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# Efficacy of Prophylactic Intravenous Tranexamic Acid in Preventing Postpartum Haemorrhage in Parturients with Risk Factors: A Randomized Control Trial

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**Abstract:- This study aims to compare the effectiveness of prophylactic intravenous Tranexamic acid (TXA) dosages of 0.5g and 1.0g in the prevention of postpartum haemorrhage (PPH) among parturient with risk factors. The research followed a randomized, double-blind, controlled experimental design, spanning nine months. Simple random sampling was used to select 154 participants to each arm. The research objectives encompassed comparing labour outcomes of the two groups and measuring blood loss via pre and post-delivery packed cell volume. Statistical analysis employed Student's t-test. Result revealed a slight non-significant difference in PCV change between 0.5g and 1.0g TXA group. The study also found that the risk of developing primary PPH when using 0.5g TXA was approximately twice the risk when using 1.0g TXA. These findings suggest that the prophylactic use of 1.0g TXA may be more effective in preventing PPH compared to 0.5g TXA. Further research is warranted to validate these results and refine recommendations for clinical practice.**

***Keywords***:- *Tranexamic Acid, Blood Loss, High-Risk Factors, Third Stage Of Labour, Parturient.*

## I. INTRODUCTION

Postpartum haemorrhage (PPH) is well recognised as the primary contributor to adverse maternal health outcomes and fatalities on a global scale, resulting in the unfortunate demise of more than 300,000 women annually (Roy et al., 2016). The global prevalence of PPH is 6% while the highest-burden is experienced in low-income countries with the magnitude in sub-Saharan Africa as high at 10.5 % (Ononge et al., 2016). In Nigeria, the incidence of PPH varies from centre to centre. In Ilorin, Port Harcourt, and Kano, the incidences were 4.2%, 4.28% and 2.48% respectively (Adeniran et al., 2014; Green et al., 2015; Garba et al., 2019). The incidence of PPH in Ekiti State was 11.2% (Awoleke, et al., 2020). This is higher than global average and appeared to be higher than other centres in Nigeria. This makes this study pertinent. Prevention of PPH is thus very important as one of the measures to reduce maternal mortality and morbidity.

The third stage of labour starts immediately after the delivery of the baby and terminated after the placenta and its membranes had been completely expelled. This stage is crucial in the prevention of PPH. Some degree of haemorrhage is bound to occur during this stage (about 100mls to 250mls), most severe PPH occur during this stage and it is therefore very essential to minimize this blood loss to the minimum. World Health Organization (WHO) recommended that third stage of labour should be actively managed (Ahmed & Bhalerao, 2017). The standard definition for active management combines three procedures: the use of a uterotonic immediately after delivery of the foetus, controlled cord traction and fundal massage immediately after delivery of the placenta, followed by palpation of the uterus every 15 minutes for 2 hours to assess the continued need for massage (Irimescu, et al., 2018). Although, active management of the third stage of labour is highly effective at preventing PPH among facility-based deliveries. It is more effective than physiological management in preventing postpartum blood loss, severe PPH and prolonged third stage of labour (Ahmed & Bhalerao, 2017). However, active management of third stage of labour is associated with a 60% reduction in the incidence of PPH (Deneux-Tharaux, et al., 2013) Also, it has been clearly shown that the administration of uterotonics, and in particular oxytocin, after birth is the only component of active management of labour that is effective in preventing PPH and it entails administration 10IU of parenteral oxytocin within one minute of the delivery of the baby. Oxytocin's action is unique to the smooth muscles of the uterus; it increases the amplitude and frequency of contractions. Additional biochemical haemostatic effects obtained from the use of pro-haemostatic drugs such as tranexamic acid may go a long way in complementing the effects of oxytocics in the prevention of postpartum haemorrhage (Ifunanya, 2019).

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The use of tranexamic acid in prevention of obstetric haemorrhage, either for the purpose of preventing or treating postpartum haemorrhage (PPH) is gaining the attention of researchers in the recent time. Many studies have proved the effectiveness of TXA in the prevention of PPH. (Igboke et al., 2022; Sadek et al., 2021; Sentilhes et al., 2015; Ali et al., 2021). Nevertheless, the majority of studies conducted to evaluate the effectiveness of prophylactic intravenous tranexamic acid (TXA) administration in avoiding postpartum haemorrhage (PPH) focused on individuals with low-risk factors for PPH and utilised a minimum dosage of 1g of TXA. The index trial compared the effectiveness of a reduced dosage (500mg) and the conventional 1g dosage in Ekiti State the high prevalent of PPH in Ekiti state. The overall aim of this study is to compare the efficacy of prophylactic intravenous 0.5g with 1.0g Tranexamic acid in the prevention of postpartum haemorrhage in parturient with risk factors. It specifically examined;

- To determine the distribution of the respondents according to the identified risk factors;
- To compare the outcome of labour in the two groups;
- To compare the mean blood loss by difference in pre and post-delivery PCV in both groups;
- To compare the need for blood transfusion between the two groups.

## II. METHODOLOGY

This research was conducted using a randomised controlled clinical trial that compared reduced dose of 0.5g intravenous Tranexamic acid and standard dose of 1g Tranexamic acid for the prevention of post-partum haemorrhage in third stage of labour among newly delivered mothers with risk factors for post-partum haemorrhage in Ekiti State University Teaching Hospital, Nigeria. Post-partum haemorrhage in the state around the time of the study was over 11% (Awoleke, et al., 2020). Ethical approval for the study was obtained from the Research and Ethics Committee of the Ekiti State University Teaching Hospital, Ado Ekiti, Ekiti state and written informed consent was obtained from each of the participants before the commencement of the procedure.

The research population consisted of all individuals who had given birth and had a risk factor for primary postpartum haemorrhage during the third stage of labour following a vaginal delivery at full term. Simple random sampling technique was used to select patients who satisfied the inclusion criteria into two groups. This was done using a computer-generated list created by an analyst outside the hospital setting. Participants in group one were randomised to receive reduced dosage of intravenous Tranexamic acid (TXA) of 0.5g while those in group two received standard dosage of TXA1.0g. The blinding procedure was conducted by keeping the drugs in a sealed enveloped placed beside the patient's identification numbers. Neither the patient nor the house officers in charge of the labour ward possessed knowledge regarding the patient's affiliation with a specific group. Within one minute of the delivery of the baby, the house officer in charge of the labour ward administered either 0.5gram (5mls constituted with 5mls of water for injection to make 10mls) or 1gram (10mls of TXA) of intravenous TXA acid (each vial of 0.5g is 5mls) to each parturient as produced by Prexam® slowly over 10minutes. The house officer was an independent person who was not involved in the randomization. The intravenous TXA administration was given after administration of 10 IU of parenteral oxytocin. Cord clamping was performed and the placenta was delivered by controlled cord traction or manually if not delivered after two attempts of controlled cord traction failed to deliver the placenta. Prompt repair of episiotomy and genital laceration site was done where the need arose.

Measurement of haemoglobin concentration was done before and after delivery by using the venepuncture method to collect blood which was put into an EDTA (Ethylene diamine tetra acetic acid) bottle, the micro-method was used to measure the haemoglobin concentration. The blood loss evaluation was also done by determining the post-delivery haematocrit level at 24hours after the delivery, and the difference between the pre-delivery and post-delivery haematocrit level were calculated and noted. Ten per cent (10%) decrease between pre and postpartum haemoglobin was taken as postpartum hemorrhage. Patient clinical condition and vital signs were checked 4hourly within the first 24 hours. The acquired data were encoded and inputted into the Statistical Package for the Social Sciences (SPSS) version 23. The Student's t-test was employed to assess statistical significance, where deemed suitable. Statistical significance was determined when the p-value was less than 0.05.

## III. RESULTS

Table 1 below shows that some (5.8%) of the respondents in the control group had prolonged labour as the singular identified risk factors for post-partum haemorrhage as against very few (1.3%) in the study group and this difference was statistically significant. ($\chi^2 = 0.061$, *p-value = 0.032).*

The most common risk factor for PPH identified in both group as a singular risk factor was induction of labour. However, there was no statistically significant difference. ($\chi^2 = 1.596$, *p-value = 0.207).*

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**Table 1: Distribution of the Respondents According to the Identified Risk Factors**

| Risk Factors | TXA 0.5g n (%) | TXA 1g n (%) | Chi square | p-value |
|---|---|---|---|---|
| Multiple pregnancies | 8 (5.2) | 2 (1.3) | 0.104* | 0.054 |
| Foetal macrosomia | 25 (16.2) | 22 (14.3) | 0.226* | 0.635 |
| Polyhydramnios | 1 (0.6) | 1 (0.6) | 1.000* | 1.000 |
| Fibroid coexisting with pregnancy | 16 (10.4) | 17 (11.0) | 0.034 | 0.854 |
| Previous history of PPH | 19 (12.3) | 17 (11.0) | 0.126 | 0.723 |
| Anaemia | 14 (9.1) | 12 (7.8) | 0.168 | 0.682 |
| Induction of labour | 73 (47.4) | 62 (40.3) | 1.596 | 0.207 |
| Augmentation of labour | 59 (38.3) | 56 (36.4) | 0.125 | 0.724 |
| Grand multiparity | 10 (8.5) | 6 (3.9) | 1.055 | 0.304 |
| Prolonged labour | 2 (1.3) | 9 (5.8) | 0.061* | **0.032** |
| Antepartum haemorrhage | 3 (1.9) | 6 (3.9) | 0.501* | 0..310 |
| Precipitate labour | 3 (1.9) | 3 (1.9) | 1.000* | 1.000 |
| **Cumulative risk factors** | **N = 154** | **N = 154** | | |
| 1 risk factors | 92 (59.7) | 106 (68.8) | 3.056 | 0.217 |
| 2 risk factors | 45 (29.2) | 37 (24.0) | | |
| 3 risk factors | 17 (11.0) | 11 (7.1) | | |

** Some Patients have more than a Risk Factor.
* - Fischer's Exact Test.

Table 2 shows that all (100.0%) of the respondents in the study group had less than 12 hours duration of labour as against majority (97.4%) of those in the control group. although only few (2.6%) of the respondents in this category had more than 12 hours duration of labour and there was a statistically significant difference ($\chi^2$ *=4.053, p-value = 0.044).* more participants in group one (81.2%)completed third stage within 5 minutes as compared to participants in group 2 (73.4%), although this is not statistically significant.

**Table 2: Comparing the Outcome of Labour in the Two Groups**

| Outcome | TXA 0.5g n (%) | TXA 1g n (%) | Test of significance | P value |
|---|---|---|---|---|
| **Onset of labour** | | | | |
| Spontaneous | 81 (52.6) | 92 (59.7) | 1.596 | 0.207 |
| Induced | 73 (47.4) | 62 (40.3) | | |
| **Progress of labour** | | | | |
| Augmented | 59 (38.3) | 56 (36.4) | 0.125 | 0.724 |
| Non-augmented | 95 (61.7) | 98 (63.6) | | |
| **Duration of labour** | | | | |
| Less than 12 hours | 154 (100.0) | 150 (97.4) | 4.053 | **0.044** |
| Greater than 12 hours | 0 (0.0) | 4 (2.6) | | |
| Mean ± S.D. | 6.60 ± 1.37 | 6.92 ± 1.88 | 2.682 | 0.091[t] |
| **Perineal tear** | | | | |
| Yes | 5 (3.2) | 4 (2.6) | 0.367 | 0.832 |
| No | 114 (74.0) | 111 (72.1) | | |
| Episiotomy | 35 (22.7) | 39 (25.3) | | |
| **Birth weight (kg)** | | | | |
| Less than 2.5 | 1 (0.6) | 0 (0.0) | 1.555 | 0.817 |
| 2.5 – 3.0 | 52 (33.8) | 56 (35.4) | | |
| 3.0 – 3.5 | 29 (18.8) | 28 (18.2) | | |
| 3.5 – 4.0 | 47 (30.5) | 49 (31.8) | | |
| Greater than 4.0 | 25 (16.2) | 21 (13.6) | | |
| Mean ± S.D. | 3.31 ± 0.56 | 3.31 ± 0.57 | 0.372 | 0.967[t] |
| **Duration of third stage of labour** | | | | |
| Less than 5 minutes | 125 (81.2) | 113 (73.4) | 2.662 | 0.103 |
| Greater than 5 minutes | 29 (18.8) | 41 (26.6) | | |

* Fischer's Exact Test.
[t] Independent Sample T Test.

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Table 3 below shows that the mean admission PCV was almost similar however there was a slightly higher difference in the mean PCV difference among the group that had I.V. TXA 0.5g (2.32 ± 1.53) compared to the group that had I.V. TXA 1.0g (2.12 ± 1.16) (T-test = *1.292, p-value = 0.099).*

**Table 3: Comparing Mean Blood Loss by Difference in Pre and Post-Delivery PCV in both Groups**

| Group | Mean admission PCV ± SD | Mean post-delivery PCV ± SD | Mean PCV difference ± SD | T-Test | 95% C.I. | p-VALUE |
|---|---|---|---|---|---|---|
| **IV TXA 0.5g (n=154)** | 32.19 ± 2.20 | 29.86 ± 2.40 | 2.32 ± 1.53 | 1.292 | 2.047 – 2.352 | 0.099 |
| **IV TXA 1.0g (n=154)** | 32.21 ± 2.27 | 30.11 ± 2.29 | 2.12 ± 1.16 | | | |

Table 4 below shows that majority of the respondents in both the study (91.6%) and control groups (94.2%) respectively did not require blood transfusion, while only 8.4% and 5.8% of the respondents in the low dose group and standard dose groups respectively required blood transfusion. However, there was no statistically significant difference ($\chi 2$ =0.783, p-value = 0.376).

Table 4: Comparing the Need for Administration of Blood Transfusion.

| Group | Blood Transfusion | | TOTAL N (%) | $\chi 2$ | p-VALUE |
|---|---|---|---|---|---|
| | Yes N (%) | No N (%) | | | |
| **IV TXA 0.5g (n=154)** | 13 (8.4) | 141 (91.6) | 154 (50.0) | 0.783 | 0.376 |
| **IV TXA 1.0g (n=154)** | 9 (5.8) | 145 (94.2) | 154 (50.0) | | |
| **Total** | 22 (7.1) | 286 (92.9) | 308 | | |

## IV. DISCUSSION

This study compared the effectiveness of prophylactic intravenous Tranexamic acid (TXA) dosages of 0.5g and 1.0 g in preventing postpartum haemorrhage (PPH) among parturient with risk factors. The study further compared labour outcome in the two groups. The study revealed prolonged labour as a significant risk factor for PPH, this is in tandem with a study conducted by Nyfløt et al. (2017) where prolonged labour (duration >12 hours) was associated with severe postpartum haemorrhage. The study revealed that women with prolonged labour were more likely to have severe postpartum haemorrhage. (adjusted odds ratio = 2.44, 95% confidence interval: 1.69-3.53, p< 0.001).

The study also showed that more blood loss was associated with the administration of lower doses of tranexamic acid compared to the standard dose of 1g, this was statistically substantiated as the study revealed a mean PCV difference of 2.32 ± 1.53 in the lower doses of tranexamic acid as compared to 2.12 ± 1.16 in those administered the standard dose of 1g. this finding revealed that the standard dose of 1g was more effective in the control of PPH than the lower dose of 0.5g. This is in tandem with a study conducted by Ali et al., (2021) in Egypt who reported that the PCV difference was significantly lower in patient who had tranexamic acid. The finding was contrary to the finding of Ifunanya et al., (2019), the reason for a lower amount of blood loss and difference in PCV could be attributed to the fact that Ifunanya et al., (2019) recruited the general population and not high-risk patients as conducted in this study. Moreso, Ifunanya et al., (2019) administered 1g of tranexamic acid alone and compared it with patients who had just 10IU of oxytocin.

The study also revealed that there was a significant difference in the estimated blood loss compared between the two groups as respondents in the study groups had a higher estimated blood loss This is similar to findings reported by Shady et al., (2019). The finding then affirmed that early administration of TXA will reduce the risk of deaths from Postpartum bleeding. The study also revealed that parturient who had tranexamic acid of 1g have decreased odds of having PPH by 1.830 times compared to those who had 0.5g of tranexamic acid. However, there was no statistically significant difference (C.I. 0.25 – 1.19; p-value 0.124). This suggested that the tranexamic acid of 1g was more effective in preventing PPH compared to the lower dose, However, most of the work done to establish the efficacy of prophylactic intravenous TXA usage in preventing PPH were done on patients with low-risk factors for postpartum haemorrhage and using at least 1g of TXA. The study also revealed that the group that had a higher dose of tranexamic acid had lower incidence (5.8%) of the need for blood transfusion compared to the group that had a lower dose of tranexamic acid (8.4%). This was also corroborated by studies conducted by Igboke et al., (2022) here the need for additional uterotonics was 1.28%. The study also revealed that there was a significant difference in the estimated blood loss compared between the two groups as respondents in the study groups had a higher estimated blood loss (Mdn = 448.50) than the control group (Mdn = 428.00), U =9344, p = 0.001. This is similar to findings reported by Ali, et al., (2021). The study then revealed that early administration of TXA reduces the risk of deaths from exsanguination in women who experience postpartum haemorrhage a finding similar to that reported in the CRASH-2 study (Brenner, et al., 2018).

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## V. SUMMARY OF FINDINGS

The researchers observed that prolonged labour was more common in the control group, emphasizing the need for early interventions in such cases. Induction of labour was a common risk factor in both groups. Also, there was no significant difference in the mean admission packed cell volume (PCV) between the two groups, the need for blood transfusions did not significantly differ. This suggests that both dosages of TXA effectively limited blood loss and reduced the need for transfusions. Moreover, the study indicated that the risk of developing primary PPH was approximately twice as high when using 0.5g TXA compared to 1.0g TXA. This finding suggests that the higher 1.0g dosage may be more effective in preventing PPH. Importantly, the incidence of side effects from TXA was minimal in both groups, reinforcing its safety profile for PPH prevention.

## VI. CONCLUSION

The study concluded that administration of 1g of tranexamic acid is more effective in controlling postpartum haemorrhage compared to the 0.5g of tranexamic acid. The study suggests that both 0.5g and 1.0g TXA dosages can be effective in limiting blood loss and reducing the need for transfusions. However, the 1.0g dosage may offer superior efficacy in preventing primary PPH. These findings provide valuable insights into optimizing interventions for maternal care during childbirth, although further research is warranted to confirm and refine the results.

## RECOMMENDATIONS

Based on the findings of this study, several recommendations can be made to improve clinical practice and further research in the prevention of postpartum haemorrhage (PPH) among parturient with risk factors:

- Healthcare institutions and obstetric departments should consider updating their clinical practice guidelines for the prevention of PPH to incorporate the use of prophylactic Tranexamic acid (TXA) and consider to adopt a dosage of 1.0g IV TXA
- Obstetric healthcare providers should assess parturient for risk factors associated with PPH during antenatal care to identify those who may benefit from TXA prophylaxis. This proactive approach can help tailor interventions to individual patient profiles.
- Obstetricians and midwives should closely monitor and intervene promptly in cases of prolonged labour, which was identified as a significant risk factor. Timely management can help mitigate the risk of excessive bleeding.
- Further research is needed to validate the findings of this study and explore the optimal TXA dosage for PPH prevention. Long-term studies with larger sample sizes and diverse populations can provide more robust evidence.

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