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**Original research article**

# Role of prophylactic tranexamic acid in reducing blood loss during and after the lower segment caesarean section: A randomized clinical trail

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**Abstract**

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 third stage of labor. 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. Primigravida total of 100 in number were enrolled in this study, randomization done by rules of odds and even. After fulfilling eligibility criteria and taking informed consent, cases were posted for LSCS. Thus tranexamic acid had significantly reduced bleeding during and after LSCS, which was compared using pre-operative and post-operative hematocrit. Estimated blood loss in cases was 313.84 ± 164.14 ml and in controls was 552.53 ± 184.7 ml.

**Keywords:** Tranexamic acid, blood loss, lower segment caesarean section

## Introduction

Cesarean delivery is one of the most commonly performed operations in obstetrics today [1]. Currently Cesarean section rates have been increased to as high as 25 to 30%. Caesarean section will cause more complications than normal vaginal delivery. Commonest complication is Primary or secondary postpartum hemorrhage (20%). As a result, there is increased maternal morbidity and mortality. Obstetric hemorrhage can be life threatening, hence in order to reduce maternal mortality due to PPH it is important to reduce the amount of bleeding during and after lower segment cesarean section (LSCS) [1].

Inaccurate estimates of surgical blood loss will adversely affect the patient's wellbeing in intra and post-operative care. Most surgeons continue to report their surgical blood loss by estimating the volume of blood in suction container and amount of blood loss by mops which is though convenient but is inaccurate. Modified gross formula using pre-operative and post-operative hematocrit is one of the accurate method to estimate blood loss in operative procedures [2].

Many studies have been conducted in various departments using this formula method shown that clinical estimation alone shows inaccurate blood loss and formula method will be better than visual estimation.

So, we have used formula method for estimating blood loss in lower segment caesarean section [3].

Transfusion of allogenic blood products during severe blood loss leads to transfusion-related adverse effects such as febrile non-hemolytic transfusion reactions, blood-borne infections etc. There will be always concerns about blood safety. Continuous blood shortages and rising costs of blood bank operations has generated interest in the reduction of transfusion requirements during and after surgery. There are lot of researches to decrease intra and post-operative bleeding through the prophylactic use of the antifibrinolytic agents such as aprotinin, tranexamic acid (TXA) and epsilon aminocaproic acid (EACA) [4].

Tranexamic acid is a synthetic derivative of the amino acid lysine which block reversibly the lysine binding locus on plasminogen molecules which exerts its antifibrinolytic effect and decreases bleeding [5, 6].

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 third stage of labor. During placental delivery, rapid degradation of fibrinogen and fibrin occurs, as well as an increase in the activation of plasminogen activators and fibrin

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degradation products due to activation of the fibrinolytic system. This activation can last up to six to 10 hours postpartum, which may cause more hemorrhage. 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 the third stage of labour for prevention of PPH. Tranexamic acid could reduce blood loss associated with complications such as placenta previa 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 will not be effective.

Intravenous administration of tranexamic acid has been used since many years to reduce hemorrhage during and after surgical procedures like orthopedic surgeries, coronary artery bypass, oral surgery, orthotopic liver transplantation, urinary tract surgery.

Tranexamic acid has been shown to be very useful in reducing blood loss during and after the surgery and thus decreasing incidence of blood transfusion in these surgeries.

In this study, the efficacy of tranexamic acid in the reducing the blood loss during and after LSCS was studied.

**Methodology**

**Study design**

Randomized clinical trial.

**Study setting**

Department of Obstetrics and Gynaecology.

**Sample size**

The Total Sample Size (N) calculated using the equation $N= [2 \times (Z_{\alpha}+Z_{1-\beta})^2 \times \sigma^2] \div d^2$ is thus determined to be equal to 50. Thus, 50 patients were taken for each group. Total of 100 patients were included in the study.

Primigravida 100 in number admitted at term in clean labour room of OBG department, undergoing Elective LSCS or Emergency LSCS labor were involved in the study.

Among 100 primigravida, 50 were taken as study group i.e., Group A which involves intervention by administrating IV Tranexamic acid 1 gm and 50 as control group i.e., Group B without intervention.

**Inclusion criteria**

1. Primigravida of gestational age between 37-42 weeks.
2. Singleton pregnancy with cephalic presentation posted for LSCS.

**Exclusion criteria:** Multigravida

- Malpresentation.
- Multiple pregnancy.
- Anemia.
- Pre-eclampsia.
- Antepartum hemorrhage.
- Macrosomia.
- Polyhydramnios.
- Uterine fibroids.
- Blood dyscrasias.
- History of drug allergy.
- History of thrombo-embolic disorder.
- Medical or surgical problems of pregnant women.

**Method of collection of data and procedure**

Primigravida total of 100 in number were enrolled in this study, randomization done by rules of odds and even. After fulfilling eligibility criteria and taking informed consent, cases were posted for LSCS.

**1. Group A: (Study Group-50)**

1 Gm/10ml tranexamic acid diluted with 10ml of 5% dextrose (20ml) was given slowly over 10 mins before 20 mins of skin incision.

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**2. Group B: (Control Group-50)**
Control group without any intervention.

**Results**

**Table 1:** Distribution of two groups according to their characteristics

| | Cases | Controls | T test | p value |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | |
| Height (CMS) | 148.48±5.4 | 148.13±4.9 | 0.336 | 0.737 |
| Weight (CMS) | 54.86±6.03 | 54.66±6.7 | 0.156 | 0.876 |
| BMI | 24.8±2.9 | 24.9±2.9 | -0.299 | 0.766 |

- Mean Height of cases was 148.48±5.4 cm and in controls was 148.13±4.9 cm with P value 0.737 which is statistically not significant which means both groups were comparable.
- Mean Weight of cases was 54.86±6.03 kg and in controls was 54.66±6.7 kg with P value 0.876 which is statistically not significant, which means both groups were comparable.
- Mean BMI of cases was 24.86 ± 2.9 and in controls was 24.9 ± 2.9 kg with P value 0.766 which is statistically not significant which means both groups were comparable.

**Table 2:** Comparison of mean values of blood volume, Haemoglobin, Haematocrit and blood loss among two groups

| Variables | Cases | Controls | T test | p value |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | |
| Estimated blood volume (wt*85) | 4663.1±512.6 | 4646.1±573.3 | 0.156 | 0.876 |
| Pre-op Haematocrit | 34.06±3.06 | 34.06±3.46 | -0.012 | 0.99 |
| Post-op Haematocrit | 31.74±2.96 | 30.02±3.56 | 2.61 | 0.001 |
| Mean Haematocrit | 33.02±3.03 | 32.02±3.55 | 1.515 | 0.133 |
| Pre-op Hb | 11.26±1.08 | 11.392±1.15 | -0.59 | 0.556 |
| Post-op Hb | 10.62±1.07 | 9.92±1.16 | 3.11 | 0.002 |
| Estimated Blood loss(ml) | 313.84±164.14 | 552.53±184.7 | -6.83 | 0.000 |

- Mean values of estimated blood volume was compared in cases and controls, p value is 0.876, which means both groups were comparable.

**Table 3:** Comparison of Pre-operative haematocrit and post-operative haematocrit among both groups

| | Case | | Control | | Mean difference | T test | P value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | | |
| Pre-OP Haematocrit | 34.06 | 3.06 | 34.068 | 3.46 | -0.008 | -0.012 | 0.99 |
| Post-OP Haematocrit | 31.74 | 2.96 | 30.026 | 3.56 | 1.714 | 2.617 | 0.01 |
| Difference of Pre and Post Op hematocrit | 2.28 | 1.246 | 4.06 | 1.268 | -1.78 | -7.079 | 0.00 |

- In our study mean pre-operative haematocrit in cases was 34.06 ± 3.06 and in controls was 34.04±3.46 and P value is 0.99, which means both groups were comparable.
- In our study mean post-operative haematocrit in cases was 31.74 ± 2.96 and in controls was 30.02 ± 3.56.
- The difference of Pre and post-operative haematocrit in cases was 2.28 and in controls was 4.06. P value of mean difference of pre and post-operative haematocrit is <0.05 which is statistically significant.
- Tranexamic acid had significantly reduced bleeding during and after LSCS, which was compared using pre-operative and post-operative haematocrit.

**Table 4:** Comparison of Pre-operative haemoglobin and post-operative haemoglobin among both groups

| | Case | | Control | | Mean difference | T test | P value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | | |
| Pre-OP Haemoglobin | 11.26 | 1.08 | 11.392 | 1.15 | -0.132 | -0.59 | 0.556 |
| Post OP Haemoglobin | 10.62 | 1.07 | 9.92 | 1.16 | 0.7 | 3.138 | 0.002 |
| Difference of Pre and Post Op Haemoglobin | 0.7 | 0.614 | 1.48 | 0.762 | -0.78 | -5.633 | 0.00 |

- In our study mean pre-operative haemoglobin in cases was 11.26 ± 1.08 and in controls was 11.392 ± 1.15 and P value is 0.556, which means pre-operative haemoglobin in both groups were comparable.
- In our study mean Post-operative haemoglobin in cases was 10.62 ± 1.07 and in controls was 9.92 ± 1.16.
- The difference of pre and post-operative haemoglobin in cases was 0.7g% and in controls was 1.48g%, mean difference P value <0.05 which is statistically significant.

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- Thus tranexamic acid had significantly reduced bleeding during and after LSCS, which was compared using pre-operative and post-operative haemoglobin.
- Estimated blood loss in cases was 313.84 ± 164.14 ml and in controls was 552.53 ± 184.7 ml.
- P value <0.05 suggesting that there is statistically significant difference in blood loss among both groups.
- Patients who received prophylactic tranexamic acid had 238.69 ml less blood loss than patients who did not receive tranexamic acid.

**Table 5:** Effect of tranexamic acid on blood loss among both groups

| | **Blood Loss (%)** | | |
|---|---|---|---|
| | **<500 ml** | **>500 ml** | **Total** |
| Cases | 44 (88%) | 6 (12%) | 50 (100%) |
| Controls | 19 (38%) | 31 (62%) | 50 (100%) |
| Total | 63 (63%) | 37 (37%) | 100 (100%) |
| Chi square-26.83, p value = 0.000 | | | |

In cases > 500ml blood loss was in 6 cases which was about 12% and in controls was in 31 cases which was about 62%, P value < 0.05 which is statistically significant and shows that tranexamic acid significantly reduced blood loss during and after LSCS.

**Discussion**

Our study showed that tranexamic acid significantly reduced bleeding during and after LSCS. Our results showed that study Cases had mean blood loss of 313.84 ± 84 ml as standard deviation, while control group patients had mean blood loss of 552.53 ± 184.7 ml as standard deviation. Thus, there was reduction in blood loss which is found to be statistically highly significant (p value= < 0.05).

In our study mean pre-operative haematocrit in cases was 34.06 ± 3.06 and in controls was 34.04±3.46, and P value is 0.99, which means both groups were comparable. Mean post-operative haematocrit in cases was 31.74 ± 2.96 and in controls was 30.02 ± 3.56**.** The mean difference of pre and post-operative haematocrit in cases was 2.28 ± 1.246 and in controls was 4.06 ± 1.268, p value <0.05 which is statistically significant. Tranexamic acid had significantly reduced bleeding during and after LSCS, which was compared using pre-operative and post-operative haematocrit. Using haematocrit by modified gross formula we have calculated estimated blood loss.

In our study mean pre-operative haemoglobin in cases was 11.26 ± 1.08 and in controls was 11.392 ± 1.15, and P value is 0.556, which means pre-operative haemoglobin in both groups were comparable. In our study mean Post-operative haemoglobin in cases was 10.62 ± 2.96 and in controls was 9.92 ± 1.16. The mean difference of pre and post-operative haemoglobin in cases was 0.7 g% and in controls was 1.48g%, mean difference is -0.78 and p value <0.05 which is statistically significant. By observing these parameters patient who received tranexamic acid had better haemoglobin level compared to those who did not receive tranexamic acid thus tranexamic acid significantly reduced bleeding during and after LSCS.

Tranexamic acid reduced the incidence of blood loss >500ml in study group 6 cases (12%) as compared to control group 31 cases (62%).

Observing all these parameters and estimated blood loss, Our study showed that prophylactic injection of tranexamic acid reduced blood loss during and after LSCS significantly, thus reducing overall incidence of PPH and anemia.

Recently in 2020 TRAAP2 (Tranexamic Acid for Preventing postpartum hemorrhage after caesarean delivery: a multicenter randomized, double blind, placebo- controlled trial) trial conducted for estimation of blood loss by giving prophylactic tranexamic acid in pregnant women undergoing caesarean section.

4524 women with caesarean deliveries before or during labour, at a term ≥34 weeks, modelled on TRAAP 1 (Study of tranexamic acid administered after vaginal deliveries) were studied. Tranexamic acid 1 g prophylactically given for cases.

Primary outcome was calculated by estimated blood loss. Preoperative hematocrit was taken if recent hematocrit was within 1 week before delivery. Postoperative hematocrit was measured on day 2. They chose this validated calculation as a quantitative objective measure to estimate blood loss because it is widely accepted that clinicians underestimate the blood loss and that gravimetric methods include liquor in addition to blood, which limits their accuracy, especially for caesarean sections. Secondary outcome was calculated using swab or gravimetric method. This study showed that there was significant reduction in blood loss using prophylactic injection of tranexamic acid. Sheehan SR *et al*., [7] Shook PR (2003) *et al*. [8], Stafford I *et al*., [2] studied similar formula method for calculation of estimated blood loss which is better than visual estimation of blood loss.

Similar study conducted by Gungorduk, Kemal *et al*. showed that there is significant reduction in blood loss in elective LSCS cases by prophylactic injection of tranexamic acid. They have used modified gross formula using pre and post-operative hematocrit to assess blood loss in LSCS [3].

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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 with p value < 0.05). In our study we also used same formula method to calculate blood loss which shows similar results [3].

**Conclusion**

As per our study the amount of bleeding is reduced during and after LSCS by prophylactic 1gm intravenous Tranexamic acid before 10 min of skin incision.
Tranexamic acid can be used safely in subjects undergoing lower segment Cesarean section with negligible side effects. This drug can be used effectively to reduce PPH thus reducing maternal morbidity and mortality.

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