

EFFICACY OF TRANEXAMIC ACID IN DECREASING BLOOD LOSS DURING AND AFTER CAESAREAN SECTION: A RANDOMIZED CASE CONTROL PROSPECTIVE STUDYTullika Singh¹, Shankar B. Burute², Hemant G. Deshpande³, Sumit Jethani⁴, Karuna Ratwani⁵**HOW TO CITE THIS ARTICLE:**

Tullika Singh, Shankar B. Burute, Hemant G. Deshpande, Sumit Jethani, Karuna Ratwani. "Efficacy of Tranexamic Acid in Decreasing Blood Loss during and after Caesarean Section: A Randomized Case Control Prospective Study". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 11, March 17; Page: 2780-2788, DOI: 10.14260/jemds/2014/2209

ABSTRACT: INTRODUCTION: 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 LSCS. **OBJECTIVES:** To study the efficacy and safety of Tranexamic acid in reducing blood loss during and after Lower segment Caesarean Section (LSCS). **METHODS:** A randomized case controlled prospective study was conducted on 200 women undergoing lower segment cesarean section. Hundreds of them that were given tranexamic acid immediately before LSCS were compared to hundred others to whom tranexamic acid was not given. Blood loss was collected and measured during the two periods, from placental delivery to end of LSCS and second from end of LSCS to two hours postpartum. **RESULTS:** Tranexamic acid significantly reduced the quantity of blood loss from placental delivery to end of LSCS, 202.25ml in the study group vs 392.20 ml in the control group ($p < 0.001$); from the end of LSCS, to 2 hours postpartum 3.80ml in the study group versus 112.25ml in the control group ($p < 0.001$); In totality, it significantly reduced the quantity of blood loss from placental delivery to two hours postpartum i.e. 27.05ml in the study group versus 510.45ml in the control group ($p < 0.001$). No complications or side effects were noted. **CONCLUSION:** Tranexamic acid significantly reduced the amount of blood loss during and after LSCS. Tranexamic acid can be used prophylactically; moreover it is safer and effective in women undergoing LSCS.

KEYWORDS: Caesarean Section, Post-Partum Hemorrhage, Tranexamic Acid.

INTRODUCTION: The journey of childbirth began thousands of years ago, when Adam and Eve were created by God. We have covered a long distance right from normal delivery to forceps delivery to caesarean section. A vacuum extractor came in as advancement to forceps delivery. The journey began from midwives who used to assist women for delivering normally which later on termed as normal labor. The severe pain during the process of childbirth was relieved by the introduction of twilight sleep. Episiotomy was introduced to prevent the terrible vaginal tears women suffered. Ever since till today in modern scientific era, childbirth remains main topic of discussion. The rates of caesarean section have increased to as high as 25 to 30 % in many areas of the world¹. Delivery by caesarean section can cause more complications than normal vaginal delivery and one of the most common complications is primary or secondary postpartum hemorrhage (20%).¹ It leads to increased maternal mortality and morbidity. In order 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).¹ Many uterotonic agents such as Oxytocin, Methyl ergometrine were studied in the past which radically reduced blood loss during Caesarean section and other than this

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hemostatic agent like Tranexamic acid was also studied in past to reduce blood loss in various surgeries e.g. orthopedic, dental and in LSCS.¹

In this study the efficacy and safety of Tranexamic acid in the reducing the blood loss during and after LSCS was investigated.

MATERIALS & METHODS:

Type of study: - Randomized Case Controlled Prospective

Period of study: - July 2011 To September 2013

Period required for data collection: -2yrs

Period required for data analysis and reporting:-6 months.

Place of study: - Department of Obstetrics & Gynecology, Padmashree Dr. D. Y. Patil Medical College, Hospital and Research Center Pimpri, Pune-411018

Sample size - 200 cases

INCLUSION CRITERIA: All primipara / multipara delivered by caesarean section without any risk factors.

EXCLUSION CRITERIA:

- Patient with hemorrhagic disorder.
- Placenta previa.
- Polyhydramnios.
- Patient who can lead to increased blood loss i.e. Twin pregnancy, Anemia, PIH.

PLAN OF STUDY:

- All the patients were evaluated as per the proforma.
- Institutional Ethical Committee approval was taken prior to commencement of study.
- All the patients were divided into two groups Case and Control, each consisting of 100 patients. The first patient in each group was allotted by a lottery basis and then they were assigned groups alternately.
- 100 of them are given Tranexamic acid 1 gm. IV immediately before caesarean section & compared with 100 of those who are not going to receive Tranexamic acid.
- 1 gm. of Tranexamic acid given slowly IV over 5 minutes in study group 20 minutes before taking skin incision.
- 100 cases are compared with 100 controls (those who are not going to receive tranexamic acid).
- 20 unit of Pitocin started immediately after delivery of baby in 500 ml of ringer lactate.
- Heart rate, respiratory rate, blood pressure measured before surgery, immediately after placental delivery and within one and two hours after birth of baby.
- Measuring Of Blood Loss:

The quantity of blood loss (ml) intraoperatively. = weight of used sponges during operation – weight of the sponges prior to surgery + volume of blood sucked in suction bottle.

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In addition pads used after completion of Caesarean section up to two hours post-partum were separately weighed to assess the blood loss postoperatively.

- Data was analyzed as per aims and objectives and results were drawn. The results were compared and significance of the difference were inferred by applying and calculating according to "Chi Square Test" & "Unpaired't' Test."

OBSERVATIONS & RESULT:

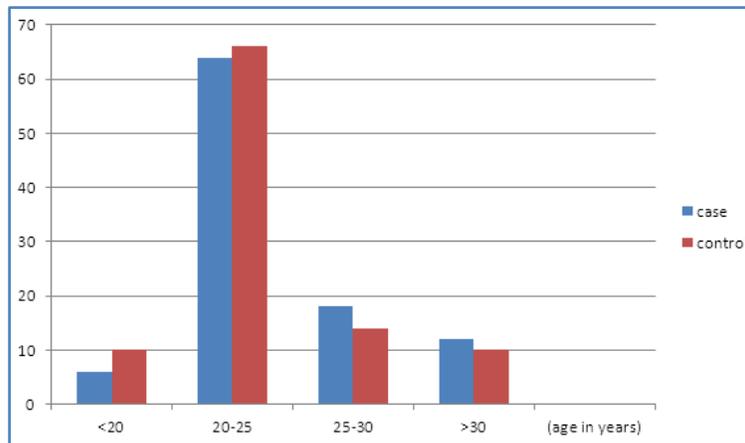
Age in years	Case	Percentage	Control	Percentage
<20	6	6%	10	10%
20-25	64	64%	66	66%
25-30	18	18%	14	14%
>30	12	12%	10	10%
Total	100	100%	100	100%
Mean \pm SD	25 \pm 1.46		30 \pm 1.24	

P value=0.8272, t=0.23, standard error of difference=21.74

Table No. 1: Age Wise Distribution of Cases and Controls

The above table shows distribution of study subject according to the age.

Out of the total 100 cases, a maximum of 64% were seen in age group of 20-25 years and least cases were found in age group <20 years i.e. 6% . Using unpaired " t" test the association between the case and control was not found to be significant.



Bar Diagram 1: Age wise distribution of cases and controls

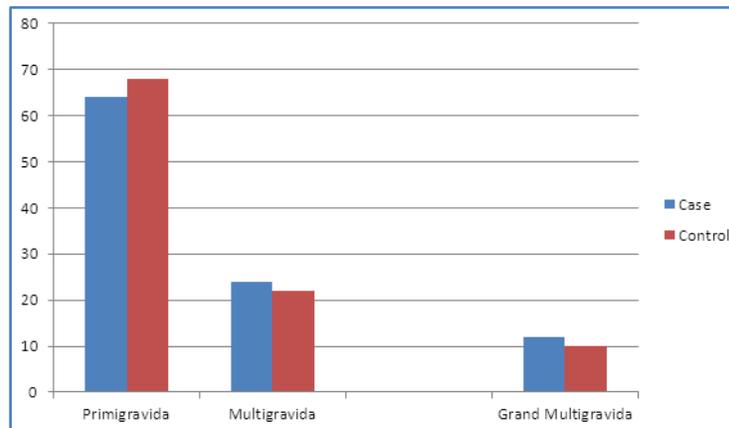
Parity	Case	Percentage	Control	Percentage
Primigravida	64	68(%)	68	68(%)
Multigravida	24	24(%)	22	22(%)
Grand Multigravida	12	12(%)	10	10(%)
Total	100		100	

chi square (df=2) 0.39, P=0.82 Not significant

TABLE NO. 2: PARITYWISE DISTRIBUTION OF CASES AND CONTROLS

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Table 2: The table shows parity wise distribution of case and control. The association between case and control based on parity was not found to be significant ($p \geq 0.05$)



Bar Diagram 2 : Parity of cases and control wise distribution

Gestational Age in weeks	Case	Control
< 37	5	6
37	11	10
38	19	20
39	33	22
40	14	21
>41	18	21
Mean \pm SD	39.1 \pm 1.24	39.3 \pm 1.28
Chi square (df=5)3.99,P=0.55 not significant		

TABLE NO. 3: GESTATIONAL AGEWISE DISTRIBUTION OF CASES AND CONTROL

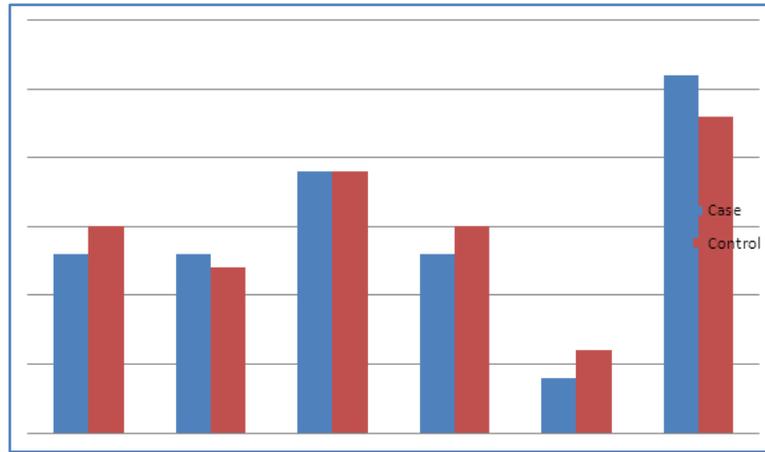
Table 3: The above table shows distribution of cases and control with respect to age, 33 cases were in 39 weeks of gestational age case group. The association was not found to be statistically significant.

Reason for LSCS	Case	Control
CPD	13	15
BREECH	13	12
FETAL DISTRESS	19	19
FAILURE OF INDUCTION	13	15
PROM	4	6
PREVIOUS LSCS	26	23
IUGR	12	10
Chi square (df=6)1.091, P=0.98 Not significant		

TABLE NO. 4: INDICATIONS OF LSCS IN CASES AND CONTROLS

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Table 4: There is no significant difference between both the groups with regard to obstetrical complication and indication of LSCS like abnormal presentation, CPD, failure of induction, fetal distress, IUGR, previous LSCS, PROM. All the LSCS were done under spinal anesthesia.



Bar Diagram 4: Indications of lscs in cases and control

Groups	Number of patients	Mean	Standard Deviation	Unpaired t test	P VALUE
Intra-operative blood loss (in ml)					
Case	100	202.25	29.244	50.5	<0.001 Highly Significant
Control	100	392.20	24.314		
Post-operative blood loss (in ml)					
Case	100	66.80	11.852	21.6	<0.001 Highly Significant
Control	100	112.25	18.523		
Total blood loss (in ml)					
Case	100	270.05	30.883	55.3	<0.001 Highly Significant
Control	100	510.45	30.342		

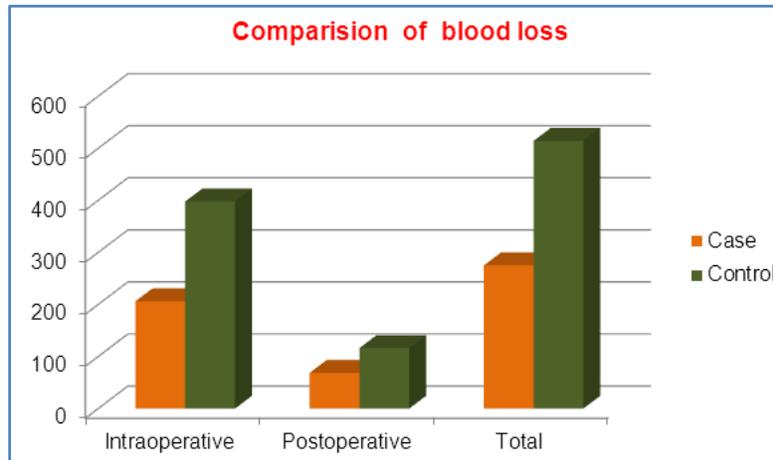
TABLE NO. 5: COMPARISION OF BLOOD LOSS OF CASES AND CONTROLS

Table 5. Shows comparison of blood loss between case and control. There is significant difference in quantity of blood loss.

In table 5. There is comparison of blood loss of case and control during intraoperative and postoperative patient. In intraoperative cases there was mean blood loss of 202.25 ± 29.244 ml (case) whereas there was 392.20 ± 24.314 ml (control) blood loss and it was found to be statistically significant, indicating that a major amount of blood loss is found in control group. Similarly in postoperative blood loss (in ml) it was found mean blood loss was 66.80 ± 11.852 (case) whereas 112.25 ± 18.523 ml was found in control in whom tranexamic acid was not administered.

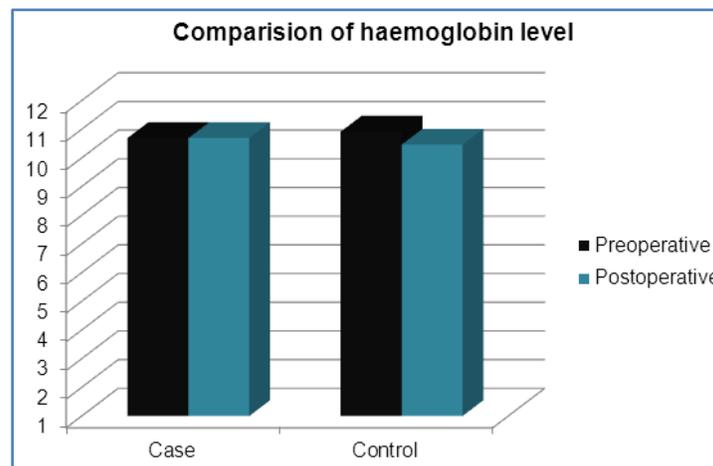
Thus, total mean blood loss intraoperative and postoperative in case group, given tranexamic acid is 270.05 ± 30.883 and in control group 510.45 ± 30.342 (not given tranexamic acid) (p Value ≤ 0.001). Hence those patient given tranexamic acid shows significant decrease in total mean blood loss.

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HAEMOGLOBIN	PREOPERATIVE		POSTOPERATIVE	
	CASE	CONTROL	CASE	CONTROL
MEAN	10.59	11.0	10.03	10.0
SD	0.707	0.76	0.76	0.70
MEAN DIFFERENCE	1.59		10.3	
SD OF CASE VS CONTROL	0.707		0.68	
P VALUE OF CASE VS CONTROL UNPAIRED T TEST	<0.003 Highly significant			
TABLE NO. 6: COMPARISON OF HAEMOGLOBIN OF CASES AND CONTROLS				

Table 6 showing the difference between preoperative and postoperative haemoglobin level in both the groups with reduction of haemoglobin postoperative in control group which is statistically significant (p value ≤ 0.001).



DISCUSSION: Increased blood loss can have its adverse effects such as raised morbidity and mortality, increased hospital stay, increased intraoperative duration, increased need for re-exploration which may be fatal at times, also excessive bleeding can hamper oxygen delivery and lead to multiple organ failure and death. Blood loss will make transfusion of blood and blood products

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imperative hence posing greater risks like transfusion reactions such as allergic reactions, transmission of fatal infections like HIV, HPV, HCV etc. and mismatched blood transfusion.

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 to 10 hours postpartum, causing more bleeding. It was because of this activation of the fibrinolytic system that we decided to use Tranexamic acid in this study.

In our study of 200 patients, cases were 100 patients, who were given Tranexamic acid with 100 control patients who had not received the drug. Our result of this study shows that Tranexamic acid significantly reduces bleeding from the time of placental delivery to 2 hours post-partum in LSCS with mean blood loss of 27.05 ml in the study group versus 510.45 ml in the control group (p Value <0.001) Also there is statistically significant difference in the quantity of blood loss intraoperatively, i.e. from the time of placental delivery to the end of LSCS with mean blood loss of 202.25 ml in the study group versus 392.20 ml in the control group (p Value < 0.001) . There was also statistically significant difference in the quantity of blood loss postoperatively i.e. from end of LSCS to two hours post-partum with mean blood loss of 3.80 ml in the study group versus 112.25 ml in the control group (p Value < 0.001).

Similar study carried out by Ming-Ying Gai et al in 2004 in China² including one hundred and eighty primiparas were randomized into two groups also showed that Tranexamic acid significantly reduced the quantity of blood from the end of LSCS to 2 hours postpartum: 42.75 +/- 40.45 ml in the study group versus 73.98 +/- 77.09 ml in the control group (p=0.001). It also significantly reduced the quantity of total blood from placental delivery to 2 hours postpartum: 351.57 +/- 148.20 ml in the study group, 439.36 +/- 191.48 ml in the control group (p=0.002). No complications or side effects were reported in either group. The study also shows significant decrease in the incidence of > 500ml blood loss in the study group as compared to control group (p value 0.029). Zheng et al showed similar results after vaginal delivery. No complications or side effects were reported in either group.

Another study done by Gohel Mayur et al in 2007 at Baroda, Gujarat³ with 100 patients out of which 50 were cases and 50 were control also showed that the Tranexamic acid significantly reduced the quantity of blood loss from the end of LSCS to 2 hours postpartum: 75.8 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: 39.8 ml in the study group versus 46.7 ml in the control group. (p=0.003). No complications or side effects were reported in either group.

Another study done in 2009 by Sekhavat L, Tabatabaie A, Dalili M, Farajkhoda T, Tafti AD. of Department of Obstetrics and Gynecology, Shahid Sedughi Hospital, Shahid Sedughi University of Medical Sciences and Health Services, Yazd, Iran ⁴ with inclusion of 90 primipara patients undergoing LSCS also showed that Tranexamic acid significantly reduced the blood loss from the end of LSCS to 2 hours postpartum 28.02 +/- 5.53 ml in the Tranexamic group versus 37.12 +/- 8.97 ml in the control group (p = 0.000). Hemoglobin 24 hours after LSCS was significantly greater in Tranexamic group than control group (12.57 +/- 1.33 in the Tranexamic group and 11.74 +/- 1.14 in the control group, p = 0.002). No complications or side effects were reported in either group.

Cochrane database systemic review study in July 2010 by Novikova N et al⁵ with inclusion of two randomized control trials also showed that Tranexamic acid was effective in reducing blood loss significantly after LSCS and vaginal delivery with no serious side effects were reported in women who received Tranexamic acid in these trials.

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Gungorduk K et al in October 2010 in Turkey⁶ performed a randomized, double-blind, placebo-controlled study of 30 women who underwent elective LSCS. The mean estimated blood loss was significantly lower in women treated with Tranexamic acid compared with women in the placebo group (499.9 ± 206.4 mL versus 600.7 ± 215.7 mL, respectively; $p < 0.001$), and the proportion of women in the Tranexamic acid group who had an estimated blood loss >1000 ml was significantly lower than in the placebo group (7 [2.1%] versus 19 [5.8%], respectively; relative risk [RR] 2.7; 95% confidence interval [CI] 1.1 to 6.3; < 0.03). Furthermore, more women in the placebo group than in the Tranexamic acid group required additional uterotonic agents (48 [14.5%] versus 28 [8.5%], respectively; RR 1.7; 95% CI 1.1 to 2.6; $P = 0.02$). Maternal and neonatal outcomes did not differ significantly. Tranexamic acid significantly reduced bleeding during LSCS, the percentage of patients with blood loss >1000 ml, and the need for additional uterotonic agents. Furthermore, the incidence of thromboembolic events did not increase.

WHO Guidelines 2012⁷ for post-partum hemorrhage – prevention and management recommends use of tranexamic acid only if oxytocin and other uterotonics fail to stop the bleeding or if it is thought that the bleeding may be partly due to trauma. (Weak recommendation, moderate quality evidence)

Xu J, Gao W published a randomized, double blind, case controlled study in March 2013⁸ to determine the efficacy of tranexamic acid in reducing blood loss in patients after caesarean section. Study was conducted on 174 primipara undergoing caesarean section. 88 of them was given 10mg/kg of tranexamic acid immediately before caesarean section and 88 others to whom injection was not given. Blood loss in the period between the end of CS and 2hr postpartum was significantly lower ($p < 0.01$) in the study group (46.6 ± 42.7) than in the control group (84.7 ± 80.2). The quantity of total blood from placental delivery to 2hr postpartum was also significantly reduced ($p = 0.02$) in the study group (379.2 ± 160.1) than in the control group (441.7 ± 189.7).

A phase 4 study which is about to be published soon in 2013 titled “Can tranexamic acid reduce bleeding after postpartum hemorrhage in caesarean section” has evaluated the effect of early administration of tranexamic acid (10mg/kg as induction dose in 12 minutes and 1 mg/kg as maintenance dose within 2 hours) vs. placebo group (received same volume of saline) in reducing postpartum hemorrhage caused by uterine atony after caesarean section delivery.⁹

There was no significant alteration in the vital science of subjects following Tranexamic acid administration. There was no abnormality in liver and renal function and urine analysis. The incidence of thrombosis during pregnancy and puerperium is five to six times higher than that of general population. When the antifibrinolytic drug Tranexamic acid is administered, the increased risk of postpartum thrombosis after LSCS should be considered. In the present study, not a single patient was developed thrombosis and incidence of side effects like nausea, vomiting and diarrhea were not statistically significant by difference in the two groups. This has been collaborated by other studies.

CONCLUSION:

1. 1 gram Tranexamic acid significantly reduces the amount of blood loss, during and after LSCS.
2. The use of Tranexamic acid in pregnancy is a safer option as we have not noted any adverse effects in our study.
3. Thus, Tranexamic acid can be used safely and effectively in subjects undergoing LSCS for decreasing morbidity and mortality from blood.

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