

ACUTE STROKE - A STUDY OF NEUROLOGICAL OUTCOMES IN ACUTE STROKES – THROMBOLYSED V/S NON-THROMBOLYSED PATIENTS BASED ON GENDER

Varghese A Pallan *, Dinesh Kumar **, PC Gilvaz ***

* Consultant Neurologist, St. James Chalakudy, Kerala.

** Resident DM, Department of Neurology, Jubilee Mission Medical College Hospital and Research Institute, Thrissur, Kerala.

*** Professor & HOD, Department of Neurology, Jubilee Mission Medical College Hospital and Research Institute, Thrissur, Kerala.

ABSTRACT

Background: Thrombolysis with intravenous recombinant tissue plasminogen activator (IvrtPA) for acute ischaemic stroke is the only approved standard protocol since 1995 done within window period studies as to fate of non thrombolysed patients were few and anecdotal especially from our part of the country. As the usage a drug increase in time and numbers, it's problems and pitfalls begin to emerge. Hence this study was undertaken to have a fresh look at the scenario at 20 years.

Aims & Objectives: The main aim of study was to evaluate the profile of patients who were not thrombolysed with intravenous recombinant tissue plasminogen activator (i v r-tpa) versus thrombolysed patients in acute ischaemic stroke using NIHSS scoring. Objective is to compare the efficacy of thrombolytic therapy in males versus females.

Study Population and Setting: All patients presenting to NEURO ICU of Jubilee Mission Medical College And Research Institute with acute stroke from 1 OCTOBER 2014 to 1 APRIL 2016 over 18 month period were included in study. To compare the neurological profile of patients not undergoing thrombolysis to those thrombolysed using serial NIHSS scoring at baseline (0 hours,12 hours,24 hours, 7 days and 90 days post thrombolysis. To compare the efficacy of thrombolytic therapy in males versus females .

Methodology:

All suspected stroke patients were sent for a non contrast computed tomographic (CT) imaging of brain and admitted in NEURO STROKE UNIT.

Initial assessment including GRBS, ECG, a baseline National Institute of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS) scoring as per institutional protocol.

Results:

60% (36/60) thrombolysed patients whereas in the non thrombolysed individuals 50% improved (74/148). 63% (14/22) of Female patients improved whereas in the male thrombolysed individuals 57% improved (22/38).

Conclusion:

In this study the neurological profile of patient assessed with NIH stroke scale, Barthel score showed a statically significant 90 day improvement in the thrombolysed group of individuals.

KEYWORDS:

Thrombolytic therapy, Stroke, IvrtPA, Gender

INTRODUCTION

Stroke is a global health problem. It is the second commonest cause of death and fourth leading cause of disability worldwide.¹ Approximately 20 million people each year will suffer from stroke and of these 5 million will not survive. In developed countries, stroke is the first leading cause for disability, second leading cause of dementia and third leading cause of death.² Stroke is also a predisposing factor for epilepsy, falls and depression in developed countries and is a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% - 30% being permanently

disabled.³ Stroke is no longer a disease of the developed world: Low and middle-income countries account for 85.5% of total stroke deaths worldwide and the number of disability-adjusted life years in these countries was approximately seven times that in high-income countries.⁴ Stroke is a life-changing event that affects not only the person who may be disabled, but their family and caregivers.⁵ Utility analyses show that a major stroke is viewed by more than half of those at risk as being worse than death.⁶ In many high-income countries, stroke management has changed substantially in the past two decades. Impressive developments through structured clinical pathways for thrombolysis and secondary prevention have been made.⁷ Organized provision of care in a stroke unit have been found to increase the number of patients who survive, return home, and regain functional independence in their everyday activities.⁸ However, implementation of such organized care for stroke is limited and inadequate in low and middle income countries, especially in a country like India where resources for rehabilitation are scarce.⁹

METHODOLOGY

All patients presenting to NEURO ICU of Jubilee Mission Medical College And Research Institute with acute stroke from 1 OCTOBER 2014 to 1 APRIL 2016 over 18 month period were included in study. To compare the neurological profile of patients not undergoing thrombolysis to those thrombolysed using serial NIHSS scoring at baseline (0 hours, 12 hours, 24 hours, 7 days and 90 days post thrombolysis and to compare the efficacy of thrombolytic therapy in males versus females. All suspected stroke patients were sent for a non contrast computed tomographic (CT) imaging of brain and admitted in NEURO STROKE UNIT. Initial assessment including GRBS, ECG, a baseline National Institute of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS) scoring as per institutional protocol. Initial examination, brief history and quick neurological examination was performed in every patient to know the status. Profile of patients who underwent thrombolysis with IV r-tpa in acute ischemic stroke using NIHSS scoring, 1 -Non Thrombolysed, 2- Thrombolysed, Pink - Improved, Green- Not improved. Mann-Whitney

U independent sample t test was applied and data was statistically analyzed in SPSS ver 21.

RESULTS

Na=148, Nb=60. Set N=Na+Nb- 208, Ranked from lowest to highest (including tied ranks when appropriate). Non Thrombolysed patients showed 50% (74/148) improvement whereas in the thrombolysed individuals 60% improved (36/60). The independent sample non parametric Mann-Whitney U test was applied and we find that the asymptotic significance with p value 0.010 in the 7th day improvement (1-7improv) across categories of patients presenting to the stroke unit within 270 minutes-thrombolysed and non-thrombolysed cases. So we neglect the null hypothesis with significance level of $\alpha < 0.05$ (p<0.012) and compliance level at 95%. Improvement in thrombolysed patients shows a significant score.

Age Wise Distribution Of Thrombolytic Therapy

Profile of Male versus female patients who underwent thrombolysis with IV r-tpa in acute ischemic stroke using NIHSS scoring. Mann-Whitney U independent sample t test was applied. Na=38, Nb=22. Set N=Na+Nb- 60, Ranked from lowest to highest (including tied ranks when appropriate). 63% (14/22) of Female patients improved whereas in the male thrombolysed individuals 57% improved (22/38) according to Mean NIHSS score.

Mean Barthel index 63(25-100) at 3 Months

Mann-Whitney U independent sample t test was applied. Na=60, Nb=148. Set N=Na+Nb- 208, Ranked from lowest to highest (including tied ranks when appropriate). The independent sample non parametric Mann-Whitney U test was applied and we find that the asymptotic significance with p value 0.016 in the third month improvement (1-90improv) across categories of patients presenting to the stroke unit. So we neglect the null hypothesis with significance level of $\alpha < 0.05$ (p<0.012) and compliance level at 95%. Improvement in thrombolysed patients shows a significant score.

Comparison of Mean Barthel index 63(25-100) at 3 Months

Mann-Whitney U independent sample t test was applied $N_a=22$, $N_b=38$. Set $N=N_a+N_b=60$, Ranked from lowest to highest (including tied ranks when appropriate). 64% patients whereas in the more than 50 group individuals 44% improved (9/18) The independent sample non parametric Mann-Whitney U test was applied and we find that the asymptotic significance with p value 0.012 in the 3 month improvement (1-90 improv) across categories of patients presenting to the stroke unit. So we neglect the null hypothesis with significance level of $\alpha < 0.05$ ($p < 0.048$) and compliance level at 95%. Improvement in female patients shows a significant score: Six (6/60) patient died due to cardio respiratory arrest, sICH 10% in Thrombolysed group. At follow up mean BI was 63 (range 25-100). Ten patients had SICH Rankin's Score showed severe handicap in 10 patients THROMBOLYSED Group had severe handicap in (10/60), 16.66% and non thrombolysed group (20/148), 13.5%. mRS (0-2) at day 90 was 60 %

DISCUSSION

Though a large proportion of ischemic stroke patients were eligible to receive thrombolytic therapy, the majority could not reach a center with adequate facilities within the recommended time window. More alarmingly, even for those patients who reached within the time window, no significant attempt was made to initiate thrombolysis. These data call not only for attention to improve existing patient transport facilities, but also for improving the awareness of efficacy and therapeutic window of thrombolysis in stroke, among the public as well as primary care doctors. Health care delivery policy-makers have to seriously ponder on what measures can be taken to provide the drug to such patients or to find ways to meet the expenditure.^{11,12} Emergency medical service systems should implement a pre-hospital stroke protocol to evaluate and rapidly identify patients who may benefit from thrombolytic therapy, similar to the protocol for chest pain.^{13,14} Stroke patients presenting within 3 hours should be triaged on an emergent basis with an urgency similar to acute ST-elevation in myocardial infarction. The use of an acute stroke care team, including physicians, neurologists, nurses, radiology staff and pharmacists, is an

effective way to coordinate initial evaluation and treatment. The round-the-clock availability of CT scanning in the emergency medicine department has to be sure in district hospital level onwards. Availability of a technician well versed with operating a CT scan machine, round-the-clock, will suffice, without the need for a radiologist, as physicians in the emerge department will be capable of distinguishing an ischemic infarct from an intracranial hemorrhage and they can also be trained to pick up early radiological signs of an evolving infarct in CT images. Mechanisms are also to be worked out to readily make available the only proven drug for acute stroke therapy, i.e., TPA, at the tertiary care centers and district headquarter hospitals, despite the current high cost of the drug. The developing world carries the highest burden of stroke mortality and stroke-related disability. The number of stroke patients receiving r-tPA in the developing world is extremely low. Pre-hospital delay, financial constraints, and lack of infrastructure remain barriers of thrombolysis therapy in developing countries. Until a cheaper thrombolytic agent and the proper infrastructure for utilization of thrombolytic therapy is available, developing countries should focus on primary and secondary stroke prevention strategies. However, governments and health systems of developing countries should efforts exurbs for promotion of their infrastructure of stroke care. The stroke in developing countries has grown to epidemic proportions.¹⁵ Two-thirds of global stroke occurs in low-and middle-income countries.¹⁶ Most of the available stroke data from these countries are hospital series.¹⁶ There has been limited progress in management of patients with stroke in developing countries and data on stroke care in these countries are sparse.¹⁷⁻¹⁹ Guidelines are continuously developed and updated in the developed world but their practicality for use in developing regions is unrealistic.²⁰ The number of stroke patients receiving r-tPA in the third world is extremely low.²¹ Stroke thrombolysis is currently used in few developing countries like Brazil, Argentina, Senegal, Iran, Pakistan, China, Thailand, and India.²¹

CONCLUSION

In this study the neurological profile of patient assessed with NIH stroke scale, Barthel score

showed a statically significant 90 day improvement in the thrombolysed group of individuals. Functional outcome was better in female patients.

LIMITATIONS

This was an observational study rather than a randomized control study. Hence this study would not change any guideline or recommendation. Certain patients could not be directly assessed but assessed telephonically.

REFERENCES

1. PM Dalal, Madhumita Bhattacharjee. Stroke Epidemic in India: Hypertension-Stroke Control Programme is Urgently Needed. JAPI. Vol 55. October 2007.
2. Strong K, Mathers C, Bonita R. Preventing stroke: saves lives around the world. *Lancet Neurol* 2007; 6:182-7.
3. Marc Fisher MD, Bo Norrving. 1st Global Conference on Healthy. Lifestyles and Non communicable diseases Control. Moscow, April 28-29, 2011.
4. Steinwachs DM, Collins-Nakai RL, Cohn LH, Garson A Jr, Wolk MJ. The future of cardiology: utilization 24 and costs of care. *Am Coll Cardiol*. 2000 Apr; 35(5 Suppl B):91B-98B.
5. Mathers CD, Lopez AD, Murray CJL. The burden of disease and mortality by condition: data, methods, and results for 2001. In: Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL, editors.
6. American Stroke Association. Primary Prevention of Ischemic Stroke: A Guideline from the American Heart Association/American Stroke Association Stroke Council. *Stroke*. 2006; 37:1583-1633.
7. Warlow C, van Gijn J, Dennis M, et al. *Stroke: practical management*, 3rd edn. Oxford: Blackwell Publishing, 2008.
8. Stroke Unit Trialists' Collaboration. How do stroke units improve patient outcomes? A collaborative systematic review of the randomized trials. *Stroke* 1997; 28: 2139-44.
9. Peter Langhorne, Linda de Villiers, Jeyaraj Durai Pandian. Applicability of stroke-unit care to low-income and middle-income countries *Lancet Neurol* 2012; 11:341-48.
10. Katzan IL, Sila CA, Furlan AJ. Community use of intravenous tissue plas-minogen activator for acute stroke results of brain matters stroke management survey. *Stroke* 2001;32:861-5.
11. Merino JG, Silver B, Wong E. Extending rTPA use to community and rural stroke patients. *Stroke* 2002;33:141-6.
12. Lacy CR, Suh DC, Bueno M. Delay in presentation and evaluation for acute stroke: stroke time registry for outcomes knowledge and epidemiology (stroke). *Stroke* 2001;32:63-9.
13. Adams HP, Brott TG, Furlan AJ. Guidelines for thrombolytic therapy for acute stroke. *Circulation* 94:1167-74.
14. L. A. Sposato, M. M. Esnaola, R. Zamora, M. C. Zurru, O. Fustinoni, and G. Saposnik, "Quality of ischemic stroke care in emerging countries: the Argentinian National Stroke Registry (ReNACer)," *Stroke*, vol. 39, no. 11, pp. 3036-3041, 2008
15. V. L. Feigin, "Stroke epidemiology in the developing world," *The Lancet*, vol. 365, no. 9478, pp. 2160-2161, 2005.
16. K. Ghandehari and Z. Izadi Mood, "The Khorasan stroke registry: results of a five-year hospital-based study," *Cerebrovascular Diseases*, vol. 23, no. 2-3, pp. 132-139, 2007.
17. N. Venketasubramanian, "Stroke in developing countries," in *Current Review of Cerebrovascular Disease*, M. Fisher and J. Bogousslavsky, Eds., pp. 212-214, CM Publications, Philadelphia, Pa, USA, 2nd edition, 2001.
18. K. Ghandehari and Z. Izadi Mood, "Cardioembolic strokes in Eastern Iran and the importance of rheumatic valvular disease," *Turkish Journal of Medical Sciences*, vol. 36, no. 6, pp. 361-364, 2006.
19. K. Ghandehari and Z. Izadi Mood, "Incidence and etiology of ischemic stroke in Persian young adults," *Acta Neurologica Scandinavica*, vol. 113, no. 2, pp. 121-124, 2006.

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20. K. Hill and E. Lalor, "Clinical guidelines for stroke care: why the fuss and is there opportunity for collaboration?" *International Journal of Stroke*, vol. 3, no. 3, pp. 173–174, 2008.
 21. J.D.Pandian, V.Padma, P.Vijaya, P.N.Sylaja, and J.M.K.Murthy, "Stroke and thrombolysis in developing countries," *International Journal of Stroke*, vol. 2, no. 1, pp. 17–26, 2007.