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Original Research Article

Efficacy of prophylactic tranexamic acid administration in prevention of postpartum hemorrhage in placenta previa cesarean section: an interventional study

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ABSTRACT

Background: Postpartum hemorrhage accounts for the major part of the mortality as well as morbidity like severe anemia, need for blood transfusion, hospital stay and infection. Aim and objectives of the study were to determine the efficacy and safety of prophylactic tranexamic acid and intravenous tranexamic acid in preventing postpartum hemorrhage in women undergoing caesarean section for placenta previa.

Methods: Seventy women with placenta previa over 1 year, randomized into 2 groups: group 1 (n=35): Women who received 10 IU oxytocin intravenous infusion after placental delivery and group 2 (n=35): Women who received 1 gm (10 ml) tranexamic acid IV before skin incision plus 10 IU oxytocin intravenous infusion after placental delivery.

Results: The mean age was similar in 2 groups i.e., 26.34±4.78 years in group 1 and 27.31±5.62 years in group 2. Most women in the present study presented with type IV placenta previa i.e., 34.3% in group 1 and 48.6% in group 2. Mean pre-operative hemoglobin was 9.57±1.54 g/dl in group 1 and 9.59±1.35 g/dl in group 2. Intra-operative mean blood loss was 729.31±172.45 ml in intravenous oxytocin group and 464.86±28.00 ml in intravenous tranexamic acid group. A total of 74.3% women in group 1 and 20% women in group 2 developed postpartum hemorrhage. Mean post-operative hemoglobin was 8.04±1.34 g/dl in group 1 and 8.85±1.26 g/dl in group 2. In group 1, 5.7% neonates were born with very low birth weight and while none in group 2. 51.4% neonates in group 1 and 45.7% in group 2 had low birth weight.

Conclusions: It is concluded that tranexamic acid used prophylactically intravenously before skin incision in patients undergoing cesarean section for placenta previa significantly reduces intra-operative blood loss.

Keywords: Prophylactic tranexamic acid, Postpartum hemorrhage, Placenta previa, Cesarean section

INTRODUCTION

Every year over five lac women die worldwide due to causes related to pregnancy and delivery. Postpartum hemorrhage accounts for the major part of the mortality as well as morbidity like severe anemia, need for blood transfusion, hospital stay and infection. Obstetric hemorrhage is responsible for about 30% all pregnancy related deaths in both high- and low-income countries and is the leading direct etiology of maternal mortality worldwide.¹ Most of the deaths occur soon after giving birth and almost all (99%) occur in low- and middle-

income countries. Fourteen million women suffer from postpartum hemorrhage each year, of whom 1-2% die within 2-4 hours after the onset of bleeding, 2 to 11% of them show anemia later in their life.²

The rates of cesarean section have increased to as high as 25% to 30% in many areas of the world.³ Postpartum hemorrhage complicates approximately six percent of the cesarean sections. According to world health organization definition, postpartum hemorrhage occurs when the clinical amount of blood loss is about 500 ml after vaginal delivery or 1000 ml after caesarean section.⁴ Risk factors

for postpartum hemorrhage include previous postpartum hemorrhage, primiparity, obesity, prolonged or augmented labour, multiple pregnancies, previous cesarean delivery, polyhydramnios, macrosomia and placenta previa.^{5,6}

Postpartum hemorrhage is commonly encountered following placenta previa as one of the major causes. Traditionally, four variations of placenta previa were recognized-complete, partial, marginal and low-lying.⁷ Recent revised classification of placenta previa consists of two variations: true placenta previa, in which the internal cervical OS is covered by placental tissue and low-lying placenta, in which the placenta lies within 2 cm of the cervical OS but does not cover it.⁸

Over many years, several techniques have been described in the literature for controlling massive bleeding associated with placenta previa cesarean sections, including uterine packing with gauze, balloon tamponades, B-Lynch suture, insertion of parallel vertical compression sutures, a square suturing technique and embolization or ligation of the uterine and internal iliac arteries, but there is wide variation in success rate of these maneuvers.⁹⁻¹³

Tranexamic acid has been shown to be very useful in reducing blood loss and incidence of blood transfusion in various surgeries such as coronary artery bypass, scoliosis surgery, oral surgery, orthotopic liver transplantation etc. In gynecology, tranexamic acid reduces maternal blood loss in women with menorrhagia compared with control agents/placebo. In obstetrics, it reduces bleeding related mortality in women with postpartum hemorrhage, especially when administered fairly soon after delivery.¹⁴

In light of these observations and in view of limited evidence on use of tranexamic acid for prevention of bleeding during caesarean section in cases of placenta previa, present study was conducted to determine efficacy and safety of intravenous tranexamic acid in preventing postpartum hemorrhage in women undergoing caesarean section for placenta previa.

METHODS

This prospective interventional randomized controlled study was conducted on women with placenta previa who underwent caesarean section in department of obstetrics and gynecology at Pt. B. D. Sharma, PGIMS, Rohtak, Haryana. The study was conducted over a period of one year (October 2018 to September 2019).

Women with placenta previa undergoing cesarean section were included in the present study and women with cardiac, hepatic, renal, thromboembolic disease, placenta accreta and allergy to tranexamic acid were excluded.

Method of recruitment

Subjects were enrolled in the study after taking written informed consent and explaining in details about the study

protocol. The diagnosis of placenta previa was made on the basis of ultrasonography. Participants were randomized into two groups based on computerized generated method: Group 1 (n=35): included patients who received 10 IU oxytocin intravenous infusion after placental delivery. Group 2 (n=35): included patients who received 1 gram (10 ml) tranexamic acid intravenous before skin incision plus 10 IU oxytocin intravenous infusion after placental delivery.

Intervention

10 IU oxytocin intravenous infusion in 500 ml normal saline over 30 minutes was given in both the group. One gram (10 ml) tranexamic acid was given by slow intravenous injection just before skin incision. The detailed history and thorough clinical examination of all subjects was done. All were subjected to investigations namely haemoglobin, blood group, HIV, HBsAg, VDRL, glucose challenge test, TSH, complete urine examination and ultrasonography. Patients' blood pressure and pulse were taken. Hemoglobin concentration was done preoperatively and 24 hours postoperatively and change in hemoglobin concentration was noted. The patients were followed up till discharge. Any maternal morbidity and mortality were also noted.

Primary outcome was measured in terms of blood loss: Quantity of blood loss in ml=[weight of gauze pads used after surgery-weight of gauze pads used before surgery] + volume of blood in suction bottle after placental delivery.

Secondary outcome was measured in terms of need for blood transfusion, need of uterotonics and need of additional surgical intervention like uterine artery ligation or uterine compression sutures.

Statistical analysis

At the end of the study, all data was compiled and the statistics were analyzed with SPSS version 21. Continuous variables were presented as mean±SD or median for the unevenly distributed data. Categorical variables were expressed as frequencies and percentages. Association between two or more variables was compared using chi square test. For all statistical tests, a p<0.05 was considered statistically significant.

RESULTS

The present prospective interventional randomized controlled study was conducted on 70 women (n=35 in each group) with placenta previa undergoing caesarean section over a period of one year (October 2018 to September 2019). The mean age was 26.34±4.78 years in group 1 and 27.31±5.62 years in group 2 (p>0.05). Most women in the present study were nullipara that is 42.9% were in group 1 and 48.6% in group 2 (p>0.05). Mean body weight was 62.97±6.44 kg in group 1 and 63.2±6.12 kg in group 2 (p>0.05). Mean systolic blood pressure in

group 1 and 2 was 115.49 ± 8.7 and 112.74 ± 8.79 mmHg respectively ($p > 0.05$ NS), mean diastolic blood pressure was 76.29 ± 8.32 and 75.37 ± 8.21 ($p > 0.05$ NS) mmHg respectively and mean pulse rate was 94.57 ± 8.7 and 91.77 ± 6.74 per minute respectively ($p > 0.05$ NS).

Bleeding per vaginum was present in 91.4% in group 1 and 77.1% in group 2. Labour pain was present in 0% and 11.4% in group 1 and 2 respectively ($p > 0.05$). Women who had no previous cesarean section in group 1 and 2 was 77.1% and 80% respectively ($p > 0.05$). In group 1, 17.1% and in group 2, 25.7% women presented with malpresentation. Malpresentation included breech, oblique and transverse lie. In group 1, 5.7% women and in group 2, 2.9% women had absent fetal heart sound on ultrasonography indicating intrauterine death of fetus at the time of presentation. Most women presented with type IV placenta previa in both the groups followed by type III and type IIb. Women with type IV placenta previa were 34.3% in group 1 and 48.6% in group 2 ($p > 0.05$).

Pre-operative hemoglobin level in most women was in range of 9-10.9 g/dl that includes 48.6% in group 1 and 71.4% in group 2. In present study, 2.9% women in group 1 and 8.6% in group 2 were found to be severely anemic. Mean pre-operative hemoglobin level was 9.57 ± 1.54 g/dl in group 1 and 9.59 ± 1.35 g/dl in group 2. No statistically significant difference was found between both groups in terms of mean pre-operative hemoglobin level ($p > 0.05$). Mean INR was 1 ± 0.12 in group 1 and 0.99 ± 0.14 in group 2. The mean platelet count was found to be 2.07 ± 0.71 lac in group 1 and 2.01 ± 0.39 lac in group 2 ($p > 0.05$ NS).

Majority of the women in the present study did not require pre-operative blood transfusion. Blood transfusion was given pre-operatively to 5.8% women in group 1 and 8.6% in group 2 in form of packed cell. Mean requirement of pre-operative blood transfusion was 0.086 ± 0.368 units in group 1 and 0.143 ± 0.486 units in group 2. The difference was found to be statistically insignificant ($p > 0.05$).

A total of 60% of women in group 1 and 45.7% in group 2 delivered at 32-36+6 weeks. Mean gestational age at delivery was 35.77 ± 2.66 weeks in group 1 and 36.69 ± 2.35 weeks in group 2. No statistically significant difference was observed between groups in terms of gestational age at delivery ($p > 0.05$).

Table 1: Intra-operative mean blood loss, (n=35).

Blood loss (ml)	Group 1, n (%)	Group 2, n (%)	P value (95% CI)
200-400	0 (0)	19 (54.3)	
400-600	9 (25.7)	10 (28.6)	<0.001
600-800	15 (42.9)	4 (11.4)	[95% CI=
800-1000	10 (28.6)	2 (5.7)	165.51 to
>1000	1 (2.9)	0 (0)	363.41]
Total	35 (100)	35 (100)	
Mean \pm SD	729.31 ± 172.45	464.86 ± 28	<0.001

Table 1 shows that the mean intra-operative blood loss was 729.31 ± 172.45 ml in group 1 and 464.86 ± 28.00 ml in group 2 with a $p < 0.001$, which is statistically highly significant. The blood loss measured in group 1 was 42.9% in range of 600-800 ml followed by 28.6% in range of 800-1000 ml followed by 25.7% in range of 400-600 ml. The blood loss measured in group 2 was 54.3% in range of 200-400 followed by 28.6% in range of 400-600 ml. When the blood loss was compared among groups, p value between group 1 versus group 2 was found to be less than 0.001, which is statistically highly significant.

A total of 31.4% in group 1 and 65.7% in group 2 required no intra-operative blood transfusion. On the other hand, 68.6% in group 1 and 34.3% in group 2 required blood transfusion intra-operatively with a $p = 0.001$. The difference observed was statistically highly significant. Mean requirement of intra-operative blood transfusion was 1.00 ± 0.861 units in group 1 and 0.457 ± 0.730 units in group 2. When compared among groups, the difference in requirement of intra-operative blood transfusion in group 1 versus group 2 showed statistical significance with $p = 0.031$. A total of 54.3% women in group 1 required additional medical intervention in form of misoprostol and/or carboprost as opposed to 17.1% women in group 2. This observation was found to be statistically highly significant with a $p < 0.001$. 60% women in group 1 required additional surgical intervention in form of hemostatic sutures, uterine artery ligation, balloon tamponade or combination of these. Only one patient required cesarean hysterectomy in group 1. In group 2, 17.1% women required additional surgical intervention intraoperatively which is statistically highly significant ($p < 0.05$). 22.9% women in intravenous tranexamic acid group showed nausea and vomiting post-operatively. No other side effects like thromboembolism till hospital stay or seizure episodes noted in both groups ($p < 0.001$).

Table 2: Maternal complications, (n=35).

Maternal complications	Group 1, n (%)	Group 2, n (%)	P value
PPH	26 (74.3)	7 (20)	<0.001 HS
Post-partum shock	1 (2.9)	0 (0)	0.313 NS
DIC	0 (0)	0 (0)	-
Renal failure	0 (0)	0 (0)	-
Transfer to ICU	1 (2.9)	0 (0)	0.313 NS
Maternal mortality	0 (0)	0 (0)	-

Table 2 shows most of the maternal complications were observed in group 1. In group 1, 74.3% women developed postpartum hemorrhage (blood loss > 500 ml) while 20% in group 2. Only one woman in group 1 developed postpartum shock and was shifted to ICU. The $p < 0.001$ in terms of postpartum hemorrhage as maternal complication which is statistically highly significant.

Table 3: Post-operative hemoglobin level, (n=35).

Post-operative hemoglobin (g/dl)	Group 1, n (%)	Group 2, n (%)	P value (95% CI)
4.0-6.9	3 (8.6)	3 (8.6)	0.001 [95% CI=- 1.57 to - 0.05]
7.0-8.9	23 (65.7)	9 (25.7)	
9.0-10.9	6 (17.1)	22 (62.9)	
≥11	3 (8.6)	1 (2.9)	
Total	35 (100)	35 (100)	
Mean ± SD	8.04±1.34	8.85±1.26	0.032

Table 3 illustrates mean post-operative hemoglobin was 8.04±1.34 g/dl in group 1 and 8.85±1.26 g/dl in group 2. The difference in post-operative hemoglobin level was found statistically significant when compared between group 1 and group 2 with a p=0.032. Mean change in hemoglobin concentration from pre-operative hemoglobin to post-operative hemoglobin was 1.563±0.66 g/dl in group 1 and 0.734±0.35 g/dl in group 2. The difference in change in hemoglobin concentration was found statistically significant when group 1 was compared with group 2 with a p<0.001. 45.7% women in group 1 and 11.4% in group 2 required blood transfusion post-operatively. Mean requirement of post-operative blood transfusion was 0.571±0.688 units in group 1 and 0.20±0.575 units in group 2. Statistically, the difference on comparing group 1 with group 2 in terms of requirement of post-operative blood transfusion was found significant with p=0.002 respectively.

Mean birth weight was 2.28±0.53 kg in group 1 and 2.41±0.52 kg in group 2. No statistically significant difference was found (p>0.05). On comparing Apgar score at 1 minute, 5.7% neonates in group 1 and 2.9% in group 2 were having score less than 7. Similarly, 5.7% neonates in group 1 and 2.9% in group 2 were having Apgar score at 5 minute less than 7 (p>0.05). A total of 5.7% neonates in group 1 and 0% in group 2 were born with very low birth weight. On other hand, 51.4% neonates in group 1 and 45.7% in group 2 were having low birth weight. Neonates born premature were 65.7% in group 1 and 45.7% in group 2. Total 11.4% neonates were transferred to NICU in group 1 and 14.3% in group 2. The observed difference was statistically insignificant (p>0.05). Most neonates were transferred to NICU due to low birth weight. Most neonates were transferred to NICU due to low birth weight i.e., 3 (8.6%) in group 1 and 5 (14.3%) in group 2.

Table 4: Hospital stay (days).

Hospital stays (days)	Group 1	Group 2	P value (95% CI)
	Mean ± SD	Mean ± SD	
Mean hospital stay (days)	6.46±3.34	4.31±2.53	0.011 [95% CI=0.41 to 3.88]

Table 4 shows that the mean hospital stay was 6.46±3.34 days in group 1 and 4.31±2.53 days in group 2. The

difference was found statistically significant in terms of hospital stay when group 1 was compared with group 2 with p=0.011.

DISCUSSION

Postpartum hemorrhage is a leading cause of maternal morbidity and mortality worldwide.¹ Placenta previa is one of the major causes of postpartum hemorrhage. It occurs with an incidence of 0.3-0.5% and is defined by implantation of placenta in lower uterine segment, thus partially or totally overlying the internal OS. Intra-operative management options deployed to control hemorrhage in placenta previa patients include bimanual uterine compression, implantation site compression with sutures, uterine arterial ligation, pelvic arterial embolization¹³ and hysterectomy. The prevention of postpartum hemorrhage in cases of placenta previa is quite challenging.^{12,13}

The age of the present study population ranged from 19 to 40 years with maximum number of women in the age group of 21-25 years (38.1%). Majority of women among all groups belonged to age group of 21-30 years which could be due to the fact that it is the most reproductive age group. Mean age was 26.34±4.78 years in group 1 and 27.31±5.62 years in group 2. This observation was found to be statistically insignificant. Similar findings were observed in study by Shady et al where mean age was 29.5±2.42 years in group 1 and 29.6±2.68 years in group 2 which was statistically not significant.¹⁵ Kaur et al also concluded that maximum number of women were in age group 21-30 years.¹⁶

In the present study, most of the women in were nulliparous with no statistically significant difference (p>0.05). Similar finding was observed by Sekiguchi et al which concluded that most women with placenta previa were nulliparous (42%).¹⁷ Kaur et al found that more than 50% of women having placenta previa were multiparous.¹⁶

In the present study, most of the women were in body weight group more than 60 kg. Mean body weight was 62.97±6.44 kg in group 1 and 63.2±6.12 kg in group 2 with no statistically significant difference (p>0.05). Salem et al observed in their study that mean body weight was 67±5.5 kg in study group versus 64±3.8 kg in control group with no statistically significant difference.¹⁸

In the present study, mean pre-operative systolic blood pressure was 115.49±8.7, 112.74±8.79 and 113.49±10.57 mmHg in group 1 and 2 respectively, while diastolic blood pressure was 76.29±8.32 and 75.37±8.21 mmHg respectively. Mean pre-operative pulse rate was 94.57±8.7 and 91.77±6.74 per minute in group 1 and 2 respectively. The difference was statistically insignificant in terms of pre-op vitals (p=0.452 and 0.864).

The findings are in agreement to the study conducted by Salem et al were similar in study group and control

group.¹⁸ Mean systolic blood pressure was 115 ± 10.24 versus 113 ± 12.06 mmHg, diastolic blood pressure was 78.90 ± 5.18 versus 80.09 ± 4.00 mmHg and pulse rate were 85 ± 5.7 versus 84 ± 4.9 per minute in study group and control group respectively with no statistically significant difference.

In the present study, majority of the women presented with bleeding per vaginum with 91.4% in group 1 and 77.1% in group 2. Women presented with labour pains were none in group 1 and 11.4% in group 2 ($p>0.05$). This observation was found to be statistically insignificant. Only 6.66% women presented with labour pains as opposed to 35.8% in the study done by Sekiguchi et al in 2013.¹⁷ Lower incidence in the present study may be due to the fact that minor degree placenta previa cases delivered vaginally. No other previous study compared presenting symptoms such as bleeding per vaginum or labour pains.

Prior cesarean delivery is a risk factor for placenta previa. In present study, 22.9% women in group 1 and 20% women in group 2 had previous cesarean delivery with no statistical significance ($p>0.05$). The incidence of prior cesarean delivery was 11.7% in the study by Sekiguchi et al, 12.05% in study by Sushma et al and 20.75% in study by Naik et al.^{17,19,20}

In the present study, 7.6% of all women had history of previous D and C with 2.9% in group 1 and 8.6% in group 2 ($p>0.05$). Sekiguchi et al in a study observed that previous history of D and C was found in 35.8% of women with placenta previa.¹⁷ Previous history of D and C in the present study was lesser as compared to this study which may be due to the fact that majority of women in the present study were primigravida.

In group 1, 17.1% and in group 2, 25.7% women presented with malpresentation. Malpresentation included breech, oblique and transverse lie. In group 1, 5.7% women and in group 2, 2.9% women had absent fetal heart sound on ultrasonography indicating intrauterine death of fetus at the time of presentation. This result is comparable to previous studies by Sushma et al (14.81%), Kaur et al (21.05%) and Naik et al (18.87%).^{16,19,20}

In the present study, most of the women who underwent cesarean delivery had type IV placenta previa i.e., 34.3% in group 1 and 48.6% in group 2 ($p>0.05$). The findings are comparable to the study by Kaur et al who observed 81.58% women with major degree placenta previa.¹⁶

In the present study, mean pre-operative hemoglobin level was 9.57 ± 1.54 g/dl in group 1 and 9.59 ± 1.35 g/dl in group 2 ($p>0.05$). In study by Yehia et al found that pre-operative hemoglobin level was 11.8 ± 1.5 g/dl in study group and 11.9 ± 1.2 g/dl in control group with no statistical significance ($p>0.05$).²¹ Shady et al pre-operative hemoglobin level was 9.89 ± 0.66 and 9.89 ± 0.67 g/dl in group 1 and 2 respectively ($p>0.05$).¹⁵

In the present study, the mean pre-operative INR was 1 ± 0.12 in group 1 and 0.99 ± 0.14 in group 2 ($p>0.05$). The mean pre-operative platelet count was 2.07 ± 0.71 and 2.01 ± 0.39 and 1.97 ± 0.42 lac in group 1 and 2. These observations were statistically insignificant ($p>0.05$).

In present study, 5.8% women in group 1 and 8.6% in group 2 required pre-operative blood transfusion in the form of packed cell. Mean requirement of pre-operative blood transfusion was 0.086 ± 0.368 units in group 1 and 0.143 ± 0.486 units in group 2 ($p>0.05$).

Prematurity is a consistent finding in babies of women with placenta previa. In the present study, 60% women underwent preterm cesarean delivery i.e., before 37 weeks of gestation. Mean gestational age at delivery was 35.77 ± 2.66 weeks in group 1 and 36.69 ± 2.35 weeks in group 2 with no statistical significance ($p>0.05$). Similarly, Shady et al observed that the mean gestational age was 36.38 ± 0.87 weeks in group 1 and 36.45 ± 0.90 weeks in group 2 with no statistical significance ($p>0.05$).¹⁵

In the present study, mean blood loss was 729.31 ± 172.45 ml in group 1 and 464.86 ± 28.00 ml in group 2 with a $p<0.001$ which was statistically highly significant. Similar results were depicted from study by Shady et al¹⁵ in which mean intraoperative blood loss was 918 ml in group 1 and 532 ml in group 2. Present study is comparable to other study by Shahid et al which concluded that intravenous tranexamic acid significantly reduced the quantity of blood loss from placental delivery to the end of cesarean section which was 356.44 ± 148.20 ml in tranexamic acid group versus 710.22 ± 216.72 ml in placebo group ($p<0.001$).²²

In the present study, 68.6% women in group 1 and 34.3% in group 2 required blood transfusion intra-operatively. This difference was found statistically significant in both cases when group 1 was compared to group 2 with a $p=0.001$. Mean requirement of intra-operative blood transfusion was 1.00 ± 0.861 units in group 1 and 0.457 ± 0.730 units in group 2. Present study shows that the use of tranexamic acid in cesarean section reduces the need of intra-operative blood transfusion. Reducing intra-operative blood loss would lower the risks and cost associated with blood transfusion. Our findings are in agreement with that of study by Shahid et al.²² He observed that 33% women required blood transfusion in placebo group as compared to intravenous tranexamic acid group in which only 8% of women required the blood transfusion.

Present study is comparable to the study conducted by Sujata et al in which 83% women in control group and 23% women in intravenous tranexamic acid group needed additional uterotonics intra-operatively ($p<0.001$). This study concluded that intravenous tranexamic acid administered at least 10 minutes before skin incision, significantly reduced the requirement for additional uterotonic drugs.²³

The present study showed that 60% women in group 1 required additional intra-operative surgical intervention in form of hemostatic sutures, uterine artery ligation, balloon tamponade or combination of these. In group 2, 17.1% women required additional surgical interventions ($p=0.001$). Our findings are comparable to that of previous study by Shady et al in which 52.5% women in control group required additional intra-operative surgical interventions in form of uterine artery ligation and internal iliac artery ligation while 17.5% required surgical intervention in intravenous group ($p=0.001$).^{7,9}

Tranexamic acid administered intravenously caused nausea and vomiting in 22.9% women ($p<0.001$). Our results are in accordance with study done by Shady et al which concluded that the incidence of nausea and vomiting was higher in intravenous tranexamic acid group (22.5%).¹⁵ Xu et al in a study found that incidence of side-effects like nausea, vomiting and dizziness was higher in intravenous tranexamic acid group compared to control group with $p<0.01$.²⁴

In the present study, most of the maternal complications were observed in group 1. Incidence of postpartum hemorrhage was 74.3% in group 1 and 20% in group 2 with a $p<0.001$. Only one patient was transferred to ICU post-operatively in group 1 because of post-partum shock. Patient stayed in ICU for five days and was discharged on post-operative day 10. There was no maternal mortality in the present study. These findings are similar to study done by Salem et al in which incidence of postpartum hemorrhage was 59.3% in control group versus 24.9% in intravenous tranexamic acid group ($p<0.001$).¹⁸

Mean post-operative hemoglobin was 8.04 ± 1.34 g/dl in group 1 and 8.85 ± 1.26 g/dl in group 2 ($p<0.05$) which is statistically significant. In the study by Shady et al mean post-operative hemoglobin was 8.63 ± 0.96 g/dl and 9.04 ± 1.01 g/dl in group 1 and 2 respectively with no statistical significance ($p>0.05$).¹⁵

Mean decline in hemoglobin concentration was 1.563 ± 0.66 g/dl in group 1 and 0.734 ± 0.35 g/dl in group 2 with $p<0.001$. Similar to the present study, Roy et al had comparable results in which decline in hemoglobin concentration was 0.26 ± 0.22 g/dl in tranexamic acid group and 0.99 ± 0.48 in control group.²⁵ This study observed that the use of tranexamic acid in cesarean section led to less decline in hemoglobin concentration post-operatively ($p<0.001$).

It was observed in the present study that 45.7% women in group 1 and 11.4% women in group 2 required blood transfusion post operatively ($p<0.001$). Mean requirement of post-operative blood transfusion was 0.571 ± 0.688 units in group 1 and 0.20 ± 0.575 units in group 2. Hence use of tranexamic acid intravenously significantly reduced the need for post-operative blood transfusion. This is because of the fact that tranexamic acid reduced perioperative blood loss and incidence of postpartum hemorrhage.

Prematurity is a consistent finding in neonates born to women with placenta previa. In the present study, 57.1% neonates in group 1 and 45.7% in group 2 were having low birth weight. Mean birth weight was 2.28 ± 0.53 kg in group 1 and 2.41 ± 0.52 kg in group 2 ($p>0.05$).

The safety of giving tranexamic acid intravenously while the fetus was still in utero was a key concern. As a consequence, the neonatal outcome was meticulously evaluated by a neonatologist. In the present study, Apgar score of less than 7 at 1-minute and 5-minute was observed in 5.7% neonates in group 1 and 2.9% neonates in group 2 ($p>0.05$). Similarly, study conducted by Roy et al found that the mean Apgar score at 1-minute and 5-minute were 7.06 ± 1.25 and 8.66 ± 1.00 in the study group and 7.18 ± 1.35 and 8.64 ± 0.98 in the control group respectively ($p>0.05$).²⁵

In the present study, 11.4% neonates in group 1 and 14.3% neonates in group 2 were transferred to NICU ($p>0.05$). Mean hospital stay in the present study was 6.46 ± 3.34 days in group 1 and 4.31 ± 2.53 days in group 2 ($p<0.001$).

CONCLUSION

In the present study, it was observed that tranexamic acid significantly reduced intra-operative blood loss. It also reduced the incidence of postpartum hemorrhage, need of additional uterotonics, need for intra-operative surgical interventions, intra- and post-operative blood transfusion and led to less decline in hemoglobin concentration post-operatively. Tranexamic acid had no effect on Apgar score, perinatal outcome, NICU transfer, low birth weight or respiratory distress syndrome.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Prata N, Gerds C. Measurement of postpartum blood loss. *BMJ.* 2010;340:c555.
2. Abou Zahr C. Global burden of maternal death and disability. *Br Med Bull.* 2003;67:1.
3. Kambo I, Bedi N, Dhillon BS, Saxena NC. A critical appraisal of cesarean section rates at teaching hospitals in India. *Int J Gynecol Obstet.* 2002;79:151-8.
4. Magann EF, Evans S, Hutchinson M, Collins R, Lanneau G, Morrison JC. Postpartum hemorrhage after cesarean delivery: an analysis of risk factors. *South Med J.* 2005;98:681-6.
5. Kramer MS, Berg C, Abenhaim H, Dahhou M, Rouleau J, Mehrabadi A et al. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. *Am J Obstet Gynecol.* 2013;209:449-e1.
6. Bateman BT, Berman MF, Riley LE, Leffert LR. The epidemiology of postpartum hemorrhage in a large,

- nationwide sample of deliveries. *Anesth Analg.* 2010;110:1368-73.
7. Oppenheimer L. Society of obstetricians and Gynecologists of Canada. Diagnosis and management of placenta previa. *J Obstet Gynecol Can.* 2007;29:261-73.
 8. Reddy UM, Abuhamad AZ, Levine D, Saade GR. Executive summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound fetal imaging workshop. *Obstet Gynecol.* 2014;123:1070-82.
 9. Al-Harbi NA, Al-Abra ES, Alabbad NS. Uterovaginal packing. *Saudi Med J.* 2009;30:243-6.
 10. Frenzel D, Condous GS, Papageorgiou AT, McWhinney NA. The use of the 'tamponade test to stop massive obstetric haemorrhage in placenta accreta. *BJOG: Int J Obstet Gynecol.* 2005;112:676-7.
 11. B-Lynch C, Coker A, Lawal AH, Abu J, Cowen MJ. The B-Lynch surgical technique for the control of massive postpartum haemorrhage: an alternative to hysterectomy? Five cases reported. *BJOG: Int J Obstet Gynecol.* 1997;104:372-5.
 12. Tjalma WA, Jacquemyn Y. Compression sutures instead of emergency peripartum hysterectomy. *Eur J Obstet Gynecol Reprod Biol.* 2005;118:258.
 13. Clark SL, Phelan JP, Yeh SY, Bruce SR, Paul RH. Hypogastric artery ligation for obstetric hemorrhage. *Obstet Gynecol.* 1985;66:353-6.
 14. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomized, double-blind, placebo-controlled trial. *Lancet.* 2017;389:2105.
 15. Shady NW, Sallam HF. Adjunctive IV tranexamic acid versus topical tranexamic acid application of the placental bed for prevention of postpartum hemorrhage in women with placenta previa: a randomized controlled trial. *Int J Reprod Contracept Obstet Gynecol.* 2017;6:5205-12.
 16. Kaur K, Garg R, Kaur A, Jindal R. Feto-maternal outcome in placenta previa with unscarred uterus (one-year prospective study). *Parity.* 2018;36:2-62.
 17. Sekiguchi A, Nakai A, Kawabata I, Hayashi M, Takeshita T. Type and location of placenta previa affect preterm delivery risk related to antepartum hemorrhage. *Int J Med Sci.* 2013;10:1683.
 18. Salem MN, Mohamed MA, Salem AH, Abbas A. Tranexamic acid as prophylactic therapy for intra- and post-partum hemorrhage: randomized controlled trial. *J Adv Med Med Res.* 2016;17:1-7.
 19. Lama S, Ranjit S. Study on maternal and immediate fetal outcome of placenta previa. *Nepal J Obstet Gynecol.* 2016;11:24-7.
 20. Naik VR, Cardoso PM. A study of proportion, maternal and fetal outcomes in cases of placenta previa. *IOSR-JDMS.* 2018;17:1-5.
 21. Yehia AH, Koleib MH, Abdelazim IA, Atik A. Tranexamic acid reduces blood loss during and after cesarean section: a double blinded, randomized, controlled trial. *Asian Pac J Reprod.* 2014;3:53-6.
 22. Shahid A, Khan A. Tranexamic acid in decreasing blood loss during and after caesarean section. *J Coll Physicians Surg Pak.* 2013;23:459-62.
 23. Sujata N, Tobin R, Kaur R, Aneja A, Khanna M, Hanjoora VM. Randomized controlled trial of tranexamic acid among parturients at increased risk for postpartum hemorrhage undergoing cesarean delivery. *Int J Gynecol Obstet.* 2016;133:312-5.
 24. Xu J, Gao W, Ju Y. Tranexamic acid for the prevention of postpartum hemorrhage after cesarean section: a double-blind randomization trial. *Arch Gynecol Obstet.* 2013;287:463-8.
 25. Roy I, Chakraborty S, Mukhopadhyaya S. Role of intravenous tranexamic acid on cesarean blood loss: a prospective randomized study. *Trop J Obstet Gynecol.* 2018;35:49-53.

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