# COMPARISON OF THERAPEUTIC EFFECTIVENESS OF OXYTOCIN VERSUS OXYTOCIN PLUS TRANEXAMIC ACID IN THE PREVENTION OF POST-PARTUM HEMORRHAGE

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## ABSTRACT

**Objective:** To compare mean blood loss with Oxytocin plus Tranexamic acid versus Oxytocin alone in the prevention of postpartum hemorrhage.

**Methodology:** This randomized controlled trial was conducted in Department of Obstretrics & Gynaecology, Lady Reading Hospital, Peshawar on 400 women, distributed into two equal groups. Group A received 10 IU of I/V Oxytocin along with 1g of I/V tranexamic acid during the third stage of labor immediately after birth and Group B received 10 IU of I/V Oxytocin only immediately after birth. The incidence of postpartum hemorrhage was based on weighing dry and soaked pads using a digital weight machine and blood loss was measured. The drug was considered effective in terms of mean reduction of blood loss after 2 hours.

**Results:** Our study shows that in group A (Oxytocin plus Tranexamic acid), the mean age was 30±4.29 years whereas in group B (Oxytocin alone), the mean age was 31±4.71 years. In group A, mean blood loss was 30 ml± 6.02 whereas in group B, mean blood loss was 40 ml ± 7.88. The mean blood loss volume shows a significant difference in between the two groups with a p-value of 0.0001.

**Conclusion:** The study concludes a significant difference in mean blood loss volume after getting treatment for post-partum hemorrhage in both the treatment groups i.e Oxytocin plus Tranexamic (Gorup A) and Oxytocin alone (Group B). Furthermore, mean blood loss volume was much less in Group A as compared to Group B, illustrating effective treatment modality in Group A.

**Keywords:** Oxytocin; Tranexamic acid; Postpartum hemorrhage; Prophylaxis.

## INTRODUCTION

Postpartum hemorrhage (PPH) is defined as a loss of more than 500ml of blood through the genital tract following the delivery of a baby. It contributes sizably to maternal mortality in all parts of the world. Mortality from PPH is exceedingly common in low resource countries, where efficient means for managing PPH are lacking as measured by a low Human Development Index.[1,2] Its incidence affects 6-11% of pregnancies globally.[1] According to World Health Organization (WHO), the prevalence of PPH in Pakistan is 34%.[2] PPH accounts for about 19.7% of maternal mortality all over the world; varying from 8% in developed countries, 32% in Northern Africa, and 26.1% in South Asia.[3] A study carried out in Pakistan has shown the mortality rate due to PPH approaching 27.1%.[2] Morbidity from PPH may be a grave and long term where 12% would later suffer from severe anemia.[4]

Uterine atony is the most attributable cause for PPH, present in 75% of cases.[5] Poor contractions of the myometrium following delivery fail to contract the vasculature of the uterus resulting in primary PPH. Retained placenta, genital tract injury, and underlying bleeding disorders are other sources of PPH.[6] Extensive blood loss may lead to shock like symptoms in the patient like tachycardia, tachypnea, hypotension, cold clammy skin and depressed consciousness. Managing the third stage of labor actively by using drugs to increase uterine tone, applying controlled cord traction and massaging the uterus after the expulsion of the placenta are ways to control PPH.[7] Oxytocin is a favored drug to be used as auterotonic agent. Such methods may be significant in reducing maternal mortality secondary to PPH.[6] The preventive methods employed for PPH vary globally where along with the use of uterotonics, antifibrinolytic agents like tranexamic acid are used in some areas to control hemorrhage.[3,4] Alone or in combination with uterotonics, they prove to be cost-effective in the

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management of the third stage of labor.[5]

At present, very little evidence is present to show the efficacy of the use of the tranexamic acid.[6,7] Although oxytocin has greater efficacy in PPH prevention but tranexamic can be a promising drug for the same purpose.[8] Hence in this study, additional use of tranexamic acid is implemented to yield local data of its efficacy in its combination with oxytocin and further recommendation can be made. Furthermore, an evident impact of the intervention will also help the experts to define or improvise the local guidelines in prevention of post-partum hemorrhage at an early stage.

## METHODOLOGY

This randomized controlled trial was conducted at Department of Obstretric & Gynarcology, Lady Reading Hospital Peshawar from 1st of November 2019 to 30th of April 2020, after approval from the ethical board. A total of 400 patients were enrolled by non-probability consecutive sampling method. World Health Organization's (WHO) software was used to calculate the sample size at a confidence interval of 95%, and statistical power of 80%. All admitted patients in age group of 18-35 either primigravida or multigravida having completed their 37 weeks of pregnancy were included. However, patients with multiple pregnancies, antepartum hemorrhage, induction of labor, chorioamnionitis, obesity, therapeutic anticoagulants, gestational hypertension, and coagulopathies as evident by clinical record were excluded.

After taking their informed written consent, all patients were worked up with detailed history and clinical examination, followed by routine baseline investigations. The patients were randomly allocated in two groups of 200 each by lottery method; Group A received 10 IU of Oxytocin along with 1g of transamine I/V during the third stage of labor immediately after birth and Group B received 10 IU of Oxytocin only immediately after birth. All the patients underwent standard protocols of vaginal delivery in the lithotomy position and the incidence of postpartum hemorrhage was based on weighing dry and soaked pads using a digital weight machine to measure the amount of blood loss rounding to 500 ml and above. The drug was considered effective in terms of mean reduction of blood loss after 2 hours by checking the quantity of Blood.

Data was analyzed by using statistical software SPSS version 20. Mean ± Standard deviation was calculated for age, weight, height, Body Mass Index (BMI),and blood loss. Frequency and percentages were calculated for parity and gravidity. An Independent T-test was used to compare the mean blood loss between the two groups. P-value of ≤0.05 was considered significant. All the results were presented in the form of tables.

## RESULTS

A sizeable majority, just below 80%, of women in group A (Oxytocin plus Tranexamic acid) were between 26 and 35 years whereas, just over 20% were 15 to 25 years old. The mean age for this group turned out to be 30±4.3 years, while in Group B (Oxytocin alone) age distribution was a little different with around a quarter of the women between 15-25 years whereas the women aged between 26 years and 35 years accounted for 76% of the total in the group. The mean age for this group was 31±4.7 years (approx.).

Age, parity, gravidity, duration, and mean blood loss was associated and compared between the two group and details are based as per Table: 1

## DISCUSSION

Postpartum hemorrhage is a worldwide problem and its effective control measures are tried several times in different controlled setups. About 14 million women experience postpartum hemorrhage every year of which 1-2% die once the bleeding begins and is not controlled within 2-4 hours.[9]

In our study, we compared women receiving IV oxytocin IV tranexamic acid to a group receiving oxytocin only. The former group showed improved results in reducing the mean blood loss from 40. A study carried out by Sekhavat L et al gave similar results to ours. Significant reduction in blood loss was seen with tranexamic acid from the end of vaginal deliveryto two hours postpartum at a loss of 28.02 +/- 5.53ml. Control group lost 37.12 +/- 8.97 mL by 2 hours postpartum. Hemoglobin (Hb) level at the end of 24 hours was higher in the group receiving tranexamic acid.[10] According to a paper by Barbieri RL et

Table 1: Comparison and Association of Different Variable in Group A & B

| Category | Subcategory | GROUP A | GROUP B | P-value |
|---|---|---|---|---|
| AGE | 15-25 years | 42(21%) | 48(24%) | 0.0270 |
| | 26-35 years | 158(79%) | 152(76%) | |
| | Mean and SD | 30 years ± 4.29 | 31 years ± 4.71 | 0.032 |
| PARITY | Primi Para | 84(42%) | 88(44%) | 0.6862 |
| | Multi Para | 116(58%) | 112(56%) | |
| GRAVIDITY | Primi Gravida | 90(45%) | 94(47%) | 0.6882 |
| | Multi Gravida | 110(55%) | 106(53%) | |
| DURATION | ≤ 3 hours | 144(72%) | 150(75%) | 0.497 |
| | > 3 hours | 56(28%) | 50(25%) | |
| MEAN BLOOD LOSS | Mean and SD | 2 hours ± 1.43 | 2 hours ± 1.87 | 0.979 |
| | Mean and SD | 30 ± 6.02 | 40 ± 7.88 | 0.0001 |

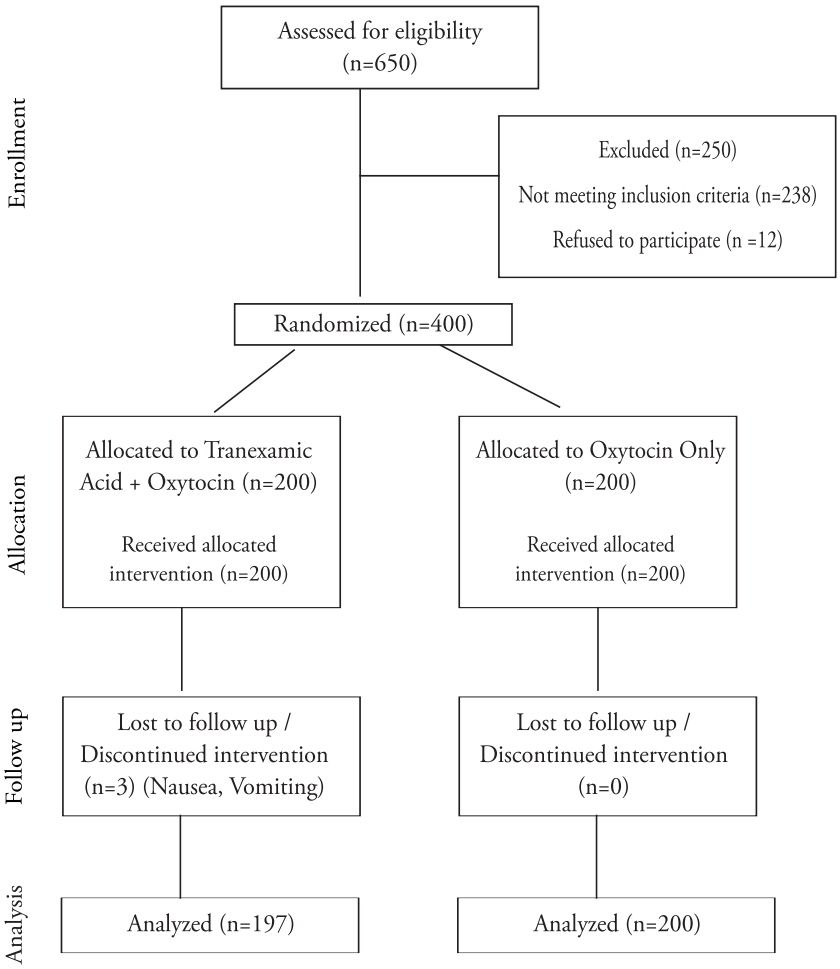


Figure 1: CONSORT diagram showing the flow of participants through each stage of the trial.

al, a French study evaluated 400 women at 35 weeks gestation to receive oxytocin and tranexamic acid combination or a placebo. Mean post-partum blood losses were alike in the group receiving tranexamic acid and placebo (220 mL and 237 mL) and so was the percentage of women to have more than 500ml blood loss (8.1% and 9.8%; P=0.07) This study suggests that both tranexamic acid and oxytocin need not be administered to the same patient unless there is excessive blood loss. One potent uterotonic should be given to all women postpartum to prevent PPH. Excessive blood loss then warrants the use of additional uterotonics and antifibrinolytic therapy. Early recognition of hemorrhage and aggressive management is still the best way to prevent a hazard to the mothers' health.[11]

In a meta-analysis, it was found that within 2 hours of vaginal delivery, 1gm of tranexamic acid was quite effective in reducing the mean blood loss. It was also found that tranexamic acid stays in the blood for a good 9-18 hours and hence its effects evident. However, its combination with IV oxytocin augments these effects.[12] However, its combination with IV oxytocin augments these effects.[12]

In another meta study carried out by Xia Y et al, the beneficial effect of tranexamic acid when postpartum blood loss was estimated in two trials. Patients treated with tranexamic acid had significantly reduced total blood loss (P = .009), blood loss postoperatively (P < .00001), total number of PPH (P = .02). However, this drug comes with a price which is nausea and vomiting. Our study showed similar results in terms of prevention and reduction of blood loss in PPH.[13] According to a study by Ducloy et al., women with postpartum hemorrhage [PPH>800ml] after vaginal delivery were randomly assigned to receive TA (loading dose 4g over 1 hour, then infusion of 1g/h over 6hours) or not. Significant reduction of blood loss was noted between study (median (IQR)173 (59-377) ml) and control groups (221 (105-564) ml), p=0.041. In the TA group, bleeding duration was shorter and less frequent progression to severe PPH as compared to the control group (p < 0.03). Although mild, transient adverse effects were observed more often in the TA group than in the control group (p=0.03). This study is the first to demonstrate that blood loss and maternal morbidity in women with PPH can be reduced with the administration of high dose tranexamic

acid. However, this study was not adequately powered to address safety issues, specifically the rate of VTE postpartum and there is concern that using an antifibrinolytic drug may increase this risk.[14]

In a meta-analysis by Hawker et al., the effect of prophylactic intravenous tranexamic acid or placebo along with 10u IV oxytocin after delivery of fetus on blood loss after vaginal delivery in women at low risk of postpartum hemorrhage was studied. The mean (SD) calculated total blood loss (519 (320) vs 659 (402) ml, p=0.036) and measured blood loss from placental delivery to 2hours postpartum (69 (39) vs 108(53) ml, p<0.001 was significantly lower than the intervention group compared with the control group. The frequency of blood loss >1000 ml was also lower in the TA group (7%vs 18%, p=0.048). Based upon results it was concluded that prophylactic TA reduces blood loss after vaginal delivery in women with a low risk of PPH and enhance maternal health.[15] However, some different papers showed no noteworthy difference between blood loss observed in the tranexamic acid group and control. This could be the reason why the drug is still not used worldwide in terms of preventive measures[16-18].

## CONCLUSION

Our study concludes that Oxytocin plus Tranexamic acid has better effectiveness in preventing post-partum hemorrhage in terms of blood loss quantity as compared to Oxytocin alone.

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## Author's Contribution

HU conceived the idea and wrote the manuscript. MS, BB and RR helped in data collection and analysis, and write up of the manuscript. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Conflict of Interest

Authors declared no conflict of interest

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None

## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.