Study of the efficacy of tranexamic acid in reducing blood loss after child birth

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ABSTRACT

Background: The aim was to study the efficacy of tranexamic acid in reducing blood loss after childbirth in normal vaginal delivery and LSCS.

Methods: 200 pregnant women divided into two groups group 1 and group 2, 100 women undergoing LSCS and 100 women undergoing vaginal delivery. Study group will be given 1 g iv tranexamic acid along with active management of third stage of labor and control subjects will be given only active management of third stage. Clinical observations and laboratory examinations, measurement of blood loss were measured.

Results: Distribution with respect to indication of LSCS like fetal distress, cephalopelvic disproportion, abnormal presentation, previous LSCS, arrest of descent, failed induction and onset of labor were comparable between both the groups. Study group showed marked decrease in blood loss when compared to controls from time of placental delivery to 2 hours postpartum in women undergoing vaginal delivery and caesarean section. There was a significant fall in mean Hb level among the control group when compared with the study group. There was no significant difference in the vital signs of the subjects in both the groups. The incidence of adverse effect like nausea, vomiting and diarrhoea were not increased in the study group when compared to the control group. Also the incidence of thrombosis was not increased with tranexamic acid.

Conclusions: Tranexamic acid significantly reduced the amount of blood loss after vaginal delivery and lower segment caesarean section. Its use was not associated with any adverse drug reactions like nausea, vomiting, diarrhoea or thrombosis. Tranexamic acid can be safely administered in pregnant women undergoing vaginal delivery and lower segment caesarean section.

Keywords: Tranexamic acid, Blood loss, Caesarean section, Thrombosis

INTRODUCTION

Postpartum haemorrhage (PPH) is a life threatening complication of both vaginal delivery and caesarean section. It accounts for 25% of maternal deaths every year worldwide accounting for 1,50,000 deaths. In recent times the rate of caesarean section has increased in both developing and developed countries which has led to increased risk of PPH. To decrease the risk of morbidity and mortality due to PPH, it is important to reduce blood loss in caesarean section and vaginal delivery.

Blood loss frequently leads to transfusion of allogeneic blood products, which lead to increased risk of
transfusion-related adverse effects, transfusion errors and blood-borne infections. There has been an increased concern regarding the safety of blood and blood products, continuous shortage of blood and rising costs of blood bank operations, tranexamic acid has shown to reduce bleeding and the need for blood transfusion and decrease the risk of transfusion transmitted viral infections.3 The changes in the fibrinolytic components during and after delivery are consistent with the fibrinolysis, to reduce blood loss hemostatic agents can be administered to support coagulation, one of these agents is tranexamic acid, a synthetic derivative of amino acid lysine which exerts its antifibrinolytic action by reversibly blocking the lysine binding sites of plasminogen molecule preventing the conversion of plasminogen to plasmin and thus inhibiting degradation of fibrin.

In developing countries like India, where anaemia is more prevalent, postpartum haemorrhage becomes an important cause of maternal morbidity and mortality.4 Tranexamic acid is particularly useful in preventing cases of PPH due to factors other than uterine atony, where uterotonic agents will not be effective. A Cochrane review reported that use of tranexamic acid could potentially have prevented some cases of PPH if it were given to women with the risk factors for PPH.

Tranexamic acid is a category B drug hence can also be used in second trimester bleeding without any effects on fetus.5 Findings of a systematic review showed that usage of tranexamic acid in surgery reduces blood loss by about one third.6,7 Tranexamic acid reduces death due to bleeding in trauma patients by about one third.8 In this study the efficacy of tranexamic acid in reducing blood loss after delivery in both vaginal deliveries and c-section has been evaluated.

METHODS

Two Hundred pregnant women undergoing vaginal delivery and LSCS meeting inclusion and exclusion criteria were included in this study.

Study setting

The study was conducted in department of obstetrics and gynaecology, Narayana medical college & hospital, Nellore, AP. It was a hospital based comparative prospective clinical study. The study period was from 2017 to 2019.

Sample size

The study will include 200 pregnant women divided into two groups group 1 and group 2, 100 women undergoing LSCS and 100 women undergoing vaginal delivery.

Inclusion criteria

The inclusion criteria are singleton pregnancy, term gestation ≥37 weeks. Primigravida, multigravida and pregnant women undergoing both normal vaginal delivery and LSCS are also included.

Exclusion criteria

Exclusion criteria are subjects with medical problems involving heart, liver, kidney, brain and having blood disorders, subjects having allergy to tranexamic acid, patients with history of thromboembolic disorders, abnormal placentation, severe preeclampsia, multiple gestation, macrosomia, polyhydramnios, grand multipara, preterm of gestational age <37 weeks were excluded.

In each group, the pregnant women will be further divided into two groups, group A or the control group and group B or the study group.

Study group/group B

Subjects in the study group will be given 1 g iv tranexamic acid along with active management of third stage of labor.

Control group/group A

Group A subjects will be given only active management of third stage.

Active management of 3rd stage comprises of 3 components: administration of uterotonic agents (preferably oxytocin), controlled cord traction, massage of uterine fundus after the placenta is delivered.

Typically at vaginal delivery a dose of 10 IU of oxytocin is administered IM and patients with intravenous access 10-20 IU is placed in 500-1000 ml of crystalloid and run quickly. With LSCS 5 IU oxytocin is administered as IM followed by similar infusion.

Clinical observations and laboratory examinations

Comparison is made between the blood loss in two groups from the placental delivery to 2 hours postpartum. Heart rate, respiratory rate and blood pressure will be checked and noted before delivery, immediately after placental delivery and 1-2 hours after birth respectively. Hemoglobin, liver and renal function were noted before and on the 3rd day after delivery.

Adverse effects of tranexamic acid

Measurement of Blood loss
In LSCS the quantity of blood loss during intra partum period=(weight of the mops and used materials post-delivery – weight of mops and materials used prior to delivery) + the volume sucked in the suction bottle after placental delivery in ml. Postpartum blood loss can be assessed by two methods using pictorial blood loss assessment charts (PBAC) and by measuring weight of the pads 2 hours postpartum-weight of the pads prior to use.

According to PBAC scoring system 1 point for each lightly stained pad, 5 points for each moderately stained pads and 20 points for each completely saturated pad. 1 point for each small clot of 1 paise size, 5 points for each large clot of 50 paise coin size and 20 points for each episode of flooding.

In vaginal deliveries blood loss is assessed by measuring the amount of blood collected in blood drape (a disposable conical, graduated plastic collection bag) and after delivery patient was given pre-weighed pads which were weighed 2 hours postpartum.

RESULTS

Mean age in both the groups does not differ significantly. Most of the women in study and control groups belong to 21-25 years.

The mean gestational age was 38.86 years in study, 38.68 years in control groups without significant difference p=0.330.

Majority of the women in both the groups are multiparous.

Failure to progress is the most common indication for LSCS among study group and CPD is most common indication among control group. However, there was no statistically significant difference between various indications of LSCS in both the groups.

Majority (82%) of the women in the study group have PBAC score of 1, whereas all the women in control group have a PBAC score of 5 indicating significant reduction in blood loss among study group in whom tranexamic acid was administered.

There was a significant reduction in blood loss in the study group when compared to the control group. Women who received tranexamic acid had 107.44 ml less blood loss compared to the control group who did not receive tranexamic acid (p<0.0001).

There is no statistical difference in mean Hb levels between both the groups, however there is reduction of mean Hb levels before and after LSCS indicating blood loss in both the groups.

The fall in Hb in control group is significantly higher when compared to the study group indicating reduction in blood loss in study group in whom tranexamic acid was administered when compared to the control group in whom tranexamic acid was not administered before and after LSCS.

There was a significant reduction in the mean SBP in control group after LSCS when compared to study group indicating significant reduction in blood loss in the study group in whom tranexamic acid was administered. There was no statistical significance between the two groups among mean DBP values before and after LSCS. In our study the mean fall in SBP in study group was 0.80 mmHg and mean fall in control group was 7.04 mm Hg, the mean fall in DBP in study and control group were 2.66 and 2.32 mmHg respectively, the mean rise in PR in study and control groups were 1.84 and 2.46 bpm respectively there was a significant fall in SBP and significant rise in PR among the control group when compared to study group and there was a significant fall in DBP among the study group in whom tranexamic acid was administered.

There was no statistical difference in the mean PR values between the two groups before and after LSCS.

The need for additional oxytocics among the study and control groups, 2% of women in the study group and 6% in the control group needed additional oxytocics, there was no statistical difference between the two groups in the need of additional oxytocics. 2% of the women in the study group and 6% of the women in the control group had a need for additional blood transfusion, however there was no statistical difference between the study and control groups in need for blood transfusion.

The incidence of adverse effects like nausea, vomiting and diarrhoea was 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. Also, there was no increase in the incidence of thrombosis in the study group.

| Table 1: Mean hemoglobin, systolic, diastolic blood pressure, pulse rate. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | Study group     | Control group   |                  |                  |
|                                | Mean     | SD    | Mean     | SD    |
| Hb Before delivery             | 10.29   | 0.84  | 11.24   | 0.79  |
| Hb After delivery              | 10.09   | 0.86  | 10.79   | 0.80  |

Continued.
| Study group       | Control group       |
|------------------|---------------------|
| **Fall in Hb**   |                     |
| 0.23             | 0.27                |
| Mean SBP         |                     |
| 117.4            | 118.50              |
| **Before delivery** |                   |
| 114.64           | 113.22              |
| Mean DBP         |                     |
| Mean             | SD                  |
| Before delivery  | 75.28              | 74.36                  |
| After delivery   | 74.12              | 75.12                  |
| **Mean pulse rate before and 2 hours after delivery** | |
| Before delivery  | 81.52              | 79.48                  |
| After delivery   | 83.88              | 81.84                  |

Table 2: Need for additional oxytocics and need for blood transfusion.

| Additional oxytocics | Study group | Control group |
|---------------------|-------------|---------------|
| _                   | Number      | Percentage (%)| Number | Percentage (%)|
|                     | 49          | 98            | 47     | 94             |
| +                   | 1           | 2             | 3      | 6              |

**DISCUSSION**

During placental delivery fibrinolytic system is activated leading to increase in fibrin degradation products. This activation can last up to 6-10 hours postpartum, causing more bleeding.9

Therefore the use of tranexamic acid appears to reduce the blood loss. In our study we used tranexamic acid to see its efficacy in reducing blood loss after child birth. Our study included patients undergoing caesarean section and vaginal delivery.

The primary outcome of our study is to study the efficacy of tranexamic acid in reducing blood loss, in our study there was a significant reduction in blood loss during both the periods that is from placental delivery till the end of surgery and from skin closure to 2 hours postpartum in the study group compared to the control group.

Gungorduk et al found that the tranexamic acid group had a higher mean Hb and haematocrit levels than the placebo group after caesarean section indicating reduction in blood loss in TXA group. These results were comparable to our study.10

Gohel M et al conducted a randomized case control study in 2005 in 100 subjects and showed that tranexamic acid significantly reduced blood loss from placental delivery to 2 hours postpartum, 374.92 ml in the study group versus 472.79 ml in the control group.11 These results were comparable to our study. In our study the mean fall in Hb level was more in the control group when compared to the study group indicating more blood loss in the control group when compared to the study group. Aleem A et al study results showed the mean drop in Hb levels were statistically significantly lower in the tranexamic acid group than in the control group.12

In our study additional oxytocics and blood transfusion were needed in 2 subjects in the study group and 3 subjects in the control group, there was no statistical significance between the two groups. Gungorduk et al study to determine the efficacy of tranexamic acid in reducing blood loss during elective LSCS found that tranexamic acid significantly reduced the need for additional uterotonic agents.

In our study 4 patients in the study group had vomiting, 4 patients had nausea and 2 patients had diarrhoea, no thromboembolic complications were noted. There was no increase in the incidence of adverse effects in the tranexamic acid group when compared with the control group. Pregnant women have 5-6 fold increased risk of thromboembolic complications compared to nonpregnant women.

In a study by Gungorduk et al 16.3% of the subjects in the study group experienced gastrointestinal side effects, thromboembolic events were not noted in this study.

Study by Heesen et al evaluated the usage of tranexamic acid did not increase the risk of thromboembolism in women undergoing caesarean section or vaginal delivery.13 The results of these studies were comparable to our study.
In our study majority of patients are primipara in both the groups, 52% of patients in the study group and 54% of patients in control group are primipara while 48% of patients in study group and 46% of patients in the control group are multipara. There was no statistical difference between the two groups in parity.

Mirghafouvand et al conducted a RCT in 120 women undergoing vaginal delivery in 2013 to study the efficacy of tranexamic acid in reducing blood loss and concluded that mean fall in Hb was lower in the study group when compared to the control group. Mean fall in Hb was more in the control group when compared to the study group, these results are comparable to our study. In our study 8% of the patients had vomiting, 4% of patients had nausea, 4% had diarrhoea and there were no thromboembolic complications.

In Gungorduk et al study conducted on 439 women undergoing vaginal delivery 35.9% women in the study group and 13.7% women in the control group had gastrointestinal side effects, thromboembolic complications were not noted in this study. In Yang et al study conducted in 400 primipara undergoing vaginal delivery nausea was noted in 2% of women in the study group no other side effects were noted in this study. In our study there was no statistical significant difference in LFT and RFT between the study and control groups.

**Limitation**

The study was a single center based study and sample size was low.

**CONCLUSION**

Tranexamic acid significantly reduced the amount of blood loss after vaginal delivery and lower segment caesarean section. Its use was not associated with any adverse drug reactions like nausea, vomiting, diarrhoea or thrombosis. Tranexamic acid can be safely administered in pregnant women undergoing vaginal delivery and lower segment caesarean section.

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