg [5,6,7]. In addition, the following side effects may occur: Blurred vision or other changes in vision; dizziness or light headedness; unusual tiredness or weakness [8,9,10].

Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as body adjusts to the medicine. Medical help may be needed if any of these side effects may persist or is bothersome: Nausea or vomiting, Diarrhoea, Unusual menstrual discomfort, Watery eyes [11,12].

Overdose: There is no known case of over dosage of tranexamic acid tablets & injection. Symptoms of over dosage may be nausea, vomiting and orthostatic hypotension.

Aim- To study the safety profile of tranexamic acid during and after lower segment caesarean section

Materials and Methods

Hundred pregnant women undergoing LSCS were included in the study. It was a prospective randomised case control study. Subject were allocated in two groups

1. Study group – Subject who received tranexamic acid.
2.Control group– Subject who did not received tranexamic acid

Number of cases: In study group = 50
In control group = 50

Inclusion criteria

1. Full term primigravida or multigravida with singleton pregnancy delivered by LSCS.
2. Normal or abnormal presentation

Exclusion criteria

1. Medical or surgical problem involving heart, liver and kidney disease
2. Allergy to tranexamic acid
3. H/O thrombo embolic disorder
4. Abnormal placenta such as placenta previa, placenta aburptio, pregnancy complication such as pre-eclampsia
5.Multiple pregnancy, macrosomia and polyhydraminos
6. Complication with myoma
7. Any blood dyscrasia

Laboratory examination

1. Hemoglobin, PCV and Urine analysis.
2. BT, CT.

Study group- Preparation of tranexamic acid injection solution, 1gm / 10ml of tranexamic acid diluted with 10ml of distilled water.

Administration- 20 minutes before incision tranexamic acid 1 gm IV slowly infused over 5 min. After delivery of neonate 10 unit oxytocin and 0.2 mg methyl ergometrine was given by slow IV.

Control group- No tranexamic acid given. 10 unit oxytocin and 0.2 mg methyl ergometrine was given.

Clinical Observation

1. Vital signs – BP, RR and heart rate were measured immediately after placental delivery and 1 and 2 hours after birth respectively.
2. The extent of postpartum hemorrhage – the blood was measured by weight and volume following placental delivery to the end of surgery and from the end of surgery to 2 hours after birth.
3. Any side effects caused by tranexamic acid.
4. Birth weight
5. APGAR score at 1 & 5 min

Results

Table-1: Distribution of cases according to age group

Age (Years)	Study group (No. of cases)	Control group (No. of cases)
18 – 22	15	12
22 – 26	23	25
26 – 30	8	7
30 – 34	4	6

Table 1 shows distribution of cases according to age group. Majority of the patients in both groups were between 22-26 years of age.

Table-2: Comparison of duration of surgery between the two groups.

	Study	Control	Z test	p value
Duration (min.)	43.84 ± 6.1	42.22 ± 6.58	Z = 1.28	p = 0.205 NS

Table 2 shows mean duration of surgery was 43.84 min in the study group & 42.22 min in the control group. There was no statistical difference in the duration of surgery between the two groups. (p= 0.167).

Table 3: Vital signs at the time of placental delivery in both the groups.

Vital signs	Study	Control	Z test	p value
Heart rate (bpm)	86.14 ± 7.25	84.81 ± 8.35	Z = 0.86	p = 0.394 NS
Respiratory rate (breath/min)	19.38 ± 2.29	19.94 ± 2.14	Z = 1.26	p = 0.21 NS
Systolic BP (mmHg)	121.08 ± 10.1	119.81 ± 9.47	Z = 0.65	p = 0.514 NS
Diastolic BP (mmHg)	77.08 ± 7.04	76.88 ± 7.61	Z = 0.14	p = 0.892 NS

Table 3 shows mean heart rate, respiratory rate, systolic blood pressure & diastolic blood pressure at the time of placental delivery in the study & control group. There was no statistically significant difference in the vital signs at the time of placental delivery in both the groups.

Table-4: Vital signs 2 hr after surgery in both the groups.

Vital signs	Study	Control	Z test	p value
Heart rate (bpm)	79.96 ± 7.55	82.16 ± 7.08	Z = 0.36	p = 0.094 NS
Respiratory rate (breath/min)	19.44 ± 2.57	19.58 ± 2.75	Z = 0.26	p = 0.798 NS
Systolic BP (mmHg)	127.16 ± 12	119.72 ± 11.5	Z = 0.465	p = 0.647 NS
Diastolic BP (mmHg)	81.04 ± 6.12	78.28 ± 5.39	Z = 1.39	p = 0.101 NS

Table 4 shows mean heart rate, respiratory rate, systolic blood pressure & diastolic blood pressure at 2 hour after delivery in the study & control group. There was no statistically significant difference in the vital signs at 2 hour after delivery in both the groups.

Table-5: Comparison of mean birth weight in both the groups.

	Study	Control	Z test	p value
Birth weight (gms)	2840 ± 323	2870 ± 355	Z = 0.54	p = 0.591 NS

Table 5 shows that mean birth weight was 2840 gm in patients who received tranexamic acid & 2870 gm in patients who didn't received tranexamic acid. There was no statistically significant difference in birth weight in both the groups. (p= 0.591).

Table 6: Comparison of adverse drug reaction in both the groups.

	Study	Control	Z test	p value
Nausea	16	13	Z = 0.66	p = 0.508 NS
Vomiting	09	08	Z = 0.08	p = 1.135 NS
Diarrhoea	01	00	Z = 1.01	p = 0.312 NS
Signs of thrombosis	00	00		

Table 6 shows adverse drug reactions due to use of tranexamic acid. Nausea, vomiting & diarrhea occurred in 16, 9, 1 cases respectively in the study group & 13, 8, 0 cases respectively in the control group. None of the subjects had any evidence of thrombosis. The incidence of the side effects like nausea, vomiting, & diarrhea were not increased in the study group as compared to the control group suggesting that the use of tranexamic acid had no significant adverse drug reaction. In addition there was no increase in incidence of thrombosis in study group.

Table 7: Comparison of APGAR score in both the groups.

APGAR score	Study	Control	Z test	p value
1 min	8.88 ± 1.19	8.64 ± 1.34	Z = 0.95	p = 0.345 NS
5 min	9.4 ± 0.639	9.22 ± 0.79	Z = 1.25	p = 0.213 NS

Table 7 reveals mean APGAR score at 1 & 5 min in newborns of subjects in both the groups. Study group had mean APGAR score of 8.88 at 1min & 9.4 at 5 min, while newborns born to subjects in control group had mean APGAR score of 8.64 at 1 min & 9.22 at 5 min. There was no statistically significant difference in APGAR score in both the groups. (p= 0.345 at 1 min & 0.213 at 5 min). Thus, tranexamic acid has no significant difference in relation to fetal outcome.

Table-8: Effect of tranexamic acid: Comparison of blood loss from time of placental delivery to 2 hrs postpartum in both the groups.

	Study group	Control group	Z test	p value
Mean blood loss (ml)	360.9 ± 110.3	443 ± 88.552	Z = 4.17	p=0.0008 Highly Significant

Table 8 shows mean blood loss from placental delivery to 2 hours postpartum was 360.9 ml in the study group & it was 443 ml in the control group (p= 0.0008), suggesting that there was statistically highly significant difference in blood loss in both the groups. Patients who received tranexamic acid had 88 ml less blood loss than patients who didn't received tranexamic acid.

Discussion

Tranexamic acid (TXA) is a synthetic analogue of the amino acid lysine that competitively inhibits the activation of plasminogen to plasmin; at high concentrations it non-competitively blocks plasmin, thus TXA inhibits the dissolution and degradation of fibrin clots by plasmin. It has been used in the treatment of bleeding for many years [3,4]. During placental delivery, fibrinogen & fibrin are rapidly degraded, whereas plasminogen activators & fibrin degradation products (FDP) increase due to activation of fibrinolytic system. This activation can last up to 6-10 hrs postpartum, causing more bleeding. The main purpose of TXA is the reduction of perioperative bleeding and transfusion requirements in both cardiac and non-cardiac surgery. This study was undertaken to study the safety profile and efficacy of TXA in LSCS. There was no significant alteration in the vital signs of subjects following tranexamic acid administration at time of delivery & at 1 hr & 2 hr postpartum. These findings were similar to findings in studies of Ming-ying Gai et al[13], Zheng et al [14], Bresnoc et al[15] & Gohel et al[16].

The incidence of thrombosis during pregnancy & puerperium is 5-6 times higher than that in the general population. When the anti fibrinolytic drug tranexamic acid is administered, the increased risk of thrombosis should be considered, especially in the LSCS postpartum population. In our study, not a single patient developed signs of thrombosis. There is currently no clinical evidence that the use of TXA increases the risk of thromboembolic events, namely myocardial infarction, stroke, deep vein thrombosis or pulmonary embolism according to meta-analyses and clinical trials cited in the general [17,18], trauma[19], orthopedic [20,21,22,23,24], cardiac [25,26,27] or obstetric & gynecological [28,29,30,31] settings.

In a review by Ferrer et al in 2009, trials of the use of TXA for the prevention of obstetric hemorrhage used TXA at a dose of 1 gram without major complications. There were no mortality and no thrombotic event was reported. The most frequently reported adverse effect of TXA was nausea [32].

The side effects described in different texts with the use of TXA include gastrointestinal symptoms such as diarrhea, nausea and vomiting that occur in about 10% of patients. These side effects of tranexamic acid as nausea, vomiting & diarrhea were not statistically significant in both the groups in our study.

In our study, there was no statistical difference in APGAR score of the baby at 1 & 5 minutes in both the groups. Therefore, tranexamic acid had no effect on the APGAR score of the baby. Similar results were found in study done by Ming-ying Gai et al [13] & Zheng et al [14].

Rare complications described in various texts include hypotension, thrombosis, blurred vision, renal cortical necrosis and retinal artery obstruction. [33]. These side effects were not observed in our study. In a prospective study of the efficacy of TXA in decreasing blood loss during and after caesarean section on 100 women, no side effects were observed [34].

Our study showed that tranexamic acid significantly reduces bleeding from time of placental delivery to 2 hrs postpartum in LSCS. Results show that study group patients had mean blood loss of 360.9ml ± 110.3 as standard deviation, while control group patients had mean blood loss of 443ml ± 88.552 as standard deviation. Thus, there is reduction in blood loss by about 20% & was found to be statistically highly significant (p value= 0.000). There was reduction in blood loss in both the parameters, i.e. from time of placental delivery to completion of skin closure & from completion of skin closure to 2 hrs postpartum.

Data analysis of this study suggests that tranexamic acid can be used safely with no serious side effects, and without increasing the occurrence of thrombosis. But, more studies with more number of cases are required to validate the safety of TXA in LSCS.

Conclusion

1. There was no significant alteration in the vital signs of subjects following tranexamic acid administration at time of delivery & at 1 hr & 2 hr postpartum.
2. In addition, incidence of thrombosis is not increased with the tranexamic acid in the study group
3. Use of Tranexamic acid was not associated with any adverse drug reaction like nausea, vomiting, diarrhea or thrombosis. Fetal outcome as evaluated by birth weight and APGAR score was not adversely affected by use of tranexamic acid.
4. Tranexamic acid can be used safely in subjects with lower segment caesarean section.

Abbreviations

APGAR	Acronym for Appearance, Pulse, Grimace, Activity, Respiration
BP	Blood Pressure
BT/CT	Bleeding Time/ Clotting Time
FDP	Fibrin Degradation products
Gm	Gram
H/O	History of
IV	Intravenous
LSCS	Lower Segment Caesarean Section
min	Minutes
ml	Milliliter
NS	Not Significant
PCV	Packed Cell Volume
RR	Respiratory Rate
TXA	Tranexamic acid

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