Efficacy of Intravenous Tranexamic Acid in reducing Blood Loss in Elective Cesarean Delivery

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ABSTRACT

Introduction: Delivery by Cesarean section may result in major obstetric hemorrhage requiring blood transfusion and in severe cases, hysterectomy, admission to an intensive care unit and even maternal death. The aim of this study is to determine the efficacy of prophylactic use of Tranexamic acid in reducing blood loss in lower segment cesarean section.

Methods: This is a hospital based case-control prospective study conducted in Department of Obstetrics and Gynecology, TUTH, Kathmandu. Sixty women who received Tranexamic acid (1 gm) before skin incision for LSCS were compared with another sixty women who did not receive Tranexamic acid. Comparison was done in terms of fall in hemoglobin and hematocrit; estimated blood loss and APGAR score at one and five minutes.

Results: The mean estimated blood loss was significantly lower in women who received TA in comparison to those who did not received TA (379.55 ml ± 232.86 versus 434.02 ml ± 231.39 ml; P=0.012) and the women who had blood loss < 500 ml was significantly higher in the study group (73% versus 68% (P<0.01).No significant difference between the use of additional uterotonics in both the groups.The incidence of side effects of TA like thrombosis, nausea, vomiting & headache was notincreased in the study group. No significant difference in one and five minutesAPGAR score of newborns born in both the groups.

Conclusions: The present study demonstrated that Tranexamic acid significantly reduced the amount of blood loss during LSCS. Its use was not associated with any side effects and or complications like thrombosis. Thus, Tranexamic acid can be used safely and effectively to reduce bleeding during LSCS.

Keywords: *blood loss; caesarean section; Tranexamic acid.*

INTRODUCTION

Caesarean section (CS) rate is as high as 25 to 30 % in many areas of the world.[1] Delivery by CS can cause more complications than vaginal delivery and one of the most common complication is primary or secondary postpartum hemorrhage (20%).[2] The average blood loss during cesarean delivery (1000 mL) is double the amount lost during vaginal delivery (500 mL).[3] The hematocrit falls by 10% and blood transfusion is required in 6% of women undergoing cesarean delivery compared with 4% of women who have a vaginal birth.[4] An approach is to minimize perioperative hemorrhage through the prophylactic use of the antifibrinolytic agents has become popular.[5]

Since TA was first reported by Okamoto in 1962, it is regarded as a potent inhibitor of fibrinolysis.[6] Moreover, TA has Food and Drug Administration approval for the prophylaxis and treatment of bleeding during dental surgery in patients with hemophilia.[7] This drug has been widely used to treat heavy menstrual bleeding and to reduce blood loss in elective surgery where it reduces blood transfusion by about one-third.[8]

The present study aims to evaluate and justify its use if TA is found to reduce blood loss and need of blood transfusion.

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METHODS

This is a prospective ,randomized case-controlled study comparing blood loss during cesarean section in cases who received TA preoperatively with controls who didn't receive TA at Department of Obstetrics and Gynaecology, TUTH, Maharajgunj, Kathmandu.

The duration of study was 12 months. The data collection and entry was done from 1st Baikash to 31st Chaitra 2071 (14th April, 2014 to 14th April 2015). The study population consisted of all women admitting inMaternity Ward, TUTH,and fulfilling the inclusion criteria during the study period. The study is purposive type. All the patients, those who meet the inclusion criteria were enrolled in the study. The study was undertaken only after the review and approvalobtained from the Institutional Review Board of IOM, TUTH Research Department.

Sample size calculated by using formula N=z2pq/e2,

Where,

N = required sample size

z = 1.96 when confidence interval is 95%

p = Prevalence of elective cesarean delivery in this hospital (17%).

q =1-p

e =Allowable error

Prevalence of elective cesarean delivery in this hospital is 17 %.

Hence, p = 0.17

q = 1- 0.17 = 0.83

e = 10% = 0.1

The required sample size calculated by the formula is 57. Taking 57 women as cases and 57 as controls, the total sample size will be 114.

- All woman with 37 completed weeks singleton pregnancyand are categorized as ASA Class I (normally healthy) according the American Society of Anaesthesiologists (ASA) scheduled for primary elective LSCS under spinal anesthesia.
- Informed consent obtained.

Women were excluded if they had

- Anemia (Hb< 7 g %).
- Multiple gestations.
- Antepartum hemorrhage (placenta previa or placenta abruption).
- Abnormal placentation (Accreta, increta or percreta).
- Complication with myoma.
- Polyhydramnios.
- Pre-eclampsia.
- Past history of uterine atony and postpartum bleeding.
- A current or previous history of significant disease, including heart disease, liver, renal disorders or a known coagulopathy.
- Allergy to Tranexamic acid.
- History of thromboembolic disorders.
- Women unwilling to enroll in the study.

Each patient was explained about the study and written consent was taken for enrollment in the study. Detail history and examination was done. Patients were randomized into two groups by simple randomization technique. In a capped plastic container, 120 equal sized folded papers were kept. In half of the folded paper, TA was written, and the rest half were blank. On the admission day, anyone other than investigator was asked to pull the folded paper. If the pulled paper contained TA, she was selected as case, and if the pulled paper was blank, she was selected as control.

On the day of surgery, the patient was shifted to the operation theatre, vital signs were recorded. After spinal anesthesia, 10 minutes before skin incision, Tranexamic acid one gm,(prepared as one g/10 ml)IV was given slowly by the anesthetist. After delivery of the baby, both case and control groupsrecei-

vedoxytocin three units (0.6 ml undiluted Syntocinon) IV slowly and placenta was delivered. If uterus remained not well contracted, additional two doses of oxytocin threeunits IV bolus administered three minutes apart, only if required. Vital signs were recorded immediately after delivery of the placenta, one hour and two hour following delivery of baby. In recovery room and in postoperative ward, 10 Units Oxytocin wasadded in first two pints of IV fluid and infused at the rate of 125 ml per hour.Vital signs were monitored every 4 hour interval. Each patient was followed up in the post-operative ward andmaternity ward for any side effects of TA. Any side effects or complications noted in the patient were recorded andmanaged as per the hospital protocol. Similarly, neonatal outcome was recorded in terms of birth weight and APGAR score at 1 and 5 minutes.

RESULTS

During the study period, there were total 4623 deliveries in TUTH. Out of them, the number of LSCS was 1776 (38.42%). Among the LSCS, 408 (22.97%) were elective and 1368 (77.03%) were emergency LSCS. Out of elective LSCS, 197 (47.8%) were primary and 211 (77.03%) were repeat LSCS. One hundred and twenty pregnant women who underwent elective primary LSCS and fulfilled the inclusion criteria of the study protocol were enrolled in the study.

Majority of the women in both case and control groups were aged between 25-30 years. In the study group, it was 26 (43%) and in the control group,it was 29 (48%). The number of women whose age was less than 20 years were 4 (7%) in the study group and 3 (5%) in control group. Women aged more than 35 years were 4 (7%) in both case and control groups.

Table 1. Distribution of study groups according to parity.

Parity	Case n (%)	Control n (%)	Total n (%)	P
P_0	48 (80)	47 (78.33)	95 (79.2)	0.799
P_1	8 (13.33)	8 (13.33)	16 (13.3)	
P_2	4 (6.67)	4 (6.67)	8 (6.7)	
P_3	0 (0)	1 (1.67)	1 (0.8)	
Total	60	60	120	

Majority of the women in both case and control groups were nulliparous. They were 40 (80%) in the study group and 47 (78.33%) in the control group. The number of primipara were 8 (13.33%) in each group. The number of multipara women were 4 (6.67%) in study group and 5 (8.84%) in control group (Table 1). The mean period of gestation was 38.17 weeks in the study group and 38.10 weeks in control groups respectively. There was no statistically significant difference in period of gestation between the two groups (P=0.637). The most common indication of LSCS in both the groups was breech presentation accounting 50 % in case and 30% in control group. Second most common indication was treated subfertility. Other indications for LSCS were big baby, bad obstetric history, CPD, cord around the neck, elderly primigravida, short stature, IUGR, unstable lie and oligohydraminos. One LSCS was done on demand. Each case of rare indication of LSCS like resolved coccyx fracture, neck of femur fracture, previous cervical bucket handle tear and genital wart were present. The mean duration of surgery was 44.81 minutes in the study group and 44.61 minutes in the control group respectively. The difference in duration of surgery between the two groups was not significant statistically (P=0.891).

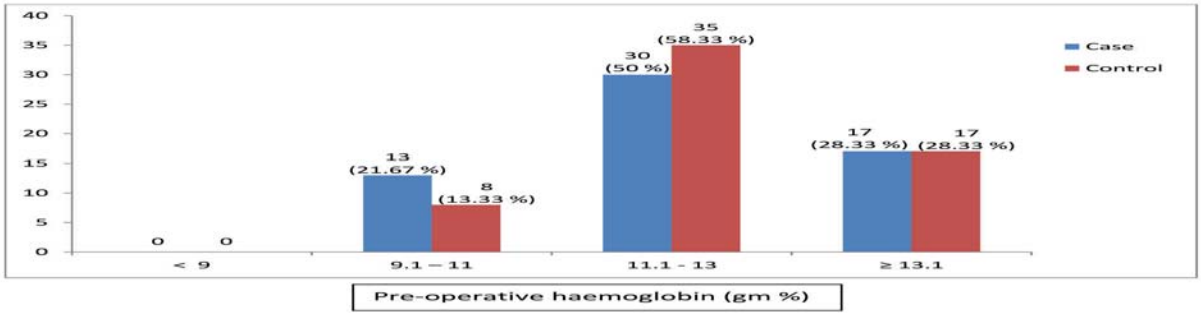

Figure 1. Comparison of pre-operative Haemoglobin in the two groups

The women who had pre-operative haemoglobin between 11.1-13 gm % were30 (50 %) in study group and 35 (58.33 %) in control groups respectively (Fig. 1). The women who had pre-operative haemoglobin more than 13 gm % were 17 (28.33 %) in each group. Thirteen (21.67 %) women in study group and eight (13.33 %) women in control group had pre-operative haemoglobin between 9.1-11 gm%. No women had pre-operative haemoglobin below 9 gm %.

The post-operative haemoglobin in majority of the women was between 11.1 – 13 gm % accounting 30 (50%) in study group and (53.33%) in control groups respectively (Fig. 2) . The women who had post-operative haemoglobin between 9.1 – 11 gm % were 23 (38.33%) in study group and 25 (41.67%) in control group.The women who had post-operative haemoglobin more than 13 gm % were 4 (6.67%) in the study group and 1(1.67%) in control group.

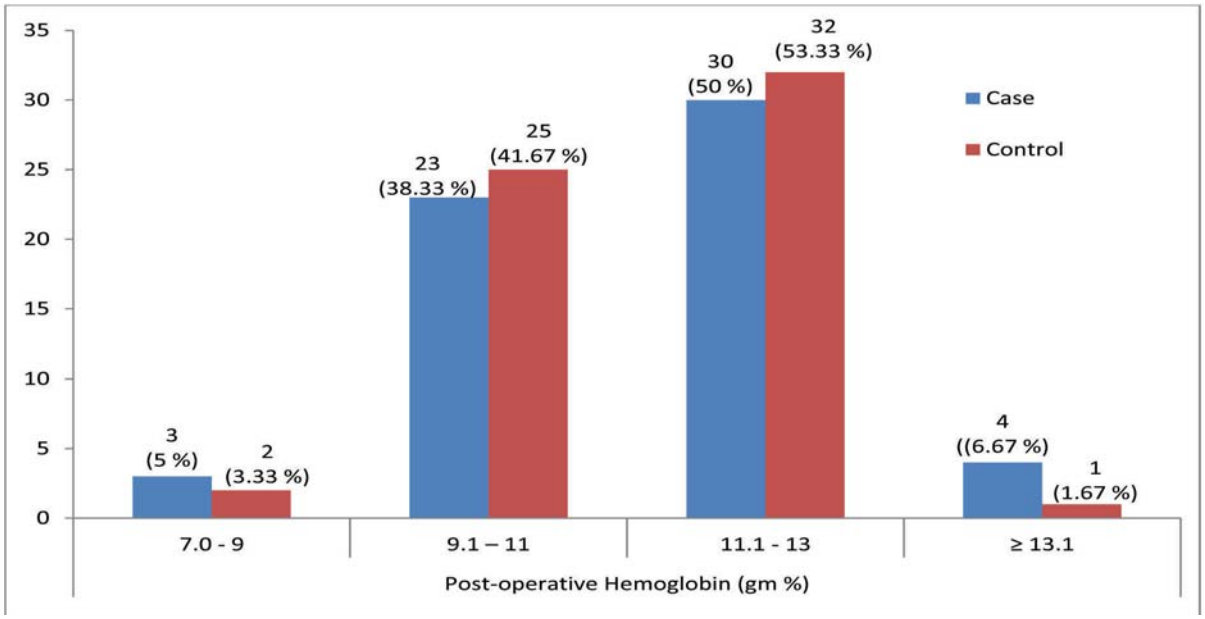

Figure 2. Comparison of postoperative haemoglobinin the two groups.

Similarly, 5% women in the study group and 3 % in control group had postoperative haemoglobin between 7-9 gm %. No women had haemoglobin below 7 gm % and none required blood transfusion.

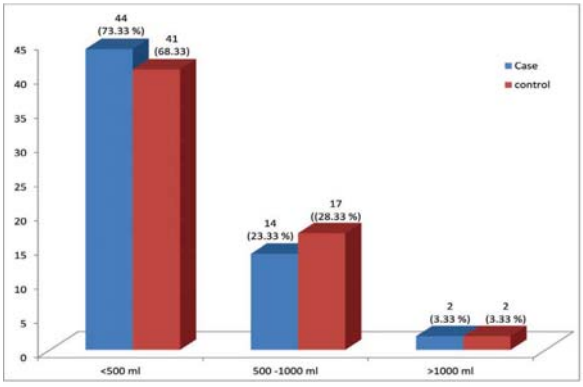

Figure 3. Comparison of blood loss in two groups

Women who had blood loss less than 500 ml were 44 (73.33%)in study groupand 41 (68.33%) in control group (Fig. 3). The difference was statistically significant (P<0.01).

DISCUSSION

In a study by Gungorduket al.[4] the preoperative haematocrit level in the study group and the control group was 32.8±1.6% and 33.0±1.7% which declined post-operatively to 30.1±1.0% and 30.7±1.5% respectively. This difference in the postoperative haematocrit was 2.7 % in study group and 2.9% in control group which was statistically significant (P<0.001). Recently, the CRASH-2 trial has expressed that the early administration of TA significantly reduces mortality in bleeding trauma patients.[9,10] Based on these studies, TA has been included in the WHO list of essential medicines.[11]

TA is commonly used to treat idiopathic

menorrhagia and bleeding associated with pregnancy (placental abruption, placenta previa) as an effective and well-tolerated treatment.[12,13] Randomized controlled studies have shown that TA reduces blood loss after CS.[14-16] TA is an antifibrinolytic agent and it has been used in the treatment of bleeding for many years.[15] When the placenta separates from the uterine wall during delivery, fibrinolytic activity increases in the maternal blood, resulting in decreased clotting. This activation can last up to 6 to 10 hours postpartum and can cause additional bleeding.[16]

The index study showed Tranexamic acid given pre-operatively significantly reducedthe blood loss during LSCS. The mean estimated blood loss was 379.55±232.86 ml in study group and 434.02±231.39 ml in control group respectively. Women who received TA preoperatively had less blood loss by 54.47 ml in comparison to those who did not received TA. The reduction in blood loss was12.55% and was found to be statistically significant (P=0.012).

In the index study, TA reduced the incidence of postpartum hemorrhage (patients with blood loss≥500 ml) in the study group as compared to control group.Twenty three percentage of women in study group and 28% in control group had loss between 500-1000 ml. This difference is statistically significant (P<0.01). Other similar studies also showed significant decrease in PPH in patients who received Tranexamic acid. Small sample size is the limitation of this study. Larger sample sized study would have generatedamore accurate and statistically significant conclusions.

As only low risk cases for postpartum haemorrhage (PPH) were enrolled in the study, it did not reflect the effect of TA in reducing blood loss in high risk cases. If high risk cases for PPH had they also been included in the study, the effect of tranexamic acid in significantly reducing blood loss during LSCS in all low risk as well as high risk cases could have been identified. Oxytocin was used in all the cases before the delivery of placenta and during postoperative period which also reduced the amount of blood loss causing uterine contraction.So, actual effect of tranexamic acid alone in reducing blood loss could not be assessed

CONCLUSIONS

The present study demonstrated that Tranexamic acid significantly reduced the amount of blood loss during LSCS as evidenced by statistically significant difference in Hct level and estimated blood loss pre and postoperatively.

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