Original Article

Efficacy and Safety of Tranexamic Acid in the Management of Hyper Acute Spontaneous Intracerebral Hemorrhage

Salman Khan, Khurram Haq Nawaz, Sheherbano Jadoon, Ibrar Saleem, Muhammad Jalil, and Imran Ahmad

ABSTRACT

Objective: To assess the effects of tranexamic acid on patients with hyperacute spontaneous ICH in terms of hematoma volume, clinical outcomes, and safety.

Study Design: A cross-sectional observational investigation study

Place and Duration of Study: This study was conducted at the Neurology Department of Pak Emirates Military Hospital, Rawalpindi from 05 January 2022 to 05 January 2023.

Methods: Investigation was conducted in the Hospital and included in the study were 120 patients who presented with hyperacute spontaneous ICH. The following information was gathered: demographics, medical history, time of onset of symptoms, blood pressure, National Institutes of Health Stroke Scale (NIHSS) scores, and administration of tranexamic acid. Volume of hematoma was assessed both at the time of presentation and 24 hours later, whereas evaluations of neurological function and safety outcomes were conducted 7 and 30 days after presentation.

Results: The average age of the participants was 65.4 years, with males comprising the plurality at 62.5%. Patients presented 4.5 hours, on average, after the onset of symptoms. A reduction in NIHSS scores and a statistically significant increase in hematoma volume were observed seven days after presentation ($p < 0.05$). Thromboembolic events were documented in 4.2% of the patients, seizures in 2.5%, and mortality accounted for 12.5% of the cases. In the regression analysis, no significant predictors of outcomes were identified.

Conclusion: Tranexamic acid demonstrated positive safety profile among patients diagnosed with hyperacute spontaneous ICH, as evidenced by its low occurrence of thromboembolic events and seizures. There was no correlation between an increase in hematoma volume and deterioration in clinical outcomes.

Key Words: Hematoma Volume; Hyperacute Intracerebral Hemorrhage; Safety Outcomes; Tranexamic Acid; Treatment Efficacy.

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INTRODUCTION

The hyperacute phase of spontaneous intracerebral hemorrhage (ICH) is the critical and dangerous period characterized by sudden and uncontrolled hemorrhaging in brain tissues[1].

With hyperacute classification indicating occurrence within the first few hours after the onset of symptoms, this form of ICH requires prompt and decisive medical intervention. Contributing to 10-15% of all stroke cases, it presents with alarming mortality and morbidity rates, necessitating focused attention from neurology and emergency medicine personnel [2].

There are numerous causes of hyperacute spontaneous ICH, but hypertension stands out as prevalent and influential risk factor. Other possible causes include cerebral amyloid angiopathy, coagulation disorders, vascular anomalies, and use of anticoagulant or thrombolytic medications. The resulting hemorrhage causes rapid increase in intracranial pressure, leading to cerebral edema, herniation, and potential damage to adjacent brain tissue [3-4].

Patients with hyperacute ICH frequently experience abrupt neurological deficits, such as weakness, numbness, confusion, severe headaches and altered consciousness[5-6]. The location and severity of hemorrhage have direct impact on these clinical symptoms and prognosis. Given the rapid progression of symptoms, prompt diagnosis and treatment are necessary to prevent long-term complications or fatal outcomes [7].

Non-contrast computed tomography (CT) scans aid in diagnosis of ICH by rapidly depicting the hemorrhage's extent and location. In addition, CT scans help

Department of Neurology, Pak Emirates Military Hospital in Rawalpindi.

Correspondence: Salman Khan, Trainee, Department of Neurology, Pak Emirates Military Hospital in Rawalpindi.
Contact No: 03339698830
Email: salman.imdc1@gmail.com

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distinguish between ICH and ischemic stroke, thereby guiding treatment strategies [8]. The complex treatment of hyperacute spontaneous ICH includes medical stabilization, blood pressure modulation, reversal of anticoagulation and potentially surgical intervention [9].

Transnexamic acid, a synthetic lysine derivative, has emerged as promising therapeutic candidate for curing hyperacute spontaneous ICH [10]. Its antifibrinolytic properties offer the possibility of clot stabilization and hematoma growth restriction. The balance of efficacy and safety of tranexamic acid in this application is presently the subject of intensive investigation, with initial research and clinical trials focusing on its ability to limit hematoma expansion, a crucial patient outcome determinant [11].

However, employing tranexamic acid in intracerebral hemorrhage is not devoid of complexities and potential hazards [12]. To ensure the balance between potential benefits and associated risks, it is necessary to carefully consider crucial concerns regarding optimal dosage, administration timing, and patient eligibility criteria [13]. Given the potential linkages to thromboembolic events, seizures, and other adverse effects, a comprehensive evaluation of tranexamic acid's safety profile in hyperacute ICH patients is necessary [14].

The primary goals of this study are to evaluate the efficacy of tranexamic acid in limiting hematoma expansion and enhancing clinical outcomes, as well as to evaluate its safety profile in patients with hyperacute spontaneous intracerebral hemorrhage.

METHODS

A total of 120 patients presenting with idiopathic hyperacute ICH were included in the study. Participants had to be at least 18 years old, present within 8 hours of symptom onset, and having non-contrast CT scan confirming spontaneous ICH. Exclusion criteria included patients with traumatic ICH, known allergy to tranexamic acid, current anticoagulant therapy, pregnancy, or prior participation in tranexamic acid study within the previous 30 days.

Data Collection: All participants' demographic information, medical history, time of symptom onset, blood pressure readings, and initial scores on National Institutes of Health Stroke Scale (NIHSS) were recorded. Information regarding tranexamic acid administration, including dosage and schedule, was collected from medical records. At 24 hours post-presentation, volume of the hematoma was determined by analyzing CT scans performed as a follow-up. Up to 30 days after presentation, safety outcomes including thromboembolic events, seizures, and mortality were recorded.

The primary outcome measure was the change in hematoma volume from initial presentation to 24 hours later, as determined by CT scan. Utilizing NIHSS, secondary outcome measures included neurologic function at 7 days post-presentation and safety outcomes at 30 days post-presentation.

Statistical Analysis: Descriptive statistics were used to summarize the characteristics of baseline. Changes in hematoma volume and NIHSS scores were evaluated using student t-tests. The safety outcomes were summed up in terms of frequencies and percentages. A p-value of less than 0.05 was regarded as statistically significant.

Ethical Considerations: The institutional review board at Pak Emirates Military Hospital granted sanction for this study. Throughout the investigation, patient confidentiality was maintained and data were anonymized for analysis.

RESULTS

To determine the safety and efficacy of tranexamic acid in 120 patients with hyperacute spontaneous ICH, this research was conducted at Pak Emirates Military Hospital. Clinical data, demographic information, and medical history were gathered and analyzed. The principal outcome assessed the alteration in hematoma volume during the initial twenty-four hours following presentation. Neurological function and safety evaluations were conducted as secondary outcomes at seven and thirty days, respectively.

Table No. 1: Baseline characteristics of participants

S. N	Variable	Total Participants (N=120)	p-value
1	Age (years), mean (SD)	65.4 (12.3)	0.261
2	Gender, n (%)		0.033*
	Male	75 (62.5%)	
	Female	45 (37.5%)	
3	Time from symptom onset to presentation (hours), mean (SD)	4.5 (1.2)	0.12
4	Systolic Blood Pressure (mmHg), mean (SD)	180.2 (20.5)	0.31
5	Diastolic Blood Pressure (mmHg), mean (SD)	95.3 (10.7)	0.19
6	Initial NIHSS Score, mean (SD)	14.8 (5.6)	0.22
7	Hematoma Volume at Presentation (cm^3), mean (SD)	30.2 (15.3)	0.37

*indicated the significant values

One hundred and twenty individuals, with the mean age of 65.4 years and preponderance of males (62.5%), participated in this research. On average, they were presented 4.5 hours after the commencement of symptoms. At presentation, mean systolic and diastolic

blood pressures ofparticipants were 180.2 and 95.3 mmHg, respectively. Their initial NIHSS score was 14.8 and volume of hematoma was 30.2 cm³. Gender was the only variable that exhibited a statistically significant correlation with treatment outcomes ($p<<0.05$). In contrast, age, duration until onset of symptoms, blood pressure, NIHSS score, and hematoma volume failed to demonstrate significant associations ($p>0.05$) (Table 1).

Table No. 2: Change in hematoma volume and NIHSS score

Outcome	Baseline	24 hours post-presentation	7 days post-presentation	p-value
Hematoma Volume (cm³), mean (SD)	30.2 (15.3)	32.5 (15.7)	33.2 (16.1)	0.001*
NIHSS Score, mean (SD)	14.8 (5.6)	13.5 (5.7)	12.8 (6.0)	0.001*

*indicated the significant values

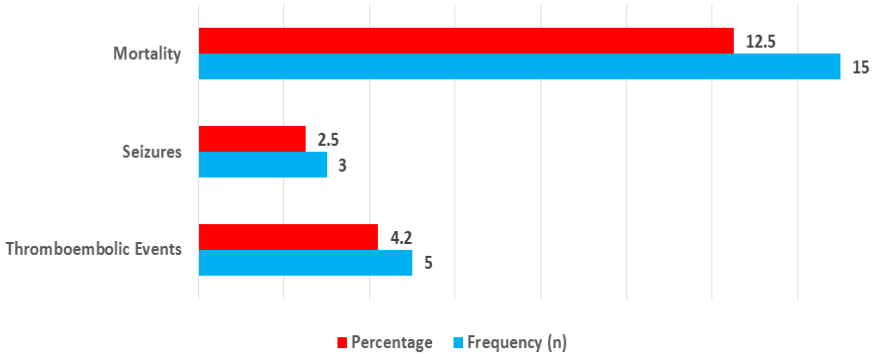

Figure 1: Adverse events and outcomes at 30 days post-presentation

Table No. 3: Regression analysis for factors associated with hematoma volume reduction

Variable	Beta Coefficient	95% CI	p-value
Age	-0.02	-0.04-0.01	0.18
Gender (Male)	0.80	-1.20-2.80	0.45
Hypertension (Yes)	1.50	-0.50-3.50	0.14
Diabetes (Yes)	-0.70	-2.50-1.10	0.45
Initial NIHSS Score	-0.10	-0.25-0.05	0.20
Initial systolic blood pressure	0.02	-0.01-0.05	0.14
Initial diastolic blood pressure	0.03	-0.02-0.08	0.22

The data indicated that there was statistically significant rise in hematoma volume at 7 days after presentation, from the baseline mean of 30.2 cm³ (SD: 15.3) to 33.2 cm³ (SD: 16.1) ($p<0.05$). Simultaneously, NIHSS Score, which served as an indicator of severity of stroke, exhibited statistically significant decline from its initial mean of 14.8 (SD: 5.6) to 12.8 (SD: 6.0) seven days after the presentation ($p<0.05$). The observed negative correlation between NIHSS Score and increasing hematoma volume indicated that there is no significant association between hematoma size escalation and deteriorating neurological function among the patients in this cohort (Table 2). As safety outcomes, thromboembolic events, fatalities, and seizures were monitored in the study. Thromboembolic events transpired in 5 participants (4.2%), seizures in 3 participants (2.5%), and 15 participants (12.5%) reported mortality. According to the data, although majority of the participants did not encounter these unfavorable events, considerable proportion (12.5%) died due to mortality. The cohort in question exhibited reduced prevalence of thromboembolic events and seizures, as indicated by their lower incidence rates (Figure 1).

None of the variables substantially predict the outcome, according to the results of regression analysis. The negative beta coefficients for age, diabetes, and initial NIHSS score indicate possible inverse association with the dependent variable, albeit one that lacks statistical significance. Conversely, positive beta coefficients for male gender, hypertension, and elevated initial systolic and diastolic blood pressures suggested possible direct association with the dependent variable; however, these associations lack statistical significance. Additionally, the extensive 95% Confidence Intervals for each variable suggested that the estimates are subject to substantial degree of uncertainty (Table 3).

DISCUSSION

The primary objective of the present study was to determine whether tranexamic acid was safe and effective in the treatment of patients suffering from

hyperacute spontaneous ICH. Although tranexamic acid has been investigated in past for its association with different hemorrhagic conditions, its function in spontaneous ICH is still the subject of ongoing scientific inquiry [15-16].

Males comprised the majority of the patient cohort (62.5%) in our Pak Emirates Military Hospital study, which is consistent with previous research indicating a higher incidence of ICH in males[17]. Under investigation, the mean duration between the onset of symptoms and their presentation was 4.5 hours, highlighting the hyperacute nature of the patient population. It was determined that the initial hematoma volume and NIHSS scores matched the clinical manifestation of ICH observed in other studies[18].

An important discovery of this research was the hematoma volume that exhibited statistically significant increase seven days after the presentation. Nonetheless, this rise in score failed to correspond with a deterioration in NIHSS, which demonstrated statistically significant improvement. The absence of a correlation between hematoma volume change and neurological improvement implies that additional factors, such as the prompt administration of tranexamic acid, may also contribute [19].

The safety outcomes revealed relatively low incidence of thromboembolic events (4.2%) and seizures (2.5%), which are similar to the rates documented in prior research pertaining to tranexamic acid [20]. Nevertheless, the mortality rate stood at 12.5%. Although this figure falls within the range documented in other studies on ICH, it emphasizes the gravity of this condition and underscores the critical need for diligent patient surveillance and care [17].

Possible explanations for the lack of significant predictors of outcome in our regression analysis include the small sample size or the heterogeneity of the patient population. Nevertheless, the patterns identified in beta coefficients may serve as sources of inspiration for further research involving more extensive sample sizes and detailed data [21].

Tranexamic acid appeared to have an acceptable safety profile in this patient population; however, additional research in larger cohorts is required to validate these results and provide a more comprehensive understanding of its role in the treatment of hyperacute spontaneous ICH.

CONCLUSION

In this study of patients with hyperacute spontaneous ICH, tranexamic acid was associated with the low incidence of thromboembolic and seizure events, which is an acceptable safety profile. Seven days after presentation, the volume of the hematoma increased substantially; however, according to NIHSS scores, this expansion was not associated with clinical deterioration. In the regression analysis, no significant predictors of the outcome were identified. In order to validate these results and ascertain the definitive function of tranexamic acid in the management of hyperacute spontaneous ICH, additional large-scale studies are required.

Author's Contribution:

Concept & Design of Study:	Salman Khan
Drafting:	Khurram Haq Nawaz, Sheherbano Jadoon
Data Analysis:	Ibrar Saleem, Muhammad Jalil, Imran Ahmad
Revisiting Critically:	Salman Khan, Khurram Haq Nawaz
Final Approval of version:	Salman Khan

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