

# Newer Nuances in the Management of Acute Stroke

## Editorial

Acute stroke can result in significant catastrophic neurological events and hence require immediate recognition and treatment to prevent irreversible injury and death. Efficient and appropriate management of the early stages of a neurological emergency has substantial impact on patient outcome and it is critical to have site-specific protocols to drive care quickly and efficiently. Emergency neurological life support (ENLS) is an educational program designed to provide caretakers advisory instruction regarding management for the first few hours of a neurological emergency [1].

Intracerebral haemorrhage protocol of ENLS is mainly concerned with the initial evaluation and treatment period and it is important to determine optimal treatment required in the initial 72 hours as part of health care planning. The first 24h are vital for managing BP, identifying and controlling seizures, ICP management and maintaining a secure airway. Avoiding hyperglycemia/ hypoglycemia, fever and hypoxia are also vital, as these may have deleterious effects on the outcomes [2-4].

The recent release of the American Heart Association Guidelines for Spontaneous Hemorrhage addresses new treatment goals for blood pressure control and coagulation reversal [2]. Even though blood pressure management has been controversial, recent guidelines favor rapid control of moderately high blood pressure [5,6]. Two pilot randomized clinical trials, the INTERACT trial and the ATACH trial, have suggested that the systolic blood pressure being reduced to below 140mmHg is safe [7,8]. INTERACT2 was a phase III clinical trial of acute blood pressure lowering in ICH patients presenting with a systolic blood pressure between 150 and 220mmHg [9]. The patients were randomized to two different blood pressure thresholds: a standard regular threshold of <180mmHg and an intensive threshold of lesser than 140mmHg. Patients in the intensive arm had better outcomes with about 4 % fewer patients having death or severe disability (modified Rankin Scale score of 3-6). However, we could not find any difference in haematoma expansion between the two groups. So current guidelines do not recommend the blood pressure to remain high without treatment [2,5,6]. The current American Heart Association and the American Stroke Association Guidelines for the Management of ICH and the European Stroke Organization guidelines have recommended a target blood pressure of less than 140mmHg similar to the INTERACT2 trial [2,6]. So in patients presenting with very high blood pressure, acute lowering of blood pressure is justifiable, but less is known about the specific safety and efficacy of treatment [2].

Basic principles of blood pressure lowering in ICH are that management should be started immediately and a drug that can be easily titratable should be used so that the target value is quickly attained and without any potential for overshoot. IV beta-blockers and calcium-channel blockers are the commonly used medications for this indication in the ED and the intensive care unit (ICU).

## Editorial

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### Arun Oommen\*

Consultant Neurosurgeon, Lakeshore Hospital and Research Centre, India

\*Corresponding author: Dr. Arun Oommen, MBBS, MS (Gen Surg), Mch ( Neurosurgery), MRCS Ed, MBA, Consultant Neurosurgeon, Lakeshore Hospital and Research Centre, Kochi, India, Website: [www.arunoommen.com](http://www.arunoommen.com), Email: [oommenarun@yahoo.co.in](mailto:oommenarun@yahoo.co.in)

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Current guidelines for warfarin reversal [2,10], recommend the use of vitamin K 5-10 mg administered intravenously by slow IV infusion, along with another more rapidly acting agent such as FFP or PCC, as it typically takes a few hours after vitamin K administration for the warfarin-induced coagulopathy to revert, but it has a more long-lasting effect than PCC or FFP [11].

Both CHEST and American Heart Association / American Stroke Association guidelines recommend the use of prothrombin complex concentrate (PCC) agents over fresh frozen plasma (FFP) [12,13]. PCCs can correct the INR within minutes, faster than FFP, and with fewer cardiopulmonary complications [14]. PCCs have better tolerance than FFP due to lower fluid volumes and reduced risk for transfusion associated circulatory overload or transfusion related acute lung injury [15,16]. INR may be checked 30 min after the end of PCC infusion to check if it is within normal range [15-19]. A second dose of the PCC may be considered if INR remains elevated and risk of continued bleeding is high. In patients who require volume resuscitation FFP can be a better choice and it may be used in combination with PCC if reversal is inadequate. It may be also noted that in a study where PCC and FFP were compared, no difference in hematoma growth was noted in patients whose INR was corrected within 2h [20]. Hence it may be inferred that it is the timing of coagulopathy reversal and not the specific agent that makes the greatest impact.

Newer anticoagulants, like direct Xa inhibitors (e.g. rivaroxaban, edoxaban or apixaban) or direct thrombin inhibitors (e.g. dabigatran) at present do not have a specific reversal agent. Moreover, experience with ICH in patients taking these medications is limited. PCCs may have limited effectiveness in reversing the effect of rivaroxaban and apixaban, but not of dabigatran [21].

The reversal agent for UFH is protamine sulfate, Administered dose is based on the time since last UFH was administered. Administered dose is 0.25 -1mg for every 100U of UFH IV received within 2 hours with a maximum dose of 50mg [22]

Current American Heart Association ICH guidelines recommend that patients with cerebellar hemorrhage having brainstem compression or are deteriorating neurologically should be considered for surgical removal of the hemorrhage at the earliest. Initial treatment of these patients with ventricular drainage alone rather than surgical evacuation is not recommended [2]. Supratentorial hematoma with neurological deterioration can be considered for surgical evacuation or decompressive hemicraniectomy as a life-saving measure. Correction of coagulopathy is critical in patients undergoing surgical hematoma evacuation [23,24].

Acute ischemic stroke is a neurological emergency that can be treated with time-sensitive interventions, including intravenous thrombolysis and endovascular approaches. Extensive studies have suggested that rapid clinical/ radiological assessment and treatment are essential for improving neurological outcome.

The latest version of ENLS is supported by remarkable advancements developing in the field of emergency neurology during the past few years. The recent success of endovascular trials for management of acute ischemic stroke has impacted the time course and treatment options needed for these patients and stresses the necessity for improved communication and collaboration among treating facilities [25-27].

A potential tPA candidate (stroke onset within 3 hours) should be subjected to interventions for immediate BP control. The target BP for IV tPA candidates is less than 185/110mmHg, and once tPA has been initiated, BP must be kept below 180/105mmHg to reduce the risk of intracranial hemorrhage [26]. BP should be lowered carefully and strategically while being careful not to drop the BP too much once the patient is at goal. Chronic antihypertensive medications should be reduced or temporarily withheld. tPA has not yet been approved by the Food and Drug Administration for use in patients presenting with stroke between 3 and 4.5 hours in the US, though it has been approved in Europe and Canada. However, tPA use in this timeframe has been endorsed by the American Stroke Association and is widely used [26].

For patients with large vessel occlusion like middle cerebral artery (MCA), intracranial internal carotid artery (ICA), basilar or vertebral artery and presenting within 6 h of the stroke onset, intra-arterial (IA) thrombolysis may be an option [28,29]. If the patient presents within 8 h, mechanical embolectomy may be considered. Numerous recent randomized trials of embolectomy in acute, large vessel ischemic stroke have shown much superior clinical efficacy and even reduction in mortality with or without IV tPA pre treatment [30-34]. IA thrombolysis or embolectomy may be avoided in the absence of a large vessel occlusion on CTA or MRA, or with large area of infarction already present on the brain imaging study.

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