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ORIGINAL ARTICLE

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Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: A randomized case controlled prospective study

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OBJECTIVE(S) : To study the efficacy and safety of tranexamic acid in reducing blood loss during and after the lower segment cesarean section.

METHOD(S) : A randomized, case controlled, prospective study was conducted on 100 women undergoing lower segment cesarean section (LSCS). Fifty of them were given tranexamic acid immediately before LSCS were compared with 50 others to whom tranexamic acid was not given. 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. Hemoglobin, urine analysis, liver and renal functions were tested in both the groups.

RESULTS : Tranexamic acid significantly reduced the quantity of blood loss from the end of LSCS to 2 hours postpartum: 75.71 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: 372.71 mL in the study group, versus 469.70 ml in the control group. (P=0.003). No complications or side effects were reported in either group.

CONCLUSION(S) : Tranexamic acid significantly reduced the amount of blood loss during and after the lower segment cesarean section and its use was not associated with any side effects or complication like thrombosis. Tranexamic acid can be used safely and effectively in women undergoing LSCS.

Ket words : Tranexamic acid, Cesarean section

Introduction

Cesarean section (CS) rates have increased to as high as 25 to 30 % in many areas of the world[1]. Delivery by CS can cause more complications than normal vaginal delivery and one of the most common complications is primary or secondary postpartum hemorrhage (20%). 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 cesarean section (LSCS) [1].

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 [2]. Intravenous administration of tranexamic acid has been routinely used for many years to reduce hemorrhage during and after surgical procedures like coronary artery bypass, scoliosis surgery, oral surgery, orthotopic liver transplantation, total hip or knee arthroplasty, and urinary tract surgery [3,4]. Tranexamic acid has been shown to be very useful in reducing blood loss and incidence of blood transfusion in these surgeries.

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

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Methods

This is a prospective randomized case controlled study. The study period was of one year commencing from July 2004 to June 2005. Randomization was done by the rule of odds and even.One hundred subjects were enrolled in the study. In 50 subjects tranexamic acid was given immediately before LSCS and the blood loss was compared with that in 50 others to whom tranexamic acid was not given. Full term primiparas / multiparas with singleton pregnancy being delivered by LSCS were included in the study while subjects having medical and problems involving the heart, liver, kidney and brain and having blood disorders were excluded from the study. Subjects having allergy to tranexamic acid, history of thromboembolic disorders, abnormal placentation, severe pre-eclampsia, multiple pregnancy, macrosomia, polyhydromnios and those requiring blood transfusion due to anemia were also excluded from the study. This study was not supported by any pharma company.

In the study group 20 minutes before taking the skin incision 1gm tranexamic acid was given slowly intravenously over 5 minutes. After delivery of the neonate, 10 units of oxytocin in a pint of dextrose normal saline was given by intravenous drip over 30 minutes while 0.4mg methyl ergometrine was given intravenously. Tranexamic acid injection was prepared by diluting 1g (10 mL) tranexamic acid with 20 ml of 5% glucose. Tranexamic acid was not given in the control group. But after delivery of the neonate, oxytocin and methyl ergometrine were given as in the study group.

Heart rate, respiratory rate and blood pressure were checked and noted before the surgery, immediately after placental delivery and 1 and 2 hours after birth, respectively. The blood loss was measured following placental delivery to the end of the surgery, and from the end of the operation to 2 hours after birth. Uterine contractility, placental separation, neonatal manifestations, and side effects caused by tranexamic acid were noted.

Measuring blood loss

The quantity of blood loss (mL)= (weight of the used materials in both the periods – weight of the materials prior to the surgery) + the volume sucked in the suction bottle after placental delivery in mL. In addition, the pads used after completion of LSCS to 2 hours postpartum were separately weighed. Amniotic fluid and the amount of blood lost before placental delivery was thus not included in measuring blood loss in the study.

Hemoglobin, urine analysis, liver and renal function were noted before and on the 3rd day after operation. Blood collected from the suction container (the volume was measured in ml as marked on the container) was noted and soaked mops, pads, and operation table sheet were weighed by electronic scale before and after the surgery.

The data so obtained was statistically evaluated using Epi Info software, Vol.3.2; February 2004 http:// ww.cdc.gov / Epi info.

Results

The subject characteristics in the two groups were similar with no statistically significant difference between two groups. (Table-1). There was also no significant difference in regard to obstetrical complications such as pregnancy induced hypertension, intrauterine growth restriction (IUGR), premature rupture of membrane, poor obstetric history and indications of LSCS including pregnancy with complication; abnormal presentation, abnormal pelvis, fetal distress, previous LSCS between the two groups. All LSCS were done under spinal anesthesia, the duration of surgery being 47.75 minutes in the study group and 48.57 minutes in the controlled group, the difference being no significant statistically. There was no significant difference in uterine contractions after placental delivery between two groups, indicating that bleeding caused by uterine inertia was similar in both the groups. There was no statistically significant difference in the heart rates, respiratory rates and blood pressures in the two groups. (Table-2)

Table 1. Distribution based on subject characteristics in the two groups.

Group	Age (years) (mean ± SD)	Height (cm.) (mean ± SD)	Weight (kg.) (mean ± SD)	Gestatinal age (wks) (mean ± SD)	Gravidity (mean ± SD)
Study (n=50)	24.30 ± 3.65	152.57 ± 4.26	49.71 ± 3.65	38.85 ± 1.29	2.1 ± 0.95
Control (n=50)	24.89 ± 3.99	152 ± 4.23	49.64 ± 4.80	38.64 ± 1.24	2.08 ± 0.86
P-value	0.99	0.992	0.841	0.790	0.233

Table 2. Vital signs after placental delivery.

Vital signs	Immediate after placental delivery			1 hour after placental delivery			2 hours after placental delivery		
	Study	Control	P-value	Study	Control	P-value	Study	Control	P-value
Heart rate (beats/min)	90.12 ± 11.16	92.40 ± 9.34	0.441	91.64 ± 8.92	87.28 ± 13.45	0.407	91.56 9.26	94 ± 10.05	0.396
Resp. rate (breaths/min)	19.04 ± 4.86	21.48 ± 2.99	0.356	21.32 ± 5.24	24.64 ± 4.00	0.173	19.80 4.54	20.12 2.89	0.295
Systolic BP mean (mmHg)	120.60 ± 11.04	125.20 ± 12.02	0.746	132.76 ± 9.16	123.76 ± 11.35	0.412	123.48 ± 11.49	123.50 ± 11.89	0.649
Diastolic BP mean (mmHg)	76.04 ± 10.12	81.28 ± 9.73	0.680	80.48 ± 8.47	80.84± 10.58	0.746	79.16 ± 7.09	80.72 ± 7.09	0.878

There was statistically significant difference in the quantity of the blood loss from the time of placental delivery to 2 hours postpartum (P=0.003). There was also statistically significant difference in the quantity of the blood loss from end of LSCS to 2 hours postpartum (P=0.001). There was no statistical difference in the quantity of the blood loss from the time of placental delivery to the end of LSCS in both the groups (P=0.056). (Table-3)

Table 3. Comparison of the extent of postpartum hemorrhage in the study and control groups.

Group	Placental delivery to the end of LSCS (mL)	The end of LSCS to 2 hours post partnum(mL)	Placentaldelivery to 2 hours post partum (mL)
Study	299.21±31.44	75.71±20.02	374.92±51.46
Control	339.76 ± 28.86	133.03 ±14.68	472.79 ± 43.54
P- Value	0.056	0.001	0.003

Table 4 shows that the incidence of postpartum hemorrhage (PPH) i.e. > 500 mL blood loss was lower in the study group than in the control group. (P=0.049)

Table 4: Comparison of the incidence of PPH in both the groups.

Blood loss from placental delivery to 2 hours postpartum (ml)	Study	Control	P-value
<500mL	45	36	0.754
≥500mL	05 (10%)	14 (28%)	0.049

There was no difference in the mean birth weight between the two groups. Tranexamic acid had no significant effect on the (1 and 5 minutes Apgar score between the two groups, (P=0.5).

Hemoglobin decreased slightly after birth in both the groups, but there was no statistical difference between the two groups. There was no significant difference in the urine analysis between the two groups. There was no significant change in the liver and renal function tests in the two groups. There was no episode of thrombosis in the study.

Discussion

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 6-10 hours postpartum, causing more bleeding [5]. It was because of this activation of the fibrinolytic system that we decided to use tranexamic acid in this trial.

This study showed that tranexamic acid significantly redues bleeding from time of placental delivery to 2 hours postpartum in LSCS (P=0.001). This study shows significant decrease in the incidene of > 500 mL blood loss in the study group as compare to control group (P-0.049). Similar study carried out by Ming-ying Gai et al [5] in China showed that tranexamic acid significantly reduces bleeding from the time of placental delivery to 2 hours post partum. The study showed significant decrease in the incidence of > 500 ml blood loss in the study group as compared to control group (P-0.029). Zheng et al [6], showed similar results after vaginal delivery.

There was no significant alteration in the vital signs of subjects following tranexamic acid administration. There were no abnormalities in hemoglobin, liver and renal function, and urine analysis. The incidence of thrombosis during pregnancy and puerperium is 5-6 times higher then that in the general population [7]. When the antifibrinolytic drug tranexamic acid is administered, the increased risk of post partum thrombosis after LSCS should be considered. In the present study, not a

single patient developed thrombosis and incidences of side effects like nausea, vomiting and diarrhea were not statistically significant by difference in the two groups. These have been corraborated by other studies [5-7].

Conclusion

Tranexamic acid significantly reduced the amount of blood loss during and after the lower segment cesarean section and its use was not associated with any side effects and.or complication like thrombosis. Thus, tranexamic acid can be used safely and effectively in subjects undergoing LSCS.

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