

## Prevention of Postpartum Hemorrhage after Vaginal Delivery Using Tranexamic Acid

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### ABSTRACT

**Background:** The postpartum hemorrhage is still remaining a leading cause of maternal mortality, especially in developing countries.

**Objective:** We aimed to determine the efficacy of using tranexamic acid in vaginal delivery to avoid postpartum hemorrhage and to reduce blood loss and hospital stay.

**Patients and methods:** A prospective-randomized clinical trial study was conducted on 92 pregnant women that were prepared for vaginal delivery. They were divided into two groups. Group (A) included 46 pregnant women that received 1 gm of tranexamic acid (TXA group) in the third stage of labour and group (B) included 46 pregnant women that received 10 IU of oxytocin (Non-TXA group) after delivery of the baby. Estimation of blood loss was done. Hemoglobin (Hb) and hematocrit (HCT) values were checked before and 24 hours after vaginal delivery as well as other basic laboratory investigations.

**Results:** In our study, there was no significant difference regarding Hb at pre- but at post-, there was significant decrease in Non-TXA group. There was no significant difference regarding HCT at pre- but at post-, there was significant decrease in Non-TXA group. Blood loss was significantly lower at TXA group.

**Conclusion:** Use of tranexamic acid would help to reduce blood loss during delivery. It is a cheap and readily available drug. The use of TXA decreases need of uterotonics and hence decreases morbidity and mortality.

**Keywords:** Postpartum hemorrhage, Vaginal delivery, Tranexamic acid.

### INTRODUCTION

Pregnancy and delivery are considered as normal physiological phenomena in women. Approximately, 10% of deliveries are considered as high risk. Vaginal delivery may result in major obstetric hemorrhage, hysterectomy, admission to an intensive care unit and maternal death. Medications, such as oxytocin, misoprostol, prostaglandin F<sub>2</sub>alpha, and methyl ergonovine have been used to control bleeding after vaginal delivery<sup>(1)</sup>. But, still the postpartum hemorrhage is a leading cause of maternal mortality, especially in developing countries<sup>(2)</sup>.

The hematocrit falls by 10% and blood transfusion is required in 6% of women undergoing Cesarean delivery compared to 4% of women who have a vaginal birth<sup>(3)</sup>.

Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine, which is an anti fibrinolytic that reversibly inhibits the activation of plasminogen. Thus inhibiting fibrinolysis and reducing bleeding. Tranexamic acid may enhance effectiveness of the patient's own haemostatic mechanism<sup>(4)</sup>. Tranexamic acid is widely used in the field of obstetric. Both antepartum and postpartum hemorrhage are being treated by TXA extensively. Although tranexamic acid crosses the placenta, no mutagenic activity or harmful effects of tranexamic acid on the fetus have been reported and animal reproduction studies have shown no teratogenic effects. Tranexamic acid has been well tolerated and has not been associated with a prejudicial effect on the delivery of healthy children<sup>(5)</sup>.

We aimed to determine the efficacy of using tranexamic acid in vaginal delivery to avoid postpartum hemorrhage and to reduce blood loss and hospital stay.

### PATIENTS AND METHOD

This prospective-randomized clinical trial study was conducted at Obstetrics and Gynecology Department at Zagazig University Hospitals during the period from March 2020 to December 2020. A total of 92 women that fulfilled the inclusion criteria were enrolled in the study. The patients were randomized into 2 groups using a computer-generated randomization list (using medcalc© version 13 (medcalc@ software, mariakirke, Ostend, Belgium). **Group (A) (TXA group)** included 46 pregnant females that received 1 gm of tranexamic acid (Kapron, Amon, Egypt) in 100 ml of lactated Ringer's solution by slow intravenous infusion over 5 minutes in the third stage of labour and after delivery of the baby, 10 IU of oxytocin (sytocinon, Novartis, Egypt) in 500 ml lactated Ringer's solution were given. **Group (B) (Non-TXA group)** included 46 pregnant females that received 10 IU of oxytocin in 500 ml lactated Ringer's solution after delivery of the baby. The solution was prepared by an anesthetist who was not involved in patient management or assessment.

**Inclusion criteria:** Full-term pregnant women (gestational age > 37 weeks) with singleton pregnancy being delivered vaginally, multiple pregnancy, macrosomia and polyhydramnios.



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**Exclusion criteria:** History of thrombosis or epilepsy and history of medical problems involving the heart, liver, kidney and brain. Known allergy to tranexamic acid. Severe medical and surgical complications involving the heart, liver or kidney. Bleeding disorders and known hemostatic abnormalities before pregnancy.

All patients were subjected to complete history taking, general examination, abdominal examination, local examination for assessment of pelvic capacity, cervical dilatation, effacement, state of membranes, exclusion of meconium stained liquor or cord presentation or prolapse. Ultrasound was done for assessment of fetal viability and biometry.

Dose of TXA (1 gm of tranexamic acid (two ampoules of Kapron®, Amoun, Egypt) was given in 100 ml lactated Ringer's by slow infusion over 5 minutes) at third stage of labour.

Estimation of blood loss =  $EBV \times [(preoperative\ hematocrit - postoperative\ hematocrit) / (preoperative\ hematocrit)]$ , where Estimated Blood Volume (EBV) in ml = the women's weight in kg x 85. Hemoglobin and hematocrit values were checked before and 24 hours after vaginal delivery as well as other basic laboratory investigations. In the Non-TXA group, after delivery of the baby (3rd stage of labour), the woman received only 10 IU of oxytocin in 500 ml lactated Ringer's solution was given intravenous drip.

The primary outcomes were the efficacy of TXA in prevention of postpartum hemorrhage which is measured by certain parameters: Amount of blood loss measured, haematocrit level pre- and post-delivery, Hb level pre- and post-delivery and the need for blood transfusion post-delivery).

The secondary outcome measures were the need for other interventions (e.g. intrauterine tamponade, embolization, brace sutures, arterial ligation and hysterectomy) done after randomization to control bleeding and achieve hemostasis, the need for blood transfusion and admission to Intensive Care Unit (ICU). Organ failure, hospital stay, the rate of decrease of maternal death and thromboembolic events (e.g. deep vein thrombosis, pulmonary embolism, myocardial infarction, and stroke).

**Ethical consent:**

**An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the study. This**

**work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.**

**Statistical analysis**

Data were collected and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software. According to the type of data, qualitative was represented as number and percentage and quantitative continues group was represented by mean ± SD. The following tests were used to test differences for significance: Difference and association of qualitative variable by Chi square test (X<sup>2</sup>) and differences between quantitative independent groups by t test or Mann Whitney. P value was set at ≤ 0.05 for significant results & < 0.001 for high significant result.

**RESULTS**

Age was distributed as 24.45 ± 5.78 with range from 18 to 40 years and 25.80 ± 6.44 with range from 17 to 43 years with no significant difference between groups. Also, there was no significant difference regarding anthropometric measures (weight, height or BMI) (Table 1).

Blood loss was significantly lower at TXA group as it was distributed as 203.67 ± 141.12 and 355.5 ± 264.96 respectively between groups (Table 2).

There was no significant difference regard HB at pre-delivery with range from 9.2 to 12.5 gm/dl in TXA group and range from 9.6 to 13.2 gm/dl in Non-TXA group but at post-delivery, it was significantly lower with range from 9 to 12.1 gm/dl in TXA group and range from 8.8 to 11.7 gm/dl in Non-TXA group and there was significant decrease in Non-TXA group Where is the table.

There was no significant difference regard HCT at predelivery with range from 25.7 to 44.6% in TXA group and range from 23.9 to 39.1% in Non-TXA group but at post-delivery, it was significantly lower with range from 25.4 to 43.2% in TXA group and range from 22.8 to 38.5% in Non-TXA group and there was significant decrease in Non-TXA group (Table 3).

Incidence of PPH is doubled in non-TXA group than in TXA group. Blood transfusion significantly associated with Non-TXA group. TXA group significantly associated with abdominal pain and Nausea (Table 4).

**Table (1):** Demographic data distribution between studied groups

	TXA group (A) (N=46)	Non-TXA group (B) (N=46)	t	P
Age / years	24.45±5.78	25.80±6.44	1.055	0.294
Weight	81.43±8.18	84.57±7.56	1.911	0.059
Height	159.68±23.99	155.47±33.35	0.696	0.488
BMI	30.74±2.79	31.21±2.63	2.431	0.017

**Table (2):** Blood loss distribution between studied groups

	TXA Group(A)	Non-TXA group Group(B)	Mann Whitney	P
Blood loss (ml)	203.67 ± 141.12 187.97 (38.6-636.8)	355.5 ± 264.96 245.8 (40.8-887.9)	3.267	0.002*

**Table (3):** Pre and post HCT distribution between studied group

	TXA Group(A)	Non-TXA group Group(B)	t	P
Pre HCT	34.16±3.41	33.51±3.14	0.954	0.343
Post HCT	33.53±3.39	31.27±3.34	1.795	0.076
P	0.28	0.008*		

**Table (4):** Number of cases developed PPH between studied groups

	TXA Group(A)		Non-TXA group Group(B)		X <sup>2</sup>	P
	N	%	N	%		
Mild	2	4.34%	1	2.1%	4.38	0.03*
Moderate	1	2.1%	3	6.5%	1.04	0.3
Severe	1	2.1%	4	8.69%	2.04	0.15
total	4	8.69%	8	17.3%	1.04	0.3
Death	0	0 %	1	2.1%	1.01	0.31

## DISCUSSION

Labor is a physiological process, but it is often associated with morbidity and mortality. Bleeding is a common cause of maternal death. Postpartum hemorrhage is defined as blood loss of 500 mL or more after delivery within 24 hours. The foremost cause of maternal mortality is postpartum hemorrhage <sup>(7)</sup>.

Topical application of TXA provides a high drug concentration at the site of the wound and a low systemic concentration. Studies from cardiac and orthopedic surgery have shown an equal or superior effect of topical compared to intravenous TXA on both bleeding and transfusion requirement <sup>(8)</sup>.

A total of 92 women that fulfilled the inclusion criteria were enrolled in the study. The patients were randomized into 2 groups: Group (A) (the study group) (n = 46) received 1 gm of tranexamic acid in 100 ml of lactated Ringer's solution by slow intravenous infusion over 5 minutes in the third stage of labour and after delivery of baby, 10 IU of oxytocin (sytocinon, Novartis, Egypt) in 500 ml lactated Ringer's solution was given. Group (B) (the control group) (n = 46) received 10 IU of oxytocin in 500 ml lactated Ringer's solution after delivery of the baby.

In our study, there was no significant difference regarding HB at pre- but at post, there was significant decrease in Non-TXA group. This is in agreement with **Jayaraman and Somu** <sup>(9)</sup> who found a significant difference in the post-delivery Hemoglobin (P < 0.01). Unlike **Mirghafourvand et al.** <sup>(10)</sup> who stated that there was no statistically significant difference between the intervention and control groups in terms of hemoglobin either pre- or post-vaginal delivery (P = 0.273). We found that HB difference was significantly lower at

TXA group as it was distributed as 0.40 ± 0.23 and 0.68 ± 0.41 respectively. Also, **Jayaraman and Somu** <sup>(9)</sup> found that the difference of hemoglobin decline in the study group and in control group was statistically significant.

In our study, there was no significant difference regarding HCT at pre- but at post, there was significant decrease in Non-TXA group. Also, **Jayaraman and Somu** <sup>(9)</sup> found that there was a significant difference in the post-delivery PCV (P < 0.01) between the groups. In Egypt, **Sanad et al.** <sup>(11)</sup> studied the effect of tranexamic acid on postpartum haemorrhage and divided his participants into two groups; the first group received a bolus injection of 1 gram tranexamic acid in contrary to the second group participants who didn't receive. They found out that the level of hemoglobin and hematocrit decreased significantly in group II than in group I (P = 0.007 and 0.005, respectively). In our study, HCT difference was significantly lower at TXA group as it was distributed as 1.13 ± 0.54 and 1.64 ± 0.84 respectively. Also, **Jayaraman and Somu** <sup>(9)</sup> found that the difference of PCV decline in the study group and in control group was statistically significant (P < 0.01).

In our study, blood loss was significantly lower at TXA group as it was distributed as 203.67 ± 141.12 ml and 355.5 ± 264.96 ml respectively between groups. Also, **Jayaraman and Somu** <sup>(9)</sup> found that the amount of blood loss in study and control group was 24 5ml and 327 ml respectively which was significant (P < 0.01). They concluded that tranexamic acid helps to reduce the amount of blood loss in vaginal delivery. **Wang et al.** <sup>(12)</sup> detected that within 48 hours after cesarean section. Amount of blood loss was significantly low (mean 369

ml) in tranexamic acid group as compared to control group (488 ml), the difference was statistically significant (p value = 0.001). A study by **Gobbur *et al.*** <sup>(13)</sup> found that tranexamic acid reduced blood loss during cesarean section. **Roy *et al.*** <sup>(14)</sup> conducted a study to find out the efficacy of tranexamic acid in the reduction of blood loss after delivery and found good reduction in blood loss with the use of tranexamic acid.

In our thesis we found that incidence of PPH was 8.6% in group A and 17.39 % in group B which means that incidence of PPH is reduced by about 50% in association with TXA administration. **Shakur *et al.*** <sup>(15)</sup> reported that tranexamic acid substantially reduced the risk of death due to bleeding (1.2%) women died in the tranexamic acid group vs (1.7%) in the placebo group. However, the risk of hysterectomy was not reduced with tranexamic acid, (3.6%) done in the tranexamic acid group vs (3.5%) in the placebo group so it was not significantly reduced with tranexamic acid.

## CONCLUSION

Use of tranexamic acid would help to reduce blood loss during delivery. It is a cheap and readily available drug. The use of TXA decreases need of uterotonics and hence decreases morbidity and mortality.

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**Conflict of Interest:** Nil.

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