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Usage of Alteplase in Stroke Patients in Rural Tertiary Care Hospital: An Observational Study

Jagadish Babu.Dasari*[1], Jyothi.K[2]

1. Department of Clinical pharmacy, SAC College of pharmacy, Karnataka, India.

ABSTRACT

The aim of the study is to assess the usage of alteplase in stroke patients which is second leading cause in worldwide. Its beneficial effect in stroke patients is to disperse the thrombus within an occluded cerebral vessel and to limit ischemic damage within surrounding tissue (ischemic penumbra) and is safety and efficacy towards the stroke patient. This is prospective observational study, which assed the current usage of tissue Plasminogen activator (tPA) alteplase in stroke patients. This study was conducted in Stroke patients in Adichunchanagiri Hospital and Research Center. Duration of our study is sixteen months. A total of 140 stroke patients were assigned to receive alteplase. In which 102 (72.85%) Patients were treated before 3 hours (Window period) the study population were elderly with the age between 53-57 were 40.70% (n=48), and followed by 63-67 were 22.03 % (n=26), where as in female elderly patients the age group between 48-52 were 59.10% (n=13) and followed by 53-57 were 18.18 (n=4), elderly patients are more prone to have stroke. Therefore 54.23% (n=64) were recoverd in the post intervention benefit of alteplase in stroke patients,as in female patients were 68.18% (n=15) and age between 78-82 years only one patient died during the treatment. This study shows that efficacy and safety of thrombolytic in stroke patients within 3 hours and recover of the patients from the stroke is high rate. The findings encourages wider use of thrombolytic therapy for suitable patients treated in stroke centres can be a beneficial in future endeavours.

Keywords: Alteplase, Stroke Patients and Thromobolytic.

*Corresponding Author Email: jagadish.pharmacy@gmail.com

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INTRODUCTION:

Stroke is one of the major causes of human morbidity and mortality[1]. Cerebrovascular diseases are the second leading cause of death worldwide, accounting for 10% of total deaths.[2] The male to female ratio was 1.7. Around 12% of all stroke occurred in population below 40 years.[1]

During the last decade, the age-adjusted prevalence rate of stroke was between 250-350/100,000. Recent studies showed that the age-adjusted annual incidence rate was 105/100,000 in the urban community of Kolkata and 262/100,000 in a rural community of Bengal. Stroke represented 1.2% of total deaths in India.[3] Like all developing countries, stroke is fast emerging as a major public health problem in India. Population - based estimates confirm a rising trend in both incidence and prevalence of stroke in India.[4]

The Framingham Heart Study and other international prospective epidemiological studies identified the major atherogenic risk factors for stroke as hypertension, diabetes mellitus, hyperlipidemia, and smoking.[5] However, overweight and obesity have been independently associated with the risk for ischemic stroke and their incidence is increasing in industrialized countries.[6]

A pooled analysis of data from the National Institute of Neurological Disorders and Stroke (NINDS) trials (parts 1and 2, 3-hour window), the 2 European Cooperative Acute Stroke Study (ECASS) trials (6-hour window), and the 2 Alteplase Thrombolysis for Acute Non-interventional Therapy in Ischemic Stroke (ATLANTIS) trials (part A, 6-hour window and part B, 5-hour window), suggest a potential benefit from treatment beyond 3 hours.[7]

Alteplase, a recombinant tissue plasminogen activator (rt-PA), is a thrombolytic enzyme that causes blood clots to dissolve and hence helps to restore blood flow to the brain following stroke. Alteplase is administered intravenously (IV) over 60 minutes at 0.9mg/kg (to a maximum of 90mg); initial 10% of dose by IV bolus injection over one minute, and the remainder by IV infusion over 60 minutes.[8]

Cost-effectiveness analyses have suggested that tPA use results in substantial improvements in health measured in quality-adjusted life years (QALYs)—while at the same time reducing costs to society.[9] And it is widely accepted as a first-line treatment.[10] However, because of lack of evidence regarding the usefulness of thrombolytic therapy after 3 hours, it is probably not appropriate for most centers to apply this therapy beyond this time until definitive data are available.[11]

Besides the safety, clinicians are also concerned about the efficacy. It is a common argument that a "higher dosage may have greater efficacy." However, this argument was not supported by the findings of the desmoplase study, Desmoteplase In patients with acute ischaemic Stroke (DIAS-2).[12] There are several possible explanations for the improvement seen in the safety of intravenous tPA within the health system in the 2 years since the initial report. The improved results may have been due to chance. They may also reflect undetected changes in patient characteristics such as stroke severity. [13] Therefore, the main objective of our study is the usage of alteplase in stroke patients, to assess safety outcome of alteplase administration and assessing the administration of alteplase intervention.

MATERIALS AND METHOD

This is prospective observational study, which assed the current usage of tissue Plasminogen activator (tPA) alteplase in stroke patients. This study was conducted in Stroke patients in Adichunchanagiri Hospital and Research Center (AH & RC) 750 bed hospital, B.G.Nagara, Mandya District, and Karnataka, India. Duration of study is November 18th 2010 to February 19th 2012 (i.e., 16 months) and a total 140 stroke patients taken for the study. And assigned alteplase to them. The median time for the administration of alteplase was within 3 hours and administration method explained below respectively. Neurology and Radiology Departments of the hospital were particularly chosen for the study, which has enormous potential for diagnosing and treating acute ischemic stroke.

Study approval: The study was approved by Institutional Ethical Committee, AH&RC, B.G.Nagara.

Study Criteria

Inclusion:

- I.V. alteplase within 3 hours of stroke onset.
- Age > 18 years of age.
- CT scan showing no haemorrhage or oedema of >1/3 of MCA artery.

Exclusion:

- Suspected recent myocardial infarction or past 3 to 6 months before.
- Sustained BP> 185 to 190 systolic; 110-120 diastolic.
- Stroke or serious trauma within the past three months where the risks of bleeding are considered to outweigh the benefits of therapy.
- Brain haemorrhage or major infarction.

Administration Method of Alteplase in Stroke Patients

0.9 mg/kg body weight. This dose given in two parts:

1) 10% of the total dose is administration on IV bolus followed immediately.
2) The remaining dose added to 50 mL sodium chloride 0.9% mini-bag and administration as an IV infusion over 60 min.[14]

Example for administration for patient weighing 72kg weight:

Step 1: Total dose = 0.9 mg/kg body weight
= 0.9 x 72
= 64.80 mg alteplase.

Step 2: Bolus Dose =10% total dose
=10/100 x 64.80
=0.1 x 64.80
= 06.48 mg
= 06.48mL therefore, given as I.V. push over minute.

Step 3: Infusion dose = total dose – bolus dose
= 64.80-06.48
= 58.32mg = 58.32mL, add to 50mL sodium chloride 0.9% minibag therefore, infusion over 60 minutes.

Example:

Weight (kg) (approximate to nearest 5kg)	**total dose (mg) (dose = 0.9mg/kg) max dose: 90mg**	**Alteplase bolus dose volume (mL) (bolus = 10% of total)**	**Alteplase infusion dose volume (mL) (infusion = 90% of total)**	**Total infusion volume (mL) (approximate)**
70	63.0	6.3	56.7	107

Total dose is calculated based on body weight and bolus dose is given as an IV push over 1 minute, and add to 5mL sodium chloride 0.9% mini-bag and infuse over 60 minutes until empty via volume control pump.

RESULTS AND DISCUSSION:

Between November 18th 2010 and February 18th 2012, a total of 140 patients were assigned to receive alteplase. In which 102 (72.85%) Patients were treated before 3 hours (Window period).Age wise distribution shows that most of the study population were elderly with the age between 53-57 were 40.70% (n=48), and followed by 63-67 were 22.03 % (n=26), where as in female elderly patients the age group between 48-52 were 59.10% (n=13) and followed by 53-57 were 18.18 (n=4),elderly patients are more prone have stroke, due to change in food habits, life

style, stress, and other factors(Table 1). But in the study Ford et al[15]. Shows that 80-year-old group had more severe strokes, where as in current study shows 53-57-year-old group are had high rate of stroke.

Table 1 Gender and Age Wise Distribution of Patient Treated With Stroke (N=140)

Age in Years	Male	Percentage (%)	Female	Percentage (%)
48-52	22	18.64	13	59.10
53-57	48	40.70	04	18.18
58-62	15	12.71	03	13.63
63-67	26	22.03	02	09.09
68-72	05	04.23	00	00.00
73-77	01	00.84	00	00.00
78-82	01	00.84	00	00.00
Total	**118**	**84.28**	**22**	**15.71**

The Patients past medical history revealed that 82.14% (n=115) of the study population had Diabetes mellitus (Table 2), 11.42% (n=16) had hypertension (Table 3) and only male patients were 06.42% (n=09) had both diabetes mellitus and hypertension (Table 4). Thus, the patients with diabetes mellitus are more prone to have stroke. In the study Sivanandy P et al.[16] shows the patient's medical history had 21.73% (n =5) had hypertension and 21.73% (n = 5) had both hypertension and diabetes.

Table 2. Patients Having Diabetes Mellitus with Stroke (N=140)

Age in Years	Male (N=94)	Percentage (%)	Female (N=21)	Percentage (%)
48-52	20	21.27	12	57.14
53-57	40	42.55	04	19.04
58-62	09	09.60	03	14.28
63-67	18	19.14	02	09.52
68-72	05	05.31	00	00.00
73-77	01	01.06	00	00.00
78-82	01	01.06	00	00.00
Total=115				**82.14**

Table 3. Patients Having Hypertension with Stroke (N=140)

Age in Years	Male (N=15)	Percentage (%)	Female (N=01)	Percentage (%)
48-52	01	06.66	01	100
53-57	03	20.00	00	00
58-62	04	26.66	00	00
63-67	03	20.00	00	00
68-72	02	13.33	00	00
73-77	01	06.66	00	00
78-82	01	06.66	00	00
Total=16				**11.42**

Table 4. Patients Having both Diabetes Mellitus and Hypertension with Stroke in males (N=140)

Age in Years	Male (N=09)	Percentage (%)
48-52	00	00.00
53-57	01	11.11
58-62	03	33.33
63-67	01	11.11
68-72	02	22.22
73-77	01	11.11
78-82	01	11.11
Total	**09**	**06.42**

The past history of stroke shows that 15.71% (n=22) only male patients are prone to be had the previous stroke (Table 5 and Figure 1). This indicates that the stroke patients are more prone have recurrent attack and alarms the physician and patients regard the severity and the need of effective treatment.

Table 5. Previous History of Stroke in males (N=140)

Age in Years	Male (N=22)	Percentage (%)
48-52	09	40.90
53-57	07	31.81
58-62	03	13.63
63-67	01	04.54
68-72	00	00.00
73-77	01	04.54
78-82	01	04.54
Total	**22**	**15.71**

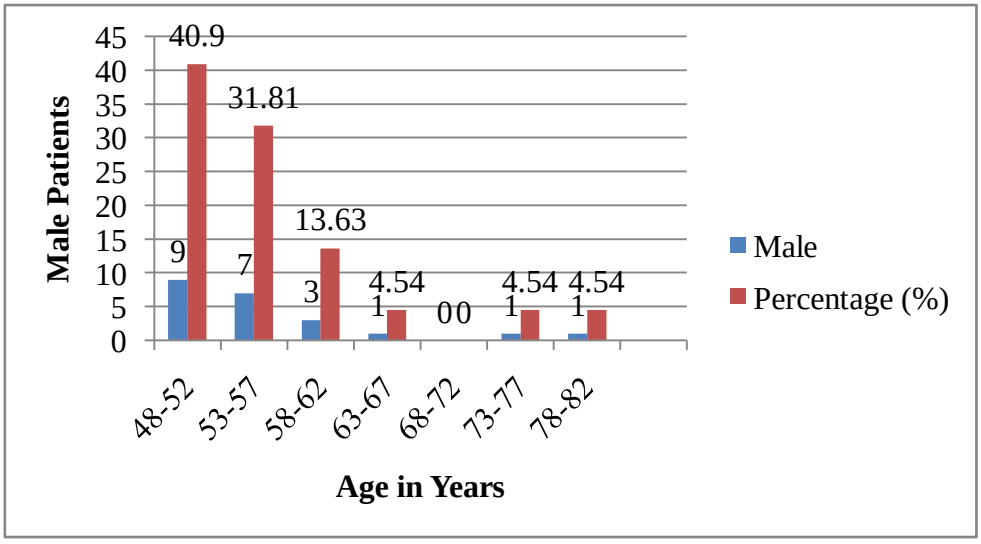

Figure 1 Previous History of Stroke in males (N=140)

In this study all the patients were received thrombolysis and among 140 patients, one died with intra cerebral haemorrhage, which is associated risk with thrombolytic therapy and it says that use of thrombolytic therapy was safe, and the rate of intra cerebral haemorrhage was low.

The current study revealed that around 86.36% (n=102) of the study population were injected the drug Alteplase within 3 hours after getting admission to the hospital(Table 6). The drug was injected initially to thrombolyse the clot and to give speedy recovery to the patient.In one study shows patients treated with tPA within 3 hours are more favorable than the results for patients treated between 3 and 5 hours by Albers W G et al.[17]

Table 6.Alteplase prescribed ≤ 3hours in stroke patients:

Age in Years	Male (N=118)	Percentage (%)	Female (N=22)	Percentage (%)
48-52	18	15.25	10	45.45
53-57	31	26.27	04	18.18
58-62	07	05.93	03	13.63
63-67	20	16.94	02	09.09
68-72	05	04.23	00	00.00
73-77	01	00.84	00	00.00
78-82	01	00.84	00	00.00
Total	83	70.33	19	86.36

In this study population 54.23% (n=64) were recoverd in the post intervention benefit of alteplase in stroke patients,as in female patients were 68.18% (n=15) and age between 78-82 years only one patient died during the treatment(Table 7 and Figure 2). In our study female stroke patients are recovered drastically as campare to male patients.The study results shows excellent outcome where 64 recovered, one of the most important predictors of clinical success is time to treatment, with early treatment of < 3 hours demonstrating significant improvement in terms of 90-day clinical outcome and reduced cerebral hemorrhage. The study has limitations that we didt measure the Rankin score.

Table 7. Post Intervention Benefits of Alteplase In Stroke Patients:

Age in Years	Male (N=118)	Percentage (%)	Female (N=22)	Percentage (%)
48-52	17	14.40	10	45.45
53-57	27	22.88	03	13.63
58-62	05	04.23	02	09.09
63-67	13	11.01	00	00.00
68-72	02	01.69	00	00.00
73-77	00	00.00	00	00.00
78-82	00	00.00	00	00.00
Total	64	54.23	15	68.18

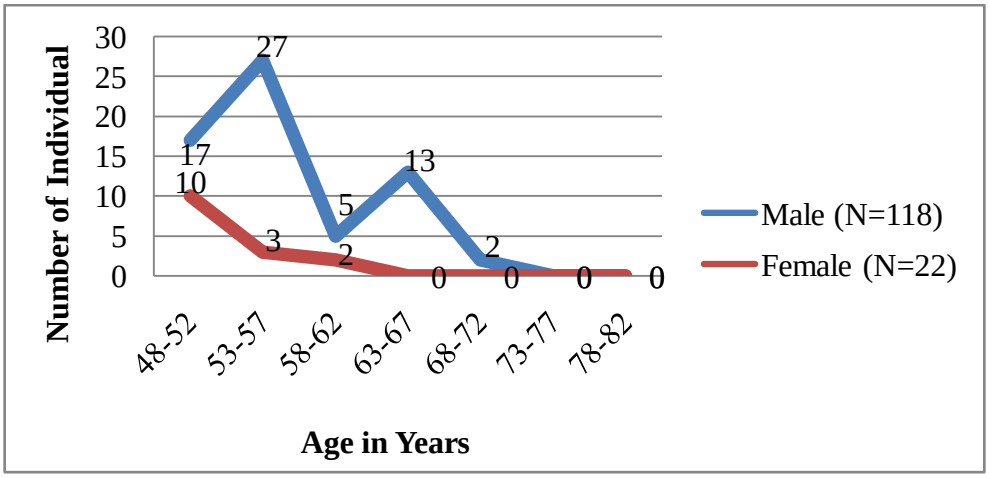

Figure 2. Post Intervention Benefits of Alteplase In Stroke Patients

CONCLUSION:

In our study suggest an overall efficacy and good safety of thromobolysis in adults. And further studies shows the recover of the patients from the stroke was drastic in adults and particularly in females stroke patients and further, studies are needed to determine the prognostic factors in adults and to assess the prognosis of the stroke. And another future challenges is to assess the safety and efficacy of thrombolysis in children and young adolescents.

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