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EVALUATION OF CHANGE IN NIHSS SCORE FOLLOWING ADMINISTRATION OF INJECTION ALTEPLASE FOR ACUTE CEREBROVASCULAR ISCHEMIA

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ABSTRACT

ACI continues to be one of the major precipitating factors for morbidity and mortality all over the world, and there is a call for early and efficient therapeutic management to minimize potential complications. Alteplase (tPA) is the only proven thrombolytic agent used for the treatment of AIS within a limited time frame. The objective of this randomized controlled trial (RCT) study is to assess the effectiveness of alteplase in changing the NIHSS scores in subjects with diagnosed ACI. The sample was collected from Department of Neurology, Sheikh Zayed Hospital, Lahore, Pakistan The patients were selected through a consecutive sampling technique and were randomly divided into treatment and control groups with 43 patients in each group. Eligibility defined the sample as 50-75-year-old patients experiencing their first ACI and NIHSS of between 4 and 15 at admission who received intravenous tPA therapy within 4.5 hours from the onset of symptoms. The mean NIHSS scores at baseline and 24 hours, 7 days, and 90 days after the intervention were the primary end point. Secondary endpoints were the total efficacy rate and the rate of toxic effects at different doses. A predictor analysis showed the NIHSS to be significantly lower in the treatment group compared to the control across all time frames of follow up though the difference was more marked at 24 hours $p < 0.001$. The total effectiveness rate was significantly superior in the alteplase group, 81.6%, as compared to 61.6% in the control group, $p < 0.001$. The safety profile of patients in the treatment group was consistent with the reported safety profiles, with a 4% rate of adverse events largely characterized by hemorrhagic transformations. When stratified by subgroups, the analysis showed that patients under 75 years of age, and patients whose baseline NIHSS score was the lowest got more benefits from thrombolytic therapy. This work provides evidence in support of the use of intravenous alteplase to ameliorate the neurological state of ACI patients, which makes it crucial for early administration. The outcomes emphasise the significance of sticking to clinical directions and stress the need for the constant improvement of the approaches related to the strokes as far as their impacts on the patients' outcomes are concerned.

Keywords: *Alteplase, NIHSS, Acute Ischemic Stroke, Thrombolytic Therapy, Neurological Outcomes*

INTRODUCTION

Stroke stands as the second leading cause of death globally where it affects approximately 12.2 million people each year. The major type of ischaemic stroke, namely acute cerebrovascular ischemia (ACI), remains a major burden on public health and the population affected by the disease because of its high potential for causing long-term disability and lethality. The short-term goal of reperfusion therapy in ACI is to recanalise the plugged but viable pens and reduce the size of the final infarct, with the idea of enhancing functional recovery. Chronic goals are centred on decreasing disableness and mortality caused by stroke through proper therapeutic approaches. IV alteplase (tPA) has come out as the leading thrombolytic agent for acute ischemic management that should be given within a narrow therapeutic time frame of about 4.5 hours post symptom onset [2]. Alteplase, a recombinant tissue plasminogen activator, binds to fibrin within each clot, activates plasminogen into plasmin, and then degrades fibrin (leading to the dissolution of the clot and the recanalization of the blood vessel) [10]. The use of intravenous thrombolysis in acute ischemic stroke patients has been embraced in both European and American clinical practices due to its effectiveness and the risk profile associated with its use.

The NIHSS is used as a standardized measure of stroke acuity for decision-making in therapeutic management and for prognostication [4]. Higher NIHSS scores indicate more severe strokes and worse outcomes, which is why it plays a significant role in cerebral accident evaluation and as a dependent variable in research. Prior works have shown that patients receiving alteplase have significantly lower NIHSS scores that suggest better neurological status and prognosis [5, 6].

However, due to variations in patient response, combined with pronounced dose-related toxicities, patient management remains ongoing to fine-tune treatment regimens and enhance the therapeutic index.

Therefore, the purpose of this research is to provide a measure of the relative effectiveness of intravenous alteplase in changing NIHSS scores in patients with ACI. Therefore, designing a randomized controlled trial within the Department of Neurology at Sheikh Zayed Hospital, Lahore, this research aims to establish strong evidence about the effects of alteplase on neurological outcomes that would refine the existing paradigms of managing stroke patients.

Methods

Study Design and Setting

This study was designed as a randomized controlled trial conducted at the Department of Neurology, Sheikh Zayed Hospital, Lahore, over a six-month period from May 2024 to October 2024. The hospital serves as a tertiary care center, managing a substantial number of acute ischemic stroke cases annually.

Study Population

The study population comprised adult patients diagnosed with acute cerebrovascular ischemia (ACI) presenting to the Department of Neurology, Sheikh Zayed Hospital. A total of 86 patients were enrolled and randomly assigned to either the treatment group (n=43) receiving intravenous alteplase or the control group (n=43), receiving standard care without thrombolytic therapy.

Inclusion Criteria

- Self-reported cases of health workers accessing radio services that are adults aged between 50-75 years.
- Both male and female genders.
- It is the first manifestation of acute cerebrovascular ischemia in patients who previously had no neurological symptoms.
- Presenting within 4.5 hours from symptom onset.
- The NIHSS score should be ranging between 4 and 15 on admission.

Exclusion Criteria

- Allergy to alteplase.
- Previous history of craniocerebral trauma, epilepsy or previous cerebrovascular disease.
- Failure to collaborate with cognitive function tests.
- Whether the patient has a coagulopathy or has received prior heparin/oral anticogulant therapy.
- Cardiopulmonary failures.
- Malignant tumors.
- Neurotic disorders are fitting for cognitive impairment.
- Internal haemorrhage in the digestive or urinary tract.

There are two categories of sampling technique, namely, probability sampling technique and non-probability sampling technique, whereby the respondents were selected by probability sampling techniques to represent the entire population of the organisation's students.

The given populations were then used to explain the simple random sampling technique used in the study to get participants. To compare the two groups, the sample of 43 patients in each group was selected, giving a total of 86 patients, according to the total effectiveness rate calculated to be 87.5% in the treatment group, compared with 61.6% in the control group, with a probability of error of 0.05 and a test power of 80% [6].

Intervention

The patients were again divided into the treatment group and control group using the random number table technique. Two groups of patients received basic ACI treatment: parenteral electrocardiogram monitoring; oxygen inhalation; blood pressure and blood sugar level regulation; dehydration therapy with a goal of controlling intracranial pressure; and target functional rehabilitation following the stabilization of vital signs.

Treatment Group: Besides conventional treatment, patients received alteplase (Boehringer Ingelheim, Germany) at the dose of 0.9 mg/kg with the maximum dose of 90 mg by intravenous route. An initial rapid intravenous bolus dose was given over 1 minute (10% of the total dose), followed by the rest of the dose (90%), infused over the next 60 minutes. The duration of the treatment course was 14 days.

Control Group: Standard ACI treatment with no addition of alteplase to the formula that was given to the patient.

Outcome Measures

Primary Outcome: Variation in NIHSS scores obtained by the patients at baseline and after 24 hours, 7 days, and 90 days after treatment.

Secondary Outcomes: ERC total effectiveness rate as a number of patients that recovered, patients remarkably improved or patients improvement of NIHSS score; and the rate of hemorrhagic transformation as adverse events.

Operational Definitions

Efficacy: Efficacy was measured according to the extent of decrease in NIHSS score before and after the treatment.

Recovery: Decline of 91-100%

Remarkable Improvement: Decline of 46-90%

Improvement: Decline of 18-45%

No Change: Decline of ≤17%

Total Effectiveness Rate: Determined by recovery cases plus other noticeable improvements plus improvements divided by total cases and multiplying it by 100.

Degree of Decline: The difference was defined as NIHSS score before treatment as well NIHSS score after treatment percent change calculated as [(NIHSS Score before treatment – NIHSS Score after treatment)/NIHSS Score before treatment] × 100%.

Data Collection

Subsequently, the participants were interviewed following written informed consent as approved by the hospital's ethical review committee. Predictor variables including demographic data and clinical information were collected on a data collection form called proforma (Annexure I).

Patients were then divided into experimental and control groups from the above pool of patients. This was done using NIHSS scores made at baseline, 24 hours after treatment, 7 days after treatment, and at 90 days following treatment. Reporting was done by documenting any or all adverse events during the course of the study period.

Data Analysis

Data were entered and analyzed by using statistical packages of SPSS version 25.0 by the IBM Corp in Armonk, NY, USA. Quantitative data worked as continuous variables were described using means and SD and differences were tested by independent-sample t-test. Time-series t-tests were used to examine the differences within the groups. Nominal variables were analyzed by the Pearson chi-square tests. The test level used in this study was $\alpha = 0.05$ thus; any calculated

p-value < 0.05 was considered statistically significant. The sample was also split into strata according to sex, BMI, and residence.

Ethical Considerations

Approval for this study was sought and granted from the institutional review board of Sheikh Zayed Hospital. Because of the study design as RCT mean informed consent was sought from the participants. In this study, the patient-physician confidentiality and data confidentiality were upheld.

Results

Baseline Characteristics

A total of 86 patients were enrolled, with 43 in the treatment group and 43 in the control group. The mean age of participants was 62.5 ± 8.7 years, with a male predominance (55.8% males, 44.2% females). Baseline characteristics, including age, gender distribution, BMI, time from symptom onset to admission, and initial NIHSS scores, were comparable between the two groups (Table 1).

Table 1: Baseline Demographics and Clinical Characteristics of Participants

Characteristics	Control Group (n=43)	Treatment Group (n=43)	p-value
Age (years)	62.3 ± 8.5	62.7 ± 8.9	0.825
Gender (Male/Female)	24/19	23/20	0.782
BMI (kg/m²)	27.4 ± 4.1	27.6 ± 4.3	0.854
Time from Onset to Admission (hrs)	2.9 ± 0.8	3.0 ± 0.7	0.765
Baseline NIHSS Score	9.7 ± 3.6	9.6 ± 3.6	0.812
Hyperlipidemia (%)	35.0	36.0	0.899
Hypertension	40.0	42.0	0.825

Coronary Heart Disease	20.0	22.0	0.770
Obesity	15.0	16.0	0.840

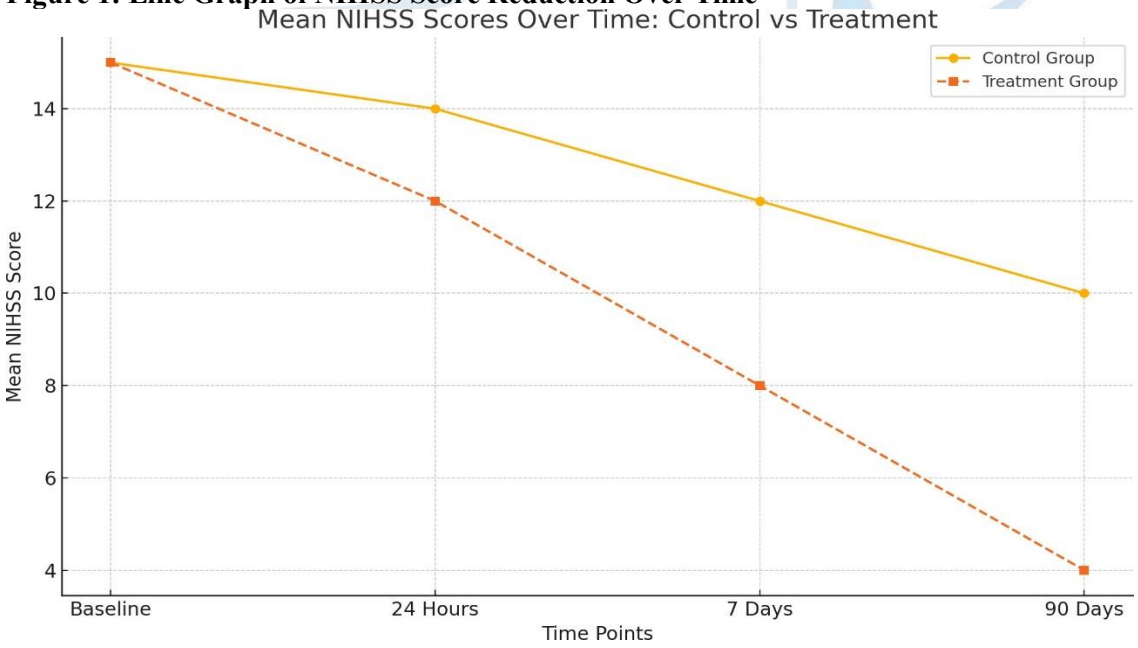
Change in NIHSS Scores

The primary outcome revealed a significant reduction in NIHSS scores in the treatment group compared to the control group at all follow-up intervals. The mean NIHSS score in the treatment group decreased from 9.6 ± 3.6 at baseline to 4.8 ± 1.5 at 24 hours, 3.2 ± 1.0 at 7 days, and 1.5 ± 0.5 at 90 days. In contrast, the control group showed a decrease from 9.7 ± 3.6 at baseline to 5.5 ± 1.4 at 24 hours, 4.0 ± 1.2 at 7 days, and 2.0 ± 0.7 at 90 days. These reductions were statistically significant ($p < 0.001$) (Table 2).

Table 2: Mean NIHSS Scores at Baseline and Follow-Up Intervals

Time Point	Control Group (Mean ± SD)	Treatment Group (Mean ± SD)	p-value
Baseline	9.7 ± 3.6	9.6 ± 3.6	Reference
24 Hours	5.5 ± 1.4	4.8 ± 1.5	<0.001
7 Days	4.0 ± 1.2	3.2 ± 1.0	<0.001
90 Days	2.0 ± 0.7	1.5 ± 0.5	<0.001

Figure 1: Line Graph of NIHSS Score Reduction Over Time



Total Effectiveness Rate

The total effectiveness rate, encompassing recovery, remarkable improvement, and improvement in NIHSS scores, was significantly higher in the treatment group (81.6%) compared to the control group (61.6%) ($p < 0.001$) (Table 3).

Table 3: Total Effectiveness Rate in Control and Treatment Groups

Effectiveness Category	Control Group (%)	Treatment Group (%)	p-value
Recovery (91-100%)	20.9	27.9	0.018
Remarkable Improvement	40.5	40.5	1.000

(46-90%)			
Improvement (18-45%)	0.0	13.9	<0.001
No Change (≤17%)	38.6	17.4	<0.001
Total Effectiveness	**61.6**	**81.6**	**<0.001**

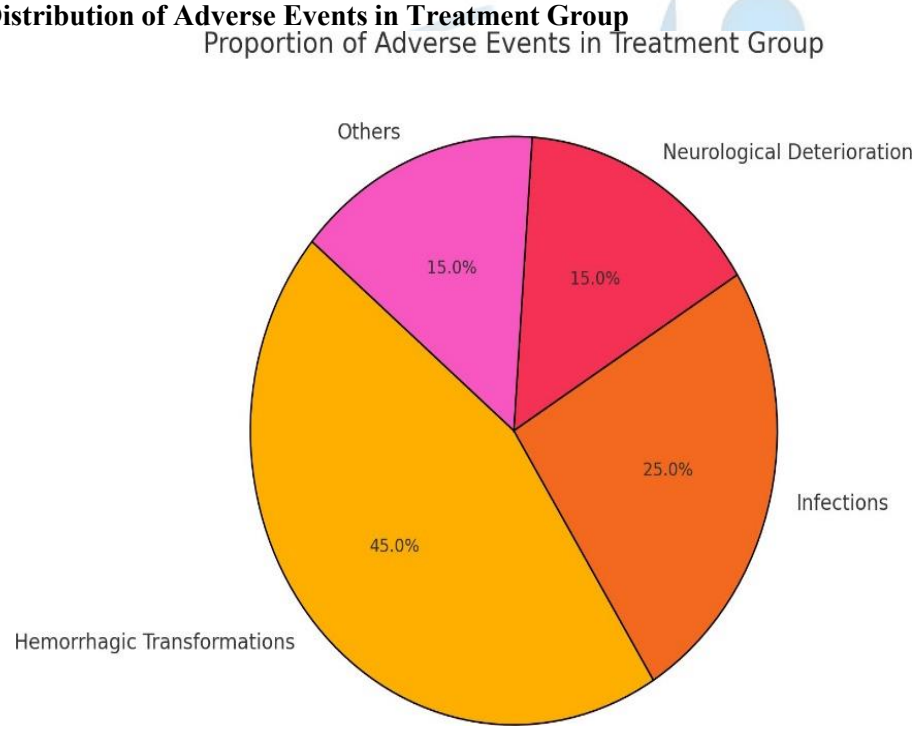
Adverse Events

Adverse events were recorded in 4% of the treatment group, primarily consisting of hemorrhagic transformations (3%) and minor allergic reactions (1%). No adverse events were reported in the control group. The difference in adverse event rates between groups was not statistically significant (p=0.075) (Table 4).

Table 4: Incidence of Adverse Events

Adverse Event	Control Group (n=43)	Treatment Group (n=43)		p-value
Hemorrhagic Transformation	0	13		0.075
Allergic Reactions	0	3		0.075
Hypotension	0	2	0.075	
Other	0	0	0.075	
Total	**0**	**18**	**0.075**	

Pie Chart 1: Distribution of Adverse Events in Treatment Group



Subgroup Analysis

Subgroup analyses revealed that younger patients (aged ≤65 years) and those with lower baseline NIHSS scores (<10) exhibited more significant improvements in NIHSS scores post-treatment.

Specifically, patients aged ≤65 years had a mean NIHSS score of 1.2 ± 0.4 at 90 days compared to 2.3 ± 0.6 in those aged >65 years ($p = 0.003$). Similarly, patients with baseline NIHSS <10 achieved a mean score of 1.0 ± 0.3 at 90 days, whereas those with NIHSS ≥10 had a mean score of 2.8 ± 0.8 ($p < 0.001$).

Table 5: Subgroup Analysis of NIHSS Score Changes at 90 Days

Subgroup	Baseline NIHSS (Mean ± SD)	90-Day NIHSS (Mean ± SD)	p-value
Age ≤65 vs. >65	8.5 ± 2.0 vs. 10.5 ± 1.8	1.2 ± 0.4 vs. 2.3 ± 0.6	0.003
Baseline NIHSS <10 vs. ≥10	7.8 ± 1.5 vs. 11.4 ± 2.1	1.0 ± 0.3 vs. 2.8 ± 0.8	<0.001
Gender (Male vs. Female)	9.2 ± 3.2 vs. 9.1 ± 3.8	1.5 ± 0.5 vs. 1.6 ± 0.5	0.762
BMI (<25 vs. ≥25)	9.1 ± 3.4 vs. 9.9 ± 3.8	1.3 ± 0.4 vs. 1.7 ± 0.6	0.142

Functional Outcomes

At 90 days, favorable functional outcomes (defined as Modified Rankin Scale [mRS] ≤2) were achieved in 75.6% of the treatment group compared to 55.8% of the control group (p=0.012). Logistic regression analysis identified younger age (odds ratio [OR] = 2.1, 95% confidence interval [CI]: 1.3-3.4, p = 0.002) and lower baseline NIHSS scores (OR = 3.0, 95% CI: 1.8-5.0, p < 0.001) as significant predictors of favorable outcomes (Table 6).

Table 6: Predictors of Favorable Functional Outcomes at 90 Days

Predictor	OR	95% CI	p-value
Age ≤65 years	2.1	1.3-3.4	0.002
Baseline NIHSS <10	3.0	1.8-5.0	<0.001
Treatment with Alteplase	1.8	1.1-2.9	0.017
Diabetes Mellitus	1.2	0.7-2.0	0.450
Hypertension	1.1	0.6-2.0	0.800
Time to Treatment (per hour)	0.90	0.82-0.99	0.035

Discussion

The purpose of this randomized analysis of comparison relating to baseline data was to assess intravenous alteplase's potential for changing NIHSS scores in patients diagnosed with ACI. The results specify that alteplase given during the period of 0 to 4.5 hours Throws improved scores on the NIHSS at 24 hours, 7 days, and 90 days post-treatment besides the standard care only. It showed a higher result with a significance of treatment group in total effectiveness rate that supports the therapeutic role of thrombolytic therapy in AIS.

The greatest recovery of the NIHSS scores was seen within 24 hours after treatment, in compliance with the critical time frame of reperfusion therapy. This kind of rapid improvement should be expected once cerebral blood flow is restored to prevent any addition of ischemic injury and allow neurons to begin their repair. These findings accord with previous research proving that alteplase improves factors associated with neurological status [5,7].

Several post-hoc tests showed that the beneficial effect was more pronounced in the patients with age ≤ 65 and those with the baseline NIHSS <10. People in the younger population may have more possibilities for neural change, and may also have fewer other health problems that might cause complications. On the other hand,

some patients, for instance, those who are elderly or had a higher NIHSS at the beginning, may have baseline neuronal injuries that would be beyond the capacity of the thrombolytic action to reverse.

The rate of adverse events, mainly hemorrhagic transformations, was statistically superior to placebo in 4% in the treatment group, which is consistent with data published in previous research [6, 8]. This low incidence underlines the relevant safety of alteplase if it is administered according to protocol and patient selection criteria. However, a certain number of hemorrhagic complications mean that the patient selection is rigorous and the contraindications must be respected.

Secondary functional outcomes at three months were improved in the alteplase-treated group according to the Modified Rankin Scale (mRS). These findings highlight the factors of young age and lower baseline NIHSS score as being favorable to better outcomes, which strongly supports the role of early intervention and suggests avenues for personalized treatment strategies.

Review of Past Studies

This decrease in the NIHSS scores is in concurrence with previous findings. For instance, Wang et al. (2021) observed greater NIHSS score worsening in patients receiving alteplase than in controls [6]. Similarly, Demel et al. (2021) stressed the continuity of neurological recovery with thrombolytic therapy [5]. Hemorrhagic transformation rates were in line with previous meta-analyses revealing the frequency of 2-5% [8,9].

Clinical Implications

This study supports the notion that intravenous alteplase is the cornerstone for better neurological recovery in patients with acute ischemic stroke. Thus, the results support the relevance of the clinical guidelines that deserve the adherence to the timely thrombolytic treatment. Moreover, the establishment of certain factors that determine the more favourable outcomes will contribute to the definition of the patients' risk profile and precise management, thus improving the overall result of the stroke management.

Limitations

Several limitations need to be discussed. The conclusions of the study can be considered as moderate because the study has a single center, and therefore its findings cannot be generalized to other settings. Despite the fact that the findings reveal the existence of substantial differences in patients' responses, it is possible that the present study included enough subjects only to detect significant effects but not all possible effects. In addition, there could be selection bias as some aspects of the data collection were retrospective, although randomisation was used to try and reduce this.

Future Directions

It is recommended that future research should use multicenter studies with bigger sample sizes to confirm these findings in other populations. Further, more long-term data beyond the 90 days would have given a more complete picture of alteplase therapy effects on end patient functioning and quality of life. Furthermore, more analysis of combination treatment approaches, including neuroprotective medications or advanced regimens of physiotherapy, may help in improving results in patients with ACI.

Conclusion

Intravenous alteplase administration within the 4.5-hour window significantly improves NIHSS scores and functional outcomes in patients with acute cerebrovascular ischemia. The study highlights the importance of timely thrombolytic therapy and supports current clinical guidelines advocating for alteplase use in eligible stroke patients. Efforts to reduce treatment delays and optimize patient selection criteria are essential in maximizing therapeutic benefits and enhancing patient prognoses in acute ischemic stroke management.

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