



## Revascularisation Strategies in Acute Ischemic Stroke

### KEYWORDS

Revascularisation strategy, Thrombolysis, Acute ischemic stroke

#### Dr. Khatib Khalid Ismail

Consulting Physician, MTE society's Sanjeevan Hospital, 23, Off Karve Road, Near Dhondumama Sathe Homeopathic Medical College, Erandwane, Pune- 411004.

#### Dr. Baviskar Ajit Subhash

Consulting Anaesthesiologist, C/O'Siddhi Clinic', 205, Business Square, Opposite S.P. College, Sadashiv Peth, Tilak Road, Pune – 411030.

#### Dr. Borawake Kapil Sharad

Consulting Physician, Ravi Polyclinic, Jangli Maharaj Road, Shivajinagar, Pune-411004.

**ABSTRACT** *Revascularisation of the infarct related artery, after acute ischemic stroke improves functional outcomes, both immediate as well as long term. Depending on the time which has elapsed after symptom onset, intravenous or intraarterial thrombolysis or mechanical thrombectomy may be used. Improvement in functional scores is apparent though there is a small risk of hemorrhage. We present a case of Acute Ischemic Stroke who was a candidate for the use of thrombolysis, and who showed improvement in functional outcome scores.*

### Introduction:

After the results of the National Institute of Neurological Disorders and Stroke Intra Venous (IV) recombinant tissue plasminogen activator (rt-PA) trial (NINDS trial) and other major randomised stroke trials of IV rTPA were published, thrombolysis became an option for the treatment of Acute Ischemic Stroke (AIS).<sup>1</sup> IV rTPA could be used for patients with AIS within the described inclusion/exclusion criteria of the trials. Since then, thrombolysis with IV rTPA has become the standard of care for patients presenting with AIS within the confines of the therapeutic time window (3-4.5 hours). Other revascularisation strategies used are intra-arterial thrombolysis and mechanical clot removal. Clinical outcomes after thrombolysis are dependent on the time of revascularisation of the infarct related artery.<sup>2</sup> We present a case report of a patient who suffered from AIS and was successfully thrombolysed, with good improvement in the National Institute of Health Stroke Scale (NIHSS) score and modified Rankin Scale (mRS) score.

### Case report:

A 64 years old, male patient presented with history of heaviness & weakness of the left upper limb, asymmetry of face and slurred speech, since half an hour. The patient was a known case of diabetes mellitus and hypertension on regular treatment for the last 8 years. The patient had a history of stroke, 7 years ago, with bilateral cerebellar infarct and obstructive hydrocephalus and had to undergo ventriculoperitoneal shunt surgery. On admission to the ICU, the vital parameters were normal except for a mild increase in blood pressure (BP- 150/80 mmHg). Examination of the central nervous system revealed a left sided hemiplegia with grade zero power in the left upper limb, and grade two power in the left lower limb. The power on the right side was normal. There was an upper motor neuron type of facial palsy on the left side.

Blood investigations were normal with an INR of 1.0 and a blood sugar value of 125 mg /dl. Urine showed evidence of urinary tract infection. The 2D Echo was normal. CT scan of the brain was done and it revealed a large gliotic area in the bilateral cerebellar region. There was no evidence of any intracranial hemorrhage (ICH). It was decided to thrombolysed the patient as: i) the patient presented within 3 hours of the beginning of symptoms, ii) no evidence of ICH on CT scan of the brain, iii) no contraindications to thrombolysis the patient. The patient was given intravenous alteplase at a dose of 0.9mg/kg of body weight which was started within 3 hours of

the onset of symptoms. Magnetic resonance imaging of the brain done after 24 hours of thrombolysis revealed i) an acute infarct in the precentral and parietal region on the right side with hemorrhagic transformation, ii) a large area of gliosis in the left occipital region and bilateral cerebellar hemispheres, iii) diffuse cortical atrophy associated with small vessel ischemic foci in the bilateral periventricular region. Magnetic resonance angiography of the brain revealed severe narrowing of the left posterior cerebral artery (PCA) from distal P1 segment and severe narrowing of the right PCA from the distal P2 segment. There was severe narrowing of the right middle cerebral artery (MCA) in the distal M1 and proximal M2 segment. The patient received antiplatelet drugs after 24 hours of thrombolysis. Power improved to grade 3 in the upper limbs and grade 4 to 5 in the lower limbs, when assessed after twenty four hours. The NIHSS score, on admission was 9 which reduced to 4 within twenty four hours after the thrombolysis. After a week the NIHSS score was 1 and the mRS score was 1.

### Discussion:

The NINDS trial and other major randomised stroke trials of IV rTPA demonstrated the effectiveness of intravenous thrombolysis in improving outcome after AIS.<sup>1</sup> Just as thrombolysis had revolutionized the Rx of AMI, the NINDS trial gave great hope of similar success in the Rx of AIS. In the ideal scenario, thrombolytic therapy for stroke uses a relatively safe agent to achieve rapid arterial recanalization soon enough to improve patient outcome.<sup>3</sup>

### Intra-venous thrombolysis:

Reperfusion therapy with intravenous (IV) recombinant tissue plasminogen activator (rTPA) is a much needed weapon that has been provided to clinicians in their fight against AIS, though there are clear limitations to its use.<sup>3</sup> There is strong evidence which fulfils level I criteria. Cumulative evidence from all trials of tPA within the 3-h time window gives a relative risk reduction of 44%, absolute risk reduction (ARR) of 13% and number needed to treat (NNT) to save one person from death or disability about 7. Though mortality increases non-significantly, intra-cranial hemorrhage (ICH) increases approximately 3-fold.<sup>4</sup>

The time window for therapeutic intervention is narrow, and there are multiple, stringent exclusion criteria. The rate of recanalization with IV rTPA is approximately 50%. Patients treated within 90 min have a better outcome than those

treated after 90 min within the 3-h window.<sup>5</sup>

When analyzed by stroke severity, higher the NIHSS score, lesser was the benefit obtained. Patients with NIHSS scores > 20 had a  $\leq 6\%$  ARR in achieving modified Rankin Scale (mRS) < 1 at 90 days as against a 13% ARR in patients with NIHSS scores of < 20.<sup>4</sup> When given after 3 hours of stroke, efficacy of IV rTPA was relatively lacking. And thrombolysis after 3 hours was associated with a high rate of symptomatic brain hemorrhage. A metaanalysis, however, showed benefit from IV therapy up to at least 4.5 h. ECASS III study confirmed the advantage of giving IV rTPA up to 4.5 h after stroke onset.<sup>6-11</sup>

Limitations of IV rTPA: i) inability to provide any diagnostic information, ii) a short time window for use, iii) modest rates of recanalization, and iv) poor specificity for the site of arterial occlusion.

Advantages of IV rTPA: i) relative ease of administration, ii) widespread availability, and

iii) proven efficacy within 3- 4.5 hours of onset of AIS.

#### Intra-arterial (IA) thrombolysis:

Patients with acute MCA occlusion have been most successfully treated with intra-arterial thrombolysis using the percutaneous route. Trials have used IA thrombolysis upto at least 6 h from stroke onset in patients with MCA occlusion. Scenarios for use of IA thrombolysis include patients with: i) acute MCA occlusion ii) extra- cranial carotid artery occlusion, iii) intracranial carotid artery T occlusion and iv) basilar artery occlusion.

The thrombolytic agents used for IA thrombolysis have been i) rTPA,<sup>1</sup> ii) urokinase (UK),<sup>12</sup> iii) pro-urokinase (scu-PA),<sup>13</sup> iv) reteplase,<sup>14</sup> v) desmoteplase,<sup>15</sup> vi) tenecteplase(TNK),<sup>16</sup> vii) streptokinase,<sup>17,18</sup> viii) staphylokinase,<sup>19</sup> ix) plasmin, and x) microplasmin.<sup>20</sup>

Advantages of IA thrombolysis : i) achieves more complete recanalization with less fibrinolytic drug, ii) clot lysis can be assessed with follow-up angiograms, iii) treatment can be initiated up to 6 h after symptom onset.

Disadvantages of IA thrombolysis: i) the logistic factors involved, such as the need to assemble the angiography team and ii) need to confirm occlusion angiographically before administration of thrombolysis.

Mechanical clot lysis: Mechanical approaches to clot removal are attractive as there is no need for thrombolytic drugs which increase the risk of reperfusion hemorrhage. The clot is fragmented and sucked using a catheter.<sup>21, 22</sup>

Advantages of mechanical clot lysis: i) no need for thrombolytic drugs, Disadvantages of mechanical clot lysis: i) Distal embolization of particles, ii) catheters are less flexible and of large size, limiting access to the tortuous vessels of the intracranial circulation.

The paradigm to be followed when treating a patient of AIS presenting within the 3-4.5 hours time window may be as follows: 1) Perform brain imaging, CT/ CT Angiography/ perfusion CT/ MRI/ MR Angiography/ perfusion MRI; depending on availability and time required to perform the investigation.

2) If there is a major vessel occlusion (Internal Carotid Artery/ Middle Cerebral Artery/ Basilar Artery): consider IA thrombolysis, if adequate infrastructure and knowhow is available. Otherwise use IV rTPA.

3) For all other cases of AIS: consider IV thrombolysis with rTPA.<sup>3</sup>

#### Conclusion:

Revascularisation of the infarct related artery should be the aim of treatment for patients of AIS, presenting within 3-6 hours of symptom onset.<sup>2</sup> Depending on the available infrastructure and knowhow; IV rTPA, IA thrombolysis or mechanical thrombectomy may be used.<sup>3</sup> There is improvement in the NIHSS and the mRS scores. There is a small associated risk of ICH.

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