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ORIGINAL ARTICLE

Major Trauma and the use of Tranexamic Acid in Children

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ABSTRACT

Objective was to determine reduction in blood loss in children with major trauma with or without using Tranexamic acid

Methods: A study included 260 patients admitted to pediatric surgery departments at Mayo Hospital, Children's Hospital, and Jinnah Hospital in Lahore, from September, 2018 to April, 2019. Patients were divided into Tranexamic acid and control groups. Both groups received standard treatment and blood transfusion requirements. Patients were followed for length of stay and final outcomes.

Results: Mean injury severity score in case and control groups was 26.61±11.17 and 29.00±11.64 respectively. Mean hospital stay was significantly shorter (p = 0.002], massive blood transfusions were significantly low [3.8% vs. 38.46%, p-value<0.001] and need of surgery [24.6% vs. 46.15%, p <0.001]. Mortality rate 1.54% vs. 7.69%, p =0.018 and discharge rate 98.64% vs. 92.31%,p = 0.018). Blood transfusion requirement and need of surgery were significant predictors for mortality in this study.

Conclusion: Results of this study demonstrate that Tranexamic Acid can be effectively used to minimize blood transfusion requirement in children with major trauma. It effectively reduces the need of massive blood transfusion, minimizing mortality and shortens the hospital stay for pediatric patients.

Keywords: Tranexamic acid, Effectiveness, Blood loss, Children, Trauma

INTRODUCTION

In 2013, 973 million individuals worldwide were injured and needed medical treatment, with 4.8 million of these people dying as a result of their injuries.(1) Among children and adolescents under the age of 18 years, trauma is the leading cause of death.(2) Haemorrhage is still a major cause of trauma-related mortality.(3)

Any injury that has the potential to inflict long-term incapacity or death is considered major trauma.(4) There are several causes of blunt and penetrating major trauma, including falls, motor vehicle crashes, knife wounds, and gunshot wounds.(5) Traumatic haemorrhage reduces circulation volume, reduces oxygen-carrying capacity, and causes coagulopathy. The restoration of circulation volume is critical for oxygen delivery. Red blood cell transfusion enhances oxygen transport and aids to the restoration of appropriate circulation volume, although it is also related with worsening when administered alone.(6) Some claim that fresh whole blood is the best transfusion product for patients who need huge transfusions of specific components since all blood elements are delivered in physiological proportions.(7, 8)

Different therapies are used in order to minimise the need for blood transfusions. Haemorrhage management in adult trauma patients seems to be possible with the use of antifibrinolytic drug. Tranexamic acid Inhibit plasminogen activation to plasmin, a serine protease that breaks down fibrin and prevents the development of a blood clot. Tranexamic acid was utilized in emergency resuscitation in the MATTERS I, II cohort trials, which included more than 2000 war injuries.(9) Tranexamic acid, an anti-fibrinolytic, decreased blood loss and the requirement for blood transfusions in children undergoing elective surgery.(10-12) Hypothermia and hypovolaemic shock are common in traumatically wounded patients, despite the fact that elective procedures are conducted under controlled conditions.(13, 14) Traumatic haemorrhage has a distinct pathophysiology from non-traumatic surgical bleeding, however. Tissue damage is extensive and uncontrolled in the traumatic haemorrhage, and patients often face delays in getting therapy.(9,10)

In juvenile patients who have had serious trauma, there is little evidence that Tranexamic acid reduces blood loss because of a lack of published data. A comparison of the effectiveness of Tranexamic acid usage without usage in decreasing blood loss in children with significant trauma in our local community is thus urgently required. To close the present paediatric trauma treatment gap, investigated the usage and advantages of Tranexamic acid in our local population's wounded children.

MATERIAL AND METHODS

All patients presenting with major trauma were assessed through injury severity score and patients with score in range 14-49. This selection is based on severity score and can include any type of trauma. Informed consent was taken from parents or legal guardians. Parents/ Guardians were given brief information regarding the condition and possible outcome regarding Childs injury. All pros and cons were briefly described for all possible outcomes. Study protocol was also briefly described to avoid any confusion later on for the parents/guardian of the child.

This randomized controlled trial was completed in 6 months Nov 2018 to May, 2019. Sample size of 260 patients 130 patients in each groups is estimated by using 5% level of significance, 90% power of test with expected mean value of blood loss with Tranexamic acid as 10±9 and in placebo as 18± 13(1) from reference study.6 The patients with history of allergic reaction with Tranexamic acid, thrombosis or embolism, injury severity score (ISS) >49 and any indication for surgical explorations were excluded from the study.

At study entry baseline demographics (Age, gender, duration of injury, ISS score, Coagulopathy) was recorded. Both were given standard treatment as per hospital policy. In addition, Tranexamic acid was given at the dose of 15mg/kg IV within 3 hours (maximum dose 1 gm) followed by 2mg/kg/hr IV infusion over next 8 hours. In the control patients were given standard treatment.

Blood transfusion requirement for both groups were noted as massive blood transfusion or reduced blood transfusion (as per operational definition). The patients were followed up for the duration of hospital admission and final outcome (discharged, mortality) as well as the length of hospital stay shall be noted.

The objective of the study was to compare blood transfusion requirement in children with major trauma with or controls. Significant blood loss was defined as the loss of 50% of blood volume in 3 hours or a rate of 2-3 ml/kg/min. Effectiveness was defined as reduced blood transfusion within 3 hours of presentation in children with major trauma. Major trauma was when a child presented with Injury Severity Score (ISS). Massive

Blood Transfusion: was transfusion of at least 1 blood volume equivalent using 70 ml/kg blood volume criteria. Reduced Blood Transfusion was transfusion of less than 1 blood volume equivalent within 3 hours using 70 ml/kg volume criteria. Mortality: was defined as patient's death within 7 days during hospital admission.

SPSS-26 was used to input the data. Mean and standard deviation were used for numerical data, such as age. The frequency and proportion of qualitative factors were presented with percentage. Requirement of blood transfusion, need of surgery, Mortality and final outcome was compared between group with the help of chi Square test. Logistic regression was applied to see the risk of mortality in relation to surgical intervention, transfusion requirement and diagnosis of the patients. Measure of risk was determined with Exp (β): Odds ratio. A p-value of 0.05 or below was deemed considerable.

RESULTS

Average patient age in each group was 8.29±2.46 years and 8.20±2.62 years. In Tranx group 89 (68.46%) were male and 41(31.54%) were female while in Group-B 76 (58.5%) were male and 54(41.5%) were female patients. Male patients dominate female patients in number. In this study, we compared the effectiveness of Tranexamic acid versus controls in reducing blood loss in children with major trauma. Mean injury severity score in Tranexamic acid versus controls was 26.61±11.17 and 29.00±11.64. Mean hospital stay was significantly shorter [6.27 vs. 7.69, p-value = 0.002], blood transfusions were significantly low [3.8% vs. 53.85%, p-value<0.001] and need of surgery [24.6% vs. 46.15%, p-value<0.001] was significantly low for Tranexamic acid patients. Mortality rate was significantly higher for controls (1.54% vs. 7.69%, p = 0.018) and discharge rate was significantly higher for Tranexamic acid patients (98.64% vs. 92.31%, p = 0.018). Blood transfusion requirement (Odds Ratio= 25.078, CI-95%:3.57-176.11) and need of surgery (Odds ratio= 0.141, CI-95%:0.028-0.709) were significant predictors for mortality in this study.

Logistic regression analysis showed that with Group-B odds of mortality increases 0.188 times higher as compared to Group-A treatment. Treatment group, blood transfusion requirement and need of surgery showed risk towards morality but need of surgery was significant predictor for mortality as per logistic regression model. Risk of mortality increases 0.198 times higher with need of surgery, with blood transfusion requirement risk of mortality increases 16.94 times but it was not statistically significant.

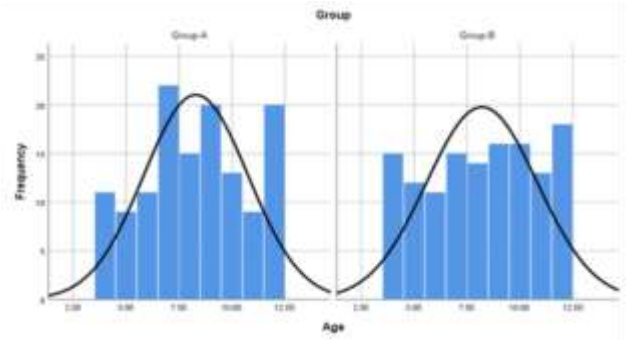

Figure-1: Histogram for Age of patients (Years)

Table-1: Type of Injury in Study Groups

	Exp group	Control	Total
Blunt trauma of the abdomen (BTA)	37(28.5%)	34(26.16%)	71
FAI	3(2.3%)	8(6.16%)	7
Fall	17(13.08%)	24(18.46%)	41
RTA (Road Traffic Accident)	73(56.15%)	64(49.23%)	137

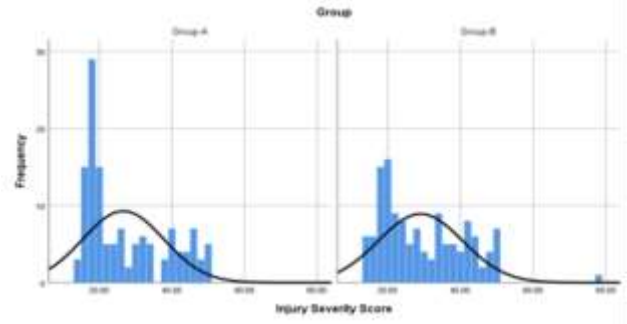

Figure-2: Histogram for Injury Severity Score

Table-2: Hospital Stay in Study Groups (Days)

	Exp group	Control
Number	130	130
Mean	6.27	7.69
SD	2.95	4.61
Min- Max	2-20	1-48
p-value	0.002	

Table-3: Requirement of blood transfusion, surgery in study Groups

		Exp group	Control	Total	P value
Blood transfusion	Massive	5(3.8%)	70(53.85%)	75	<0.001
	Reduced	125(96.2%)	60(46.15%)	185	
Requirement of surgery	Yes	32(24.6%)	60(46.15%)	92	<0.001
	No	98(75.4%)	70(53.85%)	168	
Mortality	Yes	2(1.54%)	10(7.69%)	12	0.018
	No	128(98.46%)	120(92.31%)	248	
Mortality	Yes	128(98.46%)	120(92.31%)	248	0.018
	No (discharged)	2(1.54%)	10(7.69%)	12	

DISCUSSION

The appropriateness of trauma scoring systems for pediatric patients is unclear due to their advantages and disadvantages. The Glasgow Coma Scale evaluates consciousness, while the Injury Severity Score assesses trauma severity. The Pediatric Trauma Score considers skeletal injuries, skin wounds, central nervous system damage, and physiological parameters for a comprehensive assessment. (15,16).

The National Advisory Committee for Aeronautics (NACA) score is commonly used to assess injury severity in prehospital phases. However, trauma scoring systems for adult patients have been criticized for not providing reliable prognostic information for children with multiple injuries. It is essential to continue evaluating trauma scoring systems to ensure they are tailored to the unique needs of pediatric patients with multiple injuries.(17)

Trauma requiring massive blood transfusions can hinder life-saving efforts and worsen outcomes. Early hemorrhagic shock patients should receive antifibrinolytic medication, such as tranexamic acid, which inhibits plasminogen activation and decreases fibrinolysis. This treatment reduces mortality and blood loss in major elective paediatric surgery, but its efficacy and safety in trauma patients remain unproven.(18)

According to Matthew J. Eckert's study, the use of Tranexamic Acid was observed in approximately 10% of pediatric combat trauma patients. TXA was primarily administered in the people suffering from the abdominal related severe injury or

extremity related injury and also in peoples with the metabolic acidosis. The study found that the use of TXA was associated with a lower mortality rate in these patients. This finding underscores the potential benefits of TXA in managing pediatric trauma patients, especially those with severe injuries and metabolic acidosis. It suggests that early administration of TXA may contribute to improved patient outcomes by reducing the risk of mortality. Neither a problem with safety nor a problem with medicine was discovered. A Cochrane study of Tranexamic Acid usage in paediatrics revealed a substantial decrease in transfusion needs in children having surgery with no evident side consequences.(19,20)

In the 2010 CRASH-2 study,(21) Tranexamic Acid was found to be effective in reducing all-cause death and bleeding-related deaths among injured. Similarly, patients who received TXA treatment at the Afghanistan, also had promising outcomes.

These findings suggest that TXA may be a valuable treatment option in managing trauma patients, particularly in reducing mortality and bleeding-related fatalities. However, more research is needed to determine the optimal dosage, timing, and potential adverse effects of TXA in different patient populations. Overall, the use of TXA in managing trauma patients represents a promising area of future research and clinical practice.(9)

When Tranexamic Acid has been used in paediatric surgery, meta-analyses show that less blood loss and fewer blood transfusions are required. Traumatic haemorrhage has a distinct pathophysiology from non-traumatic surgical bleeding, however. As a result of significant, uncontrolled tissue damage, patients often face delays in getting therapy.(10,12)

Tranexamic Acid's therapeutic potential must be considered in conjunction with the current surgical literature, which shows that this medication reduces blood loss and transfusion needs during major paediatric surgery. Aside from haemorrhage management, the usage of Tranexamic Acid may have other benefits such as better neurologic and pulmonary outcomes, as well.

CONCLUSION

It is possible to efficiently employ tranexamic acid to reduce the need for children who have suffered serious trauma to get blood transfusions. The use of tranexamic acid results in a significant reduction in the requirement for major blood transfusions, which helps lower the risk of mortality and shorten the length of hospital stays for young patients.

Recommendations: All current critical hemorrhage recommendations now advise the use of tranexamic acid, which is crucial to paediatric PBM procedures. We should work on improving our local guidelines regarding use of Tranexamic acid in pediatric trauma for better outcome of these patients. Improvement in transfusion protocol may result in faster, better and safer care for the patients. Additional prospective studies are required to examine transfusion and fluid strategies in the context of pediatric trauma. The aim of such investigations should be to establish treatment protocols for fluid and hemotherapy that are founded on a reliable and comprehensive database. By developing and implementing such protocols, healthcare professionals can provide treatment recommendations that are based on the most current and accurate data.

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