Research Article

A study to compare the effectiveness of TXA in reducing mortality or disability in traumatic brain injury patients

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Abstract

Introduction: Traumatic brain (TBI) is a leading cause of death and disability. Intracranial bleeding is a common complication of TBI, and intracranial bleeding can develop or worsen after hospital admission. Hemostatic drugs may reduce the occurrence of size of intracranial bleeds and consequently lower the morbidity and mortality associated with TBI. Hemorrhage size is strongly associated with outcome. Patients with a large international hemorrhage, whatever the location, have a substantially higher mortality than patients with a small hemorrhage **Aims and Objectives:** To evaluate and compare the effectiveness of TXA in reducing mortality or disability in patients **Methodology:** This was case control study having two groups one is treatment TXA (Tranexamic acid), Other control group is not having TXA treatment, patients were randomly allocated in this two groups with their consent total 200 patients 100 in TXA group and 100 in control study 16 patients who received tranaexamic acid had hemorrhagic of contusion. **Result**: In this study 46 patients from control group had hemorrhagic progression of contusion. The effect of tranaexamic acid on hemorrhagic progression of contusion was considered extremely significant. (P <0.0001, df= 1, OR =0.2236 with 95%CI)The effect of tranaeximic acid on GCS on admission was considered not quite significant with p value of 0.627.There is significant effect of TXA on HPC with GCS change. Chi-square Test The two-sided P value is 0.0208, considered significant. The row/column association is statistically significant. There was not statistically significant Effect of TXA on HPC in contusion and haematoma of non-operated patients Chi-square Test: The two-sided P value is 0.7340.In our study 10 patients from tranexamic acid group had hypotension while 34 patients from control group hypotension. The effect tranexamic acid in hypotension was considered significant (P < 0.0001, df = 1, OR = 0.2126 with 95% CI) study result were encouraging and significant, regarding hypotension and effect of tranexamic acid on CT findings, clinical sings and composite outcome. Chi-square Test: The two-sided P value is < 0.0001. **Conclusion:** The larger effect on intracranial bleeding observed is consistent with the evidence of effectiveness of tranaexamic acid to reduce hemorrhagic progression of contusion. The effect is significant in contusions than in hematoma. Regarding the clinical outcomes, there is a trend towards a reduction in mortality, without any evidence of increase in dependency among survivors.

Keywords: Traumatic brain Injury (TBI), Hemorrhagic progression of contusion (HPC), Tranexamic acid (TXA), Glasgow Coma Scale (GCS).

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INTRODUCTION

Traumatic brain (TBI) is a leading cause of death and disability. Intracranial bleeding is a common complication of TBI, and intracranial bleeding can develop or worsen after hospital admission. Haemostatic drugs may reduce the occurrence of size of intracranial bleeds and consequently lower the morbidity and mortality associated with TBI[1].Worldwide, over 10 million people suffer of TBI each year.[1] approximately 90% of deaths occur in low- and middle-income countries.[2] majority of patients are young adults, and many patients experience burden is considerable. With rapidly increasing motorization, the incidence is predicted to rise.[3] An effective, practicable e treatment could save

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many thousands of lives and substantially reduce the burden of disability. Approximately one-third of patients with TBI have laboratory evidence of abnormal coagulation at hospital admission.[4]These patients have an increased risk of intracranial hemorrhage and higher mortality. Increased fibrinolysis, as indicated by high level of fibrinogen degradation products, is common in intracranial bleeding and is a strong independent predictor of progressive intracranial hemorrhage.[5] These observations raise the possibility that tranexamic acid (TXA) might reduce international hemorrhage and improve outcome in TBI patients. In addition, it has been shown that progressive tissue damage and edema develops in regions surrounding intracranial bleeding lesions, and is associated with a worse outcome.[14] Tissue plasmingen activator (tPA) has been shown to be an important factor in this process of peri-lesional edema.[6,7] Hemorrhage size is strongly associated with outcome. Patients with a large international hemorrhage, whatever the location, have a substantially higher mortality than patients with a small hemorrhage.[8] In many TBI patients, the intracranial bleeding continues after hospital admission.[9,10] Among [patients with moderate or severe TBI, who are found to have intracranial bleeding on a CT scan taken soon after hospital admission, intracranial bleeding progresses in 84% of patients showing hemorrhagic progression of contusion (HPC).[11].

AIMS AND OBJECTIVES

To evaluate and compare the effectiveness of TXA in reducing mortality or disability in patients

MATERIAL AND METHODS

This was case control study having two groups one is treatment TXA (Tranexamic acid), Other control group is not having TXA treatment, patients were randomly allocated in this two groups with their consent total 200 patients 100 in TXA group and 100 in control. All patients meeting the following criteria will be eligible for inclusion in the study: Trauma patients judged to be 16 years or older, With significant hemorrhage (systolic blood pressure less than 90 mmHg and/or heart rate more than 110 beats per minute), or considered to be at risk of significant hemorrhage, Within 8 hours of the injury GCS of 14 or less, Baseline clinical CT scan shows intracranial abnormality consistent with TBI, on pregnant, Patients with following criteria were excluded from the study. Pregnant women, Patients for whom a second brain scan was not possible were excluded. Eligible patients were adults with traumatic intracranial bleeding who are within 8 h of injury, with any intracranial bleeding on CT scan.

RESULTS

Table 1: Effect of TX Aon HPC

Titles	TXA	Control	Total
HPC	16 (8%)	46 (23%)	62 (31%)
No HPC	84 (42%)	54 (27%)	138 (69%)
Total	**100**	**100**	**200**

In our study 16 patients who received tranaexamic acid had hemorrhagic of contusion. 46 patients from control group had hemorrhagic progression of contusion. The effect of tranaexamic acid on hemorrhagic progression of contusion was considered extremely significant. (P <0.0001, df= 1, OR =0.2236 with 95%CI)

Chi-square Test: The two-sided P value is < 0.0001, considered extremely significant. The row/column association is statistically significant.

Table 2: Effect of TXA on GCS on admission

Parametor	Column A	Column B
Mean	13.200	14.000
No. of points	10	10
Standard deviation	1.135	1.054
Std error	0.3590	0.3333
Minimum	12.000	12.000
Maximum	15.000	15.000
Median	13.000	14.000
Lower 95% CI	12.388	13.246
Upper 95% CI	14.012	14.754
Normality test	0.2595	0.2286
Normality test P value	0.0550	>0.10
Passed normality test	Yes	Yes
Sun of ranks	85.000	125.00

The effect of tranaeximic acid on GCS on admission was considered not quite significant with p value of 0.627.

Table 3: Effect of TXA on HPC with GCS change

Titles	TXA	No TXA	Total
No GCS Change	8 (18%)	11 (25%)	19 (43%)
GCS change	2 (5%)	23 (52%)	25 (57%)
Total	**10 (77%)**	**34 (23%)**	**44 (100%)**

There is significant effect of TXA on HPC with GCS change. **Chi-square Test:** The two-sided P value is 0.0208, considered significant. The row/column association is statistically significant.

Table 4: Effect of TXA on HPC in contusion and haematoma of non-operated patients

Titles	OP	Non OP	Total
Contusion with HPC	4 (25%)	3 (19%)	7 (44%)
Hematoma with HPC	7 (44%)	2 (13%)	9 (56%)
Total	**11 (69%)**	**5 (31%)**	**16 (100%)**

There was not statistically significant Effect of TXA on HPC in contusion and haematoma of non-operated patients **Chi-square Test:** The two-sided P value is 0.7340, considered not significant. The row/column association is not statistically significant.

Table 5: Effected of TXA in hypotension

Titles	TXA	Control	Total
Hypotension	10 (5%)	34 (18%)	44 (23%)
NoHypotension	89 (46%)	61 (31%)	150 (77%)
Total	**99 (51%)**	**95 (49%)**	**194 (100%)**

In our study 10 patients from tranexamic acid group had hypotension while 34 patients from control group hypotension. The effect tranexamic acid in hypotension was considered significant (P < 0.0001, df = 1, OR = 0.2126 with 95% CI) study result were encouraging and significant, regarding hypotension and effect of tranexamic acid on CT findings, clinical sings and composite outcome. **Chi-square Test**: The two-sided P value is < 0.0001, considered extremely significant. The row/column association is statistically significant.

Table 7: The effect of TXA in OHS

Titles	Control	TXA	Total
Operated	3 (8%)	22 (56%)	25 (64%)
Non Operated	6 (15%)	8 (21%)	14 (36%)
Total	**9 (23%)**	**30 (77%)**	**39 (100%)**

In both groups, Tranaexamic acid and control group OHS is significantly related and predicts accurately the GCS at 28 days. It is therefore helpful in taking the problem of missing data in clinical studies in TBI. In our findings, OHS could be a simple and useful outcome measure to use in settings for which long term fallow-up is problematic. **Chi-square Test**: The two-sided P value is 0.0722, considered significant.

DISCUSSION

Here we focus specially on the phenomenon of HPC, a secondary injury process that designates the designates the enlargement or new appearance of a parenchymal hemorrhagic contusion due to delayed bleeding. There are two mechanisms that have been implicated in its devlopment. First an explicit or progression latent coagulopathy leads to continued or delayed bleeding of micro vessels fractured at the time of primary injury. Next recently discovered mechanism postulating that micro vessels in the region of injury (penumbra) receive kinetic energy from the impact that is not sufficient to fracture them, but is sufficient to include a series of maladaptive molecular events that eventually results in their structural failure, leading to delayed formation of petachial haemorrhages which then coalesce to produce hemorrhagic progression. Distinguishing between these two mechanisms is important, because implications for treatment are quite different. For the first mechanism, treatment must be aimed at normalizing coagulation, whereas for the second, treatment must block the maladaptivemolecular events in microvescular endothelial cells.[12] Contuse injury to the brain invariably is complicated by secondary injury due to micro vascular dysfunction (Yotoka,2007) [13], which worsens with time and leads to growth of expansion of the primary lesion.HPC may be referred to by various terms, including delayed traumatic intracerebral hematoma (DTICH), progressive hemorrhagic injury, traumatic intracerebral hemorrhage, or colloquially, as a contusion that has "blossomed. "In our study 16 patients who received tranaexamic acid had hemorrhagic of contusion. 46 patients from control group had hemorrhagic progression of contusion. The effect of tranaexamic acid on hemorrhagic progression of contusion was considered extremely significant. (P <0.0001, df= 1, OR =0.2236 with 95%CI)In our study 16 patients with contusion had hemorrhagic progression of contusion while 10 patients with haematoma had hemorrhagic progression of contusion. The effect of tranaexamic acid on contusion was significant. (P, 0.0241, df =1, OR =4.487 with 95% CI)In our study, in tranaexamic acid group 44% patient had contusion with hemorrhagic progression of contusion and 50% of patients had haematoma with haemorrhagic progression of contusion. Only 25% patients from contusion group were operated while 44% with haematoma were operated. So the overall effect of the tranaexamic acid in contusion was significant as compared to hematoma.

Hypotension

Hypotension was found to be a statistically significant predictor of outcome, statistically independent of other major including age, hypoxia, and the presence or absence of severe trauma to one or more extracranial organ systems. When the influence of hypotension on outcome was controlled separately, the statistical significance of severe trauma to one or more extracranial organ systems as a predictor of outcome was eliminated, suggesting that the influence of systematic multiple trauma on the outcome of severe head injury patients is primarily mediated through hypotension. The analysis of outcome from severe head injury in the TCDB revealed that the five most powerful predictors occurring from injury through resuscitation were age, intracranial (compared tomographic) diagnosis, post-resuscitation GCS score, and presence or absence of hypotension. Notably, of these five major predictors, only the occurrence and severity of hypotension is amenable to medical manipulation. In our study 10 patients from tranexamic acid group had hypotension while 34 patients from control group hypotension. The effect tranexamic acid in hypotension was considered significant (P <0.0001, df = 1, OR = 0.2126 with 95% CI) study result were encouraging and significant, regarding hypotension and effect of tranexamic acid on CT findings, clinical sings and composite outcome. Additionally a recent paper has challenged this basic hypothesis by reporting

coagulopathy is also found in TBI patients without hypotension.[14]

CONCLUSION

The larger effect on intracranial bleeding observed is consistent with the evidence of effectiveness of tranaexamic acid to reduce haemorrhagic progression of contusion. The effect is significant in contusions than in hematoma. Regarding the clinical outcomes, there is a trend tpwerds a reduction in mortality, without any evidence of increase in dependency among survivors.

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