# Intra-arterial thrombolysis in acute ischemic stroke: A single center experience

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# Abstract

Intra-arterial thrombolysis (IAT) is a treatment modality in patients with acute large vessel occlusive ischemic stroke. To our knowledge, this is probably the first reported study of intra-arterial thrombolysis in acute ischemic stroke from India. Of the 17 patients treated who recieved IAT, successful recanalization was achieved in nine patients, Thrombolysis in Myocardial Infarction (TIMI) score of 2 or 3. At 90-day follow-up, eight patients achieved modified Rankin Scale (mRS) score of <2.

deficit - National Institute of Health Stroke Scale (NIHSS) score more than or equal to four, and informed consent by either the patient or care giver. Clinical exclusion

criteria included rapidly improving neurological signs,

an NIHSS score greater than 30, history of stroke within

the previous six weeks, seizures at onset, previous history of intracranial hemorrhage at any time, neoplasm,

or subarachnoid hemorrhage, surgery within 30 days,

head trauma within 90 days, active or recent hemorrhage

within 30 days, known hemorrhagic diathesis, baseline

international normalized ratio greater than 1.7, activated

partial thromboplastin time more than 1.5 times the normal, or baseline platelet count less than 1,00,000/c.c.

Computed tomographic (CT) scan exclusion criteria

were intracranial tumors, hemorrhage, significant

mass effect with midline shift, and acute hypodense

parenchymal lesion or effacement of cerebral sulci in more than one-third of the vascular territory. Patients

who met all clinical and CT scan criteria were taken for

four-vessel diagnostic cerebral angiography after taking consent from patient/relatives. The patients were taken

up for IAT if there was a large vessel occlusion with Thrombolysis in Myocardial Infarction (TIMI) score of

zero or one. Patients received 3000 U of heparin bolus. A 6F guiding catheter was placed into the symptomatic

artery. Microcatheter was then navigated into the thrombus. Intra-arterial infusion of Urokinase (UK) or

rtPA was performed in small doses and repeated until the

maximum dose was reached (rtPA 40 mg and Urokinase

1.2 million I.U.), complete recanalization (TIMI 2 or 3)

was achieved or time after onset was more than eight

Key words: Acute stroke, intra-arterial thrombolysis, rtPA

## Introduction

Intravenous thrombolysis (IVT) in acute ischemic stroke within three hours of onset has been an established treatment after the NINDS trial.<sup>[1]</sup> The recent European Cooperative Acute Stroke Study (ECASS III) trial has extended the window period to four and half hours.<sup>[2]</sup> In large vessel occlusions, early recanalization rates with IV rtPA are low, approximately 10% in internal carotid arteriy (ICA) occlusion and 30% in proximal middle cerebral artery (MCA) occlusion.<sup>[3,4]</sup> Pro-Urokinase (r-proUK) for Acute Cerebral Thromboembolism (PROACT II) study suggests that intra-arterial thembolysis (IAT) can be given up to six hour window period in patients with middle cerebral artery occlusion and is an effective treatment but with some safety concerns.<sup>[5]</sup> There is no published study from India on IAT in acute ischemic stroke. Even though about 2500 patients with stroke are admitted yearly in our institute only a handful of patients present within the window period. The overall purpose of this paper is to report the summary of IAT in acute stroke in a tertiary referral center from India.

## **Materials and Methods**

This is a retrospective study of 17 patients with acute ischemic stroke treated by intra-arterial thrombolysis (IAT) between 1999 and 2009 with at least 3-month follow-up. The clinical inclusion criteria were age between 18 and 85 years, focal neurological deficits consistent with stroke within six hours of onset, measurable neurological hours. Since the last five years we have been using rtPA as it is highly fibrin specific and recanalization is better with rtPA compared to UK.<sup>[6]</sup>

CT scan was done post thrombolysis and at 24 hours. It was repeated if patient's condition deteriorated at any time during follow-up. NIHSS score and modified Rankin Scale (mRS) score were documented at 24 hours, 30 days and 90 days. All causes of mortality and procedure-related complications were analyzed. The primary outcome was percentage of patients achieving mRS of two or less at 90 days follow-up. The secondary outcome was percentage of patients achieving complete angiographic recanalization and also the percentage of patients who presented within 3 hours duration achieving mRS 0-1 at 90 days.

## Results

During the study period 17 patients with acute stroke had IAT [Table 1]. The mean age was 55.3 years (range 37 to 85 years) and eleven were males. The mean duration of presentation was 3.35 hours (range 0.5 hours to 6 hours). The median NIHSS score was 17 (range 10 to 22). Twelve patients had middle cerebral artery (MCA), three had carotid 'T' and two had basilar artery (BA) occlusions. Nine (53%) patients had TIMI 2 or 3 recanalization rate and eight (47.06%) patients had mRS score of <2. There were three deaths and the causes of death include intracerebral hemorrhage (1), massive edema and herniation (1), and reocclusion of the artery and brainstem infarct (1). We had eight patients who presented within three hours duration. The mean age of these patients was 59.12 years (range 42 to 75 years) and four were male. The mean duration of presentation was 1.75 hours (range 0.5 hours to 3 hours) and the median NIHSS score was 16 (range 10 to 22). Five patients had MCA, two patients had Carotid 'T' and one had BA occlusions. There was no mortality and none of the patients had intracranial hemorrhage. Seven (87.5%) patients achieved mRS score of 0 to 2 at 90 days, four (50%) patients achieved mRS of 0 to 1 at 90 days and six (75%) patients had TIMI 2 or 3 recanalization rate [Figures 1 and 2].

We had 12 patients who presented with MCA occlusion [Figures 3-5]. The mean age of patients was 53.41 years (range 43 to 75 years) and ten were males. The mean duration of presentation was 3.5 hours (range 0.5 hours to 6 hours) and the median NIHSS score was 17 (range 10 to 22). One patient had intracranial hemorrhage. Five (41.66%) patients achieved mRS score of 0 to 2 at 90 days and six (50%) patients had TIMI 2 or 3 recanalization rate.

#### Discussion

The efficacy of IVT in acute ischemic stroke has been proven in NINDS trial.<sup>[1]</sup> When the NINDS trial was further analyzed with respect to stroke severity, the degree of benefit declined with increasing NIHSS scores. Patients with NIHSS scores of more than 20 had 6% absolute risk reduction in achieving mRS score of <1 at 90 days. If all the presently available data were analyzed, the efficacy of recanalization after IVT of patients with large arteries occlusion (internal carotid artery, MCA - M1 segment, or BA especially proximal BA) would be 30% compared to 60 to 70% in IAT.<sup>[7]</sup> The efficacy of IVT in large vessel occlusions is lesser compared to IAT. In a large retrospective study, comparing IA and IV treatments

Table 1: Clinical features and outcome of patients treated with intra-arterial thrombolysis							
Age	Sex	Territory	Duration (hours)	NIHSS	TIMI (post treatment)	mRS (3 months)	Mortality
42	F	Left ICA T	3	16	1	2	
62	М	Right MCA	6	14	1	1	
65	Μ	Left ICA T occlusion	3	17	1	2	
45	М	Left MCA	4	16	0	3	
70	F	Basilar artery	1	10	3	0	
48	М	Left MCA	5	13	0	3	
65	М	Right MCA	2	22	2	1	
40	М	Left MCA	4	22	0	3	
55	М	Left MCA	6	18	0		Dead, parenchymal bleed
43	Μ	Right MCA	4	18	2	3	
87	F	Basilar artery	4	21	3		Dead 4 <sup>th</sup> day reocclusion and brain stem infarct
75	F	Left MCA	1	22	3	1	
55	М	Right MCA	0.5	10	3	2	
35	F	Left ICA T	4	22	3		Dead due to herniation
		thrombosis					
55	F	Right MCA	2	16	3	0	
52	М	Left MCA	6	20	0	3	
46	М	Right MCA	1.5	16	3	3	



Figure 1: Vertebral angiogram showing basilar artery thrombosis



Figure 2: Post thrombolysis angiogram showing complete recanalization of basilar artery (TIMI 3)



Figure 3: Right internal carotid angiogram showing middle cerebral artery occlusion



Figure 5: Post thrombolysis computed tomographic scan shows no hemorrhage



Figure 4: After 40 mg of rtPA, complete recanalization of middle cerebral artery (TIMI 3) was achieved

in M1 occlusion presenting within 3 hours matched for age and stroke severity, favorable outcome was more frequent after IAT than after IVT (53% vs.23%; P = 0.001), and mortality was lower after IAT than after IVT (7% vs.23%; P = 0.022). IA treatment was associated with a significantly better outcome despite the longer 'door to needle time'.<sup>[8]</sup> Efficacy of combined IV and IA treatment will be assessed by the ongoing Interventional Management Study III.

There are two randomized trials of IAT which included patients with MCA occlusion. In PROACT II trial, 40% of r-prourokinase group and 25% of control patients had mRS score of <2. The recanalization rate was 66% for r-prourokinase group. The mortality was 25% for the r-proUrokinase group and 27% for the control group.<sup>[5]</sup> In

the Middle Cerebral Artery Embolism Local Fibrinolytic Intervention Trial (MELT) trial, 49.1% of urokinase group and 38.6% of control patients had a mRS score of <2. Even though they have not used TIMI score, 73.7% of patient achieved partial or complete recanalization in urokinase group. The mortality was 5.3% in the urokinase group and 3.5% in the control group at three months and intracerebral hemorrhage within 24 hours of treatment occurred in 9 and 2%, respectively.<sup>[9]</sup> In the analysis of studies of IAT in patients with acute ischemic stroke, there were more favorable outcomes in the IAT than the control group (41.5% vs. 23%, P = 0.002), with a lower mortality rate for IAT (27.2% vs. 40%, P = 0.004). Symptomatic intracerebral hemorrhage was more frequent in the IAT group compared with the control group (9.5% vs. 3%, P = 0.046).<sup>[10]</sup>

Despite the advantages, there are limitations to the IAT. These include availability of specialized equipment, experienced trained personnel and costs. In our study, the recanalization rate was 53% (TIMI 2 or 3). 47% patient had mRS score of <2 at three months. When we analyzed the patients with MCA occlusion; 42% of patients had a favorable outcome and the recanalization was 50%. Symptomatic cerebral hemorrhage occurred in one patient. In BA occlusion; one of the two patients had a favorable outcome. In ICA T occlusion; one of the three patients had a favorable outcome. In the study by Gonner *et al.* the recanalization rate was 63% and 21% of patients recovered to mRS score of 0 or 1 and 40% patients to mRS score of 2 or 3. Outcome was good (mRS 0-3) in 80% of patients with MCA occlusions, 33% with ICA, and in 50% with BA occlusion. Symptomatic cerebral hemorrhage occurred in 4.7% of patients.[11]

Our study has many limitations like small cohort, retrospective collection of data, non randomized design, single center involvement and non-blinded nature of the study. Our study suggests that intra-arterial thrombolysis is a feasible option in the subgroup of patients with large vessel occlusion. There, however, is a need for a randomized multicentric study to support our results.

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