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OUTCOME OF INTRAVENOUS THROMBOLYSIS WITH TENECTEPLASE IN ACUTE ISCHEMIC STROKE.

Emergency Medicine

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ABSTRACT

Tenecteplase is a modified tissue plasminogen activator and newer thrombolytic agent. It has a longer half life ,which is more fibrin specific, produces less systemic depletion of circulating fibrinogen, and is more resistant to plasminogen activator inhibitor. Because of its pharmacodynamic properties which results in rapid reperfusion and lower intracranial hemorrhages. Hence the objective is to study the efficacy of tenectaplase in acute ischemic stroke including, neurological and functional outcome at 3 months which is assessed by mRS scale and also to know the complications arising out of thrombolysis with tenectaplase. **Methods-** This is prospective observational study of 40 cases of acute ischemic stroke undergoing thrombolysis with tenecteplase within 4.5 hours of onset. Dose of 0.2 mg /kg of tenecteplase was used for thrombolysis and outcome was evaluated with improvement in NIHSS score at arrival , 24 hrs, 1 week and at discharge, 1 and 3 month and mRS scale at 1 and 3 months. **Result-** In our study, 67.5% (27 out of 40) patients met the primary clinical efficacy outcome by achieving an improvement in NIHSS score of 4 or more points at 24 h and 67% (27out of 40 patients) met the secondary clinical efficacy outcome by having an mRS scale of 0 or 1 at 3 months. Adverse events were noted in 7 patients (17.5%) of which 4 developed ICH and 3 patients showed poor clinical outcome. **Conclusion-** Tenecteplase appears to be a safe and effective agent for acute ischemic stroke because of significant improvement in NIHSS , low disability rates were observed in the present study.

KEYWORDS

Tenectaplase, stroke, NIHSS score , modified rankin scale

INTRODUCTION:

Stroke is one of cause for mortality worldwide[1]. The largest burden is seen in low income countries [2]. Stroke is defined as mechanism that hampers the blood flow to the brain. Ischemic stroke are more common and seen in 87% of all strokes[3]. Tenecteplase is a third generation thrombolytic agent which is genetically engineered mutant tissue plasminogen activator,it has got some pharmacokinetic advantages over alteplase. and it is more fibrin specific and which produces less systemic depletion of circulating fibrinogen, and is more resistant to plasminogen activator inhibitor than alteplase. These are the pharmacodynamic differences may result in more rapid reperfusion and lower intracranial hemorrhage rates.[4]

AIMS AND OBJECTIVES:

To study the efficacy of tenectaplase in acute ischemic stroke. neurological outcome ,complications occurred because of thrombolysis and Functional outcome at 3 months assessed by mRS scale.

METHODOLOGY:

Our study includes 40 patients with acute ischemic stroke with a window period of 4.5 hours presenting to ED Or admitted patients with symptoms. it is an interventional prospective observational study. DURATION OF STUDY: between November 2016 to September 2018.

Inclusion Criteria:

Ischemic stroke cases undergoing thrombolysis after fulfilling inclusion and exclusion criteria for thrombolysis with Tenecteplase with a clearly defined time of onset

- presenting within 4.5hours of onset
- a deficit measurable on NIHSS and,
- age above 18 years.

Exclusion Criteria:

- Cases thrombolysed in other hospital and admitted for further treatment in our hospital
- thrombolysis cases who left against medical advise during hospitalization and treatment
- patients not under follow up
- 'Wake up stroke' undergoing thrombolysis
- Cases which are thrombolysed out of window period
- CT suggestive of intracranial bleed.

Ethical Clearance: Clearance was obtained from the Ethical committee of the hospital.

METHODOLOGY:

Patients with ischemic stroke fulfilling inclusion and exclusion criteria were considered for thrombolysis with tenecteplase of dose 0.2 mg/kg iv bolus. Patients characteristics like sex, weight, blood pressure arrival NIHSS co morbidities were notified. Stastical method; The collected variables are the time of onset of the symptoms, the time of arrival to the ER,door to scan time door to needle time, risk factors for ischemic stroke, neurological examination with calculation of the NIHSS score (which was done on admission, 30 min interval after thrombolysis for 2h, 24h, 48h, discharge), mRS score after 3 months, monitoring of systolic and diastolic blood pressure and blood glucose on admission, time of completion of the imaging and its results, Tenecteplase administration time. The primary outcome measure was studied by the proportion of patients achieving significant early nuerological recovery defined as an improvement of 4 or more points on the NIHSS score at 24h, and achiving mRS (0-1) at 3 Months. And the adverse effect of intracranial haemorrage caused by thrombolysis were notified. Qualitative data are represented in the form of percentages. Quantitative data are calculated using mean +/- SD and /or median with range. Results are represented graphically. Results are compaired with previous studies. MS office 2013 and SPSS version 20 is used for most analysis.

RESULTS

Table 1: NIHSS Description

Variable name	Lowest	Highest	Kurtosis	Skewness	Range	Mean	Std. Dev.	Std. error	C.V.	Prob
NIHSS Arrival	3.000	25.000	1.383	1.256	22.000	8.825	5.232	0.827	59.292	0.001 **
NIHSS 24hr	0.000	23.000	2.428	1.646	23.000	4.225	5.641	0.892	133.513	0.000 ***
NIHSS 1 Week	0.000	20.000	1.863	1.613	20.000	3.500	5.407	0.855	154.473	0.000 ***
NIHSS At Discharge	0.000	20.000	2.203	1.680	20.000	3.275	5.104	0.807	155.847	0.000 ***
NIHSS 1 Month	0.000	10.000	1.518	1.682	10.000	1.650	2.923	0.462	177.121	0.000 ***

NIHSS 3 Months	0.000	9.000	1.317	1.656	9.000	1.575	2.791	0.441	177.200	0.000***

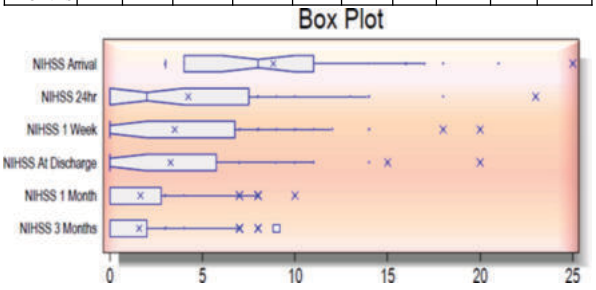
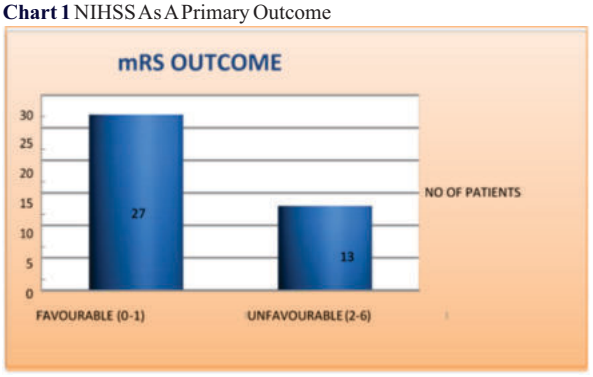


Chart 1 NIHSS As A Primary Outcome



Chaert 2 mRS As Secondary Outcome

Table 2 Analysis

Variable Name	Lowest	Highest	Kurtosis	Skewness	Range	Mean	Std. Dev.	Std. error	C.V.	Prob
mRS 1 month	0.000	5.000	-0.180	1.141	5.000	1.100	1.661	0.263	151.001	0.013*
mRS 3 months	0.000	5.000	-0.180	1.141	5.000	1.100	1.661	0.263	151.001	0.013*
Events/ Day	0.000	1.000	1.220	1.778	1.000	0.175	0.385	0.061	219.890	0.000***

Significance Levels * = <.05, ** = <.01 & *** = <.001

mRS shows significant favourable secondary outcome 67.5% with score range of (0-1) in study population with probability of 0.000.

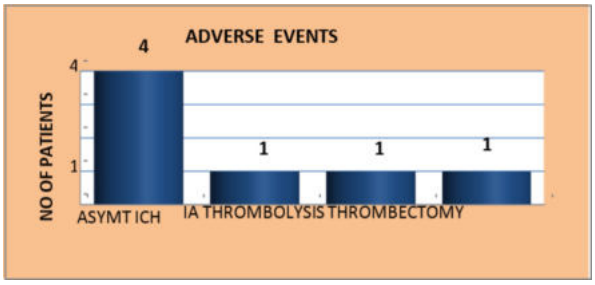


Chart 3 Adverse Events Due To Thrombolysis With Tenecteplase

In total only 3 patients had grave outcome rest 4 patients developed asymptomatic ICH with pvalue < 0.001 suggesting good safety and efficacy

DISCUSSION:

Sample size for the study is 40 patients who presented with acute ischemistudied various risk factors leading to stroke like hypertension, diabetes mellitus ,Atrial fibrillation, chronic kidney diseases, smoking and alcoholism.Hypertension was found to be 73%, 29 out of 40 patients, and alcohol 77% ,31 out of 40 patients 54 **[6].** In the present study 27 patient were screened with CT brain with cerebral angiography and 13 with MRI brain with MR angiography. Culprit vessel was identified and thrombolysed with tenecteplase . Most of the patients had large artery stroke subtype, with the infarct region belonging to the territory of middle cerebral artery 27 out of 40. Our study also included 9 posterior circulatory stroke and in 4 patients Internal carotid artery involvement was noted **. [4]** The mean time from onset of symptoms to arrival at the medical emergency was 100.5(±70.14) minutes. while mean "door to needle" time was 50.9 (±22..77) min. The study subjects had a mean NIHSS score of 8.8 (±5.23) at arrival and a median mRS score of 1 .primary clinical efficacy outcome as improvement in NIHSS score of 4 or more points after 24 h 55. **[7]** Secondary clinical efficacy outcome was disability assessment at 3months based on mRS scale, favorable outcome (with a score of 0 or 1) or an unfavorable outcome (a score of 2–6).56**[8].** The study showed improvement from mean arrival NIHSS of 8.8 (±5.23) to mean of 4.22(±5.64) at 24hrs.It showed future improvement from mean NIHSS of 3.50 (± 5.40) at 1 week to mean of 1.57(±2.79) at 3 months with a significant p value of < 0.001 which is significant suggesting that tenecteplase has good efficacy. Durai Pandian et al from AIIMS reported 65% patients to have an improvement of 4 or more points in NIHSS score at 48 h with alteplase.**57 [11]** . The study shows that Tenecteplase is as effective as alteplase although the number of patients enrolled in the study is relatively small. NIHSS was recorded at arrival and reevaluated at 24 hrs, at 1 week, at discharge , at 1 month and 3 months with a significant p value of < 0.001.

In our study mRS showed mean of 1.10 (±1.66). In the present study, 67.5 % patients had an excellent recovery at 3 months with mRS score being 0 or 1, which is in accordance with a recent Randomized control trial in which excellent recovery was observed in 54% subjects[4] .In another study by Parson et al it showed that in the pooled tenecteplase groups, as compared with the alteplase group, infarct growth was reduced, and a higher proportion of patients had an excellent or good recovery (modified Rankin scale score of 0 to 2) at 3months **.[9]** But our study couldn't show any change in mRS between 1 and 3 months with mean value of 1.10 (±1.66). Adverse events were noted in 7 patients (17.5%) of which 1 patient developed symptomatic ICH with midline shift and underwent decompressive craniotomy. 1 patient showed no improvement with hours of thrombolysis and was taken for thrombectomy,1 patient underwent intraarterial thrombolysis as symptoms worsened. 4 patients developed asymptomatic ICH and were treated conservatively but none of patient died. t -test values in present study showed that probability of p=0.128 which is insignificant suggesting that tenecteplase is safe and effective drug for thrombolysis. Tenecteplase is a promising drug which is relatively cheaper as compared to alteplase and is found to be safe and effective. It was also shown to be non-inferior to alteplase though not superior. **[10]** The present study has limitations. The study included small number of patients and most of the patients had milder stroke with mean NIHSS of 8.8. Another limitation was no direct comparison was made with alteplase treated patients. Future multicenter randomized trials are required in a middle income group country like ours where stroke burden is huge and health care specialties look for safe and cost effective treatment strategies in acute ischemic stroke.

CONCLUSION:

Tenecteplase appears to be a safe and effective agent for acute ischemic stroke. ➢ Significant improvement in NIHSS ,low disability rates were observed in the present study . ➢ The ease of administration, cost effectiveness and non inferiority makes it a good alternative to alteplase in our setting.

Conflict Of Interest: Nil

Funding: Nil

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