Management of acute ischemic stroke

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Abstract

Stroke is a major cause of mortality and morbidity, and thrombolysis has served as a catalyst for major changes in the management of acute ischaemic stroke. Intravenous alteplase (recombinant tissue plasminogen activator) is the only approved thrombolytic agent at present indicated for acute ischaemic stroke. Recombinant tissue plasminogen activator (rt-PA) therapy is effective in reducing early and long-term neurologic disabilities if it is started quickly. This article summarizes the recent advances in thrombolysis for acute ischaemic stroke.

Keywords: Cerebral edema; Penumbra; Secondary neuronal injury; Stroke, rt-PA

1. Introduction

Stroke is defined by the World Health Organization as a clinical Syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting More than 24 hours or leading to death with no apparent cause Other than a vascular origin.1 Stroke is classified broadly into three Categories; ischemic stroke, hemorrhagic stroke and subarachnoid Haemorrhage. Ischemic stroke occurs due to blockage of blood vessel Which limits the blood supply to the brain whereas hemorrhagic Stroke occurs due to rupture of blood vessel leading spillage of Blood in the intracranial cavity.2 Depending on the site of blood Spillage the hemorrhagic stroke could be classified as intracerebral Haemorrhage or subarachnoid haemorrhage.2 Approximately 60–80% Of all strokes is ischemic. This article is dedicated to acute ischemic Strokes and its management.

2. Early detection

Ischemic stroke can occur both in the community and in the hospital and must be recognized by bystanders and/or providers. Early Recognition activates a stroke-specific chain of survival (3). Stroke is a clinical diagnosis and several features of the patient’s Clinical presentation can be used to identify stroke patients. Emergency Medical Systems are key in detection, triaging, and Transport of stroke patients to receiving facilities.4

3. Epidemiology

Stroke is the second most common cause of mortality and third most common cause of disability worldwide.3Globally, 68% of all Strokes are ischemic and 32% are hemorrhagic. Numbers from The USA differ a little with 87% of all strokes being ischemic, 10% Hemorrhagic and about 3% being subarachnoid hemorrhage.5 Data regarding prevalence of stroke in India is lacking however, It can be extrapolated from the data available from the West. In a Study done by Banerjee et al. In 2001 crude prevalence rate of Stroke in India was 147/100,000 and the annual incidence rate Was 36/100,000. Women had substantially higher age-adjusted Prevalence rate (564/100,000 for women vs 196/100,000 for men) And incidence rate (204/100,000 for women vs 36/100,000 for Men). Overall prevalence of stroke ranges from 147–
922/100,000 in various studies.\(^8\), \(^9\)India has the highest burden of acute coronary syndrome (ACS) in the world and the three most common risk factors for ACS are Smoking (40%), high blood pressure (38%), and diabetes (30%). Taking account of the above mentioned data and considering the fact that stroke shares common risk factors with ACS, we can safely assume that India has a very high incidence of stroke as well.\(^5\)

### 4. Prehospital management

Workflows and organized systems of care can efficiently reduce delays in time to treatments. With the deployment of Mobile stroke units (MSUs) equipped with CT scanners and Telemedicine links, recognition of patients and administration of treatments may be more precise and efficient. Recent studies have shown that the implementation of MSUs has led to higher rates and reduced the time to IV-tPA administration and Door-to-needle time compared with regular ambulance transport to emergency departments (EDs) \((4-8)\). In theory, initiation of therapies for intracerebral haemorrhaged (ICH) such as Blood pressure control and reversal of anticoagulation may also be implemented at the prehospital setting. In addition to clinical Examination with conventional scales such as the Neurological Institutes of Health Stroke Scale (NIHSS), several prehospital Scales and prompt recognition of severe strokes with large vessel Occlusions (LVOs) have successfully been validated.\(^6\)

### 5. Ischemic stroke classification\(^7\)

According to the multicentre Trial of Acute Stroke Treatment (TOAST) there are three kinds of ischemic stroke:

- Large vessel stroke
- Small vessel stroke or Lacunar stroke
- Cardio embolic stroke

Large artery strokes could be due to thrombotic or embolic occlusion of the major arteries of the brain like the internal carotid artery, middle cerebral artery, anterior cerebral artery or the vertebrobasilar system. Lacunar strokes are more often due to involvement of smaller or perforating blood vessels supplying the deeper structures of the brain.

### 6. Risk factors\(^8\)

Non-modifiable Risk Factors include

- Age
- Race
- Sex
- Ethnicity
- History of migraine headaches
- Fibromuscular dysplasia
- Heredity: Family history of stroke or transient ischemic attacks (TIAs).

Modifiable risk factors include

- Hypertension
- Diabetes mellitus
- Cardiac disease (see below)
- High cholesterol
- Previous stroke
- Carotid stenosis
- Hyperhomocystinemia
- Lifestyle issues: Excessive alcohol intake, tobacco use, illicit drug use, physical inactivity
- Obesity
- Oral contraceptive use/postmenopausal hormone use

Majority of the ischemic strokes seen in patients with cardiovascular disease are embolic. Embolic strokes may arise directly from the heart or the aorta. Following is the list of conditions that carry a high risk for embolic strokes.\(^9\)
7. Management of acute stroke

The most important factor in the management of acute ischemic stroke is time. The patient with ischemic stroke loses 190,000 brain cells every minute, about 14000,000,000 nerve connections are destroyed every minute and 12 km (7.5 miles) of nerve fibres are lost every minute. The brain ages 3.6 years for every hour it is deprived of blood supply. There are two modalities of treatment available for treatment of acute ischemic stroke. Intravenous thrombolysis and mechanical thrombectomy.10

7.1. * 8 D’s of stroke care

7.1.1. Detection

Involves recognizing the signs and symptoms of an acute stroke

7.1.2. Dispatch

Activation of emergency medical services. In most cases, this involves calling 911 or a stroke team

7.1.3. Delivery

Means prompt transport of the patient to a hospital, preferably a stroke center or to a setting in the hospital for further evaluation by a stroke team.

7.1.4. Door

This refers to the arrival of the patient at the ED. According to recommendations from the National Institute of Neurological Disorders and Stroke, an assessment should be completed by an ED physician within 10 min of arriving in the ED.

7.1.5. Data

Data collection includes results from laboratory tests and both a physical and a neurologic examination (Neurological Institutes of Health Stroke Scale).

7.1.6. Decision

Information, such as the type of stroke, last seen normal, and time from onset of symptoms, is considered before a treatment decision is made.

7.1.7. Drug/device

Fibrinolytic therapy should be administered within 4.5 hr of the onset of symptoms. Even if the patient is not a candidate for fibrinolysis, they may still qualify for endovascular therapy to remove mechanically a clot.

7.1.8. Disposition

It is recommended that patients are admitted to an ICU or stroke unit within 3 hr of arrival in the ED.11

7.2. * Befast, detection of stroke

- Balance, acute or sudden onset of loss of balance or Coordination.
- Eyes, blurred or unclear vision, double vision, and gaze preference.
- Facial weakness or facial asymmetry.12
- Arm and/or leg weakness.
- Speech difficulty/slurring of speech.
- Time is brain, time to activate stroke system and stroke clock.13

7.3. * Arterial Occlusion Evaluation Scale

- Facial palsy: Absent (0), mild (1), and moderate (2).
- Arm motor impairment: Normal to mild (0), moderate (1), and severe (2).
- Leg motor impairment: Normal to mild (0), moderate (1), and severe (2).
- Head/gaze deviation: Absent (0) and present (1).
• Aphasia: Performs tasks correctly (0), performs one task correctly (1), and performs neither task (2).
• Agnosia: Recognizes his/her arm and deficit (0), does recognize his/her arm but not or deficit (1), and does not recognize his/her arm or deficit (2). 14

8. Endovascular treatment for stroke

Intravenous tPA has been the backbone of stroke treatment for almost 20 years. Intravenous therapy although effective has specific inclusion and exclusion criteria which limits its use in a large number of patients. Moreover, the intravenous tPA cannot be used after the 4.5 hour window and has limited efficacy in patients with large vessel occlusion. Riedel et al showed that it is almost impossible to dissolve large clots with intravenous therapy. 15 In another study by Alexandrov and Grotta up to one third of patients had re-occlusion of blood vessels after initial recanalization. The FDA approval of IV-tPA has innovated the entire field of Emergency neurology. 16 However, up to 69% of stroke patients are ineligible to receive IV-tPA due to delayed hospital presentation. 16 Over the last 3 years, the time window for AIS Treatment has expanded thanks to EVT and has provided physicians with a stronger therapeutic arsenal. The success of EVT is measured by the degree or quality of revascularization. The Thrombolysis in Cerebral Infarction (TICI) scale is a tool to standardize the different degrees of reperfusion ranging from no Perfusion (TICI 0) to complete perfusion (TICI 3). 17 TICI scores of 2B to 3 are usually regarded as successful reperfusion. Previous studies failed to show improved results with EVT and diminished the initial optimism regarding intervention for AIS. However, the study design of those clinical trials was criticized for not requiring the image proof of LVO, using Older technology for clot retrieval, and having prolonged stroke to puncture times. 18 Since, multiple trials have shown the efficacy of EVT in addition to standard medical care in improving the overall outcome of AIS patients with proximal MCA or internal carotid artery (ICA) occlusion when EVT was performed Within either 6 hours, 8 hours (42), or 12 hours Of symptom onset. 19

9. ICU management

9.1. Oxygenation and ventilation

Supplemental oxygen may be required if a patient's saturation is less than 94%. Rapid neurologic Deterioration and ensuing loss of consciousness with impairment of reflexes that maintain the airway mandate definitive Airway control. 20 Failure to recognize imminent airway loss may result in complications such as Aspiration, hypoxemia, and hypercapnia, which may result in Secondary neuronal injury. Hyperbaric oxygen was shown to either have no effect or be harmful in AIS patients and should be avoided. 21

9.2. Blood pressure

As part of cerebral autoregulation, blood pressure is commonly elevated during the acute phase of AIS, maximizing perfusion in the ischemic areas. However, severe hypertension can lead to hemorrhagic transformation of the infarct, hypertensive encephalopathy, as well as cardiopulmonary and renal complications. Current AHA/ASA guidelines recommend permissive hypertension with a blood pressure goal of less than or equal to 220/120 mm Hg for the first 24–48 hours. Yet, these blood pressure variables only apply if the patient is not undergoing any acute intervention such as IV-tPA or EVT. If the patient receives IVtPA, the risk of hemorrhagic transformation increases and the blood pressure should be lowered to less than or equal to 185/110 mm Hg prior to IV-tPA administration and to less than or equal to 180/105 mm Hg once IV-tPA has been given. Reperfusion injury and hemorrhagic transformation are of concern in the case of EVT; thus, blood pressure. 22

9.3. Glycemic control

Evidence indicates that persistent in-hospital hyperglycemia during the first 24 hours after AIS is associated with worse outcomes compared with normoglycemia due to multiple potential mechanisms, such as endothelial dysfunction, increased Oxidative stress, and impaired fibrinolysis. However, in the NINDS funded Stroke Hyperglycemia Insulin Network Effort (SHINE) clinical trial, an intensive IV insulin protocol to achieve a systemic glucose between 80 and 130mg/dL was not associated with favourable outcomes at 90 days compared with a Standard regimen of insulin in a "sliding-scale" fashion to keep the glucose between 80 and 180mg/dL. The intensive insulin protocol was associated with significant hypoglycaemic Events and a higher level of care. To this end, it is reasonable to treat hyperglycemia to achieve blood glucose levels in a range of 140–180mg/dL and to monitor closely to prevent hypoglycemia in patients with AIS. 23
9.4. Cerebral edema

Large infarcts of the MCA or ICA are associated with high Morbidity rates of up to 80%. Patients with large hemispheric Infarcts (LHIs) are at increased risk of cerebral edema and fast Neurologic deterioration that led to the term “malignant MCA Infarction” (MMI). The ultimate intervention to alleviate increased Intracranial pressure and avoid herniation in LHI with significant edema is surgical decompression with DHC. Three European clinical trials assessed the benefit of DHC in patients 60 years and younger. A pooled analysis of these trials showed that DHC does not only reduce mortality by 50% but also improve long-term functional outcome. The NNT to avoid a death is 2 (mRS = 6), whereas the NNT to avoid Death and the most severe to moderately severe disability is 4 (mRS = 4–6). The proportion of patients alive with minimal-to-moderate disability (mRS = 0–3) was increased from 21% to 43%. Viewed another way, DHC resulted in a 49% absolute Risk reduction in death, and an absolute increase in the proportion of patients rated as mRS = 2 of 12%, mRS = 3 of 10%, and mRS = 4 of 29%.

10. Conclusion

Management of acute ischemic stroke is time dependent. Efficient and effective stroke care depends on a well-functioning team from the emergency room to the neurologist and the interventional Neurologist. Accurate diagnosis, emergent management to stabilize the patient and correct choice of imaging can make a lot of difference in the outcome of a patient. Every minute lost in wrong imaging or Lab test results in decrease in functional outcome and ultimately irreversible paralysis. Success of stroke treatment is dependent on the entire team working smoothly and efficiently.

Compliance with ethical standards

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There is no conflict of interest.

References


