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Evaluation of the efficacy of traneximic acid in preventing postpartum haemorrhage in high risk patients delivered by CS

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Abstract

Background: Obstetric hemorrhage remains one of the major determinants of maternal death in both developed and developing countries. Because of its weight as a leading cause of maternal mortality and morbidity, obstetric hemorrhage (ante-partum and post- partum hemorrhages) must be investigated for national guideline development.The present study was planned todetermine the efficacy of tranexamic acid (TXA) in reducing blood loss during and after caesarean section (CS), as well as its safety.**Methods:**The current study was randomized controlled clinical trial conducted at Department of Obstetrics and Gynecology in Zagazig University Hospitals, from April 2021 to September 2022. Included 78 women ages were from 18 - 48 years old and gestational age from 35 - 42 weeks with risk factor for Postpartum hemorrhage (PPH). All patients were assessed by full history with particular attention to bleeding tendency.**Results:** There is statistically significant lower value of HB, HCT post cesarean delivery of high-risk pregnancy compared to its value pre CS among control group $p<0.05$. Percent of reduction of HB, HCT value post were 19.6%, 16.7% respectively.**Conclusions**:Tranexamic acid (TXA) decrease incidence of PPH and also decrease need for other medical or surgical interventions or blood transfusion.

Key words: Tranexamic acid , Postpartum haemorrhage , caesarean section

INTRODUCTION

Post-partum hemorrhage is one of the most common obstetric emergency. It remains a leading cause of early maternal death accounting for about 300,000 deaths worldwide every year and of morbidity related to anemia, blood transfusions and hemorrhage related ischemic complications. The incidence of caesarean delivery is increasing day by day and the average blood loss during caesarean delivery (1000ml) is double the amount lost during vaginal delivery (500ml)[(1-3)].

Traditionally, PPH was defined as blood loss morethan 500 mL after a vaginal delivery and more than 1000mL after a cesarean delivery; however, an updated andefficient definition has been suggested by American College of Obstetrics and Gynecology which stated PPH ascumulative blood loss more than or equal to 1000 mL orblood loss accompanied by signs or symptoms of hypovolemia throughout the first 24h after delivery regardless the delivery route[(4)].

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PPH also contributes significantly to maternal morbidity with the probability for intensive care admission,shock, acute renal failure, disseminated intravascular coagulation (DIC), adult respiratory distress syndrome(ARDS), hysterectomy, and loss of fertility[4,5].

The hematocrit falls by 10% and blood transfusion may also be required[6]. Also Delivery by CS can cause more complications than normal vaginal deliveryand one of the most common complications of primary or secondary postpartum hemorrhage (20%)[7].

It leads to increased maternal mortality and morbidity as in severe cases, resulting in major obstetrical hemorrhage, hysterectomy and even admission to an ICU[6,7].

To reduce morbidity and mortality associated with obstetric hemorrhage various pharmaceutical, hematological and surgical techniques have been used to prevent PPH during caesarean section. Medications such as oxytocin, misoprostol, prostaglandins F2α and methysergide have been used to control bleeding after caesarean section[8].

Antifibrinolytic drugs such as tranexamic acid (TXA) are widely used in hemorrhagic conditions associated with increased fibrinolytic activity or hyperfibrinolysis (HF) like PPH[9].

TXA is a synthetic lysine analogue that competitively inhibits the conversion of plasminogen to plasmin preventing the proteolytic action of plasmin on fibrin threads resulting in inhibition of fibrinolysis and stabilizing existing blood clots, thus reducing the risk of hemorrhage[10].

TXA has been found to reduce intra- and postoperative bleeding like open-heart surgeries, scoliosis correction surgery, liver transplantation, prostatectomy, arthroplasty, and urinary tract surgeries[10]. The use of TXA has been proven beneficial in traumapatients reducing the risk of hemorrhage and the needfor blood transfusion when used within 3 h of injury[11].

Detailed guidelines have suggested the use of uterotonic drugs in obstetric interventions. In contrast, hemostatic drugs are not routinely used as a first-line intervention in PPH[12].This study target was to reach the minimal blood loss during elective cesarean section (CS) in order to decrease patients' morbidity by using Tranexamic acid (TXA) injection before operation time.

METHODS:

The current study was randomized controlled clinical trial conducted at Department of Obstetrics and Gynecology in Zagazig University Hospitals, from April 2021 to September 2022. The estimated sample was 78 women , 39 women in each group. All the included women ages were from 18 - 48 years oldand gestational age from 35 - 42 weeks with risk factor for PPH as Multiple pregnancies, multiparous, Previous postpartum hemorrhage,History antepartum hemorrhage in the current or previous pregnancy, Anemia Fetal macrosomia ,Polyhydramnios without medical history of any chronic disease, with no known allergy to tranexamic acid and no history of thrombo-embolic disorders they were all planned for elective caesarean section and after women consent, the cesarean sections were done using spinal anesthesia for all women, Women with the selection criteria were chosen to participate in the trial, with one group are given1 gmtranexamic acid (2 ampules=10 ml)

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were administered intravenous 10 minutes before skin incision slowly infused (over 5 min), and the other group receiving10 ml normal saline solution, CS done , after delivery of the neonate 10 units Oxytocin IV drip given and Assessment of uterine tone and size were accomplished using a hand resting on the fundus and palpating the anterior wall of the uterus. The presence of a boggy uterus or increasing uterine size with heavy vaginal bleeding establishes the diagnosis of uterine atony. The blood loss were measured following placental delivery till end of (CS) at closure of uterus and skin,Maternal blood pressure and vital signs were measured immediately after delivery.

Blood sample were taken for measurement of hemoglobin and Hematocrlevel, Maternal and neonatal side effects caused by tranexamic acid and need for additional uterotonics or other surgical measures to stop bleeding (B-lynch sutures, uterine artery ligation, internal iliac artery ligation, hysterectomy and/or transfusion of blood or blood products) were recorded.

Statistical Analysis:

According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance; Differences between frequencies (qualitative variables) and percentages in groups were compared by Chi-square test. Differences between parametric quantitative independent groups by t test Paired data by paired t. P value was set at <0.05 for significant results&<0.001 for high significant result.

RESULTS:

Table (1): Risk factors for Postpartum Hemorrhage in Cesarean Delivery of high-risk pregnancy of studied groups

Variables	Studied groups				χ^2	p-value
	Tranexamic Acid intervention group (n.39)		Control group (n.39)			
	N.	%	N.	%		
Big size baby	4	10.3%	3	7.7%	f	0.99
Anemia	14	35.9%	12	30.8%	0.23	0.63
Twins pregnancy	6	15.4%	7	17.9%	0.092	0.76
Polyhyramons	2	5.1%	5	12.8%	f	0.43
Multiparous	5	12.8%	6	15.4%	0.106	0.75
Others	8	20.5%	6	15.4%	0.35	0.56

χ^2Chisquare test f=Fisher Exact test p>0.05 non significant

Table 1; This study showed statistically insignificant difference between Tranexamic Acid intervention group and control group regard their Risk factors for Postpartum Hemorrhage p>0.05.

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Table (2): Amount of blood loss in Cesarean Delivery of high-risk pregnancy among studied groups

Variables	Studied groups		% blood loss difference	u	p-value
	Tranexamic Acid intervention group (n.39)	Control group (n.39)			
Amount of blood loss during C/S **Mean ±SD** **Median** **(range)**	484.87±183 500 (100-1000)	705±292 600 (400-1750)	37%	3.824	0.0001 (HS)

U= Mann-Whitney U test (HS) p<0.001 highly significant

Table 2; This study showed that the mean of blood loss during C/S of tranexamic Acid intervention group was 484.87 cc and ranged from (100-1000) and mean of blood loss during C/S of control group was 705 cc and ranged from (400-1750), the difference highly statistically significant p=0.0001. Percent of blood loss was 37% more among control group compared to Tranexamic acid intervention group.

Table (3): Vital signs before cesarean delivery of high-risk pregnancy among studied groups

Variables	Studied groups		t	p-value
	Tranexamic Acid intervention group (n.39)	Control group (n.39)		
Pre systole Mean ±SD Median (range)	112.56±4.98 110(100-120)	113.58±7.7 110(110-150)	0.694	0.490
Pre diastole Mean ±SD Median (range)	73.07±5.69 70(60-90)	71.28±5.7 70(60-100)	1.391	0.168
Pre pulse/minute Mean ±SD Median (range)	75 ±5.9 75(65-87)	77.35±6 75(65-92)	1.348	0.182
Pre-Respiratory rate/minute Mean ±SD Median (range)	17 ±0.6 17(17-19)	17.46±0.64 17(16-19)	0.001	0.99

t= t test p>0.05 non significant

Table 3; This study showed that statistically insignificant difference between Tranexamic Acid intervention group and control group regard their vital signs before Cesarean delivery p>0.05.

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Table (4):CBC pre and post Cesarean Delivery of high-risk pregnancy among Tranexamic Acid intervention group

Variables	Tranexamic Acid intervention group (n.39)		% reduction	p-value
	Pre	Post		
HB Mean ±SD	10.2±0.94	9.6±0.98	5.9%	>0.05
HCT Mean ±SD	30.05±4.2	28.69±4.4	4.5%	>0.05
PLT Mean ±SD	227.47±65	230.88±68	1.136	0.263

Paired t= paired t test p>0.05 non significant

Table 4;This study showed that statistically insignificant difference between CBC pre and post cesarean delivery of high-risk pregnancy among Tranexamic Acid intervention group. Percent of reduction of HB, HCT value post were 5.9%, 4.5% respectively.

Table (5): Vital sign pre and post cesarean delivery of high-risk pregnancy among Tranexamic Acid intervention group

Variables	Tranexamic Acid intervention group (n.39)		p-value
	Pre	Post	
Systole Mean ±SD Median (range)	112.56±4.98 110(100-120)	113±5.6 110(110-122)	>0.05
Diastole Mean ±SD Median (range)	73.07±5.69 70(60-90)	72.38±5.54 75 (70-90)	>0.05
Pulse/minute Mean ±SD Median (range)	75 ±5.9 75(65-87)	78.6±3.3 76(65-86)	>0.05
Respiratory rate/minute Mean ±SD Median (range)	17 ±0.6 17(17-19)	17.58±0.55 18(17-19)	0.342

Paired t= paired t test p>0.05 non significant

Table 5; This study showedthat statistically insignificant difference between vital sign pre and post cesarean Delivery of high-risk pregnancy among Tranexamic Acid intervention group p>0.05.

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Table (6):CBC before and after cesarean delivery of high-risk pregnancy among control group

Variables	Control group (n.39)		Percent of reduction	p-value
	Pre	Post		
HB Mean ±SD	10.1±1.39	8.12±0.65	19.6%	<0.001
HCT Mean ±SD	30.64±3.9	25.4±3.88	16.7%	<0.05
PLT Mean ±SD	227.7±51.6	227.95±52.2	1.241	0.222

Paired t test **p<0.05 significant**

Table 6; This study showedthat statistically significant lower value of HB, HCT post cesarean delivery of high-risk pregnancy compared to its value pre Cs among control group p<0.05. Percent of reduction of HB, HCT value post were 19.6%, 16.7% respectively.

DISCUSSION

This study showed that tranexamic acid significantly reduces bleeding during and after cesarean section in women who are having risk factors to develop post-partum hemorrhage. This was evident with the significantly reduced amount of blood loss, drop in hemoglobin and hematocrit values in the treatment group when compared with the placebo group.

One more study by **LeilaSekhavat et al,**[13]concluded that TXA statistically reduces blood loss from end to 2 hours after CS.

Abdel Aleem and colleagues; concluded that the pre-operative use of TXA is associated with reduced blood loss during and after elective CS. They enrolled seven hundred and forty women (373 in study group and 367 in control group). Mean total blood loss was 241.6 (SE 6.77) ml in the TXA group versus 510 (SE 7.72) ml in the control group.

This study shows that the mean of blood loss during CS of tranexamic Acid intervention group was 484 cc and ranged from (100-1000cc) and mean of blood loss during C/S of Control group was 705 cc and ranged from (400-1750cc), the difference highly statistically significant p=0.000.

A study conducted by **Yehia et al.** [14]reported mean blood loss to be 369.5 ± 198 ml in patients treated with TA which was significantly lower than that of placebo group. These findings of **Yehia et al.** [14]are similar to that of our study results. **Xu et al.** [15]from China reported mean blood loss was noted to be 336.7 ± 151.2 ml in patients treated with tranexamic acid which is close to our study results. **Goswami et al.** [16]reported 376.83±31.961ml mean blood loss after therapy with TA and found that blood loss was significantly less than that of placebo group indicating effectiveness of the TA in the targeted population.

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Vital signs before cesarean delivery of high-risk pregnancy in our study as pre-CS systole were 112.56±4.98 mm/Hg and 113.58±7.7mm/Hg in tranexamic acid intervention group and control group and the pre-CS diastole were73.07±5.69mm/Hg and 71.28±5.7mm/Hg in tranexamic acid intervention group and control group while Pre-CS Respiratory rate/minute were 17 ±0.6 and 17.46±0.64 in tranexamic acid intervention group and control group with no significant difference in all vital signs.

Fahmy et al.[17]revealed pre-CS systole were 118.45±10.55mmHg and 116.39±12.42 mmHg in tranexamic acid intervention group and control group and the pre-CS diastole were 81.27±5.34mmHg and 82.49±4.12mmHg in tranexamic acid intervention group and control group while pre-CS Respiratory rate/minute were 16.89±2.04 and 16.35±2.22 in tranexamic acid intervention group and control group with no significant difference in all vital signs.

The current study showed that the HB before cesarean delivery were 10.2±0.94g/dl and 10.1±1.39g/dl in tranexamic acid intervention group and control group and the HCT were30.05±4.2% and 30.64±3.9% in tranexamic acid intervention group and control group with no significant differences.

These came in agreement with **Fahmy et al.**[17]study's who revealed that the HB before cesarean delivery were 12.63±0.82g/dl and 12.18±1.08g/dl in tranexamic acid intervention group and control group and the HCT were 37.96±2.55% and 36.49±3.22% in tranexamic acid intervention group and control group with no significant differences.

Our study showed that the HB after cesarean delivery were 9.6±0.98g/dl and 8.12±0.65g/dl in tranexamic acid intervention group and control group and the HCT were28.69±4.4% and 25.4±3.88% in tranexamic acid intervention group and control group with significant difference.

These came in agreement with **Fahmy et al.**[17]study's who revealed that the HB after cesarean delivery were 11.66±0.79g/dl and 10.53±1.07g/dl in tranexamic acid intervention group and control group and the HCT were 34.99±2.40% and 31.62±3.22% in tranexamic acid intervention group and control group with significant difference.

CONCLUSIONS:

Tranexamic acid (TXA) decrease incidence of PPH and also decrease need for other medical or surgical interventions or blood transfusion. Tranexamic acid improve anemic state by decrease percentage of reduction on HB and HCT level.

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