

## Use of Tranexamic Acid in Preventing Postpartum Hemorrhage Following Vaginal Delivery

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### Abstract:

**Introduction:** Tranexamic acid (TXA) injections due to its antifibrinolytic properties can be used as a treatment for postpartum hemorrhage (PPH) on a global scale along with uterotonics.**Aims and Objectives:** The purpose of this study was to evaluate the safety and effectiveness of TXA and to identify potential side effects if any in preventing PPH following vaginal delivery.**Material and Methods:** This randomized controlled trial, conducted in a multispecialty Dhiraj hospital in Vadodara, India, involved 300 term patients over one year from February 2023 to March 2024. Subjects were randomly assigned into two groups. Each cohort received 10 prophylactic units of oxytocin. One group received 1 gm of intravenous TXA, while the other received 10 mL of normal saline intravenously within 2-3 minutes after delivery. Blood loss was measured using calibrated drapes, and mean changes in hemoglobin (Hb) and packed cell volume (PCV) were assessed from pre-delivery to postnatal day 2. Data analysis was done using SPSS (Statistical Package for the Social Sciences) software.**Results:** Patients in the research had an average age of 23.43 years with a standard deviation (SD) of 3.26 years. The occurrence of PPH was observed in 10 individuals (6.66%) in the TXA group and 17 individuals (11.33%) in the placebo group ( $p = 0.226$ ). Furthermore, the mean blood loss was significantly lesser in the TXA group, measuring 250.10 mL with an SD of 133.54 mL, compared to 334.2 mL with an SD of 141.78 mL in the placebo group ( $p < 0.0001$ ).**Conclusion:** Tranexamic acid can serve as a supplementary treatment alongside uterotonics during the third stage of labor, as demonstrated in this study.**Keywords:** Postpartum Hemorrhage, Tranexamic Acid, Placebo, Vaginal Delivery.

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### Introduction

Postpartum hemorrhage (PPH) is defined as "blood loss more than 500ml following vaginal delivery or, 1000ml following caesarean section or any bleeding that affects the hemodynamic stability of the patient".[1]

History of previous PPH, primigravida, obesity, multiple pregnancies, VBAC (vaginal birth after caesarean section), large baby especially due to gestational diabetes are some of the factors that can lead to PPH in the present pregnancy and can be measured using a Calibrated drape, however visual per speculum examination being a crude approach.[2,3] Hemostatic agent alongside uterotonics are used to minimize bleeding during vaginal delivery to prevent complications during childbirth as well as maternal deaths due to PPH.[4] Active management of third stage of labor includes use of Oxytocin to prevent PPH [5].

Tranexamic acid (TXA) inhibits plasminogen activation thereby reducing bleeding through antifibrinolytic activity. Therefore in 2012, WHO recommends use of TXA for the treatment of PPH if uterotonics fail or bleeding is due to traumatic injury.[6]

The "World Maternal Antifibrinolytic Trial" published its results in 2017 which stated that early use of intravenous TXA (within 3 hrs of birth or immediately if bleeding is encountered) reduces death due to bleeding in women with PPH regardless of cause and no maternal adverse effects.[7] WHO recommends that TXA should be given intravenously 1g in 10ml (100mg/ml) at 1 ml/min over 10 min and a second dose of 1g TXA is repeated if bleeding continues for 30 minutes or bleeding after the drug is introduced. Tranexamic acid (TXA) is a valuable tool in preventing PPH,

being cost-effective, easily accessible, straightforward and easily integrated into vaginal delivery protocols.[8] The study aims to assess efficacy of TXA as well as its adverse effects when given after vaginal delivery for the prevention of PPH.

#### Materials and Methods:

A randomized controlled experiment was conducted from February 2023 to March 2024 including 300 term patients at Dhiraj hospital – a tertiary care center at Vadodara, Gujarat, India aiming for vaginal delivery. Patients were included in the study after obtaining written informed consent.

Those antenatal patients who had specific medical conditions (eg: Diabetes, hypertension, coagulopathy etc) or history of any major illness were excluded from the study.

Both groups received 10 units of prophylactic oxytocin intramuscularly as a part of AMTSL (Active management of third stage labour).The

participants were randomly assigned 2 groups (Group A and Group B), each comprising 150 patients.

Group A received 1g intravenous TXA, while Group B received a slow infusion of 10 ml of Normal saline over 30-60 seconds within 2-3 minutes following vaginal delivery. After Administration of the drug a V-drape bag was kept under a woman's buttocks and blood loss (measured in millilitres) was observed at 30 minutes and 2 hours post-delivery and vital parameters were monitored during the golden hour every 15 minutes and again at the end of 2 hours. Adverse effects of TXA were noted if any and the participants were followed up after 3 months. Also participants requiring blood transfusion or hysterectomy due to uncontrolled PPH were recorded. SPSS (Statistical Package for the Social Sciences) software was used to calculate the p value and for data analysis.

#### Results:

**Table 1: Distribution based on mother's age, gravidity and BMI**

Characteristics	TXA group	Placebo group	p-value
Mother's age			
18–22 years	60(40%)	70(46.6%)	0.409
23–27 years	50(33.3%)	48(32%)	
28–32 years	32(21.3%)	22(14.6%)	
33–37 years	8(5.33%)	10(6.66%)	
Mean age (in years)	24.11 ± 4.1	23.53 ± 3.06	0.1008M
Gravidity			
Primigravida	58(38.6%)	55(36.6%)	0.811
Multigravida	92(61.3%)	95(63.3%)	
BMI (Kg/m <sup>2</sup> )			
<18.5 (underweight)	67(44.6%)	64(42.6%)	0.637
18.5–24.9 (normal weight)	58(38.6%)	66(44%)	
25–29.9 (pre-obesity)	19(12.6%)	17(11.3%)	
>30	6(4%)	3(2%)	

**M Indicates Mann–Whitney U-test**

**Table 2: Frequency of PPH**

Type of PPH	TXA group	Placebo group	p-value
Atonic PPH	3(2%)	9(6%)	0.140
Traumatic PPH	7(4.66%)	8(5.33%)	1
Atonic + traumatic	0 (0%)	0(0%)	0

**Table 3: Mean blood loss and clinical/lab parameters for both groups were within typical ranges**

Parameters	TXA group	Placebo group	p-value
Mean blood loss	250.10 ± 133.54	334.2 ± 141.78	<0.0001M
Clinical parameters			
Postpartum transfusion	4 (2.66%)	11 (7.33%)	0.111
Arterial embolization	0	0	0
Emergency hysterectomy	0	1(0.66%)	1
Lab parameters			
Change in hemoglobin	1.48 ± 1.22	1.82 ± 1.20	0.0066 T
Change in packed cell volume (PCV)	3.51 ± 3.42	5.05 ± 4.18	0.0015 T

**M Indicates Mann–Whitney U-test; T Indicates T-test**

**Table 4: Mean variation in pulse rate, SBP and DBP among both groups**

Characteristics	TXA group	Placebo group	p-value among both groups
Pulse rate (beats per minute)			
Pre Intervention	81.64 ± 8.54	79.52 ± 6.48	0.13 M
Post Intervention	76.38 ± 9.67	75.41 ± 5.81	0.86 M
Change	-1.35 ± 11.44	-3.33 ± 10.79	0.21 M
p-value (within group)	0.09W	0.002W	
Systolic blood pressure (SBP)			
Pre Intervention	111.81 ± 10.42	111.25 ± 9.30	0.65 M
Post Intervention	112.84 ± 8.91	112.38 ± 8.08	0.66 M
Change	1.02 ± 12.57	1.12 ± 12.51	0.93 M
p-value (within group)	0.25W	0.25W	
Diastolic blood pressure (DBP)			
Pre intervention	76.32 ± 5.87	75.40 ± 4.81	0.33M
Post Intervention	74.04 ± 5.79	72.52 ± 6.11	0.05M
Change	-2.28 ± 7.50	-2.89 ± 7.98	0.71M
p-value (within group)	0.003W	0.0004W	

M Indicates Mann-Whitney U-test; w Indicates Wilcoxon sign test

**Table 5: Comparison: Minor negative events, hospital stays, uterotonic drug use in both groups**

Parameters	TXA group	Placebo group	Among groups p-value
Minor adverse drug reactions			
Nausea	6(4%)	2(1.33%)	0.282
Vomiting	8(5.33%)	3(2%)	0.219
dizziness	2 (1.33%)	2(1.33%)	0.6843
Nausea + vomiting	3(3%)	1(0.66%)	0.6225
Length of time spent in hospital			
≤3 days	133(88.6%)	124(82.6%)	0.187
>3 days	17(11.3%)	26(17.3%)	
Additional use of uterotonics			
Yes	13(8.66%)	31(20.6%)	0.005
No	137(91.3%)	119(79.3%)	

### Discussion:

Obstetric bleeding remains a leading cause of maternal deaths worldwide. Primary PPH has a global prevalence of 6%, it accounts for 35–55% of peripartum maternal fatalities.[9] In this study, most participants in the TXA and placebo groups were aged 18–22 years (40% and 46.6%, respectively), with the fewest in the 33–37 age group (5.33% and 6.66% respectively). The median age didn't significantly differ between the groups. Dahiya et al. found similar mean ages in their investigation: 24.25 ± 4.02 years in group I and 24.23 ± 4.14 years in group II (p=0.945).[10]

The study showed no significant difference in gravidity between the TXA test and control groups (p = 0.811). Similarly, Nambiar and Somu found no significant difference in primigravida or multigravida women proportion between the TXA test and control groups (p = 0.39, 0.79), consistent with our findings.[11] Mean BMI ranged from 18.5 to 24.9 kg/m<sup>2</sup> in both groups with no discrepancy observed. Al-Garhy et al. also reported no difference in BMI across groups (p = 0.658), validating our results.[12] In this trial, PPH occurred in 6.66% of the test group and 11.33% of

the control group (p = 0.226). Atonic PPH was 2% in the test group and 6% in the control group (p = 0.140). Traumatic PPH was 4.66% in the test group and 5.33% in the control group (p = 1). No simultaneous traumatic and atonic PPH cases were observed in the test group as well as control group.

A study by Almutairi WM reported an overall atonic PPH incidence of 2.5%, with a 12% increase between 2017 and 2018 in a Saudi Arabian specialty hospital.[13] A recent study found that the TXA test group had significantly lower average blood loss compared to the control group. In the TXA test group, the mean blood loss was 250.10 ± 133.54 mL, whereas, in the control group, it was 334.2 ± 141.78 mL (p < 0.0001), indicating a significant difference. The median blood loss in the TXA test group was 200 mL, which was lower than that in the control group.

Additionally, research by Igboke et al. showed that use of TXA reduced blood loss following a vaginal delivery.. The TXA test group had a lower mean estimated blood loss than the control group (174.87 ± 119.83 mL vs 341.07 ± 67.97 mL, respectively; p < 0.0001).[14] In this study, TXA didn't significantly reduce PPH. Rates were 6.66% in the

TXA group and 11.33% in the control group, showing no significant difference. In contrast, Saccone et al. found that TXA after vaginal delivery decreased primary PPH incidence (8.7% vs 11.4%; relative risk 0.61, 95% CI, 0.41–0.91).[15] In the trial, there was no significant difference in blood transfusions, peripartum hysterectomy, or arterial embolization between the TXA test and control groups. Although 7.3% of control group patients required postpartum transfusions, compared to 2.6% in the TXA test group, the difference wasn't statistically significant.

A meta-analysis by Xia et al. also found no significant difference in needs between control and test groups, consistent with this study's findings (TXA vs control; relative risk: 0.87, 95% CI: 0.46–1.64,  $p = 0.66$ ) in two trials.[16] Franchini et al. performed a recent meta-analysis at the Italian National Blood Centre on TXA's effectiveness in PPH. They found that the TXA group required fewer transfusions compared to the control groups.[17]

In the current investigation, the test group showed significantly lower changes in laboratory measures, particularly Hb and PCV levels, compared to the control group ( $1.48 \pm 1.22$ ,  $1.82 \pm 1.20$ ), with a statistically significant difference ( $p = 0.0066$ ). Naeiji et al. also found that the control group had notably lower mean hemoglobin levels compared to the test TXA group ( $11.77 \pm 0.50$  vs  $11.31 \pm 0.56$ ), consistent with our study's results.[18] Oseni et al. discovered that preoperative administration of TXA significantly lowered the blood loss during emergency C-sections.[19]

In our study, no notable differences were observed in the heart rates or blood pressure between both groups pre- and Post-intervention. Although DBP notably decreased in both groups during the intervention, SBP remained relatively unchanged. Shakur- Still et al. conducted a trial with 167 women, finding no significant vital sign changes post-tranexamic acid injection during and after delivery. [20] The current study found no statistically significant difference in the side effects observed with the usage of TXA, such as nausea, vomiting, and dizziness, between the two groups. Sentilhes et al. found that nausea, vomiting, and dizziness were prevalent side effects in a multicenter randomized trial.[21] In this trial, 133 people (88.6%) in the TXA test group were discharged within 3 days of hospitalization, compared to 124 participants (82.6%) in the control group.

The length of hospital stay stated no statistically significant differences in this investigation. In this study, the control group (31 participants, 20.6%) needed significantly more uterotonics compared to

the test group. Another study by Ifunanya et al. stated that 7.1% cases in the TXA test group and 33.3% in the control group required additional administration of uterotonics coinciding with our current results.[22] Tran et al. found higher uterotonic use in the control group as compared to TXA test group, aligning with our study's results.[23]

### Conclusion:

Tranexamic Acid compliments uterotonics in the third stage of labor by reducing blood loss without any serious side effects. Its cost effectiveness, easy availability and its antifibrinolytic activity enhances its use as a drug of choice as a hemostatic agent and helps in preventing maternal mortality as a result of blood loss with its immediate administration after vaginal birth.

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