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EFFICACY OF TRANEXAMIC ACID IN REDUCING BLOOD LOSS IN CAESAREAN SECTION: A PROSPECTIVE RANDOMIZED CONTROL STUDY IN A TEACHING HOSPITAL IN SOUTHERN INDIA

Obstetrics & Gynaecology

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ABSTRACT

Postpartum hemorrhage remains a major cause of maternal mortality worldwide, occupying in both vaginal and caesarean deliveries. Tranexamic acid (TXA), an antifibrinolytic agent reduces bleeding-related mortality in women with postpartum hemorrhage (PPH). This study aimed to assess the efficacy of prophylactic tranexamic acid administration vs standard uterotonic agents alone among women undergoing caesarean delivery. This was a prospective interventional study comprising of a total of 100 patients planned for lower segment caesarean section (LSCS) and divided into 2 groups; Group 1(study group): women who received 1 gram of tranexamic acid added in 100ml NS over 15 minutes prior to skin incision :Group 2(control group): women who received 100ml NS as placebo. 10 IU oxytocin was added after delivery of the placenta to both the groups. The pre-delivery and post-delivery parameters -Pulse rate, Blood pressure, Hb(gm%) and PCV% were measured for each patient. Blood loss was assessed in two phases; the first phase included intraoperative blood loss and the second phase included the postoperative period till 6 hours. Out of 100 women who underwent randomization, there was a comparable increase in the pulse rate and decrease in blood pressure in the control group when compared to the study group. The blood loss was significantly low in the study group, and the need for other uterotonics , blood transfusion were low as well. Prophylactic TXA given in women undergoing lower segment cesarean delivery, under subarachnoid-blockade or epidural anaesthesia, significantly decreases blood loss, including postpartum hemorrhage.

KEYWORDS

Maternal morbidity, caesarean delivery, Postpartum hemorrhage, Tranexamic acid

1. INTRODUCTION

The American College of Obstetricians and Gynecologist'(ACOG) defines postpartum hemorrhage(PPH) as cumulative blood loss greater than or equal to 1000ml or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process (including intrapartum loss) regardless of route of delivery.[1] Blood loss of about 600-750 ml during cesarean delivery should alert the health care provider so as to evaluate the increased blood deficit and be cautious for PPH and treat the same. About 14 million women experience postpartum hemorrhage resulting in about 70,000 maternal deaths globally.[2] Prophylactic administration of a uterotonic agent is recommended to reduce the risk of postpartum hemorrhage.[3,4,5] Tranexamic acid(TXA) is a synthetic derivative of the amino acid lysine that exerts its anti-fibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecule, and thereby inhibiting the interaction of plasminogen and the heavy chain of plasmin with lysine residues on the surface of fibrin. It has been recognized to reduce blood loss and transfusion need in many elective surgeries.[6] This study was conducted to evaluate the efficacy of TXA in reducing blood loss in caesarean delivery.

2. MATERIAL AND MATHODS

This was a prospective interventional randomized controlled study. The study was carried out from January 2021 to April 2022 at Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka. Prior to enrolment, ethical committee clearance was obtained from Hospital Ethical Committee. Written informed consent was attained from all women participated in the study.

The eligible participants were all primigravida / multigravida with singleton live pregnancy at term gestation being delivered by LSCS who were willing to participate in the study.patients with anemia complicating pregnancy, multiple gestation, polyhydramnios, macrosomia, previous history of PPH, fibroid, medical co-morbidities and blood disorders, previous history of epilepsy, abnormal placenta (placenta previa, placental abruption, placental adhesions caused by repeated artificial abortions), eclampsia, prolonged and obstructed labour, history of thromboembolic disorders, allergy to tranexamic acid, and foremost patients who were not willing to participate., were excluded from the study.

A total of 100 patients planned for lower segment caesarean delivery (LSCS) were included in the study after the study criteria were met and informed consent was taken. Patients were randomly divided into 2 groups by simple random sampling method; Group 1(study group): women who received 1 gram of tranexamic acid added in 100ml NS(normal saline) over 15 minutes prior to skin incision in addition to 10 IU of oxytocin injection after delivery of the placenta; Group 2(control group): women who received 100ml NS over 15 minutes prior to skin incision in addition to 10 IU oxytocin after delivery of the placenta.

A structured proforma was designed to record the demographic details, past history and delivery details of all the subjects enrolled for the study. All patients were subjected to history taking, general, abdominal examination and pre-operative investigations (hemoglobin concentration and packed cell volume). Blood loss was assessed in two phases; the first phase included intraoperative blood loss and the second phase included the postoperative period till 6 hours.

The primary outcomes were the blood loss during caesarean delivery and during the first 6 hours post-operative period, vitals during the first 6 hours post-operative period, 24 hour postoperative hemoglobin and hematocrit values. Other outcomes were maternal morbidity such as wound dehiscence, delayed wound healing, prolonged hospital stay, any thromboembolic events; any requirement of blood and blood products transfusion.

Heart rate, respiratory rate and blood pressure were checked and noted before the surgery, immediately after placental delivery and during the first 6 hours after birth. Blood loss was assessed in two phases; the first phase included intraoperative blood loss and the second phase included the postoperative period till 6 hours. Women were transferred from the operating room to the postoperative intensive care unit. Gravimetrically estimated blood loss was assessed. Uterine contractility, urine output were noted.

Measuring Blood Loss

The quantity of blood loss (in ml) =

(Weight of the soaked mops and sponges in the 1st period from skin incision till the end of LSCS procedure - weight of the unsoaked mops prior to the surgery)

+

the volume (in ml) sucked in the suction bottle after placental delivery + weight of the clots obtained during surgery and in post-operative period (till 6 hours).

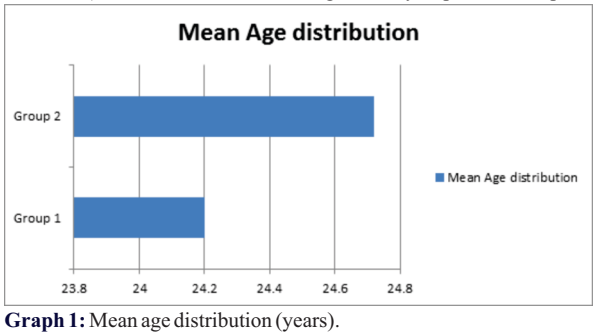
Weigh all blood-soaked mops and sponges and clots (1 gram weight = 1 milliliter blood loss volume). In addition, the pads used after completion of LSCS to 6 hours postpartum were weighed separately.

Blood collected from the suction container (the volume was measured in ml as marked on the container) was noted and soaked mops, pads were weighed by manual weighing machine before and after the surgery. Preoperative hematocrit was the value most recently measured within 15 days before delivery, and postoperative hematocrit was that measured on day 2 after delivery (without transfusion).

RESULTS

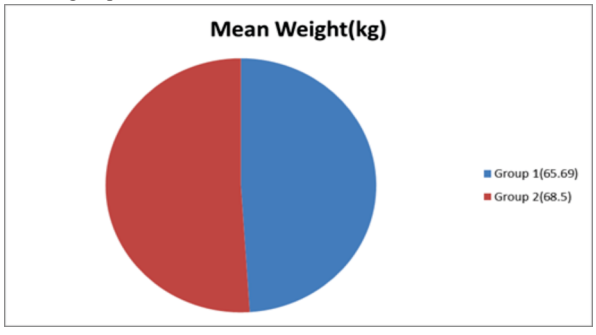
From January 2021 to April 2022, we recruited 100 eligible participants and randomly assigned them to receive tranexamic acid (n=50) or placebo (n=50) and the results were analysed in the Statistical Package for Social Sciences (SPSS 20.0) version used for analysis.

The mean age (study group- 24.20±2.56 versus control group- 24.72±3.1) of the cases did not differ significantly, depicted in Graph 1.



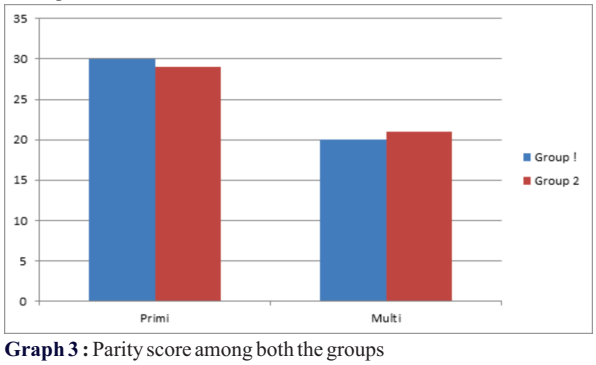
Graph 1: Mean age distribution (years).

The mean weight was 65.69±0.95 kg/m^2 in the study group and 68.50±0.72 kg/m^2 in the control group, depicted in Graph 2. The mean BMI (kg/m$^{2)}$ among the study group was 24.13±0.65 and among the control group was 25.03±0.46.



Graph 2 : Mean Weight Distribution among both groups

Thirty (30) patients in study group and twenty-nine (29) patients in control group(placebo) were primigravida. Twenty (20) patients in study group and twenty one (21) patients in control group were multi-gravida. The parity index was comparable in both the groups, depicted in Graph 3.



Graph 3 : Parity score among both the groups

The mean blood loss at the end of procedure was 311.52 ml in the study group and 393 ml in the control group. The mean blood loss in the 1st 6 hours post-delivery was 54.40ml in the study group and 65ml in the control group. The blood loss was significantly low in the study group compared to the control group (Table 1). The patients in both the groups lost almost 310-400 ml of blood.

Mean increase in pulse rate was 2.4/minute in study group and 7.3/minute in control group. Mean fall in systolic BP was 2.72 mmHg in study group and 7.52 mmHg in control group. Mean fall in diastolic BP was 3.24 mmHg in study group and 6.9 mmHg in control group. There was a statistically significant increase in the pulse rate and decrease in blood pressure in the control group as compared with the study group (Table 1).

Table 1. Primary outcome

Parameters	Study Group (Mean ± Sem)	Control Group (Mean ±Sem)	P Value (<0.05= Significant)
Blood loss	311.52 ±41.58	393.60 ±50.57	0.001
Pulse rate (bpm)			0.009
Pre-delivery	84.20 ±0.94	82.48 ±1.11	
Post-delivery(1 hour)	86.24±1.56	90.16±2.12	
Change in pulse rate	2.04	7.68	
Systolic BP (mmHg)			0.003
Pre-delivery	125.44±1.95	124.72±1.69	
Post-delivery(1 hour)	122.72 ±3.80	116.24 ±1.89	
Change in Sys BP	2.72	7.52	
Diastolic BP (mmHg)			0.002
Pre-delivery	80.88±1.22	78.48±0.96	
Post-delivery	77.64 ±1.47	71.56 ±1.76	
Change in diastolic BP	3.24	6.9	
Hemoglobin (gm%)			0.012
Pre-delivery	12.35±0.16	12.46±0.17	
Post delivery (24 hr)	11.84 ±0.25	11.02 ±0.18	
Change in hemoglobin	0.512	1.44	
Packed cell volume(PCV) (%)			0.244
Pre-delivery	34.26±1.00	35.18±0.55	
Post-delivery((24 hours)	32.62 ±0.71	31.84 ±0.59	
Change in PCV	1.64	3.34	

The mean fall in hemoglobin was 0.512 gm% in study group and 1.44 gm% in control group. Mean fall in hematocrit was 1.64% in study group and 2.7% in control group. The post-delivery hemoglobin and hematocrit were significantly reduced in the control group as compared to the study group.

DISCUSSION

Postpartum hemorrhage (PPH) is a complication of childbirth and the most common cause of maternal death, with about 25% of all mothers' deaths worldwide. The PPH frequency is reported to be 2-4% after vaginal birth and 6% after cesarean section; and when uterine atony is the cause of approximately 50%. Intravenous oxytocin is the drug of choice for postpartum hemorrhage. Other uterotonics like misoprostol, ergometrine, carboprost may also be used for uterine atony.[8] Apart from uterine atony, retained placenta or placental abnormalities, and coagulopathy were the other causes for the PPH.[9]

As the fibrinolytic system gets activated after placental delivery, anti-fibrinolytic agents can be used to reduce obstetric blood loss. Tranaexemic acid is a lysine analogue which acts as an antifibrinolytic via competition inhibition of the binding of plasma and plasminogen to fibrin.[10] Peak plasma TXA concentrations is obtained immediately after intravenous administration, then concentration decreases until the 6th hour. Its half-life is about 2 hours.[10]

Our results show that prophylactic use of tranexamic acid at cesarean delivery had a biologic effect, in that the calculated estimated blood loss was significantly lower among women who received the drug than among those who received only oxytocin (the mean between-group difference was approximately 80 ml); this difference resulted from a significantly smaller decrease in hematocrit from before surgery to after surgery in the tranexamic acid group than in the other group, which was similar to a study done by Gai et al[11] which reported that TA administration reduced blood loss by an average of 88 mL. The statistical difference was not obscured by age, the parity, weight, and average duration of two groups of surgery.

There was a statistically significant fall in Hb% in the control group as

compared to the study group. There was a statistically significant change in vital parameters which are in concurrence with similar study by Sekhavat et al.[12]

There was no significant statistical difference between the blood transfusion among the groups, study group(4%) and control group(11%). The need for other uterotonics and duration of hospital stay were not statistically significant in both the group. No drug allergies or serious gastrointestinal side effects were observed in group with Tranexamic acid use. No incidence of venous thromboembolism among the patients was found during the study, which was not comparable to other studies done by Shakur H et al.[13]

CONCLUSION

Tranexamic acid injection, an anti-fibrinolytic agent when given prophylactically reduced the blood loss during and after the lower segment caesarean delivery. World Health Organization guidelines recommend administration of tranexamic acid in treatment of PPH and trauma. WHO recommendations on how to use uterotonic agents and prevention of postpartum hemorrhage, tranexamic acid can significantly reduce the number of PPH incidents. There is a minimal chance of increasing the risk of thromboembolism, but there has been no observation in our study. So, further studies are also needed to support its efficacy. Also, further studies on larger sample size are warranted to derive conclusive data.

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