Utilization and outcomes with low dose tissue plasminogen activator as intravenous thrombolytic therapy for ischaemic stroke at Aga Khan University Hospital, Karachi: a retrospective analysis

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INTRODUCTION

- In managing stroke, a major breakthrough came in 1996 when the National Institute of Neurological Disorder (NINDS) trial proved that treatment with intravenous tissue plasminogen activator (t-PA) within three hours of the onset of ischemic stroke improved clinical outcome at three months.
- There are only two longitudinal studies on the utilization and outcome of thrombolytic therapy for acute stroke in Pakistan to date, both of which had small sample sizes.
- The paucity of literature on the safety and efficacy of intravenous t-PA, especially in the Pakistani population, hence necessitated further investigation.

OBJECTIVES

- To determine the safety and efficacy of intravenous tissue plasminogen activator (t-PA) at a dose of 0.6mg/kg in acute stroke patients at Aga Khan University hospital (AKUH).
- To compare the results with those of 0.9mg/kg dose mentioned in literature, notably the safe implementation of thrombolysis in stroke monitoring study (SITS-MOST)[1].

METHODS

- This retrospective observational study was conducted at Aga Khan University Hospital.
- Hospital records of patients receiving intravenous tissue plasminogen activator for ischemic stroke thrombolysis from January, 2007 to October, 2016 were reviewed.
- Primary and Secondary safety and efficacy outcome variables were recorded.

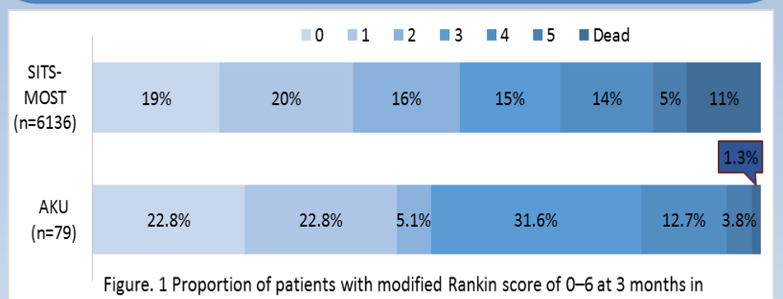

Figure. 1 Proportion of patients with modified Rankin score of 0–6 at 3 months in AKUH and SITS-MOST

	AKU (n=79)	SITS-MOST (n=6483)
Age(years)	62 (54-70)	68 (59–75)
Gender (Female)	27 (34.2%)	2581 (39.8%)
Independence (modified Rankin score 0–1) before stroke	79/79 (100%)	5899/6337 (93.1%)
Hypertension	56/79 (70.9%)	3710/6318 (58.7%)
Diabetes Mellitus	24/79(30.4%)	1020/6374 (16.0%)
Systolic Blood Pressure (mm Hg)	150(130-171)	150 (137–166)
Diastolic Blood Pressure (mm Hg)	81 (70-96)	81 (74–90)
Degree of neurological severity (pre t-PA NIHSS)	12 (8-15)	12 (8–17)
Mild (NIHSS 1–7)	17/79 (21.5%)	1494 (23%)
Moderate (NIHSS 8–14)	39/79 (49.4%)	2409 (37%)
Severe (NIHSS ≥15)	23/79 (29.1%)	2571 (40%)
Previous stroke	5/79(6.3%)	643/6395 (10.1%)
Cause of stroke		
Large vessel disease with substantial carotid stenosis	5 (6.3%)	844 (13%)
Large vessel disease other than substantial carotid stenosis	8 (10.1 %)	1435 (22.1%)
Cardiac origin	41 (51.9%)	2270 (35%)
Lacunar stroke	4 (5.1 %)	535 (8.3%)
Other	15 (19 %)	1171 (18.1%)
Unknown	6 (7.6 %)	228 (3.5%)
Stroke onset to treatment time (min)	165 (135-215)	140 (115–165)
Mean delay between stroke onset and treatment (min)	175 (56)	136 (33)
Door-to-needle time (i.e. from entering the facility to receiving treatment with alteplase) (min)	96 (31)	68 (30)
Data are median (IQR), mean (SD), or n (%).		

Table 1: Baseline characteristics of patients enrolled in AKUH and SITS-MOST

	AKUH Proportion (events/total; 95% CI)	SITS-MOST Proportion (events/total; 95% CI)
SICH rates per SITS-MOST*	0 % (0/79)	1.7% (107/6444; 1.4–2.0)
SICH per Cochrane/ NINDS definition†	3.8 % (3/79; 1.3 – 10.6)	7.3% (468/6438; 6.7–7.9)
Mortality within 3 months	1.3 % (1/79; 0.2 – 6.8)	11·3% (701/6218; 10.5–12.1)
Independence (modified Rankin score 0–2) at 3 months	50.6 % (40/79; 39.8 – 61.4)	54.8% (3362/6136; 53.5–56.0)

SICH=symptomatic intracerebral hemorrhage. * Intracerebral hemorrhage (parenchymatous hemorrhage type 2), at post-treatment scan combined with NIHSS drop ≥ 4. †NIHSS drop ≥1 and any hemorrhage.

Table 2: Proportions of patients with symptomatic intracerebral hemorrhage, mortality and independence at 3 months at AKUH and SITS-MOST

RESULTS

- Of the 79 patients included in the final analysis, 52 were male (66%) and 27 (34%) were female.
- Median pre t-PA NIHSS was 12 (IQR 8-15).
- Mean door to needle time was 96 minutes (S.D. 31 minutes) vs 68 minutes (S.D. 30 minutes) in SITS-MOST.
- The proportion of patients with symptomatic intracerebral hemorrhage according to the SITS-MOST criteria was 0 % at AKUH vs 1.7 % in SITS-MOST, whereas according to the Cochrane/NINDS definition it was 3.8 % at AKUH vs 7.3 % in SITS-MOST.
- Functional independence (mRS 0-2) was seen in 50.6% of patients at AKUH vs 54.8 % of patients in SITS-MOST at three months. Figure 1 and Tables 1 & 2 show our findings.

DISCUSSION

- The safety and efficacy outcomes in our patients were comparable with that of SITS-MOST.
- When compared with the regional data, a prospective study by Maria et al in Dubai reported 12 (6.8 %) patients developing symptomatic intracranial hemorrhage, when defined as hemorrhage (PH2) on the post thrombolysis CT scan with a drop of 4 or more points on NIHSS, as opposed to 0% at our center.
- This is the largest reported data from a single center in South Asia regarding safety and efficacy of low dose thrombolytic therapy in ischemic stroke patients.

CONCLUSION

- Low dose intravenous thrombolytic therapy for ischemic stroke patients was safe and efficacious in our patient population and yielded comparable results with those of SITS-MOST.

REFERENCES

1. Zaman Babar MU, Khan AZ, Hakim H, Gilani J, et al., (2019).Utilization and outcomes with low dose tissue plasminogen activator as intravenous thrombolytic therapy for ischaemic stroke at Aga Khan University Hospital, Karachi: a retrospective analysis. J Pak Med Assoc, 69(11):1705-1710.

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