Brain Attack : Time to Act Now

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Stroke is a medical emergency. 'Time is brain' as millions of neurons are lost with every minute of stroke. Following an acute ischaemic stroke (AIS) and without treatment 4 million neurons, 12 million brain cells, and 15 billion synapses die every minute [1]. Stroke is being increasingly addressed as Brain Attack in order to accord highest level of priority in medical management of stroke. World renowned stroke expert Prof Vladimir Hachinski first coined the term 'brain attack' to convey that stroke is an emergency [2]. Unfortunately the medical community as well as the general public continues to nurse a nihilistic attitude toward occurrence of stroke. For a great majority, stroke means masterly inactivity. Early detection and prompt treatment can prevent morbidity as well as reduce mortality.

Stroke is a global epidemic and an important cause of morbidity and mortality. It is the third leading cause of death in the United States after heart disease and cancer [3]. In India, stroke is perhaps the second commonest cause of death and probably the most common cause of disability [4]. The overall crude prevalence rate of stroke in India ranges from 90 to 220 per 100,000 persons; approximately 30% of strokes occur in people less than 50 years of age [5]. More than 50% stroke patients remain vocationally impaired and about 30% need full support for activities of daily living [4]. Death due to stroke is 22 times of death due to malaria and 1.4 times of that due to tuberculosis [6]. Though there are national programs on malaria eradication and tuberculosis control, organised governmental support in stroke management and rehabilitation is lacking.

Management of stroke, ischemic stroke in particular, has undergone a sea change since the landmark National Institute of Neurological Disorders and Stroke (NINDS) Recombinant Tissue Plasminogen Activator (rt-PA) Stroke Study earned US-FDA approval in 1996. The window of opportunity for salvaging the ischemic tissue at risk is first 3 h since onset of stroke. Intravenous

thrombolysis (IVT) with recombinant tissue plasminogen activator (rt-PA) is the only approved form of specific therapy for AIS in the window period. Specific therapy includes thrombolysis with rt-PA 0.9 mg/kg administered within 3 h of onset of AIS. The NINDS rt-PA stroke study showed patients with ischemic stroke treated with intravenous rt-PA in the first 3 h were at least 30 percent more likely to have minimal or no disability at three months. In the NINDS trial, best outcome was seen with thrombolysis within 90 minutes of stroke [7].

In the recently published trial by European Cooperative Acute Stroke Study investigators (ECASS III), using a time window of 3 to 4.5 h for IVT, the outcome was better in the treatment group. The rate of symptomatic intracerebral haemorrhage in this study was 2.4% in the thrombolysed group, much lower than that found in the earlier studies [8]. However, only 1% to 2% of patients with ischemic stroke receive IVT therapy in Europe and the United States [9]. This figure is certainly lower in India. The results of the ECASS III study are encouraging in terms of more number of patients benefiting from thrombolysis using a wider window of opportunity. Based on the published literature a time window of 6 hours for the anterior and 12 hours for the posterior circulation has also been suggested for IVT [9]. The Third International Stroke Trial (IST 3) is studying the efficacy of IVT until 6 h [10]. Basilar artery occlusion (BAO) is a catastrophic disease with dismal natural course, carrying 85% to 95% mortality even during anticoagulant and antifibrinolytic therapy if not recanalised [11]. IVT in selected cases of BAO even upto 48 hours has been shown to have encouraging results [11,12].

Intra-arterial thrombolysis (IAT) is an option in these groups of patients but is limited to use at specialized centres [12,13]. IAT is an option for treatment of selected patients who have major stroke of < 6 h duration due to occlusions of the middle cerebral artery and who

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are not otherwise candidates for intravenous rt-PA [14]. The therapeutic window for patients with vertebral or basilar artery occlusion has not been established. Instead of witnessing the natural course of BAO, some stroke centres have adopted interventional protocols to manage BAO, mostly with intra-arterial thrombolytics [11]. Typically, roughly half of the patients with either route for recanalisation therapy will succeed, and roughly half of those will have good outcome [11]. Because BAOs carry an increased risk of death and disability, IAT in this condition is recommended upto 12 – 24 h after the onset of stroke [15]. There are anecdotal reports showing angiographic and clinical improvement even upto 72 h after onset of stroke [13]. Combination thrombolysis using a reduced dose IV rt-PA within 3 h, followed by IAT within 6 h of stroke onset has also been described. The time window for success of thrombolysis is related to multiple factors, including collateral circulation, degree of ischemia, and site of occlusion [13]. Application of penumbral imaging modalities may allow a better selection of patients beyond 3 h [10]. The decision to thrombolys should be based on evidence based guidelines, clinical judgement and after full discussion of the potential risks and benefits of treatment with rt-PA with the family and the patient, if possible [14]. While these wider time windows are intended to maximize the benefit of thrombolysis to more number of patients, these are not yet the currently approved time frames for thrombolysis.

We in the Armed Forces are faced with a formidable burden of stroke in young soldiers resulting in substantial loss of manpower to the organization. The morbidity and mortality from stroke can be significantly reduced by timely action by the patients, their caregivers and the medical professionals at all levels. There are several factors which result in missing the window of opportunity: lack of awareness that stroke is a medical emergency, failure to recognize the warning symptoms of stroke, delay in transportation to hospital, failure to accord priority in the emergency services, delays involved in notifying stroke specialist and carrying out a brain imaging, and lack of availability of rt-PA in most government hospitals.

The commonest medical problem that brings a patient to a doctor is 'pain'. Heart Attack, synonymous with myocardial infarction, being an extremely painful condition gets noticed early by the patient prompting him to seek emergent medical attention. In our opinion, the most important factor resulting in delay in reaching hospital in golden period is the lack of pain in stroke. Attitude of medical professionals toward stroke is equally appalling, a sentiment echoed by stroke specialists worldwide [16]. It is not unusual for physicians to admit

cases of stroke to general medical ward rather than an intensive care unit, as the patient's general condition is seemingly stable. Close monitoring of blood pressure and other vital signs in acute stroke is best done in an intensive care setting. Poor blood pressure control can further damage the ischemic penumbra at risk. A similar situation in a setting of acute myocardial infarction would manifest with pain and dyspnoea, drawing immediate attention. We need to impart similar significance to a painless yet not less important condition like stroke.

We have had gratifying results with timely IVT in AIS. Nothing can be more satisfying for a neurologist than to see a patient with global aphasia regain his speech in few hours or to see a patient with dense hemiplegia walk out of hospital after few weeks. Thrombolysis can be lifesaving in posterior circulation strokes, which has a particularly high mortality rate, as we have seen in some of our cases. However, these are exceptional examples of patients who reported to hospital in time. A vast majority of them continue to seek medical attention several hours to days after a stroke.

Management of AIS requires a close coordination amongst all those involved with the workup and care of a stroke patient. Where facilities are available a 'stroke team' should be established comprising emergency care physician, neurologist, radiologist, interventional radiologist, neurosurgeon with special interest in stroke, neurointensivist, stroke nurse specialist, and key paramedical staff. It has been shown that stroke is best managed in setting of Stroke Care Unit, which significantly reduces the morbidity and mortality from stroke. Establishment of Stroke Care Units in India in 1970s enabled to drop mortality from stroke from 40% to 12% in 1990s. Further advances in treatment of stroke in last 15 years have reduced it to 8% [4].

The hospital administrative authorities play a lead role in ensuring timely action and successful management of acute stroke. Patients of acute stroke on arrival at the Emergency Services of Command Hospital (SC) Pune are stratified according to the stroke protocol of CH (SC) and AFMC, and are accorded highest level of priority in carrying out imaging and thrombolytic therapy. This model of stroke care being followed at this centre can be implemented and practiced at all tertiary care service hospitals, as well as at zonal hospitals where facility for CT scan exists. At the level of zonal hospitals, physicians, who have earned the experience and expertise of thrombolysis in AIS during their formal training, can play a key role in reducing the morbidity and mortality resulting from stroke. Thrombolysis of ischemic strokes by physicians should be restricted to the currently approved time window of 3 h, and should be done in accordance with the NINDS protocol for

Table 1**Proposed institutional acute stroke protocol**

Territory of stroke	Duration of stroke	Neuroimaging	Mode of rt-PA therapy	Remarks
Anterior circulation (ACA / MCA Territory)	< 3 hours 3 to 6 hours	CT / MRI MRI + DWI + MRA + (DSA)	IV IV or IA or combination	IA or IV + IA therapy preferred with ICA & M1 occlusions of 3 – 6 hours
Posterior circulation (VA or BA Territory)	< 3 hours	CT / MRI	IV	—
Vertebral artery occlusion	3 to 6 hours 6 to 12 hours	MRI + DWI + MRA MRI + DWI + MRA + DSA	IV IA or combination	— In selected cases
Basilar artery occlusion	3 to 12 hours 12 to 24 hours	MRI + DWI + MRA + DSA MRI + DWI + MRA + DSA	IV or IA or combination IA	In selected cases In selected cases

ACA – Anterior cerebral artery, BA – Basilar artery, CT – Computerised tomography, DSA – Digital subtraction angiography, DWI – Diffusion weighted imaging, IA- Intra-arterial, ICA – Internal carotid artery, IV – Intravenous, M1 – First segment of MCA, MCA – Middle cerebral artery, MRI – Magnetic resonance imaging, MRA – Magnetic resonance angiography, VA – Vertebral artery

thrombolysis of ischemic strokes.

Emergency medical personnel should be trained to identify early signs of stroke, practice triage and co-ordinate with radiologist and stroke team. Present need is of integration of hospital administration system with the medical and paramedical staff trained specifically in stroke. A quick reference ‘Seven Ds’ in the stroke chain of survival and recovery are a useful guide to stroke management [17]. The ‘Seven Ds’ in the stroke chain of survival and recovery are:

1. *Detection* of onset of signs and symptoms of stroke
2. *Dispatch* through activation of the stroke help line and emergency services
3. *Delivery* of the patient to the hospital while providing prehospital assessment, care and prior notification to the hospital
4. *Door* – Emergency Department (ED) Triage
5. *Data* - ED evaluation including the neuro-radiological scanning
6. *Decision* about potential therapy
7. *Drug* therapy

We propose a model of institutional protocol for acute stroke thrombolysis suited to a tertiary care hospital, as shown in Table 1. Stroke specialists, with informed consent of family or patient, may use their clinical judgement and angiographic evidence in selecting stroke cases for thrombolysis beyond the currently approved time windows.

The patient and physician attitudes have to change for any stroke programme to have the desired impact on the outcomes of stroke. Most of these issues can be addressed by creating awareness on aspects of early recognition of stroke amongst the public and the need for timely action by the hospital services. As large number of dependent clientele is far away from the nearest tertiary care service hospitals, creating stroke

awareness amongst the troops and implementing acute stroke management at zonal level hospitals will go a long way in maximizing the benefits of aggressive stroke management. To meet the objective of implementing a successful stroke care programme, establishing a CT scan facility at all zonal hospitals of the armed forces is recommended. Hospital authorities should ensure availability of rt-PA at all zonal and tertiary care hospitals.

Given the burden of stroke that is managed at tertiary care service hospitals, it is time we formally introduced early and safe implementation of thrombolysis in acute ischemic stroke. At the tertiary care level, stroke team and stroke care units need to be established to manage brain attack. A working evidence based stroke protocol for the armed forces should be formulated which will go a long way in reducing the stroke-related morbidity and mortality [18]. Remember “Time is Brain as Brain Matters”.

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