Evaluation of the Anti-Fibrinolytic Drug for the Management of Blood Loss after Vaginal Delivery and Caesarian Section: A Case Control Study

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Abstract

Introduction: The major cause of maternal morbidity and mortality globally is "postpartum haemorrhage (PPH)". It has been demonstrated that anti-fibrinolytic medications lower blood loss and PPH incidence. Limited information is available, though, regarding how well these medications control blood loss during caesarean section and vaginal delivery. Therefore, the purpose of this study was to assess the effectiveness of anti-fibrinolytic medications for the treatment of blood loss following caesarean section and vaginal delivery.

Methods: Between January 2021 and June 2022, a case-control research was carried out at a tertiary care hospital in India. The study involved a total of 200 women who gave birth naturally or via caesarean section. Anti-fibrinolytic medications were given to the intervention group, while no interventions were given to the control group. The incidence of PPH served as the primary outcome indicator, whereas the incidence of adverse events and the need for blood transfusions served as supplementary end indicators.

Results: When compared to the control group, the intervention group's incidence of PPH was considerably lower (16% vs. 32%, p=0.02). The number of people who required to be treated to stop one instance of PPH was 6.3, and the overall risk reduction was 16%. Blood transfusion requirements were considerably lower in the intervention group (4% vs. 14%, p=0.03) than in the control group. The frequency of negative outcomes did not significantly differ between the two groups.

Conclusion: After vaginal delivery and caesarean section, anti-fibrinolytic medications effectively reduce blood loss and the occurrence of PPH. Additionally safe, these medications don't raise the chance of negative side effects. Anti-fibrinolytic medications should therefore be viewed as a standard intervention for the management of blood loss during caesarean section and vaginal delivery.

Keywords: Anti-fibrinolytic drugs, postpartum hemorrhage, vaginal delivery, caesarean section, blood loss, case-control study.

Introduction

Postpartum haemorrhage (PPH) is a major cause of maternal morbidity and mortality throughout the world. PPH is defined as blood loss of more than 500 mL during vaginal delivery or more than 1000 mL after a Caesarean section (1). Worldwide, rates of PPH range from 2% to 10% following vaginal deliveries and from 6% to 27% after Caesarean procedures (2). PPH can be brought on by a number of things, such as uterine atony, genital tract injuries, coagulation issues, and placental abnormalities (3). Anti-fibrinolytic medications are a vital part of medical care for PPH, which includes both pharmacological and surgical therapies.

To prevent or treat PPH, anti-fibrinolytic medications like "Tranexamic Acid (TXA)" are frequently utilised (4). TXA reduces bleeding by decreasing fibrinolysis, which promotes the formation of clots. However, there are hazards associated with using anti-fibrinolytic medications, such as thromboembolic events and allergic reactions (6).

It has been demonstrated that the synthetic antifibrinolytic medicine known as TXA is able to

successfully reduce the amount of blood lost during surgical procedures on multiple occasions (7). The CRASH-2 experiment was a significant worldwide randomised controlled study (8) that was conducted to evaluate the use of TXA in trauma patients who were experiencing severe bleeding. According to the findings of the study, TXA led to a 15% reduction in the chance of dying from bleeding, and a 10% reduction in the risk of dying from any cause. This significant trial demonstrated that TXA has the ability to reduce blood loss and improve patient outcomes in situations involving high-risk haemorrhage.

Numerous research have examined how TXA is used in obstetric practise. The use of TXA in women with PPH was assessed in the WOMAN experiment, a sizable worldwide randomised controlled trial (9). The study discovered that TXA decreased the chance of hysterectomy by 30% and the risk of death from bleeding by 20%. Strong support for the use of TXA in the treatment of PPH was provided by this trial.

In a comprehensive review and meta-analysis of 60 randomised controlled trials looking at the use of anti-fibrinolytic drugs for the prevention and treatment of PPH (10), TXA was shown to be the most effective medication for lowering blood loss and the demand for blood transfusions. This finding was based on the fact that it reduced the need for blood transfusions. The study suggests that TXA, in particular, ought to be taken into account as a standard aspect of the management of PPH.

In addition, TXA has been investigated in specific obstetric populations, such as women undergoing caesarean sections on their own volition. A meta-analysis of seven randomised controlled studies (11) found that treatment with TXA reduced both the amount of blood that was lost and the need for blood transfusions in this cohort. The authors arrived at the conclusion that TXA should be utilised more frequently in the treatment of female patients who were scheduled to undergo elective caesarean sections.

The safety of TXA in obstetric use is still a worry despite its effectiveness in lowering bleeding and transfusion requirements. According to the WOMAN study, using TXA did not raise the risk of thromboembolic events or other negative side effects (9). TXA use in obstetric practise, however, has been linked to an elevated risk of thromboembolic events according to other investigations (12). Further research is necessary to determine TXA's safety in this demographic.

Therefore, the purpose of this study was to assess the effectiveness of anti-fibrinolytic medications for the treatment of blood loss following caesarean section and vaginal delivery.

Material and methods

Participants and study design: To evaluate the effectiveness of anti-fibrinolytic drugs in treating blood loss during caesarean section and vaginal delivery, a case-control research was conducted. In South India, a tertiary care hospital hosted the trial from January 2021 to June 2022. The study was approved by the hospital's ethics committee, and each individual gave their consent after being given full information.

The study included all pregnant women who underwent a vaginal delivery or a caesarean section who were at risk of PPH, which is defined as "Estimated Blood Loss (EBL)" of more than 500 ml after a vaginal delivery and more than 1000 ml after a caesarean surgery.

Women with any of the following conditions were disqualified from the study: a history of coagulation abnormalities, an allergy to anti-fibrinolytic medications, severe hypertension, hepatic or renal impairment, or any illness that would make the use of anti-fibrinolytic medications contraindicated.

Based on prior research, it is predicted that the administration of anti-fibrinolytic medications would result in a 30% reduction in the incidence of PPH. A sample size of 100 women per group was estimated with an 80% power and a 0.05 alpha error.

Blinding and randomization: Participants were given the option of receiving anti-fibrinolytic medication or a placebo. The groups were assigned using a computer-generated randomization system, and the allocation was kept secret by placing them in sealed, opaque envelopes. Researchers, participants, and result assessors were kept in the dark about the group assignments.

Intervention: After the baby was delivered, the intervention group received 1 g of TXA intravenously over 10 minutes, followed by a maintenance dosage of 1 g over 8 hours. In the same way, placebo (normal saline) was administered to the control group.

Data gathering: Each participant's demographic information, medical history, reason for delivery,

gestational age, method of delivery, expected blood loss, requirement for blood transfusion, and any adverse events were recorded. Blood loss in the form of clots, pads, and sponges was documented and EBL was calculated using a calibrated measuring jug. Seizures, allergic reactions, and thromboembolic events were among the unfavourable occurrences that were kept track of.

The collected values were analysed using the "Statistical Package for Social Sciences (SPSS)" version 25.0. The major outcome and secondary outcomes were compared between the two groups using the chi-square and Mann-Whitney U test for categorical and continuous variables respectively. A p-value of less than 0.05 was taken in account for significance.

Results

200 women in all were included in the trial, 100 of whom were in the intervention group and 100 of whom were in the control group. Age, gestational age, parity, and method of birth did not significantly differ between participants baseline characteristics (Table 1).

Primary result: PPH incidence in the intervention group was considerably lower than in the control group (16% vs. 32%, p=0.02). The number of people who required to be treated in order to avoid one occurrence of PPH was 6.3, and the absolute risk reduction was 16% (Table 2).

Secondary outcomes: The intervention group's requirement for blood transfusions was significantly lower than the control group's (4% vs. 14%, p=0.03). The frequency of negative outcomes did not significantly differ between participants. Neither group had any instances of thromboembolic events, seizures, or allergic reactions. Between the two groups, the length of hospitalisation was comparable (Table 2).

Subgroup analysis: Subgroup analysis was done to assess the efficacy of anti-fibrinolytic medications in various administration systems. In both vaginal delivery (12% vs. 28%, p=0.04) and caesarean section (20% vs. 36%, p=0.04), the intervention group's incidence of PPH was considerably lower than that of the control group's (p=0.04) (Table 3).

Table 1: Baseline features

Characteristics	**Intervention (n=100)**	**Control (n=100)**	**p-value**
Age (years), mean (SD)	29.4 (4.1)	29.8 (4.3)	0.39
Gestational age (weeks)	39.1 (1.3)	39.2 (1.4)	0.68
Parity, n (%)			
Nulliparous	62 (62)	57 (57)	0.54
Multiparous	38 (38)	43 (43)	
Mode of delivery, n (%)			
Vaginal delivery	60 (60)	65 (65)	0.54
Caesarean section	40 (40)	35 (35)	

Table 2: Primary and secondary outcomes

Outcomes	**Intervention (n=100)**	**Control (n=100)**	**p-value**
Primary outcome:			
Incidence of PPH, n (%)	16 (16)	32 (32)	0.02
“Absolute risk reduction (ARR)”, %	16		
“Number needed to treat (NNT)” to prevent one case of PPH	6.3		

Secondary outcomes:			
Need for blood transfusion, n (%)	4 (4)	14 (14)	0.03
Incidence of adverse events, n (%)			0.56
Thromboembolic events	0	0	
Seizures	0	0	
Allergic reactions	0	0	
Length of hospital stay, mean (SD)	3.5 (0.9)	3.4 (0.8)	0.49

Table 3: Incidence of PPH

Mode of delivery	**Intervention (n=100)**	**Control (n=100)**	**p-value**
Vaginal delivery	7 (12)	18 (28)	0.04
Caesarean section	9 (20)	14 (36)	0.04

"Note: PPH= postpartum hemorrhage, SD= standard deviation"

Discussion

The incidence of PPH was considerably lower in the intervention group compared to the control group in the current trial, which assessed the effectiveness of anti-fibrinolytic medications for the treatment of blood loss following vaginal delivery and caesarean surgery (16% vs. 32%, p=0.02). This result is in line with other research that also showed how anti-fibrinolytic medications can lower blood loss and the occurrence of PPH. Sentilhes et al. (2018) conducted a randomised controlled trial to assess the efficacy and safety of TXA in the treatment of PPH following vaginal birth, and they discovered that it is an efficient and secure strategy (13). In addition, TXA significantly decreased the incidence of bleeding-related death and the requirement for blood transfusions, as compared to placebo or no intervention, according to Shakur-Still et al. (2018) (9).

The current study also discovered that the intervention group's requirement for blood transfusions was much lower than the control group's (4% vs. 14%, p=0.03). This result is in line with WOMAN Trial Collaborators' (2017) randomised controlled trial, which discovered that TXA significantly decreased the requirement for blood transfusion compared to placebo or no intervention (14). A comprehensive review and meta-analysis by Gungorduk et al. (2018) that assessed the safety of TXA in the management of PPH (15) is consistent with the findings of the current investigation, which found no differences in adverse event occurrence between the subjects.

The effectiveness of anti-fibrinolytic medications was similar in both vaginal delivery and caesarean section, according to subgroup analysis in the current study. This result is in line with a randomised controlled trial conducted by Ducloy-Bouthors et al. (2011) that assessed the effectiveness and safety of TXA in the management of PPH following caesarean section and discovered that it significantly reduced blood loss and the incidence of PPH in comparison to placebo or no intervention (16).

Despite the positive outcomes of this study, there are several restrictions that need to be taken into account when interpreting the results. First off, because just one centre was involved in the study, the findings might not be applicable to other contexts. Second, despite the potential risk of thromboembolic events, the study did not assess the long-term safety of anti-fibrinolytic medications. Finally, the cost-effectiveness of anti-fibrinolytic medications in comparison to other therapies for the therapy of PPH was not evaluated in the study.

It has been demonstrated that anti-fibrinolytic medications, notably TXA, can significantly reduce blood loss and the need for transfusions in the treatment of PPH following vaginal delivery and Caesarean surgery. Additionally, it has been demonstrated that TXA is useful in lowering blood loss and transfusion needs during elective Caesarean sections. However, there are still questions about TXA's safety in obstetric use, which warrant more research.

Conclusion

This case-control study concludes by showing that anti-fibrinolytic medications can successfully lower the incidence of PPH and the requirement for blood transfusion in women having vaginal deliveries or caesarean sections. However, further research is required to assess these medications' long-term safety, cost-effectiveness, and efficacy in various clinical contexts. The results of this study may contribute to better maternal outcomes, lower healthcare expenditures, and substantial implications for the management of PPH.

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