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Original Research Article.

Outcome Evaluation of Thrombolytic Therapy in Acute Ischaemic Stroke Patients with Renal Dysfunction

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ABSTRACT

Background: Stroke is the fourth leading cause of death and the leading cause of disability. Intravenous administration of alteplase represents the sole medical therapy approved for the management of acute ischemic stroke in patients. Hence; the present study was conducted for outcome evaluation of thrombolytic therapy in acute ischaemic stroke patients with renal dysfunction.

Materials & Methods: A total of 100 patients participated in this study. Thrombolytic therapy for acute stroke was initiated, and all individuals who received tissue plasminogen activator (tPA) for acute ischemic stroke were included in the analysis. A comprehensive medical history and physical examination were conducted, which involved gathering information on the onset of symptoms, assessing stroke risk factors, reviewing current medications, and identifying any contraindications to tPA therapy. A stat non-contrast head computed tomography (CT) scan was performed and analyzed to check for intracerebral hemorrhage (ICH), which would represent an absolute contraindication for tPA administration. Intravenous alteplase was administered at a dosage of 0.9 mg/kg, with a maximum limit of 90 mg. Patients were evaluated on the second or third day to determine the appropriate course of action based on their functional status and were monitored until discharge. Renal profile was evaluated.

Results: A total of 100 patients were evaluated. Among them, eGFR (ml/min/1.73 m^2) was ≥ 60 in 65 percent of the patients while it was less than 60 in the remaining 35 percent of the patients. Mean age of the patients with eGFR ≥ 60 and less than 60 was 61.5 years and 63.8 years respectively. Mean weight of the patients with eGFR ≥ 60 and less than 60 was 81.3 Kg and 84.7 Kg respectively. While assessing outcome, it was seen that incidence of intracranial hemorrhage was similar in both the study groups. Also, non-significant results were obtained while comparing the functional status (mortality) among patients divided on the basis of eGFR.

Conclusion: The presence of an estimated glomerular filtration rate (eGFR) below 60 in individuals undergoing thrombolytic treatment for acute stroke did not correlate with a heightened risk of intracerebral hemorrhage (ICH), unfavorable functional outcomes, or mortality.

Key words: Stroke, Thrombolytic, Renal.

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INTRODUCTION

Stroke is the fourth leading cause of death and the leading cause of disability in the elderly in the USA. Every year, about 795,000 new or recurrent strokes occur, which cost an estimated US$73.7 billion in 2010 alone. Ischemic stroke, or disruption of blood flow to the brain, accounts for about 85 % of all strokes. Maintaining adequate tissue oxygenation is important during periods of acute cerebral ischemia in order to prevent hypoxia and potential worsening of the neurologic injury.[1-3] Intravenous administration of alteplase represents the sole medical therapy approved by the US Food and Drug Administration (FDA) for the management of acute ischemic stroke in patients. The application of this treatment is linked to enhanced clinical outcomes across a diverse patient population. Recent clinical trials indicate that the therapeutic window for alteplase may be extended to 4.5 hours for certain patients. Prompt initiation of treatment is associated with a higher likelihood of achieving favorable results.[4, 5]

Alteplase, along with other plasminogen activators such as streptokinase and urokinase, facilitates thrombolysis by cleaving the arginine-valine peptide bond in plasminogen, thereby generating the active proteolytic enzyme plasmin. In the context of

physiological fibrinolysis, the activity of circulating plasmin is swiftly inhibited by α2-antiplasmin (α2-plasmin inhibitor). The fibrinolytic function of plasmin is preserved within the thrombus, while its systemic activity is curtailed due to the selective incorporation of plasminogen into the thrombus during its formation. Additionally, the active site and lysine-binding sites of plasminogen (and consequently plasmin) are the same as those where α2-antiplasmin binds. As a result, fibrin-bound plasmin within the thrombus enjoys relative protection from inactivation by α2-antiplasmin. Thrombolytic agents like streptokinase and urokinase activate both fibrin-bound and circulating plasminogen without discrimination, leading to a systemic release of substantial quantities of plasmin into the bloodstream.[6, 7]

Hence; the present study was conducted for outcome evaluation of thrombolytic therapy in acute ischaemic stroke patients with renal dysfunction.

MATERIALS & METHODS

The present study was conducted for the outcome evaluation of thrombolytic therapy in acute ischaemic stroke patients with renal dysfunction. A total of 100 patients participated in this study. Thrombolytic therapy for acute stroke was initiated, and all individuals who received tissue plasminogen activator (tPA) for acute ischemic stroke were included in the analysis. A comprehensive medical history and physical examination were conducted, which involved gathering information on the onset of symptoms, assessing stroke risk factors, reviewing current medications, and identifying any contraindications to tPA therapy. The National Institute of Health (NIH) stroke scale was calculated upon presentation. Additionally, serum biochemical and hematological profiles were assessed. A stat non-contrast head computed tomography (CT) scan was performed and analyzed to check for intracerebral hemorrhage (ICH), which would represent an absolute contraindication for tPA administration. Intravenous alteplase was administered at a dosage of 0.9 mg/kg, with a maximum limit of 90 mg. Patients were evaluated on the second or third day to determine the appropriate course of action based on their functional status and were monitored until discharge. Renal profile was evaluated. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

RESULTS

A total of 100 patients were evaluated. Among them, eGFR (ml/min/1.73 m^2) was ≥ 60 in 65 percent of the patients while it was less than 60 in the remaining 35 percent of the patients. Mean age of the patients with eGFR ≥ 60 and less than 60 was 61.5 years and 63.8 years respectively. The mean weight of the patients with eGFR ≥ 60 and less than 60 was 81.3 Kg and 84.7 Kg respectively. While assessing the outcome, it was seen that incidence of intracranial hemorrhage was similar in both the study groups. Also, non-significant results were obtained while comparing the functional status (mortality) among patients divided on the basis of eGFR.

Table 1: Demographic and clinical data

Variable	eGFR ≥ 60 (n=65)	eGFR < 60 (n=35)
Mean age (years)	61.5	63.8
Mean weight (Kg)	81.3	84.7
Diabetes	12	8
Hypertension	19	14
eGFR (ml/min/1.73 m^2)	92.3	43.7
Serum creatinine (mg/dL)	0.9	2.3

Table 2: Clinical outcome

Outcome		eGFR ≥ 60 (n=65)	eGFR < 60 (n=35)	p-value
Intracranial hemorrhage events	**Petechial haemorrhage**	5	3	0.81
	Symptomatic haemorrhage	3	2	
	Subarachnoid haemorrhage	1	1	
Functional status	**Poor outcome**	23	14	0.14
	Mortality	12	8	

DISCUSSION

Acute ischaemic stroke can be addressed through thrombolytic therapy and mechanical thrombectomy. The administration of intravenous recombinant tissue plasminogen activator (IV r-TPA) is currently regarded as the standard treatment for acute ischaemic stroke (AIS). A significant limitation of this therapeutic approach is the narrow time window following the onset of stroke symptoms, within which treatment must be initiated to yield any therapeutic benefit. Research indicates that IV r-TPA should be administered within a maximum of 4.5 hours post-stroke onset. Alternative treatment options, such as intra-arterial thrombolysis and mechanical clot retrieval, have not demonstrated the same level of efficacy and warrant further investigation. It is not surprising that recanalisation techniques have advanced rapidly in recent years. While achieving vessel recanalisation is crucial for enhancing the likelihood of substantial tissue reperfusion, clinical trials should prioritize functional outcomes over mere rates of reperfusion or recanalisation to effectively evaluate the success of these interventions.[7- 10] Hence; the present study was conducted for assessing outcomes with thrombolytic therapy in patients with renal dysfunction presenting with acute ischaemic stroke.

A total of 100 patients were evaluated. Among them, eGFR (ml/min/1.73 m^2) was ≥ 60 in 65 percent of the patients while it was less than 60 in the remaining 35 percent of the patients. Mean age of the patients with eGFR ≥ 60 and less than 60 was 61.5 years and 63.8 years respectively. The mean weight of the patients with eGFR ≥ 60 and less than 60 was 81.3 Kg and 84.7 Kg respectively. While assessing the outcome, it was seen that incidence of intracranial hemorrhage was similar in both the study groups. Also, non-significant results were obtained while comparing the functional status (mortality) among patients divided on the basis of eGFR. Hao Z et al evaluated the safety and effectiveness of thrombolytic therapy in acute stroke patients with renal dysfunction using a meta-analysis. They systematically searched PubMed and EMBASE for studies that evaluated the relationship between renal dysfunction and intravenous tissue plasminogen activator (tPA) in patients with acute ischemic stroke. Poor outcome (modified Rankin Scale ≥2), mortality, and symptomatic intracranial hemorrhage (ICH) and any ICH were analyzed. Fourteen studies were included (N=53,553 patients). The mean age ranged from 66 to 75 years. The proportion of male participants was 49% to 74%. The proportion of renal dysfunction varied from 21.9% to 83% according to different definitions. Based on 9 studies with a total of 7796 patients, the meta-analysis did not identify a significant difference in the odds of poor outcome (odds ratio [OR]=1.06; 95% confidence interval [CI]: 0.96–1.16; I2=44.5) between patients with renal dysfunction and those without renal dysfunction. Patients with renal dysfunction were more likely to die after intravenous thrombolysis (OR=1.13; 95% CI: 1.05–1.21; I2=70.3). No association was observed between symptomatic ICH (OR=1.02; 95% CI: 0.94–1.10; I2=0) and any ICH (OR=1.07; 95% CI: 0.96–1.18; I2=25.8). Renal dysfunction does not increase the risk of poor outcome and ICH after stroke thrombolysis. Renal dysfunction should not be a contraindication for the administration of intravenous thrombolysis to eligible patients.[11] Power A et al examined the impact of renal impairment on clinical outcomes with thrombolysis within the current 4.5-hour therapeutic window. Their retrospective multicenter cohort study (2009-2011) examined 229 stroke patients receiving thrombolysis with alteplase (0.9 mg/kg; mean age 70 ± 13 years; 59% male, 24% diabetic). Sixty-five patients had an estimated glomerular filtration rate (eGFR) <60 ml/min.: There was no significant difference in mean time to thrombolysis between the groups (221 ± 66 vs. 220 ± 70 min from symptom onset; p = 0.9). An eGFR <60 ml/min was independently associated with a statistically significant reduction of the therapeutic effect of alteplase at 24 h on multivariate regression [coefficient -2.3, 95% confidence interval (CI) -3.7 to -0.9; p = 0.002], and this persisted at 7 days (coefficient -3.5, 95% CI -5.3 to -1.7; p < 0.001). Their results suggested that renal impairment is associated with reduced efficacy of thrombolysis in acute ischemic stroke without any excess hemorrhagic complications.[12]

CONCLUSION

The presence of an estimated glomerular filtration rate (eGFR) below 60 in individuals undergoing thrombolytic treatment for acute stroke did not correlate with a heightened risk of intracerebral hemorrhage (ICH), unfavorable functional outcomes, or mortality. These results indicate that administering thrombolytics in cases of acute stroke is suitable for patients with renal impairment.

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