ORIGINAL ARTICLE

Prophylactic Use of Tranexamic Acid in Reducing Blood Loss and Preventing Postpartum Haemorrhage in Elective Caesarean Section

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ABSTRACT

Objective: To compare the mean blood loss in women administered pre-operative prophylactic tranexamic acid versus control group undergoing elective lower segment caesarean section.

Study Design: It was an experimental study.

Place and Duration of Study: Study was carried out at Department of Obstetrics and Gynecology at Federal Government Polyclinic Hospital Islamabad from 9th Mar 2021 to 8th Sep 2021.

Materials and Methods: A total of 100 patients were selected who were presented for elective cesarean delivery under spinal anesthesia. Women were equally divided into two groups A & B with 50 patients in each group. Patients in group A were preoperatively given 1gm of tranexamic acid intravenously. Group B did not receive tranexamic acid. Immediately after delivery of neonate both groups received 10 units of oxytocin. All abdominal sponges, gauzes, pads were weighed before surgery and postoperatively and blood from suction container also measured in ml. Postoperatively per vaginal bleeding up to 24 hours were measured by total number of pads used, weighed for dry and wet weight and blood loss measured in ml. Total blood loss was measured. Data analysis was performed through SPSS version 22.

Results: The mean age for Group A and Group B was 29.9years±6.51SD and 28.7years ±5.13SD respectively. The mean age for the total study subjects was 29.3 ±5.9SD. The mean and standard deviation for blood loss after elective lower segment caesarean section in Group A was 576.6ml± 91.59SD and in Group B it was 836.6ml ±91.59SD respectively with 31 %reduction in blood loss in group A. It is clear from the results that blood loss was significant in both the groups with p-value=0.001.

Conclusion: The blood loss is significantly reduced in women undergoing elective lower segment caesarean section by administering pre-operative prophylactic tranexamic acid.

Key Words: *Caesarean, Delivery, Hemorrhage, Postpartum, Tranexamic Acid.*

Introduction

Postpartum hemorrhage is defined by WHO as blood loss which exceeds 500ml after birth but within 24hours of delivery and is responsible for 25% maternal mortality & severe anemia in 12% survivors.[1] Loss of around 45% blood volume results in weakness, sweating, tachycardia and hemodynamic instability. Rise in caesarean section rate worldwide is alarming. It has led to high risk of complications than normal vaginal delivery in the form of either primary or secondary postpartum hemorrhage resulting in increased maternal mortality & morbidity.[2] Pregnancy related causes leads to death of thousands of women worldwide during delivery or in postpartum period. Postpartum hemorrhage stands as a major cause of mortality and morbidity leading to anemia needing red cell transfusion, prolonged hospitalization, and sepsis. In addition to uterine atony, haemostatic equilibrium is shifted towards increased fibrinolysis causing coagulopathy and bleeding due to extensive tissue damage in caesarean.[3,4] Main first line treatment for PPH is oxytocin. Others include ergometrine and misoprostol. Following placental expulsion, fibrinolytic system gets activated resulting in degradation of fibrin and fibrinogen. Rise in plasminogen activators and fibrinogen degradation products causes increased tendency to bleed in postpartum period which lasts up to 10 hours leading

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Received: March 24, 2023; Revised: August 28, 2023
Accepted: August 29, 2023
https://doi.org/10.57234/jiimc.september23.1667

to more hemorrhage. So, we need other strategies to reduce blood loss in addition to standard utero-tonic agents. There is limited evidence for definitive recommendations of prophylactic tranexamic use in women of all risk profiles undergoing cesarean section.[5,6] Pro-hemostatic drugs such as tranexamic acid provide a complementary biochemical haemostatic effect to well proven uterotonic. Tranexamic acid is a synthetic analog of amino acid lysine. It acts as fibrinolytic agent by competitively binding to lysine receptor site on plasminogen and reduces conversion of plasminogen to plasmin thus preventing fibrin degradation and stabilizing fibrin clot. Tranexamic acid was conventionally used to control peri operative bleeding, reduce hemorrhage & decrease blood transfusion rate in different medical & surgical conditions with resulting decrease in both mortality & morbidity. Recently it's being used in many Gynecological procedures like myomectomy, hysterectomy, cervical & ovarian cancer surgeries & used as 1st line in women with menorrhagia. Although WHO recommended its usage for standard treatment for postpartum hemorrhage within 3 hours of birth but preventive role of this drug in decreasing hemorrhage during & after cesarean has been a conflicting area yet .[7]

The rationale of this study was that uterotonic drugs that are used in routine practice compared to haemostatic agents. Prophylactic usage of tranexamic acid might reduce need of hysterectomy, risk of severe anemia & avoid need for blood transfusion & will help in improving quality of care for women by preventing maternal mortality & morbidity due to postpartum hemorrhage. It is a cost-effective agent with fewer side effects, easy availability, and effective & in developing country like Pakistan where low socioeconomic status prevails, its promising drug. Many international studies are available in literature, but local data is still lacking which could help us in using this favorable drug. So, this study was planned with an objective to find out the mean blood loss and compare it among women receiving prophylactic tranexamic acid with those who do not receive it.

Materials and Methods

It was an experimental study with non-probability consecutive sampling conducted at the department of Obstetrics & Gynecology, Polyclinic hospital, Islamabad. Duration of study was 6 months from 9th Mar 2021 to 8th Sep 2021**.** A total of 100 cases were selected and divided in two groups, 50 in each group; 50 cases in each group were calculated with Confidence level = 95%, Power of study = 90% and mean (SD) for total blood loss i.e., 436.5±118.07 ml with tranexamic acid and 616.5±153.34ml in control group after elective caesarean section. Pregnant women of age 18-40 years, parity <5, gestational age>37 weeks planned for elective lower segment caesarean section under spinal anesthesia were enrolled in the study. Women with heart disease (medical record), renal disorders (creatinine> 1.8mg/dl), diabetes (OGTT>186mg/dl), hypertension (BP>140/90mmH), coagulation disorders (INR>2), and anemia (Hb<10g/dl), requiring blood transfusion, abnormal placentation, polyhydramnios, and multiple pregnancies (on ultrasound) were excluded from study. Moreover, no booked cases and those who were sensitive to tranexamic acid or in whom tranexamic acid is contraindicated and women with history of postpartum hemorrhage in previous delivery were also excluded from study. Informed consent was taken. After taking approval from hospital ethical committee letter No 1/2017-E/C82, 100 women fulfilling selection criteria were enrolled in the study through maternity ward of Department of Obstetrics & Gynecology, Polyclinic hospital, Islamabad. Demographic information (name, age, BMI, gestational age, parity) was noted. Women were randomly divided into two groups. In group A, just before giving skin incision 1gm of tranexamic acid in 10ml of 5% dextrose was given intravenously slowly over 5 minutes. In group B, tranexamic acid was not given preoperatively. In both groups after delivery of neonate 10 units of oxytocin were given. All abdominal sponges, gauzes and pads were weighed before surgery and postoperatively .Blood from suction container was also measured in milli liters. Postoperatively per vaginal bleeding up to 24 hours was measured by total number of pads used, weighed for dry and wet weight and blood loss was measured in milli liters. Total blood loss was measured. Data was entered and analyzed through SPSS version 22. The quantitative data like age, BMI, gestational age and total blood loss was presented as mean and SD. Qualitative variables like parity were

https://doi.org/10.57234/jiimc.september23.1667

presented as frequency and percentage. Both groups were compared for mean blood loss by using independent sample t-test. P-value≤0.05 was taken as significant.

Results

The mean age of women in Group A and Group B was 29.9 ± 6.51 years and 28.7 ± 5.13 years respectively. Most of the patients were ≤35 years of age. In group A, 38 (76.0%) were primiparous and 12 (24.0%) were multiparous females. In group B, 35 (70.0%) were primiparous and 15 (30.0%) were multiparous females. The mean BMI of patients in Group A was 28.12 ± 4.45 kg/m^2 and in Group B was 28.72 ± 4.73kg/m^2. Table I

The mean blood loss in Group A was observed as 576.60 ± 91.59 ml and in Group B, the mean blood loss was 836.60 ± 91.59 ml. The difference of blood loss in both groups was highly significant p=0.001. Table II

Table I: Age and Parity of Study Subjects (N= 100)

		Group		Total
		Group A	Group B	
N		50	50	100
Age years)	≤ 25.00	19 (38.0%)	17 (34.0%)	36 (36.0%)
	26.00 - 35.00	21 (42.0%)	26 (52.0%)	47 (47.0%)
	≥36.00	10 (20.0%)	7 (14.0%)	17 (17.0%)
Mean age (years)		29.9 ± 6.51	28.7 ± 5.13	29.3 ± 5.9
Parity				
Primiparous		38 (76.0%)	35 (70.0%)	73 (73.0%)
Multiparous		12 (24.0%)	15 (30.0%)	27 (27.0%)
BMI		28.12 ± 4.45	28.72 ± 4.73	28.42 ± 4.59

Table II: Blood Loss in Both the Groups (N=100)

	Group		p-value
	A	B	
Blood loss (ml)	576.60 ± 91.59	836.60 ± 91.59	0.000

Discussion

Results of our study show that patients in Group A, who received tranexamic acid, their mean blood loss was 576.6ml± 91.59SD compared to 836.6ml±91.59SD group B patients who didn't receive prophylactic tranexamic acid. This value coincides with the 30% reduction in hemorrhage reported by Ahmed & associates in Ismaila Egypt.[3] Another trial conducted in 160 women showed that total blood loss in tranexamic acid recipient group was much less when compared to control group.[8] In another study conducted on 100 females, mean blood loss was significantly lower in study group as compared to control group. The difference was significant with p value <0.057.[9] Finding of these studies are consistent with our study with significant reduction in blood loss in tranexamic acid group.

Shah p et. al., in his study took 160 pregnant women who underwent caesarean delivery and were given one gram of Tranexamic acid intravenously. Measurement of blood loss was done during and after the procedure. Women with tranexamic acid showed less blood loss than placebo group with statistically significant difference was found between pre-operative and post-operative hemoglobin levels in Tranexamic acid group than in the control group. Hence tranexamic acid usage in preoperative period decreases blood loss after operative procedure. These findings are consistent with the findings of our study. In a developing country like ours where postpartum hemorrhage is a major threat to the life of the mothers, it seems to be a promising option.[10]

Study conducted by Magann et al in their results reported that 6.7% of caesarean deliveries have postpartum hemorrhage with complication rate of 4.8 %.[11] Jaiparkash in his research gave 1 Gram tranexamic acid before caesarean delivery. Mean blood loss during and after surgery along with side effects were compared with decrease blood loss in study group as compared to control group with no adverse events. It concluded that it is a cheap and easily available drug that leads to significant reduction in blood loss and is suitable in low resource settings[12]All these are in consistent with our study findings.

Meta analysis of 18 randomized control trials was done to study the role of tranexamic acid in decreasing hemorrhage in caesarean delivery. Outcome was compared in women who received intravenous tranexamic acid to prevent hemorrhage after caesarean with placebo group women. The Tranexamic acid group had a 60% decline in risk of postpartum hemorrhage, RR 0.40: 95% CI. There was 68% reduction in women getting risk of severe postpartum hemorrhage (which defined as greater than 1000 ml blood loss) with RR, 0.32; 95% CI & decline in rate of transfusion to 70% with RR, 0.30; 95% CI. No safety concerns were observed about

usage of the antifibrinolytic agent from the 18 RCTs analyzed.[4] All of it is consistent with our study results. Mean blood loss in our study was closer to the research conducted by the Gungorduck et al but higher than research conducted by Gai et al, Gohel et al, Shekavat et al. But in all studies, tranexamic acid use in women statistically decreases the hemorrhage in caesarean delivery and this finding grossly matches with our study.[21-14,15] All of it are in consistent with our study results.

Different studies conducted on incidence of postpartum hemorrhage and role of tranexamic acid in decreasing hemorrhage after caesarean delivery. In research conducted by Gai et al postpartum hemorrhage incidence was much lower in study group when compared to control with a p value of less than 0.05. There was no statistical distinction in postpartum hemorrhage incidence from completion of Caesarean to two hours postpartum between two groups. Research carried out by Gohel et al revealed notable decline of more than 500ml hemorrhage in study group when compared to control in caesarean delivery.[15]

In the study conducted by Joshua M et al, randomized control trial research was done on both surgically & vaginaly delivered women regarding effectiveness of tranexamic acid in preventing postpartum hemorrhage. It revealed that use of tranexamic acid led to decline in post-partum hemorrhage in all cases.[16] These findings are consistent with our study.

Viswanathano and colleagues concluded that direct relation exists between tranexamic acid & decrease in postpartum blood loss. A multicenter randomized double-blind placebo-controlled trial included 4000 women & compared the effect of tranexamic acid in a dose of 1Gram two min after normal vaginal & after prophylactic administration of oxytocin and in all these studies results showed that tranexamic acid has a promising role in decreasing hemorrhage in postpartum hemorrhage. [17, 18] All these studies' results findings are in consistent with finding of our study.

Sentilhes L et al in his research showed biological effect of using tranexamic acid prophylaxis in cesarean with resulting decline in hemorrhage among women who received tranexamic acid compared to group who received placebo.[18]In double blinded randomized controlled trials, not only significant decline in blood loss(Amount of intraoperative blood loss was significantly less in the tranexamic group 2232 ± 1204 ml compared to the placebo group 3405 ± 1193 ml with p value 0.002) with use of tranexamic acid was shown but also significantly less frequency of hemorrhage, decline in need for uterotonic agents, reduced need for hysterectomy, reduced risk of severe anemia and less need for blood transfusion was also shown. [3,19-21]

There are several limitations to our study. It is underpowered in detecting adverse outcomes of this agent and identifying specific risk factors for PPH in certain patients. It was not powered to detect potentially meaningful differences in the risk of severe maternal complications. In addition to this, maternal satisfaction on day 2, psychological status at 2 months, quality of life and mother–infant relationship were not explored. Further studies are required to validate the role of TXA in women at high risk of PPH.

Conclusion

The blood loss is significantly reduced in women undergoing elective lower segment caesarean section by administering pre-operative prophylactic tranexamic acid. So Tranexamic acid can be used as prophylaxis before caesarean section for decreasing blood loss during surgery.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.