

## The Race with Time and the Hurdles to Overcome in the Management of Acute Ischemic Stroke in Nepal

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Acute ischemic stroke (AIS) is the third leading cause of disability and the fifth leading cause of mortality in Nepal.<sup>1</sup> Nepal is currently in the midst of a rapid epidemiological transition and the burden of stroke and other non-communicable diseases is consistently on the rising trend owing to rapid urbanization, sedentary lifestyle, unhealthy dietary choices.<sup>2</sup> As time is brain, once ischemia due to AIS starts to evolve umbra develops in which 1.9 million per min neurons start to die. “Pen umbra”, surrounding the umbra is potentially destined for infarction and the target for any acute therapies. This has led a great paradigm shift in the management of acute ischemic stroke in the last two decades.<sup>3</sup>

Stroke Units, Emergency ambulance services, Tele stroke network, mobile stroke units, advanced imaging techniques (including CT and MR angiography, perfusion scanner), intravenous thrombolysis (IVT), mechanical thrombectomy (MT) are some of the many ways that has been introduced into practice to challenge time and save penumbra. Currently IVT and MT are two proven therapies for management of AIS. However, both these treatment strategies are time bound with barriers set within 4.5 hours of onset where IVT can be instituted and within 6 hours when MT can be performed for patients who develop large vessel occlusion (LVO).<sup>4</sup> This can be extended upto 24 hours if the penumbra is salvageable and has been practiced at advanced stroke centers as evidenced by DAWN, DEFUSE 3 trial.<sup>5,6</sup> Further, there are ample evidences to institute IVT earlier with clinical diagnosis of stroke and negative CT scan even if the patient has LVO and would eventually require thrombectomy.<sup>7</sup> This time barriers have set new outlines for management of AIS. Even within the window period, earlier the intervention better is the outcomes for the patients.

However, the current scenario is very grim for stroke patients in Nepal. The difficult geographical terrain and poor quality of roads equally contribute to delays in hospital arrival. Further lack of awareness about stroke among general population and practicing physicians worsen the matter even more. Although there is no data regarding this, our observation has revealed that often patient who suffered from stroke are taken to nearby hospital where much time is wasted before making

appropriate referral to specialist stroke center. Lack of central ambulance service with stroke trained paramedics is another important cause of prehospital delay. There are less than 10 centers capable of IVT and three capable of MT all centered in the capital city.<sup>8</sup> Further there are only 25 neurologists, few endovascular neurosurgeons and neurointervention radiologists in the entire country.<sup>9</sup> Studies done in the capital city show that less than 20% patients reach hospital within the window period to avail the benefits of IVT.<sup>10</sup> Even for those who reach hospital in time, financial constraint is a big barrier. The diagnostic cost of imaging (CT scan/MRI) is expensive. Further, the cost of 50 mg vial of alteplase is USD 650 to USD 1000 which is too expensive considering Per Capita Income of an average Nepalese citizen. Tenecteplase, a proven alternative thrombolytic agent, is cost effective (30 mg vial cost USD 450) and equally efficacious.<sup>11</sup>

Often times, if the disease overshadows the time, physicians at stroke centers have to be content treating with antiplatelet agents to prevent future events and patients have to live with lifelong disability, dependence and financial burden for the family.<sup>12</sup> Decompressive craniectomy for malignant infarction is available. However, this rarely improves quality of life for patients. STA-MCA bypass, Carotid endarterectomy, Carotid artery stenting, are prevention strategies for recurrent stroke and is performed at few selected centers.<sup>13</sup> To overcome this challenges patient and physician education, establishment of minimal equipped stroke units,<sup>14,15</sup> establishment of tele stroke network with “hub and spoke” model, “drip and ship” model.<sup>16,17</sup> establishing working algorithm, more policy in ensuring this treatment from the government with insurance policy as there is a huge out cry for it and would be a game changer.

In conclusion, time is not only brain, but it is also money in a country like Nepal. To achieve the goals set in terms of time, tremendous effort will be required from all quarters including the Government.

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