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Efficacy of Tranexemic Acid in Prevention of Hemorrhage after Vaginal Delivery Postpartum

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ABSTRACT

Background: Postpartum haemorrhage is still the primary cause of maternal death, particularly in underdeveloped nations. We aimed to see how tranexamic acid and oxytocin compare in terms of preventing postpartum haemorrhage and lowering blood loss, hospital stay, morbidity, and death during vaginal birth.Patients and methods: A prospective, randomised clinical trial study was conducted on 92 pregnant women who were being prepared for vaginal delivery and were divided into two groups: Group (A) (TXA group) (46 patients) received 1 gm of tranexamic acid and Group (B) (Non-TXA group) (46 patients) received 10 IU of oxytocin. Hemoglobin and hematocrit readings were tested before and 24 hours after vaginal delivery, and additional basic laboratory tests were performed.Results: In our study, there was no significant difference in HB at the pre-test, but the Non-TXA group was considerably lower at the post-test, and the Non-TXA group had a significant reduction. At the pre-test, there was no significant difference in HCT, but the Non-TXA group was considerably lower at the post-test, and the Non-TXA group had a significant reduction. In the TXA group, the difference in HCT was much smaller. The TXA group had considerably less blood loss.Conclusion: The use of tranexamic acid during delivery may assist to minimise blood loss. It is a low-cost and widely available medication. The use of TXA reduces the requirement for uterotonics, lowering morbidity and mortality.

Keywords: ***Postpartum Hemorrhage; VaginalDelivery ; Tranexemic Acid***

Introduction:

In women, pregnancy and birth are considered normal physiological events. High-risk deliveries account for around 10% of all deliveries. Major obstetric bleeding, hysterectomy, admission to an intensive care unit, and mother mortality can all occur

during vaginal delivery. To reduce bleeding after vaginal birth, medications such oxytocin, misoprostol, prostaglandin F2alpha, and methyl ergonovine have been utilized **(1).**

However, postpartum haemorrhage is still a significant cause of maternal death, particularly in underdeveloped nations **(2).**

In comparison to 4% of women who have a vaginal birth, the hematocrit drops by 10% and blood transfusion is necessary in 6% of women who have a Cesarean delivery **(3).**

Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine that acts as an anti fibrinolytic by inhibiting plasminogen activation in a reversible manner. As a result, fibrinolysis is inhibited, and bleeding is reduced. Tranexamic acid may help the patient's own haemostatic system work better **(4).**

In the field of obstetrics, tranexamic acid is frequently utilised. TXA is used widely to treat both antepartum and postpartum haemorrhage. Despite the fact that tranexamic acid penetrates the placenta, there has been no evidence of mutagenic activity or adverse effects on the foetus, and animal reproduction studies have found no teratogenic consequences. Tranexamic acid has been well tolerated and has not been linked to a risk of premature birth in healthy children **(5).**

The aim of this study is to determine the role of tranexamic acid in determining the efficacy of using tranexamic acid in vaginal delivery to reduce blood loss, hospital stay, and postpartum haemorrhage..

Patients and Method:

From March to December 2020, a prospective, randomised clinical trial study was conducted at Zagazig University Hospitals' Obstetrics and Gynecology Department. The study enrolled a total of 92 women who met the eligibility requirements. The patients were randomly assigned to one of two groups using a computer-generated randomization list created with medcalc version 13 (mariakirke, ostend, Belgium). In the third stage of labour, Group (A) (TXA group) (46 patients) received 1 gm tranexamic acid (Kapron, Amon, Egypt) in 100 mL lactated Ringer's solution by slow intravenous infusion over 5 minutes. Following the birth of the child, 10 IU of oxytocin (sytocinon, Novartis, Egypt) in 500 ml lactated Ringer's solution was given.

The pregnant females in Group (B) (Non-TXA group) (46 patients) received 10 IU of oxytocin in 500 mL lactated Ringer's solution after the baby was delivered. An

anaesthetist who was not involved in patient management or assessment prepared the solution.

Full-term pregnant women (gestational age>37 weeks) with a singleton pregnancy delivered vaginally, as well as multiple pregnancy, macrosomia, and polyhydramnios, were included in the study.Exclusion criteria was 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, and bleeding disorders were present and known hemostatic abnormalities before pregnancy.

All patients underwent a full physical examination, including a general examination, an abdominal examination, and a local examination. To determine pelvic capacity, cervical dilataion, effacement, state of membranes, and the absence of meconium-stained liquor, cord presentation, or prolapse. Biometry and foetal viability were assessed using ultrasound.

TXA dosage :(at the third stage of labour, 1 gm of tranexamic acid (two ampoules of Kapron®, Amoun, Egypt) was given in 100 ml lactated ringer by slow infusion over 5 minutes)

EBV x [(preoperative hematocrit – postoperative hematocrit) / (preoperative hematocrit)] = estimated blood loss where Estimated Blood Volume (EBV) in ml = the women's weight in kg x 85.(**6**).

Hemoglobin and hematocrit values were checked before and 24 hours after vaginal delivery and 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 outcome was TXA's efficacy in preventing postpartum haemorrhage, which was assessed using a set of parameters (1-Amount of blood loss measured, Haematocrit level pre and post delivery, Hb level pre and post delivery, The need for blood transfusion post delivery)

The need for other interventions (e.g. intrauterine tamponade, embolization, brace sutures, arterial ligation, and hysterectomy) after randomization to control bleeding and achieve hemostasis, the need for blood transfusion, admission to the Intensive Care Unit (ICU), organ failure, and hospital stay, and the rate of decrease in maternal death were the secondary outcome measures.

Microsoft Excel software was used to code, enter, and analyse data collected during the history, basic clinical examination, laboratory investigations, and outcome measures. Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software was used to analyse the data. The following tests were used to test differences for significance based on the type of data: qualitative data was represented as a number and percentage, quantitative data was represented as a mean and SD, and the following tests were used to test differences for significance based on the type of data: Chi square test (X2) was used to determine the difference and association of qualitative variables. By using a t test or a Mann Whitney test, differences between quantitative independent groups can be determined. P value was set at <0.05 for significant results &<0.001 for high significant result.

Results:

There was no significant difference in age between groups, and there was also no significant difference in anthropometric measures. Age was distributed as 24.455.78 with a range of 18 to 40 years and 25.806.44 with a range of 17 to 43 years (weight, Height or BMI). There is no difference in the distribution of medical illnesses between the two groups **(Table 1)**. The distribution of obstetric history among the groups studied presented in **(Table 2)**.

GA was distributed as 38.02.89 with a range of 37 wks to 41 wks and 37.433.05 with a range of 37 wks to 41 wks with no significant difference, PG were 37% in TXA group and 19.6% in Non-TXA group with no significant difference in parity, and the majority were 2 in both groups. Blood loss was significantly lower in the TXA group, with a ratio of 203.67141.12 to 355.5264.96 between the two groups.

There was no significant difference regard HB at predelivery with range from 9.2 to 12.5 in TXA group and range from 9.6 to 13.2 in Non-TXA group but at post deliverywas significantly lower with range from 9 to 12.1 in TXA group and range from 8.8 to 11.7 in Non-TXA group and there was significant decrease in Non-TXA grou. 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 postdelivery 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. TXA group significantly associated with Abdominal pain and Nausea **(Table 3)**.

Incidence of PPH is doubled in Non-TXA group than in TXA group **(Figure 1).** Blood transfusion significantly associated with Non-TXA group. TXA group significantly associated with Abdominal pain and Nausea.Non-TXA group is significantly associated with uterine artery ligation **(Table 4)**

Table 1: medical diseases data distribution between studied groups

	TXA group (A) (N=46)		Non-TXA group (B) (N=46)	
	N	%	N	%
HTN disorders	5	10.8%	6	13.04%
DM	2	4.34%	3	6.52%
Thyroid disorders	2	4.34%	4	8.69%
cardiac disorders	1	2.17%	1	2.17%
NO medical disease	36	78.2%	32	69.5%
total	46	100%	46	100%

Table2: obstetric history distribution between studied groups

			TXA group (A) (N=46)	Non-TXA group (B) (N=46)	t/ X^2	P
GA			38.0±2.89	37.43±3.05	0.911	0.365
G	PG	N	17	9	3.45	0.321
		%	37.0%	19.6%		
	≤2	N	12	16		
		%	26.1%	34.8%		
	3-4	N	13	16		
		%	28.3%	34.8%		
	>4	N	4	5		
		%	8.7%	10.8%		
P	zero	N	20	12	3.88	0.27
		%	43.5%	26.1%		
	≤2	N	19	25		
		%	41.3%	54.3%		
	3-4	N	7	8		
		%	15.2%	17.3%		
	>4	N	0	1		
		%	0.0%	2.2%		
Total		N	46	46		

	%	100.0%	100.0%		

Table 3: adverse effect distribution between studied groups

	TXA Group(A)		Non-TXA group Group(B)		X^2	P
	N	%	N	%		
Headache	3	6.5%	1	2.1%	2.25	0.13
Abdominal pain	8	16.8%	2	4.2%	5.71	0.01*
Nausea	11	23.9%	3	6.5%	8.82	0.002*
Vomiting	6	13.0%	2	4.2%	3.62	0.060
Itching	3	6.5%	0	0.0%	1.33	0.24
Use of uterotonics	2	4.3%	10	21.7%		0.001

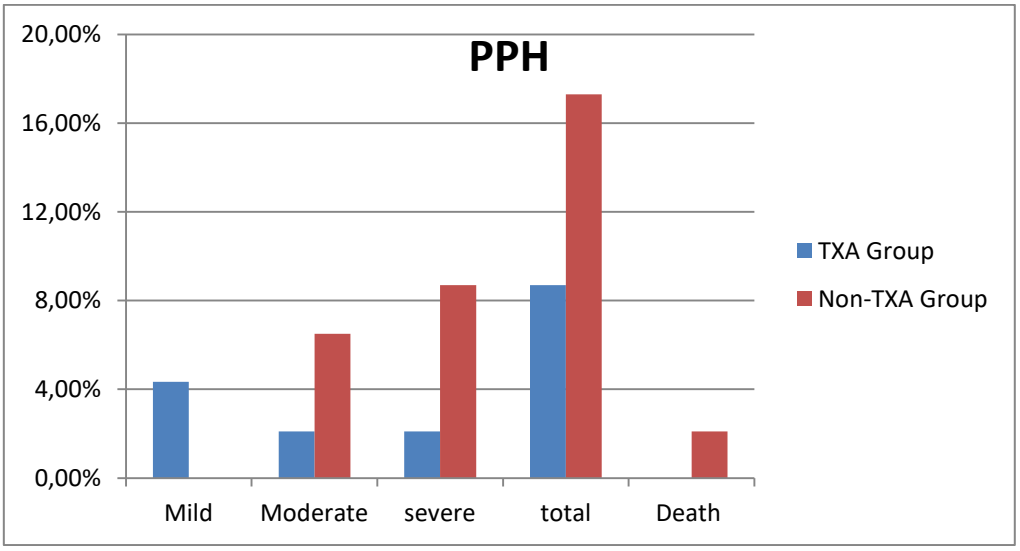

Fig. 1 : Percentage of cases developed PPH and mortality ratebetween studied groups

Table 4: Need for surgical interventions between studied groups

	TXA Group(A)		Non-TXA group Group(B)		X^2	P
	N	%	N	%		
Uterine artery ligation	1	2.1%	3	10.8%	2.38	0.03*
B-lynch	1	2.1%	3	6.5%	1.04	0.3
Tamponade	0	0%	2	4.2%	2.04	0.15
Hystrectomy	1	2.1%	2	4.2%	2.04	0.15
ICU	1	2.1%	3	6.5%	1.04	0.3
Death	0	0%	1	2.1%	1.01	0.31

Discussion:

Postpartum haemorrhage (PPH) is the leading cause of maternal morbidity and mortality worldwide, and more aggressive measures to prevent and control it are urgently needed. Uterine atony, which responds to uterotonic drugs like oxytocin, methylergometrine, and prostaglandins, is the most common cause of PPH. However, these drugs have a number of side effects, including oxytocin-receptor downregulation and desensitisation after oxytocin exposure, which results in a lack of further improvement in uterine contractions regardless of dose increase. After a vaginal delivery, the incidence of PPH is 2 percent to 4%, and after a caesarean section, the incidence is 6%. According to India Sample registration scheme (SRS) 2001-2003, PPH accounts 38% of maternal deaths **(7)**.

Different strategies have been described for preventing PPH, including active management of the third stage of labor. Antifibrinolytic agents, mainly tranexamic acid have been demonstrated to prevent PPH **(8)**.

Tranexamic acid is safe in pregnancy, being FDA category B. One concern regarding the use of tranexamic acid is the potential for thromboembolic events in a population at already high risk of thrombosis **(9).** These data on thromboembolic events were also supported by **Sentilhes et al. (10)** in pregnant women.

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. 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) (46 patients)consists of pregnant females who received 10 IU of oxytocin in 500 ml lactated Ringer's solution was given after delivery of the baby.

In our study, there was no significant difference regarding HB at pre but at post, non-TXA group was significantly lower and there was significant decrease in non TXA group. Also, **Jayaraman and Somu (11)** found a significant difference in the post-delivery Hemoglobin ($P<0.01$).

Unlike **Mirghafourvand et al. (12)** who stated that there was no statistically significant difference between the intervention and control groups in terms of haemoglobin 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 (11)** found that the the difference of Hemoglobin decline in the study group and in control group was statistically significant

In our study, 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. Also, **Jayaraman and Somu (11)** found that the amount of blood loss in study and control group was 245ml and 327 ml respectively which is significant (P<0.01). They concluded that tranexamic acid helps to reduce the amount of blood loss in vaginal delivery.

Simonazzi et al. (13) found that prophylactic tranexamic acid given before cesarean skin incision in women undergoing cesarean delivery, under spinal or epidural anesthesia, significantly decreased blood loss, including PPH and severe PPH, in addition to the standard prophylactic oxytocin given after the delivery of the baby.

Sentilhes et al. (14) made a study on TXA prevention of PPH after vaginal delivery and detected that TXA reduced the risk of blood transfusion by a relative 39% and the mean transfused volume by 1.1 units which is concordant with our results.

Sentilhes et al. (10)mentioned in their study that Women in the tranexamic acid group had a lower rate of provider-assessed clinically significant postpartum hemorrhage than those in the placebo group and also received less additional uterotonic agents.

Thus, use of tranexamic acid in third stage labor would help in reducing blood loss and decreasing the use of uterotonic drugs. Tranexamic acid is a readily available and inexpensive drug. Hence, its use should be encouraged to reduce blood loss. There was insignificant side effects with the use of tranexamic acid in our study.

Abd El-Gaber et al.(15) performed a study at south valley university in EGYPT and stated that Incidence of PPH in group A and group B were (4.4% and 6.8) respectively, 1.2% in group A and 2.8% in group B had severe degree of PPH. Amount of blood loss immediately after placental delivery up to first 6 hours postoperative was statistically significant increase in placebo group than tranexamic acid group \and that is consisent with our study.

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 assosciation with TXA adminstration.

Shakur et al. (16) discussed 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 .

Also found that the use of intrauterine tamponade, embolisation, manual removal of the placenta, and arterial ligation did not differ significantly between the tranexamic acid and the placebo group,Brace sutures were used more often in the tranexamic group .In our thesis we found that risk of hystrectomy is reduced in TXA group(2.1%) compared with non-TXA group(4.2%).

Further studies should include women with higher baseline risk of thromboembolic events, including women with antiphospholipid syndrome and with using different protocols (varying the duration of administration, quantity, route, etc.) to confirm these findings.

Conclusion:

The use of tranexamic acid during delivery may assist to minimise blood loss. It is a low-cost and widely available medication. The use of TXA reduces the requirement for uterotonics, lowering morbidity and mortality.

Conflict of Interest: No conflict of interest.

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