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Effectiveness of Intravenous Tranexamic Acid Versus Combination of Tranexamic Acid and per Rectal Misoprostol in Reducing Blood Loss During Caesarean Section: A Prospective Comparative Study

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ABSTRACT

Postpartum hemorrhage, which can be fatal and is one of the primary causes of maternal mortality globally, is a common complication of Caesarean section delivery, which can result in more complications than a typical vaginal delivery. To ascertain whether tranexamic acid, either by itself or in conjunction with per rectal misoprostol, reduces blood loss and the need for transfusions in patients having caesarean sections up to 24 hours after the procedure and whether doing so is safe. This study is prospective and comparative, with an institutional basis. Study location: Bankura Sammilani Medical College and Hospital, Department of Obstetrics and Gynecology, Post-Natal Ward 2, Emergency Operation Theatre, Bankura, WB. Study period: 18 months. 20 patients (55.6%) in Group A had P0+0 in parity, 10 patients (27.2%) had P1+0 in parity and 6 patients (16.7%) had P2+0 in parity.In Group-B, P0+0 was present in 16 (44.4%) patients, P0+1 was present in 1 (2.8%) patient, P1+0 was present in 9 (25.0%) patients, P1+1 was present in 3 (8.3%) patients, P1+1 was present in 4 (11.1%) patients and P2+0 was present in 3 (8.3%) patients. We came to the conclusion that neither group had any reported complications or adverse effects. In addition to having no negative side effects or complications, tranexamic acid plus 600 micrograms of misoprostol taken rectally statistically reduces the amount of bleeding from placental delivery to 2 hours postpartum.

INTRODUCTION

Postpartum hemorrhage, which can be fatal and is one of the primary causes of maternal mortality globally, is a common complication of Caesarean section delivery, which can result in more complications than a typical vaginal deliveryp[1]. Reducing the amount of bleeding during and after CS is crucial to lowering maternal mortality and morbidity from bleeding. A typical labor involves about 300-400 milliliters of blood loss; postpartum hemorrhage (PPH) is defined as blood loss exceeding 500 milliliters after vaginal delivery or more than 1000 milliliters after cesarean section. In addition to Active Management of 3rd Stage of Labor (AMTSL), uterotonics such as oxytocin, prostaglandins (E1, E2 and F2α) and methylergonovine have been used to control bleeding after cesarean section.It is widely believed that most PPH-related deaths could be prevented by treating and preventing PPH.

These crucial actions will improve women's health care during childbirth and help achieve the Sustainable Development Goals. Reducing the global maternal mortality ratio (MMR) to less than 70 maternal deaths per 100,000 live births is the goal[2]. There have been studies on the use of tranexamic acid to stop blood loss in a number of gynecological conditions, including menorrhagia and CS. Since tranexamic acid (TA) has been shown to decrease menstrual blood loss, bleeding in trauma patients and blood loss during elective surgery, it has been studied as a potentially helpful adjunct to uterotonics for the prevention of PPH.Women who require TA had significantly less post-operative blood loss without experiencing an increase in unfavorable side effects, according to an RCT for PPH prevention[3]. Prostaglandins are the myometrium's natural stimulant and have been shown to be useful in both inducing labor and an abortion. By binding to their cell membrane receptors, which are mediated by G proteins, they are able to displace calcium through the cell membrane. This allows them to either stimulate phospholipase C or inhibit adenylcyclase[4]. An obstetrician should always take postoperative bleeding, also known as postpartum bleeding, into account. Numerous studies examined how combining different medications can reduce blood loss in patients with chronic sinus syndrome. Therefore, by comparing the changes in hemoglobin (Hb%) and hematocrit (HCT) at CS, it attempted to assess the effects of different medication types on blood loss during and after CS.

MATERIALS AND METHODS

Study Design: It is a Institutional based Prospective Comparative study.

Place of Study: emergency operation theatre, Post-Natal ward 2, Dept. of Obstetrics and Gynaecology, Bankura Sammilani Medical College and Hospital, Bankura, WB.

Period of Study: 18 months

Sample Size: Sample size (SS) of the proposed study is based on the following formula

$$n = [(Z\alpha+Z\beta)2 \times (S12 +S22)] / (Mean\ 1-Mean\ 2)\ 2$$
$$+15\%\ of\ sample\ size$$

where, Zα = 1.96 (two tailed) at 95% confidence interval, Zβ =1.28/ 0.84 at 90% / 80% power of test, S1 and S2 are standard deviations of post-operative hemoglobin levels in both groups.

Now, putting the values in the formula, the SS for the proposed study would be, n = 72. The S1 and S2 were as per the existing literature.

Inclusion criteria: Term pregnant women having emergency caesarean section, singleton pregnancy having no medical disorders.

Exclusion criteria: The exclusion criteria included:

1. Severe medical and surgical disorders; thyroid dysfunction, which was excluded by routine thyroid function test (free T3, free T4 and thyroid stimulating hormone (TSH), all of them should be within normal limits)
2. Bleeding tendency, for example, disseminated intravascular coagulopathy, which was excluded by platelet count, coagulation time, bleeding time, prothrombin time, partial thromboplastin time and thrombin time (all should be within normal)
3. Acute liver or kidney diseases
4. Blood disorders, such as anemia
5. Allergy to TA; allergy to misoprostol
6. Contraindication to misoprostol, for example, bronchial asthma and heart disease
7. History of thromboembolic disorders
8. Risk factors for PPH, such as poly hydramnios, fetal macrosomia, antepartum hemorrhage, or prolonged obstructed labour
9. Abnormal placenta such as placenta previa and placenta abruptia; pregnancy complications such as severe pre-eclampsia.
10. Multiple pregnancies
11. Those requiring blood transfusion
12. Patients who refused spinal anesthesia.

RESULTS

About 20 patients (55.6%) in Group A had P0+0 in parity, 10 patients (27.2%) had P1+0 in parity and 6 patients (16.7%) had P2+0 in parity (Table 1). In Group-B, P0+0 was present in 16 (44.4%) patients, P0+1 was present in 1 (2.8%) patient, P1+0 was present in 9 (25.0%) patients, P1+1 was present in 3 (8.3%) patients, P1+1 was present in 4 (11.1%) patients and P2+0 was present in 3 (8.3%) patients. Blood loss during LUCS from placental delivery to the end Within Group-A, the average blood loss (mean±standard deviation) among patients from placental delivery to the end of LUCS was 480.1667±99.2890. Within Group-B, the average blood loss (mean±standard deviation) among patients from placental delivery to the end of LUCS was 301.4722±17.5312 (Table 2).The mean blood loss distribution with group from placental delivery to the end of LUCS was statistically significant (p<0.0001). Blood Loss from LUCS Termination to Two Hours After Partum Patients in Group-A had a mean blood loss of 133.8056±35.3123 from the end of LUCS to two hours after giving birth (mean±standard deviation). Of the patients in Group-B, the mean blood loss (mean±standard deviation) from the end of LUCS to two hours after partum was 74.8333±9.4461. The group's mean blood loss distribution from the end of LUCS to 2 hours after delivery was statistically significant (p<0.0001). Group-A patients had an average heart rate of 88.1944±11.8727 (mean±standard deviation) two hours after giving birth (Table 3). Group-B patients had an average heart rate of 87.6389±9.7867 two hours after giving birth (mean±standard deviation). Hb% (prior to surgery) expressed in gm% The pre-op mean Hb% (Mean±S.D.) of patients in Group-A was 11.2250±1.1185. The mean Hb% (pre-op) in Group-B was 11.6361±1.2690 (Mean±S.D.) (Table 4). Hb% in gm% (24 hours postpartum) The mean Hb% (24 hours postpartum) (mean±standard deviation) of patients in Group-A was 9.9056±.9463. The mean Hb% (24 hours postpartum) (mean±standard deviation) of patients in Group-B was 10.6306±1.2019.The mean Hb% distribution with group 24 hours postpartum was statistically significant (p = 0.0058). The mean SBP (2 hours post-placental delivery) (mean±standard deviation) for the patients in Group-A was 119.2222±7.5786. Group-B patients had a mean SBP of 117.0000±5.8846 (2 hours post-placental delivery) (Mean±S.D.) (Table 5).

Table 1: Association between Parity

Parity	Group A	Group B	Total
P0+0	20	16	36
Row %	55.6	44.4	100.0
Col %	55.6	44.4	50.0
P0+1	0	1	1
Row %	0.0	100.0	100.0
Col %	0.0	2.8	1.4
P1+0	10	9	19
Row %	52.6	47.4	100.0
Col %	27.8	25.0	26.4
P1+1	0	3	3
Row %	0.0	100.0	100.0
Col %	0.0	8.3	4.2
P2+0	6	4	10
Row %	60.0	40.0	100.0
Col %	16.7	11.1	13.9
P2+1	0	3	3
Row %	0.0	100.0	100.0
Col %	0.0	8.3	4.2
TOTAL	36	36	72
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

Chi-square value: 7.8971; p-value: 0.1620

Table 2: Distribution of mean Blood loss (mL) from placental delivery to end of LUCS and Blood loss from end of LUCS to 2 hrs post partum (mL)

	Number	Mean	SD	Minimum	Maximum	Median	p-value
Blood loss from placental delivery to end of LUCS (mL)							
Group A	36	480.1667	99.2890	200.0000	680.0000	501.0000	<0.0001
Group B	36	301.4722	17.5312	268.0000	330.0000	300.0000	
Blood loss from end of LUCS to 2 hrs post partum (mL)							
Group A	36	133.8056	35.3123	56.0000	220.0000	132.0000	<0.0001
Group B	36	74.8333	9.4461	56.0000	92.0000	74.5000	

Table 3: Distribution of mean Heart rate 2 hrs postpartum

Heart rate at 2 hrs postpartum	Number	Mean	SD	Minimum	Maximum	Median	p-value
Group-A	36	88.1944	11.8727	64.0000	114.0000	89.0000	0.8291
Group-B	36	87.6389	9.7867	64.0000	108.0000	89.0000	

Table 4: Distribution of mean Hb% (pre-op) and Hb% (24 hrs post-partum) (g%)

Parameters	Number	Mean	SD	Minimum	Maximum	Median	P-value
Hb% (pre-op)							
Group-A	36	11.2250	1.1185	8.9000	13.4000	11.5000	0.1493
Group-B	36	11.6361	1.2690	8.8000	13.4000	11.9000	
Hb% (24 hrs post- partum)							
Group-A	36	9.9056	0.9463	8.0000	12.0000	10.0000	0.0058
Group-B	36	10.6306	1.2019	8.1000	12.6000	10.8500	

Table 5: Distribution of mean SBP(2 hrs after placental delivery) in mm hg

Parameters	Number	Mean	SD	Minimum	Maximum	Median	p-value
SBP(2 hrs after placental delivery)							
Group-A	36	119.2222	7.5786	100.0000	134.0000	120.0000	0.1690
Group-B	36	117.0000	5.8846	100.0000	130.0000	118.0000	

DISCUSSION

The Gynaecology Emergency Operation Theatre, Post-Natal Ward 2, Department of Obstetrics and Gynaecology, Bankura Sammilani Medical College and Hospital was the site of this randomized Control Trial (Superiority Trial). This study included term pregnant women who had emergency caesarean sections and singleton pregnancies without any medical conditions. Total 72 patients were present in our study and divided into two groups.Group A = 36 (transfusion of 1 gram of tranexamic acid intravenously) group B=36, which is administered 600 micrograms of misoprostol intrarectally along with tranexamic acid via IV (Every blood loss is measured in milliliters).

In Group-A, we discovered that 20 patients (55.6%) had P0+0 in parity, 10 patients (27.8%) had P1+0 in parity and 6 patients (16.7%) had P2+0 in parity. In Group-B, P0+0 was present in 16 (44.4%) patients, P0+1 was present in 1 (2.8%) patient, P1+0 was present in 9 (25.0%) patients, P1+1 was present in 3 (8.3%) patients, P1+1 was present in 4 (11.1%) patients and P2+0 was present in 3 (8.3%) patients. At p = 0.1620, this was not statistically significant.

The mean age (mean±s.d.) of the patients in Group-A and Group-B in our study were 22.3056±4.2950 years and 21.1944±4.0765 years, respectively and were not statistically significant (p=0.2641).

According to our research, patients in Group-A had a mean gestational age (completed weeks) of 38.6667±.8619, while those in Group-B had a mean gestational age (completed weeks) of 38.3611±.8333, which was not statistically significant (p = 0.1307).

Gai *et al*.[5] showed that While 89 women in the control group did not receive tranexamic acid prior to CS, 91 women in the study group did. Two times were used for the collection of blood. The amount of blood from the end of CS to two hours postpartum was significantly decreased by tranexamic acid: 42.75±40.45 mL in the study group compared to 73.98±77.09 mL in the control group (p = 0.001).

The amount of total blood from placental delivery to 2 hours postpartum was also significantly decreased (p = 0.002): 351.57±148.20 mL in the study group and 439.36±191.48 mL in the control group. The amount of bleeding that occurs from placental delivery to two hours postpartum is statistically reduced by tranexamic acid and there are no negative effects or complications linked to its use. For this reason, tranexamic acid can be used to lessen bleeding from CS in a safe and efficient manner.

Mayur *et al*.[6] showed that Before LSCS were compared with 50 others who did not receive tranexamic acid, 50 of them received it right away. The amount of blood loss from the conclusion of LSCS to 2 hours postpartum was significantly decreased by tranexamic acid: 75.71±20.02 mL in the study group compared to 133.03±14.68 mL in the control group (p = 0.001). The study group experienced a significant reduction in blood loss from placental delivery to two hours post-partum, with 299.21±31.44 mL, compared to 339.76±28.86 mL in the control group. P is equal to 0.003.

The amount of blood lost during and following a lower segment caesarean section was greatly decreased by tranexamic acid and there were no negative effects or complications, such as thrombosis, linked to its use. Women undergoing LSCS can safely and effectively use tranexamic acid.

Sekhavat *et al*.[7] showed that 45 women in the study group received tranexamic acid right before CS, while 45 women in the control group received a placebo. Between the end of CS and the first 2 hours after delivery, tranexamic acid significantly decreased blood loss (28.02±5.53 mL in the tranexamic group compared to 37.12±8.97 mL in the control group; p = 0.000). Blood loss is statistically reduced by tranexamic acid from the end to 2 hours after CS and there are no negative effects or complications linked to its use. As a result, tranexamic acid can be used to lessen CS-related bleeding safely and effectively.

Gungorduk *et al*.[8] found that before surgery, a random selection of patients was made to receive an intravenous infusion of either TA (1 g/10 mL in 20 mL of 5% glucose; n = 330) or 30 mL of 5% glucose. The percentage of women in the TA group who had an estimated blood loss >1000 mL was significantly lower than in the placebo group (7 [2.1%] versus 19 [5.8%], respectively; relative risk [RR] 2.7; 95% confidence interval [CI] 1.1 to 6.3; p < 0.03). The mean estimated blood loss was significantly lower in the TA group compared with women in the placebo group (499.9±206.4 mL versus 600.7±215.7 mL, respectively; p<0.001).

Blood loss greater than 1000 millilitres, the proportion of patients requiring additional uterotonic agents and bleeding during CS were all considerably decreased by TA. Moreover, there was no rise in the frequency of thromboembolic incidents. According to their findings, TA can be applied to lessen CS bleeding in a secure and efficient manner.

Movafegh *et al*.[9] showed that The tranexamic acid group exhibited a significantly lower mean blood loss (262.5±39.6 vs. 404.7±94.4 mL) and postoperative bleeding (67.1±6.5 vs 141.0±33.9 ml; p<0.001) in comparison to the control group.

Sentürk *et al*.[10] found that 10 minutes prior to the commencement of the caesarean section, the patients in the study group (n = 101) and the control group (n = 122) received intravenous injections of 20 cc of tranexamic acid and a 20 cc 5% dextrose solution. Tranexamic acid decreased blood loss both during and after surgery. They did not notice any TA-related side effects, such as hypersensitivity, gastrointestinal issues, or venous thromboembolism. This study demonstrates that tranexamic acid effectively lowers intrapartum and postpartum hemorrhage in women undergoing cesarean sections. Their research indicates that it can be used safely in the patients mentioned above, despite the fact that some obstetricians are still concerned about the thrombosis risk.

El-Sttar *et al*.[11] showed that 75 patients in group A received 600 mcg of misoprostol rectally prior to the incision and 75 patients in group B received 1-g of TA slowly injected intravenously 10 minutes prior to the incision. A statistically significant difference was observed between the groups with respect to postoperative hemoglobin (p = 0.038), hematocrit (p = 0.033), systolic (p = 0.043) and diastolic (p = 0.037) blood pressures, heart rate (p = 0.045) two hours after surgery, blood loss in the first (p<0.001) and second periods (p = 0.019) and total blood loss (p<0.001). Group B showed a difference in blood loss of 146.15 mL (22.6%) less than group A.

We found that the mean heart rate of patients in Group-A was 88.1944±11.8727 two hours after giving birth, while the mean heart rate of patients in Group-B was 87.6389±9.7867 two hours after giving birth, which was not statistically significant (p = 0.8291).

Ali *et al*.[12] found that after the baby was delivered, 100 patients received oxytocin and tranexamic acid 20 minutes prior to the start of anesthesia; the remaining 100 patients received oxytocin alone. Vaginal bleeding in the first two hours after delivery was substantially less severe in the study group than in the control group (p<0.019). Preoperative hemoglobin concentration did not differ significantly between the study and control groups (p = 0.195); postoperative hemoglobin concentration was significantly higher in the study group than in the control group (p<0.001); and reduction in hemoglobin levels was significantly lower in the study group than in the control group (p<0.001).

Preoperative hematocrit did not differ statistically between the study and control groups (p = 0.967). The study group had significantly higher postoperative hematocrit levels than the control group (p0.015) and the study group had significantly lower reductions in hematocrit levels than the control group (p<0.001).

CONCLUSION

We came to the conclusion that neither group had any reported complications or adverse effects. In addition to having no negative side effects or complications, tranexamic acid plus 600 micrograms of misoprostol taken rectally statistically reduces the amount of bleeding from placental delivery to 2 hours postpartum. Therefore, it is safe and effective to use tranexamic acid along with 600 micrograms of misoprostol per rectally to reduce bleeding from CS. However, more RCTs are required to validate the use of misoprostol and tranexamic acid together to significantly lower blood loss.

The World Health Organization recommends tranexamic acid as a treatment for postpartum hemorrhage. There is a new RCT involving 11,000 women and there are ongoing RCTs using tranexamic acid to prevent PPH. Following this, additional advice on PPH prevention might be taken into account for a regular preventive regimen.

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