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Original Article

Tranexamic Acid and Blood Loss During and After Cesarean Section: A Prospective Randomized Study

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Abstract:
Background: Incidence of cesarean sections is on the rise. This has increased incidence of associated complications, especially the Postpartum hemorrhage (PPH). Tranexamic acid is a potent antifibrinolytic agent. Efficacy and safety of the drug has not been assessed in patients from Muzaffarabad, as of yet.
Objective: To find out the effectiveness and safety of tranexamic acid in the reduction of blood loss during and after the cesarean section.
Methods: A prospective, randomized, placebo controlled, study was directed on 100 women experiencing lower segment cesarean segment (LSCS) at Department of Obstetrics and Gynecology, Combined Military Hospital Muzaffarabad over 6 months from May 2018 to October 2018. Fifty of them were given tranexamic acid preceding LSCS were contrasted and 50 control group who got IV placebo. Blood loss was collected and estimated during two periods. The study group got IV tranexamic acid and the control group got IV placebo. Following delivery, all participants got 10 units of oxytocin in 500 mL of normal saline. Hemoglobin, urine examination, liver and renal functions were checked in both the groups.
Results: Tranexamic acid essentially decreased the quantity of blood loss from the finish of LSCS to 2 hours postpartum: 60.96±13.4 ml in the investigation group versus 112.02±13.46 mL in the control group (p=0.001). It additionally essentially reduced the amount of blood loss– Intraoperative 500.62±111.20 mL in the study group, versus 696.85±196.32 ml in the control group. (P<0.001). No serious complication or reactions were accounted for in either group.
Conclusion: Tranexamic acid essentially decreased the quantity of blood loss during and after the lower segment cesarean segment and its utilization was not associated with any serious reactions or side effect like thrombosis. TXA can be utilized as safe and effective in participants undergoing LSCS and useful for anemic women or the individuals who refuse blood transfusion.
Keywords: Tranexamic acid, Blood loss, Cesarean section.

Introduction

The incidence of cesarean section is constantly increasing day by day **a**nd the rate of complications is also much higher as compared with normal vaginal delivery. Out of these complications primary and secondary postpartum hemorrhage is most common. It prompts expanded maternal morbidity and mortality. Impact of this complication is decreased by lowering the amount of blood loss during and after cesarean section especially the lower segment cesarean section (LSCS).[1,2] Cesarean section (CS) rates have expanded to as high as 25 to 30% in numerous territories of the world.[3] Delivery by CS can cause a bigger number of complications than normal vaginal delivery and a standout amongst the most well-known intricacies is primary or secondary postpartum hemorrhage (20%).

Postpartum hemorrhage (PPH) is considering a noteworthy complication after the vaginal or cesarean delivery around the world, which contributes generously to maternal mortality and close misses. Every year, around 1– 2% of mothers with PPH bite the dust, with a normal interim of roughly 2 to 4 hours from beginning of PPH to death.[4] PPH is defined as the loss of in excess of 500 mL of blood subsequent to normal delivery or in excess of 1000 mL loss following CS.[5] There are four reasons for PPH – uterine atony, injury to the birth passage, seized placental tissue or membranes, and coagulopathies, for example, spread intravascular coagulation (DIC).[6] PPH can achieve grievous extents during CS.

Diverse figures fluctuating from under 500 ml to in excess of 1000 ml have been cited as estimation of blood loss related with Cesarean section. There is

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additionally a wide variety in blood ordering practices for this surgery. A few components like habit, training and medico lawful concerns might be mindful notwithstanding difficulty in loss assessment in CS. In the course of the most recent couple of years there has been developing concern for safety, cost and sufficiency of blood usage. Reviews on blood use expected to recognize issue zones which can be then rectified. The initial step while looking into transfusion practice is to see whether precise appraisal of blood loss is being done.[7] Management of discharge after CS may extend from organization of oxytocic and blood transfusion to increasingly extreme estimates, for example, hysterectomy.[8,9] Use of anti-fibrinolytic agents, for example, tranexamic acid (TXA), be that as it may, stays away from both the perils of blood transfusion similarly as the long-term side-effects of hysterectomy.

TXA (a manufactured subordinate of the amino acid lysine) is an anti-fibrinolytic that intensely represses the actuation of plasminogen to plasmin. Tranexamic acid is an aggressive inhibitor of plasminogen activation, and at much higher concentrations, a noncompetitive inhibitor of plasmin.[10]Aim of our study is to study the efficacy and safety of tranexamic acid in reducing blood loss throughout and after cesarean section**.**

Methods

A randomized, placebo-controlled, open label clinical study was directed after Institutional Ethics Committee endorsement from May 2018 to October 2018 with 100 clinically stable singleton antenatal mothers age limit 20 to 40 years at term planned for elective CS. Pregnancy difficulties, for example, pre-eclampsia, polyhydramnios, macrosomia, different pregnancy, preterm work, placenta previa, and abruptio placentae were excluded from the investigation alongside women experiencing blood dyscrasias, coagulation issue, thromboembolic clutters, severe anemia, sensitivity to TXA, and extreme medical and surgical entanglements including the heart, liver, or kidney.

By assuming a difference of 100 mL of aggregate, intra and postoperative blood loss would be a clinically vital contrast between the two groups the sample size was calculated. It was determined that 45 candidates per group would be required to identify that difference with 80% power and 5% possibility of Type 1 error was set. Standard deviation was assumed on the bases of an earlier study[11] that was 190 for control group and 150 for the test group by adjusting 10% for dropout rate; the enrollment target was taken 50 participants for each group. The selected 100 mothers were randomized into two groups utilizing a PC produced randomization rundown to get any 1 g (in 10 mL) of IV TXA broke up in 20 mL of 5% dextrose arrangement (think about grouping; n = 50) or IV placebo, for example 30 mL of 5% dextrose arrangement for the control group; n = 50, 20 minutes before starting spinal anesthesia. Amid cesarean Section, in the wake of depleting the amniotic liquid totally and delivery of placenta, blood was depleted in a different suction holder. Dry and drenched cleans and sheets were weighed by a sensitive gauging machine. Mean blood loss from mops and sheets was determined by utilizing the equation used by Gai et al.[12] blood from mops and sheets = (load of drenched material – load of dry material)/1.05; where 1.05 was taken the particular blood gravity on 37°C.

To this, the blood depleted in the suction container after delivery of placenta was added to get the all intra operative blood loss. After delivery, 10 units of oxytocin in 500 mL of normal saline was injected intravenously every 20 to 30 minutes. Extra 15 units of oxytocin was given postoperatively (5 U in each dose of IV liquid for three sequential doses over a time of 12 hours). Prerequisite oxytocin was given further. Two-hour postoperative blood loss was determined from the doused cushions by a similar recipe referenced previously. Two hours postoperative vitals like pulse, systolic and diastolic blood pressure, respiratory rate, and pallor were compared with the preoperative status in the two groups. Before and 24 hours after operation complete blood count, coagulation profile, liver function test, and renal function test were analyzed between the two groups.

Results

The study data was expressed as mean ± SD, frequencies and percentages. Numerical variables were compared by applying independent sample t-test, while categorical variables were dealt by Chi-square test. Two-tailed p-value of <0.05 was taken significant. For the analysis of data, the standard statistical software i.e. Microsoft Excel and SPSS version 21.0 were used.

Two groups were similarly coordinated as for statistic attributes like age, weight, height, period of gestation at which CS was done, signs for elective CS, preoperative vitals i.e. beat, systolic circulatory strain, diastolic pulse, respiratory rate, preoperative

hematological stir up, for example, total blood count, liver function tests, and renal function tests. (Table 1)

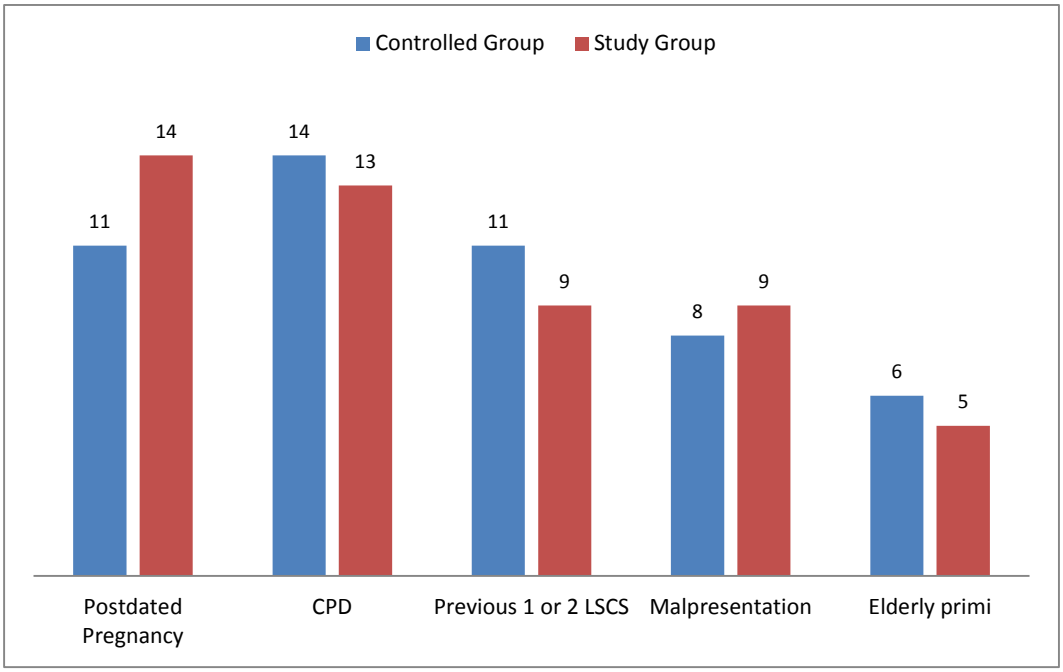

Figure 1. Indication for lower segment cesarean section (LSCS). CPD, Cephalopelvic Disproportion

Table 1: Pre-operative Demographics of the vitals and blood work-up of participants

Parameter	Study Group (mean±SD)	Controlled Group (mean±SD)	P-value
Age (years)	26.01±4.69	26.79±5.39	0.388
Weight (kg)	66.02±5.61	65.12±7.14	0.801
Height (meter)	1.54±0.05	1.54±0.06	0.798
Gestation period (weeks)	37.95±1.41	38.97±1.44	0.732
Pulse rate (per minute)	82.73±8.21	84.23±6.89	0.129
SBP (mmHg)	118.62±8.32	117.11±9.14	0.364
DBP (mmHg)	73.92±6.07	72.94±8.78	0.794
Respiratory rate (per minute)	13.64±1.39	12.92±2.10	0.057
Hb (g/dL)	10.33±1.26	9.80±1.34	0.050
Urea (mg/dL)	22.66±1.80	22.52±1.78	0.655
Creatinine (mg/dL)	0.80±0.20	0.79±0.19	0.805

Both intraoperative and 2-hour postoperative blood loss were altogether less in the examination group than the control group. (Table 2) Postoperative vital assessment and side effects are given in Table 3 and 4 respectively.

Table 2. Preoperative and postoperative blood loss assessment

Parameters	Study group (n=50) (mean±SD)	Control group (n=50) (mean±SD)	p-value
Blood volume in suction (mL)	99.54±28.89	218.78±64.48	0.001
Blood volume in mops + sheets (mL)	403.13±112.44	465.85±141.18	0.01
Blood loss – Intraoperative (mL)	500.62±111.20	696.85±196.32	0.001
Blood loss - 2 h postoperative (mL)	60.96±13.4	112.02±13.46	0.001
Total blood loss	561.64±113.79	801.71±200.12	0.001

Table 3: Postoperative vitals assessment

Parameters	Study Group (mean ± SD)	Controlled Group (mean ± SD)	p-value
SBP (mmHg)	110.90±8.874	107.8±10.196	0.096
DBP (mmHg)	68.54±6.011	69.45±7.26	0.761
Respiratory rate (per minute)	14.35±1.21	14.01±1.76	0.495
Hb (g/dL)	10.08±1	8.81±1.18	0.000
Urea (mg/dL)	22.17±1.54	21.98±1.49	0.741
Creatinine (mg/dL)	0.75±0.17	0.75±0.16	0.910

Table 4: Side effects observed among study patient

Parameters	Study Group n (%)	Controlled Group n (%)	p-value
Nausea	17 (33%)	14 (26%)	0.059
Vomiting	9 (18%)	8 (16%)	0.790
Diarrhea	1 (2%)	0 (0%)	0.315
Thrombosis	0 (0%)	0 (0%)	

Discussion

Increased blood loss can have its adverse impacts, for example, raised morbidity and mortality, expanded hospital stay, expanded intraoperative duration, increased need for re-exploration which might be fatal at times, also excessive bleeding can hamper oxygen delivery and lead to various organ failure and death. Blood loss will make transfusion of blood and blood items basic henceforth presenting more serious dangers like transfusion reactions, for example, unfavorably susceptible responses, transmission of fatal infections like HIV, HPV, HCV and so forth and mismatched blood transfusion. Amid placental delivery, fibrinogen and fibrin are quickly debased, while plasminogen activators and fibrin degradation items (FDP) increment because of activation of the fibrinolytic framework. This initiation can last up to 6 to 10 hours postpartum, causing all the more bleeding. It was a result of this actuation of the fibrinolytic system that we chose to utilize Tranexamic acid in this study.

TXA applies its antifibrinolytic impact by hindering the lysine restricting locus of the plasminogen and plasmin particles, in this way keeping the binding of plasminogen and plasmin to the fibrin substrate. TXA additionally restrains change of plasminogen to plasmin.[13]Afterdelivery of the infant, there is transient initiation of fibrinolytic course for 6 to 10 hours.[14] Hence, the adequacy of an antifibrinolytic agent, for example, TXA is being assessed for the counteractive action of PPH. The outcomes demonstrate that, intraoperatively, mothers in the examination aggregate had a mean blood loss of 500.62±111.20 mL, while mothers in control bunch had a mean blood loss of 696.85±196.32 mL (P = 0.000).Two hours postoperatively, the study amass had a mean blood loss of 60.96±13.4 mL, while the control aggregate had a mean blood loss of 112.02±13.46 mL (P = 0.000). Coupling the two outcomes, mothers in the examination amass had a mean all out blood loss of 561.64±113.79 mL, while mothers in the control bunch had a mean all out blood loss of 801.71±200.12 mL. In this way, in the examination group, there was all out decrease in blood loss by roughly 30% (P = 0.000). Six mothers in the control group required additional 10 U of oxytocin infusion, while just two of the mothers in the TXA group required the equivalent.

Movafegh et al.[14] played out their investigation with intravenous administration of 10 mg/kg of TXA 20 minutes before skin incision at cesarean delivery. Mean blood loss was fundamentally less in the TXA aggregate contrasted and the control group for both intraoperative bleeding (259.86 ± 40.05 versus 406.7 ± 84.7 mL) and postoperative bleeding (68.3 ± 6.7 versus 142.3 ± 34.12 mL; P < 0.001). Oxytocin administration was fundamentally less in the TXA group contrasted and the control group (40 ± 6.7 versus 44 ± 6.5 units; P= 0.001). These outcomes were predictable with the present study.

A comparable report was completed by Gai et al.[15] in China by regulating TXA 10 min before skin entry point. This mediation prompted less draining 2 hours postoperatively: 42.75 ± 40.45 mL in the investigation group versus 73.98 ± 77.09 mL in the control group (P = 0.001) yet did not demonstrate any diminishing in post-placental delivery blood loss. This was likely because of the way that TXA was directed just 10 min before the skin entry point. Along these lines, the present investigation was intended to regulate TXA 20 min before spinal anesthesia.

Sekhavat et al.[16] led a prospective randomized investigation on 90 primipara women which demonstrated that TXA essentially diminished blood loss from the finish of CS to 2 hours postpartum; 28.02 ± 5.53 mL blood loss in the tranexamic group versus 37.12 ± 8.97 mL in the control group (p-value = <0.001). These outcomes were practically identical to our examination despite the fact that they considered just primipara, while our investigation had no incorporation criteria dependent on equality.

In our investigation, postoperatively, there was altogether more pallor in the control bunch than the

examination group. There was likewise huge increase in pulse, mean 84/min in study amass versus 92/min in control gathering (p-value = <0.001). Different parameters, for example, systolic blood pressure, diastolic blood pressure, and respiratory rate did not have any huge contrast in the two gatherings. In the investigation by Movafegh et al.[14] and Gai et al., [15]there was no critical increase in pulse just as other postoperative vitals. There was noteworthy distinction in postoperative hemoglobin levels between the two groups, mean fixation being 10.08±1 g% in the investigation bunch versus 8.81±1.18 g% in the control group (P = <0.001). The contrast between the preoperative and postoperative hemoglobin esteems was additionally fundamentally less in the study group than the control (P esteem = 0.000). Other hematologic and biochemical parameters did not have any critical distinction in the two groups.

These outcomes were practically identical with the study by Movafegh et al. and Gai et al. [14,15] Side effect profile of TXA, for example, nausea, vomiting, and diarrhea was comparative in the two groups. These outcomes were like previous investigations. The frequency of thrombosis amid pregnancy and puerperium is 5 to 6 times higher than that in the all general population. At the point when the counter fibrinolytic drug TXA is regulated, the expanded risk of thrombosis ought to be considered, particularly in the postpartum LSCS population. In our examination, in any case, none of the woman had indications of thrombosis. Svanberg et al.[17] revealed 67 instances of abruptio placentae being treated by TXA with no indications of thrombosis in any. Comparable outcomes were found in different investigations. [14,15]

All information showed that TXA can be utilized safely without expanding the occurrence of thrombosis, yet more examinations are required in such a manner. The safety of giving TXA (1G) while the fetus was still in utero was a key concern. As a result, the neonatal result was fastidiously assessed by a neonatologist. In the present examination, the mean APGAR scores at 1 and 5 min were less in the investigation group and as contrast with the control. In this way, there was no critical distinction in the APGAR esteems at 1 min and at 5 min among the two groups. None of the children required NICU confirmation. Results were similar to past investigations. [14, 15, 18, 19]

Conclusion

Tranexamic acid essentially decreased the quantity of blood loss during and after the lower segment cesarean segment and its utilization was not associated with any serious reactions or side effect like thrombosis. TXA can be utilized as safe and effective in participants undergoing LSCS and useful for anemic women or the individuals who refuse blood transfusion.

Conflict of Interest: Authors declare no conflict of interest.

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Authors' Contribution:

NS: Conception, study designing & conduction, analysis, manuscript writing, & facilitating procurement

HP: Conception, study designing & conduction, analysis & manuscript writing

SH: Conception, planning, analysis & material procurement

RR: Discussion & manuscript writing