ORIGINAL RESEARCH PAPER

Gynaecology

Volume : 6 | Issue : 12 | December : 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

EFFICACY OF TRANEXAMIC ACID IN REDUCING BLOOD LOSS DURING AND AFTER LSCS

KEYWORDS

CS - Caesarean Section, LSCS – lower segment caesarean section, TXA – tranexamic acid, PPH – post partum haemorrhage, HCT - haematocrit

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ABSTRACT

Background: *Caesarean section (CS) rates have increased to as high as 25 to 30 % in many areas of the world. Delivery by CS leads to more complications than normal vaginal delivery and one of the most common complications is primary or secondary postpartum haemorrhage (20%).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. Tranexamic acid has been shown to be very useful in reducing blood loss and incidence of blood transfusion in a variety of surgeries.*

AIMS : *To study the efficacy of tranexamic acid in reducing blood loss during and after the lower segment caesarean section.*

Methods: *A randomized, case controlled study, was conducted on 100 women undergoing lower segment caesarean section (LSCS). 50 of them were given tranexamic acid 1gm in 100ml NS 10 minutes before LSCS and were compared with 50 others who did not receive tranexamic acid . Blood loss was collected and measured during two periods. The first period was from placental delivery to end of LSCS and second from the end of LSCS to 2 hours postpartum. Vital signs at time of delivery, at 2 hour postpartum were studied in both the group.*

Results- *Our study showed that tranexamic acid significantly reduced bleeding from time of placental delivery to 2 hrs postpartum in LSCS. Results also showed that study group patients had mean blood loss of 363.80 ± SD 171.95 ml after placental delivery till skin closure, while control group patients had mean blood loss of 512.20 ± SD242.56 ml . Thus, there was reduction in blood loss by about 29% and was found to be statistically highly significant (p value<0.001).Total blood loss after placental delivery to 2 hrs post partum in study group is 397.6 ± SD 176.37 ml as standard deviation and in control group was 553.40 ± SD 247.63 ml.*

Thus there was 28% reduction in total blood loss which was statistically significant (p=value<0.001).

CONCLUSION(S): *Tranexamic acid significantly reduced the amount of blood loss during and after the lower segment caesarean section and its use was not associated with any side effects like nausea, vomiting, diarrhoea and thrombosis. Thus, Tranexamic acid can be used effectively in women undergoing LSCS to decrease the blood loss.*

INTRODUCTION:

Caesarean sections are rising in most part of the world. It is about 25-30% in many areas of the world[1]. In USA caesarean section rate is increased by 53% from 1996 to 2007, reaching to 32%[2]. In India, there is increased trend of caesarean section due to increased rate of institutional delivery and better obstetric care. In India the caesarean section rate is 10.6% according to NFHS-3 and in instutional delivery 21-24%. It is more in southern state compared to northern states[3]. In our hospital incidence is about 45 – 50%.

Delivery by caesarean section causes more complications than normal vaginal delivery. Among them most common complications are primary or secondary postpartum haemorrhage (20%)[4]. Obstetric haemorrhage can be life threatening, sometimes requiring hysterectomy. Therefore to reduce the morbidity and mortality due to obstetric haemorrhage, we need to reduce blood loss during caesarean sections.

Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts antifibrinolytic effect by inhibiting the conversion of plasminogen to plasmin by the plasminogen activators. Therefore, the use of tranexamic acid appears to reduce the blood loss. It belongs to category B drug and even used in second trimester bleeding without any effects on fetus[5]. In India, anaemia is the most common condition that is aggravated in pregnancy and in this background postpartum haemorrhage becomes an important cause of maternal morbidity and mortality[4].

In this study, we aimed to determine the efficacy of tranexamic acid in reducing the blood loss during and after lower segment caesarean section. By reduction in operative blood loss would also reduce the risks and costs associated with blood transfusion.

Okamoto in 1962 was first to report that Tranexamic acid is a potent inhibitor of fibrinolysis[6]. It has been in use for many years for reducing the blood loss in surgeries like transurethral prostatic surgery, cardiac surgery with cardiopulmonary bypass, total hip/knee arthroplasty, orthotropic liver transplantation, or urinary tract surgery and rates of rebleeding were reduced in patients with traumatic haematoma. Tranexamic acid has been shown to be very useful in reducing blood loss and incidence of blood transfusion in these surgeries but only few studies have been done that have shown its efficacy in reducing blood loss at caesarean section.

Tranexamic acid potentiates the blood clotting system and is used to treat and prevent bleeding. The mechanism of action of tranexamic acid is related to its antifibrinolytic effect, which makes this drug potentially very effective in the third stage of labour. During placental delivery, rapid degradation of fibrinogen and fibrin occurs, as well as an increase in the activation of plasminogen activators and fibrin degradation products due to activation of the fibrinolytic system. This activation can last up to six to 10 hours postpartum, which may cause more haemorrhage. The antifibrinolytic effect of tranexamic acid in the third stage of labour could make it a safe and effective alternative or adjunct to other regimens currently used in 3rd stage of labour for prevention of post partum haemorrhage (PPH). Tranexamic acid could reduce blood loss associated with complications such as placenta praevia and lower genital tract trauma, as well as bleeding from the upper segment placental site. Use of tranexamic acid could potentially have prevented some PPH cases if it was given to women with the risk factors for PPH, as reported in the Cochrane review on treatment of PPH. Therefore, it may be particularly useful in preventing cases of PPH due to factors other than uterine atony, where uterotonics are not effective.

OBJECTIVE : To study the efficacy of tranexamic acid (antifibrinolytic agent) in reducing blood loss during and after the lower segment caesarean section. Variables: mean

Volume : 6 | Issue : 12 | December : 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

hematocrit and decline in hematocrit.

MATERIALS AND METHODS:

Study setting:

The study was conducted on pregnant women registered in the Obstetrics and Gynaecological department in Alluri Sita Rama Raju Academy of Medical Sciences, Eluru.

100 patients who were admitted in this hospital during the study period from march 2015 to September 2016 were included in the study.

Study population:

All pregnant women meeting the inclusion criteria and consenting for study were recruited.

Inclusion criteria:

- Term primipara with a live singleton pregnancy
- Previous 1 LSCS with a live singleton pregnancy.
- Booked cases

Exclusion Criteria

- Severe medical and surgical complications including the heart, liver and kidney, brain disease and blood disorders.
- Previous history of stroke
- Abnormal placenta: Such as placenta previa, placenta abruption, placental adhesions.
- Severe pregnancy complications such as severe preeclampsia
- History of thrombo embolic disorders
- Multiple pregnancies, macrosomia, poly hydrominos
- Pregnancy with myoma.
- More than 2 Previous LSCS

Study design:

Randomized control trial

Study group :

Preparation of tranexamic acid injection solution: 1 gm in100ml of normal saline.

Administration :

10 minutes before incision, tranexamic acid 1gm IV slowly infused (over 5-10 min). After delivery of the neonate, oxytocin 10 units IV drip is given.

Control group :

No tranexamic acid was given. Oxytocin was administered as in the study group.

CLINICAL OBSERVATIONS AND LABORATORY EXAMINATIONS: Clinical observations :

1. Vital signs : Blood pressure (BP), were checked before giving spinal and 2 hour after birth respectively.
2. The extent of postpartum haemorrhage: The blood was measured by weigh and volume during two periods following placental delivery to the end of surgery and from the end of the operation to 2 hours after birth.
3. Uterine contractility and placental separation.
4. Side effects caused by tranexamic acid.

Laboratory examinations:

1. Complete blood count (CBC) before delivery and on the third day after delivery.
2. Fluid administration in intra operative period noted.

CALCULATION OF QUANTITY OF BLOOD

Blood Collection : After placental separation a new sheet will be taken and blood will be collected via suction container, soaked gauge pads and operation table sheets can be weighed.

Blood measurements can be obtained post partum during two separate periods from placental delivery to 2 hr post partum. The study will ignore estimates of amniotic fluid and bleeding that occurred prior to placental delivery and account mainly after post placental blood loss. (It will be done by instructing the staff to change suction bottle after placental delivery or to note the level before bleeding).

Calculation of quantity of blood The Quantity Of Blood = (weight of guaze pads used after surgery – weight of guaze pads prior to surgery) + the volume of blood in suction bottle after placental delivery.

Methodology: After taking an informed consent, the pregnant women posted for caesarean section will be randomized into two groups. One group will be given tranaxemic acid and the other group will not be tranexamic acid. Haematocrit before delivery and on the third day after delivery will be compared in both the groups. Fluid administration in intra operative and post operative period noted.

Data management and data analysis: The data will be entered into Microsoft Excel. The change in haemoglobin and hematocrit will be compared in both groups using the student "t" test. The need for blood transfusion will be compared using Chi – Square test.

Ethics: Previous studies have shown the safety of this drug for use in both pregnant and non-pregnant patients.

RESULTS: A prospective randomized case controlled clinical study of 100 patients recruited from a population of all pregnant patients undergoing LSCS at term at **ASRAM medical college, eluru** between the period of March 2015 and September 2016.

Study comprised of 50 patients who received Tranexamic acid and 50 control subjects who didnot receive the Tranexamic acid.

Statistically there is no significant difference between the study and control group in terms of Age, Gestational age, Indication of LSCS, duration of LSCS, and also in the incidence of vomitings, diarrhoea, thrombosis.

There is statistical significance in both study and control group in terms of difference in mean systolic blood pressure after 1 hour of surgery ($p < 0.04$), mean reduction in haematocrit postoperatively ($p< 0.002$), mean reduction of blood loss from time of placental delivery till the time of skin closure ($p<0.001$), mean reduction in total blood loss from placental delivery till 2 hrs postpartum ($p<0.001$).

Table 1: Effect of Tranexamic acid –comparison of blood loss from time of placental delivery till the time of skin closure

Variable	Group	Mean blood loss (In ml.)	SD	t-value	p-value
Placental delivery till skin closure	Study	363.80	171.95	3.52	**0.001**
	Control	512.20	242.557		

Above table showed the mean blood loss from placental delivery till skin closure of LSCS. The total blood loss was 363.80±SD171.95 ml in study group (received Tranexamic acid) and 512.2± SD242.56 ml in control group (not received Tranexamic acid). The above table showed there was statistically reduced blood loss in study group (Received Tranexamic acid) as compared to control group ($p<0.001$).There was 148 ml less mean blood loss in study group as compared to control group.

Table 2: Showing effect of Tranexamic acid : comparison of mean blood loss from placental delivery till 2 hour after surgery (LSCS).

Volume : 6 | Issue : 12 | December : 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

Blood loss	Group	Mean blood loss (In ml)	SD	t-value	p-value
Placental separation till 2 hour after LSCS	Study	397.60	176.37	3.624	**0.001**
	Control	553.40	247.63		

Above table showed mean blood of **397.6 ± SD 176.37** ml in study group and **553.40 ± SD 247.63** ml in control group. There was statistically significant reduced blood loss in study group(who received Tranexamic acid) as compared to control group(who did not receive (Tranexamic acid) **(p<0.001).** Patients who received Tranexamic acid had **155.8** ml less blood loss as compared to control group who did not receive Tranexamic acid.

Table 3 : Comparison of mean reduction of Hematocrit (PCV) postoperatively in both study and control group

Variable	Group	Mean PCV(%)	SD	t-value	p-value
Decline In PCV	Study	3.72	2.21	3.237	**0.002**
	Control	5.17	2.26		

The above table showed mean reduction of PCV in study group was 3.72±SD2.21 % whereas it was 5.17±SD2.26 % in control group. This observation was statistically significant **(p<0.002).** So there was significant less blood loss in study group(who received Tranexamic acid) as compared to control group (who did not receive tranexamic acid).

Table 4: Comparison of mean systolic blood pressure after 1 hour of surgery (LSCS) in both study and control group

Variable	Group	Mean SBP (In mm of Hg)	SD	t-value	p-value
Systolic BP(After 1 hour of surgery)	Study	116.42	12.89	2.084	**0.040**
	Control	111.38	11.23		

Above table showed the mean systolic blood pressure in study group was **116.42±12.89** mm of Hg whereas it was **111.38±11.23** mm of Hg in control group. There was statistically significant difference was found between both groups **(p<0.040).**

Discussion : This is a randomized control trial in which a total of 100 patients were recruited .The use of tranexamic acid 1gm at the time of LSCS (n=50) and placebo group (n=50) was compared at ASRAM, Eluru in the period between march 2015 to September 2016.

The patients in both the groups were found to be comparable with respect to age, gravidity, parity, duration of surgery, indication of LSCS, intraoperative fluid administration etc. thereby eliminating majority of the confounding factors.

In our study the primary outcome measured was amount of blood loss after placental delivery till 2hr of surgery and comparison of decline in hematocrit with tranexamic acid and non tranexamic acid group significantly.

Our study showed that tranexamic acid significantly reduced bleeding from time of placental delivery to 2 hrs postpartum in LSCS. Results show that study group patients had mean blood loss of 363.80ml ±SD 171.95ml after placental delivery till skin closure, while control group patients had mean blood loss of 512.20ml ±SD 242.56 ml . Thus, there is reduction in blood loss by about 29% and it was found to be statistically highly significant (p value< 0.001). Total blood loss i.e after placental delivery to 2 hrs post partum in study group was 397.6±SD 176.37ml whereas in control group was 553.40 ± SD 247.63 ml. Thus there was 28% reduction in total blood loss that is significant (p value<0.001).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. Tranexamic acid also reduced the incidence of postpartum haemorrhage (patients with blood loss ≥ 500 ml) in the study group as compared to control group .Many studies have shown significant decrease in PPH in patients who received tranexamic acid like study carried out by Ming-ying Gai, Lian-fang Wu & coworkers (28) in China showed that tranexamic acid significantly reduces bleeding from the time of placental delivery to 2 hrs postpartum. The study group showed total blood loss reduction by 30% as compared to control group. Tranexamic acid also reduced the incidence of postpartum haemorrhage by 25.7% in the study group (22 cases Vs 35 cases in the study & controlled group respectively) (P value was 0.029). These results correlated well with our study.

As AK, et. Al[7] evaluated tranexamic acid use in postpartum haemorrhage in normal vaginal delivery & showed that tranexamic acid significantly decreased the amount of blood loss & the incidence of postpartum haemorrhage in subjects with vaginal delivery to about 20% as compared to control group. The results were found almost similar to that in our study.

Yang H et.al [8] also showed similar results. Tranexamic acid significantly reduced postpartum blood loss after vaginal delivery. The occurrence of postpartum haemorrhage was 6.4% in study group as compared to 25.3% in control group, which was statistically significant without any significant adverse effects. Therefore, tranexamic acid is efficient and safe in reducing postpartum haemorrhage.

Halder S et.al[9] a prospective randomised, case-control, study was conducted on 100 women undergoing lower segment caesarean section. Fifty of them were given tranexamic acid immediately before the surgery and compared with 50 others to whom tranexamic acid was not given. Blood loss was measured up to two days. Haemoglobin level was estimated before caesarean section and two days after. In this study, it was found that tranexamic acid reduced the quantity of blood loss from placental delivery to 2 days postpartum: 990 ml in the study group versus 1004 ml in the control group. The fall of haemoglobin was significantly less in the study group (1.214 g/dl) in comparision to control (1.7256 g/dl) (p < 0.0001). No complications or side-effects were reported in either group. No adverse neonatal outcome was also noted. Thus Tranexamic acid can be used safely and effectively in women undergoing lower segment caesarean section.

Gohel M, et. Al[10]evaluated tranexamic acid in caesarean section. They showed that showed that tranexamic acid reduces significant blood loss from the end of LSCS to 2 hours postpartum, 75.71 ml in the study group verses 133.03 ml in the control group (P = .001). It also significantly reduces the quantity of blood loss from placental delivery to 2 hour postpartum, 372.71 ml in the study group versus 469.70 ml in the control group (P = 0.003) . These results were comparable to our study.

Leila Sekhavat et.al[11] conducted a prospective randomised study on 90 primiparas divided into two groups who underwent CS. Their results 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 (p = 0.000). These results were comparable to our study.

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 Gai MY et al[12], Yang H et. Al[8],As

Volume : 6 | Issue : 12 | December : 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

AK et. Al[7] and Gohel M et al[10].

The incidence of thrombosis is 5-6 times higher during pregnancy and puerperium compare to the general population. When the anti fibrinlytic drug tranexamic acid is administered, the increased risk of thrombosis should be considered, especially in the postpartum population. In our study, not a single patient developed signs of thrombosis.

Svanberg et.al[13] reported 67 cases of abruptio placenta treated by tranexamic acid but there was no evidence of thrombosis occurred in any of these cases.

Gai MY et.al[12] in China in their study of tranexamic acid in LSCS showed no thrombosis in study group. Similar results were found in study of Gohel M et al[10].

Yang H et.al[8] Chinese study of 400 pregnant women with normal vaginal deliveries who received tranexamic acid during labour for PPH , no thrombosis seen in any of the case.

Ducloy-Bouthors et al. Demonstrated for the first time that TXA administered to women with overt PPH decreases blood loss and maternal morbidity[14]. Prevention of PPH is another indication where TXA has been used[11]. Varied doses of TXA ranging from 1mg/kg to more than 100mg/kg have been used in various surgeries. Even in studies involving LSCS, the doses used were either a bolus of 1gm or 10mg/kg intravenously.

The side effects of tranexamic acid as nausea, vomiting and diarrhoea were not statistically significant in both the groups in our study.These results are similar with other previous studies.

CONCLUSION

Following conclusions were drawn from our current study:

1) Tranexamic acid significantly reduced the amount of blood loss during and after the lower segment caesarean section.
2) Its use was not associated with adverse drug reaction like nausea, vomiting,
3) Tranexamic acid can be used safely in subjects with lower caesarean section.
4) Tranexamic acid decreases the use of additional oxytocics

REFERENCES:

1. Kambo I, Bedi N, Dhillon Bs, et al. A critical appraisalof caesarean section rates at teaching hospitals in india. Int.J Gynaecol obstet 2002 Nov, 79:151-8.
2. Menacker F, Hamilton BE. Recent trends in cesarean delivery in the United States. NCHS Data Brief. 2010 Mar;(35):1–8.
3. Stanton CK, Holtz SA. Levels and trends in cesarean birth in the developing world. Stud Fam Plann. 2006 Mar;37(1):41–8.
4. Lu MC, Fridman M, Korst LM, Gregory KD, Reyes C, Hobel CJ, et al. Variations in the incidence of postpartum hemorrhage across hospitals in California. Matern Child Health J. 2005 Sep;9(3):297–306.
5. Walzman M, Bonnar J. Effects of tranexamic acid in human milk after oral administration of tranexamic acid in lactating women. Stockh Swed Kabi AB. 1971;
6. Roberts I. Tranexamic Acid - a recipe for saving lives in traumatic bleeding. J Tehran Heart Cent. 2011 Nov;6(4):178.
7. As AK, Hagen P, Webb JB. Tranexamic acid in the management of postpartum haemorrhage. Br J Obstet Gynaecol. 1996 Dec;103(12):1250–1.
8. Yang H, Zheng S, Shi C. [Clinical study on the efficacy of tranexamic acid in reducing postpartum blood lose: a randomized, comparative, multicenter trial]. Zhonghua Fu Chan Ke Za Zhi. 2001 Oct;36(10):590–2.
9. Halder S, Samanta B, Sardar R, Chattopadhyay S. Tranexamic acid used before caesarean section reduces blood loss based on pre and post operative haemoglobin level: a case- control study. J Indian Med Assoc.2013. Mar; 111(3) : 184 -6
10. Gohel M patel P. Efficacy of tranexamic acid in decreasing blood loss during andafter caesarean section:A randomized case controlled prospective study [Internet]. 2007 [cited 2015 Jun 8]. Available from: http://medind.nic.in/jaq/t07/i3/jaqt07i3c1.shtml
11. Sekhavat L, Tabatabaii A, Dalili M, Farajkhoda T, Tafti AD. Efficacy of tranexamic acid in reducing blood loss after cesarean section. J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat Med Fed Asia Ocean Perinat Soc Int Soc Perinat Obstet. 2009 Jan;22(1):72–5
12. Gai M, Wu L, Su Q, Tatsumoto K. Clinical observation of blood loss reduced by tranexamic acid during and after caesarian section: a multi-center, randomized trial. Eur J Obstet Gynecol Reprod Biol. 2004 Feb 10;112(2): 154–7.
13. Svanberg L, Astedt B, Nilsson IM. Abruptio placentae--treatment with the fibrinolytic inhibitor tranexamic acid. Acta Obstet Gynecol Scand. 1980;59(2):127–30.
14. Ducloy – Bouthors AS, Jude B, Duhamel A, Broisin F, Huissoud C, Keita – Meyer H, et al. High dose tranexamic acid reduces blood loss in postpartum haemorrhage. CRIT CARE 2011;15:R117