www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v7i3.91

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

Outcome of Thrombolysis with Alteplase in Acute Ischemic Stroke

Authors
Balakrishnan Ramasamy[1*], Madhavi Karri[2], Angel P Varghese[3], Mintu George, Reshma K Thomas, Deepthi Wilson, Anju Jose
[1,2,3]Department of Neurology, PSG Institute of Medical Sciences and Research.
[*]Department of Neurology, PSG Institute of Medical Sciences and Research, Tamil Nadu – 641004, INDIA,
Email: *drrbksamy@gmail.com*

Abstract
Background: *Stroke has been a major concern worldwide. Thrombolysis has brought a new direction for management in acute ischemic stroke. It has served as a catalyst for major changes in the management of acute stroke. It is at the forefront with good evidence of its efficacy within 4.5 hours of symptom onset.*
Aim: *To study the outcome of thrombolysis of acute ischemic stroke with alteplase after 3 months. We also assessed associated complications of alteplase.*
Methods: *We have taken data of acute ischemic stroke patients who underwent thrombolysis with alteplase. Data collection was retrospective and analysed from January 2010 to April 2015.Primary outcome was measured with NIH Stroke Scale (NIHSS) at admission and at discharge; and secondary outcome was measured with modified Rankin score (mRS) and NIHSS at three months.*
Results: *We collected data of consecutive 64 patients who received alteplase for thrombolysis. Mean age was 59.05 years with a standard deviation (SD) of 12.7 with majority of them being males. Mean duration of hospital stay was eight days. Mean time of onset of symptoms to arrival to ED was 2 hours (SD-1.0) and onset to window period were 4.1 hours. Complications were noted in 19 patients (29.7%) and more common noted one was asymptomatic haemorrhagic transformation.*
Conclusions: *Stroke thrombolysis is a safe and effective therapy in actual practice. Its role has helped in reduction of morbidity and mortality associated with acute ischemic stroke.*
Keywords: *Alteplase, Thrombolysis, Acute ischemic stroke, Complications, NIHSS, mRS.*

Introduction

Acute ischemic stroke is a significant concern in present decade in view of rising incidence. It is most common neurological condition and second leading cause of mortality in global ranking after coronary artery disease.[1]Thrombolytics restore the cerebral blood flow in acute ischemic stroke and may lead to improvement and restoration of neurologic deficit. With introduction of Alteplase (tPA) for reperfusion therapy has caused a pioneer change in approach to stroke management. It was discovered in 1983[2] but its use for effective treatment in ischemic stroke was in 1995.[3]With the licensed time window upto 4.5 hours, National Institute of Neurological Disorders and Stroke (NINDS) has approved intravenous alteplase (recombinant tissue plasminogen activator) a thrombolytic agent for acute ischemic stroke.[4,5] Administration of tPA is simple with a total dose of 0.9mg/kg body weight – initiated with 10 percent bolus followed by remaining dose over one hour infusion.[6] Complications associated with it are

bleeding manifestations like intracerebral haemorrhages and other systemic haemorrhages and, anaphylactic reactions. This study was done in view of assess the effectiveness of alteplase use in ischemic stroke, in correlation with risk factors and severity of stroke.

Methodology

This is a retrospective analysis of all patients given intravenous alteplase therapy for acute ischemic stroke from January 2010 to April 2015.Ethical approval was obtained from standard institutional ethical committee. Standardized recommendation for inclusion and exclusion criteria was strictly followed. All patients above 18years presented with acute ischemic stroke in window period were taken for the study. Any prior history of haemorrhage, pregnancy, seizure disorder, bleeding disorder, persistent hypertension at arrival (SBP:185mm Hg or DBP:110mm Hg), NIHSS score of less than 4 at admission were excluded. Informed written consents were taken from all the patients or their relatives. Basic demographic information of the patients with acute ischemic stroke to emergency department, who have given informed consent, were collected. All the patients were thoroughly examined and computed tomography (CT) or magnetic resonance imaging (MRI) scan of brain, to rule out hematoma and magnetic resonance imaging stroke protocol to assess early infarct and any evidence of cerebral arterial occlusion was done. Thrombolysis was carried out in emergency department. Baseline risk factors, stroke characteristics, baseline NIHSS scores, mRS scores were collected. Follow up outcome after 90 days was assessed by NIHSS and mRS after 90days. Primary outcome was measured by improvement of NIHSS by four or more than four points at the time of discharge. Secondary outcome was measured by mRS score of 0 or 1. Complications after thrombolysis like symptomatic intracranial haemorrhage, systemic haemorrhage, angioedema or any event related symptoms were noted. Simple statistics were used for descriptive analysis. Spearman correlation was used for qualitative correlation of discrete variables. Statistical analysis was done using SSPS version 20.

Results

A total of 64 patients were enrolled for the study. Of 64,54(84.4%) were males and 10 (15.6%) were females. Mean age of study population was 59.05 years with a standard deviation (SD) of 12.7. Mean age among males was 58.7 and among females was 60.1. Among risk factors, most prevalent were alcohol, smoking, hypertension and diabetes, seen in 27 patients (42.2%), 23 patients (35.9%), 19(29.7%) and 19(29.7%) respectively. Other risk factors noted were dyslipidaemia in 15 patients (23.4%),10 patients (15.6%)had history of ischemic heart disease and 1 patient each (1.6%) had hypothyroidism, history of old stroke, chronic renal failure respectively. Two patients had (3.1%) hyper-homocysteinemia. Four patients reported to develop acute ischemic stroke without any significant risk factors. (Table 1)

Table 1: Prevalence of Risk factors in the study population

Risk factors	Yes	No	Cumulative percentage(%)
Smoking	23	41	35.9
Alcohol	27	37	42.2
Dyslipidaemia	15	49	23.4
Hypertension	19	45	29.7
Diabetes Mellitus	19	45	29.7
Ischemic Heart Disease	11	53	15.6
Hyper-homocysteinemia	2	61	3.1
COPD	1	63	1.6
CRF	1	63	1.6
Hypothyroidism	1	63	1.6
Recurrent CVA	1	63	1.6
No Risk factors	4	60	6.2

Duration of hospital stay among the study population was analysed. Maximum and minimum duration of hospital stay were 2 days and 81 days with a mean duration of 8 days (SD-13.164). Mean systolic blood pressure was 149.3 mm Hg and mean diastolic blood pressure was 87.9 mm Hg. Clinical parameters were assessed. Speech was affected in 44 patients (68.7%) and 20 patients (31.2%) had no

speech involvement. About 28 (43.7) patients had left sided weakness and 34 (53.1%) had right sided weakness.

This study also assessed the time of onset of stroke and arriving time of patients to emergency department as well as door to needle time. Mean time of onset of symptoms to arrival to ED was 2 hours (SD-1.0) and onset to window period were 4.1 hours. Number of risk factors were correlated with outcome of stroke after three months with mRS scoring. (Table 2).

Table 2: Spearman correlation of number of risk factors and mRS scores after three months (showed no significant correlation) (mRS – modified Rankin Scale)

Correlations

			Number risk factors	mRS score
Spearman's rho	Number Risk factors	Correlation Coefficient	1.000	.197
		Sig. (2-tailed)	.	.119
		N	64	64
	mRS score	Correlation Coefficient	.197	1.000
		Sig. (2-tailed)	.119	.
		N	64	64

Mean NIHSS score at admission observed was 11.8. Mean NIHSS score at discharge was 6.3. Primary outcome was achieved in 25 patients (39.1%). Secondary outcome was met in 39 patients (60.9%) (Table 3). Mean window period was correlated with mRS scores after three months. (Table 4) NIHSS scores at admission was significantly associated with mRS scoring after three months (Table 5).

Table 3: mRS scores at admission and after three months were quantified. (mRS – modified Rankin Scale)

Grade	mRS on admission	mRS after 3 months
0	0	12
1	1	10
2	3	17
3	11	16
4	38	9
5	11	0
6	0	0

Table 4: Chi – square correlation between window period and mRS scores after three months. (mRS – modified Ranking scale)

mRS3months * window period Crosstabulation

Count		Window period <2.5hours	>2.5hours	Total
MRS3months	<2	28	11	39
	>2	20	5	25
Total		48	16	64

Table 5: Correlation of NIHSS scores at admission with mRS scores after three months (showed significant association with value less than 0.05)

Chi-Square Test

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	23.994[a]	12	.020
Likelihood Ratio	25.028	12	.015
Linear-by-Linear Association	15.999	1	.000
N of Valid Cases	64		

a. 15 cells (75.0%) have expected count less than 5. The minimum expected count is .14.

Complications identified post alteplase thrombolysis were mild asymptomatic intra-cerebral bleed, severe intra-cerebral bleed, other systemic haemorrhage, angioedema and others. Among 64 patients, 35(54.7%) patients were did not have any complications. While 18 patients (28.1%) developed haemorrhagic transformations, which were categorised as mild asymptomatic intracerebral haemorrhage. (Table 5)

Table 5: Complications in the study population (ICH – intra-cerebral haemorrhage)

Grade	**Number**	**Cumulative percentage**
Nil complications	37	57.8
Asymptomatic ICH	17	26.5
Symptomatic ICH	2	3.12
De-compressive craniectomy	2	3.12
Systemic bleeding	4	3.12
Angioedema	2	3.12
Others	2	3.12

Discussion

Thrombolysis has played a major role in outcome of ischemic stroke. Early intervention has helped in improving morbidity and quality of life. In our study the mean age was 59.05which was smaller to that study done by Volans.P.et.al[7] which showed a mean age of 69 years and 64.9+/-12 done by Werner Hacke et.al[8]**.** A study done by Sussane S et.al, showed mean age of 58 years.[9] The mean SBP in our study was 149.33 and DBP is 87.91 which was identical with the study done by Werner Hacke et.al which showed a SBP of 152.6+/-19.2 and DBP of 84.4+/- 13.5[10]**.** The study also assessed the mean duration of hospital stay of 8 days which resembles the study done by Thorkild Terkelson et.al which showed a mean duration of days of 9days (thrombolysed patients) and 13 days(Non-thrombolysed patients)[11]. Mean window period was 250 minutes and mean onset to arrival time was 120minutes, which was higher compared to the study done by Akansha et.al 76.8min[12]. It was lesser compared to a study done by Victor et al.[13] which showed mean window period time of 580 minutes. In the window period, we assessed those who are arriving within 2.5hours and between 2.5 to 4.5 hours and correlated with mRS scores. No significant association has been noted among the two groups.

Mean NIHSS score at admission observed was 11.8.It was lesser compared to a study done by Jagini et.al.[14] and also to a study done by Vikram Huded et al.[15]. Mean mRS after three months was 2. Primary outcome was achieved in 39.1% which was lesser compared to 65% done in a study by Padma et al. [16]Secondary outcome was reached in 60.9% which was higher compared to a largest single centre stroke study done by Jan Sobesky et.al which showed only 53%.[17] and German stroke study which showed only 35%[18]. Complications were noted in 29.7% which was higher compared with two studies done in Kolkata which 20% and 16.1% respectively and zero percent mortality which was lesser compared to a study done by Fischer et al.[19]In our study, we had better outcome in patients thrombolysed with alteplase with no mortality and but had minor complications noted in 29.7% the study population.

Limitations of the study

Though patients noted to have better outcome with alteplase, sample size was small and restricted to a regional geographical area. More studies are needed for assessment of alteplase

Conclusion

Here we have assessed the utility of alteplase in ischemic stroke in our study population. Predominantly males were noted with mean window period of two hours. Alteplase has reached the primary and secondary outcome in maximum patients, which helped in moulding the morbidity with least complications noted in our study. NIHSS and mRS scoring scales have played a major role in assessing the morbidity and outcome in our study.

Acknowledgement: Nil

References

1. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *Lancet Neurol*. 2009.
2. Hill MD, Buchan AM. Thrombolysis for acute ischemic stroke: Results of the Canadian Alteplase for Stroke Effectiveness Study. *Cmaj*. 2005;172(10):1307-1312.
3. Röther J, Ford GA, Thijs VNS. Thrombolytics in acute ischaemic stroke: Historical perspective and future opportunities. *Cerebrovasc Dis*. 2013.
4. Grinnon ST, Miller K, Marler JR, et al. National Institute of Neurological Disorders and Stroke Common Data Element Project - approach and methods. *Clin Trials*. 2012;9(3):322-329.
5. Albers GW, Olivot JM. Intravenous alteplase for ischaemic stroke. *Lancet*. 2007.
6. Toni D, Ahmed N, Anzini A, et al. Intravenous thrombolysis in young stroke patients results from the SITS-ISTR.

Neurology. 2012.
7. Volans AP. An analysis of outcomes of emergency physician/department-based thrombolysis for stroke. *Emerg Med J*. 2012;29(8):640-643.
8. Lees KR, von Kummer R, Bluhmki E, et al. Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke. *N Engl J Med*. 2008.
9. Schmülling S, Grond M, Rudolf J, Heiss WD. One-year follow-up in acute stroke patients treated with rtPA in clinical routine. *Stroke*. 2000.
10. Hacke W, Albers G, Al-Rawi Y, et al. The Desmoteplase in Acute Ischemic Stroke Trial (DIAS): A phase II MRI-based 9-hour window acute stroke thrombolysis trial with intravenous desmoteplase. *Stroke*. 2005.
11. Terkelsen T, Schmitz ML, Simonsen CZ, et al. Thrombolysis in acute ischemic stroke is associated with lower long-term hospital bed day use: A nationwide propensity score-matched follow-up study. *Int J Stroke*. 2016.
12. A. W, A. P, M. K, et al. Quality indicators of intravenous thrombolysis from North India. *Ann Indian Acad Neurol*. 2017.
13. Urrutia VC, Faigle R, Zeiler SR, et al. Safety of intravenous alteplase within 4.5 hours for patients awakening with stroke symptoms. *PLoS One*. 2018.
14. Prasad Jagini S, I. S. Clinical profile of patients with acute ischemic stroke receiving intravenous thrombolysis (rtPA-alteplase). *Int J Adv Med*. 2018.
15. Huded V, R DS, Nagarajaiah R, Zafer S, Nair R, Acharya H. Thrombolysis in acute ischemic stroke: Experience from a tertiary care centre in India. *J Neurosci Rural Pract*. 2014.
16. Padma M, Singh M, Bhatia R, et al. Hyperacute thrombolysis with IV rtPA of acute ischemic stroke: Efficacy and safety profile of 54 patients at a tertiary referral center in a developing country. *Neurol India*. 2007.
17. Sobesky J, Frackowiak M, Zaro Weber O, et al. The cologne stroke experience: Safety and outcome in 450 patients treated with intravenous thrombolysis. *Cerebrovasc Dis*. 2007.
18. Thomalla G, Schwark C, Sobesky J, et al. Outcome and symptomatic bleeding complications of intravenous thrombolysis within 6 hours in MRI-selected stroke patients: Comparison of a German multicenter study with the pooled data of ATLANTIS, ECASS, and NINDS tPA trials. *Stroke*. 2006.
19. Schaad H, Zwahlen M, Fischer U, et al. Impact of Thrombolysis on Stroke Outcome at 12 Months in a Population. *Stroke*. 2012;43(4):1039-1045.