In the acute period of stroke, several physiologic parameters have been implicated in influencing the extent of cerebral damage and outcome, such as blood pressure, blood glucose, and temperature[1]. Many evidences suggest that monitoring of these parameters with treatments aimed at maintaining physiologic homeostasis may improve stroke outcome and this policy is now recommended by expert reviews of critical care in acute stroke[2].

Hyperglycemia in acute stroke

As much as 50% of acute stroke patients are hyperglycemic (>126 mg/dl) on presentation[3]. Although diabetes, which is present up to one third of stroke patients, can account for the hyperglycemia, probably many patients have stress hyperglycemia and relative insulin deficiency also plays a role[4]. Extensive stroke experiments support that hyperglycemia has adverse effects on tissue outcome, while the results in focal ischemia are less consistent and differ by the presence of reperfusion[5]. Among the detrimental mechanisms of hyperglycemia, lactic acidosis in the ischemic penumbra is pivotal. During ischemia, hyperglycemia augments an anaerobic glycolysis which aggravates local acidosis[5]. Enhanced acidosis worsens the penumbral area into infarction by increasing free radicals and perturbing intracellular signal transduction, and also exaggerates brain edema and hemorrhagic transformation by damaging blood brain barrier[5,6]. Most clinical studies agree that hyperglycemia in acute stroke is associated with poor outcome in non-diabetic as well as diabetic patients, independently of infarction volume and stroke severity in some studies. In a systematic overview of 32 studies, stress hyperglycemia (>108~144 mg/dl) after ischemic stroke was associated with 3-fold risk of fatal one month outcome and 1.4-fold risk of poor functional outcome in non-diabetic patients[7]. Admission hyperglycemia was also reported to be a risk factor for symptomatic hemorrhage and worsen outcome after thrombolytic therapy. In the re-analysis of the NINDS rt-PA trial, admission hyperglycemia was independently associated with decreased odds for neurologic improvement (OR=0.76 per 100 mg/dl increase) and increased odds for symptomatic hemorrhage (OR=1.75 per 100 mg/dl increase)[8]. Furthermore, recent studies showed correlation of penumbral tissue loss with hyperglycemia which was linked to increased lactate production and more infarct expansion in hyperglycemic patients[9,10], which suggest that hyperglycemia is one of true determinants of early infarct progression. However, the cause and effect issue of hyperglycemia and stroke outcome is still controversial while some would argue that the existing data is sufficient to recommend the importance of maintaining normoglycemia acutely after stroke. Recently, pilot studies addressing the safety and efficacy of continuous insulin infusion in acute stroke patients with moderate hyperglycemia were reported[11,12]. There are still a number of unanswered questions with regard to glycemic control in acute stroke, including what insulin regimen should be used and the duration of intensive glycemic control. The level of target glucose concentrations of quite different current recommended values in the published guidelines (EUSI: <180 mg/dl, ASA: <300 mg/dl)[2] should be also deter-
mined. Although there is no conclusive evidence, intravenous solutions containing should be avoided in the acute period of stroke and restoration of normoglycemia as soon as possible should be encouraged. To unravel the aforementioned issues, a clinical trial to prove that active control of hyperglycemia in acute stroke improves the outcome is required, as it has been demonstrated to do in acute myocardial infarction and critically ill patients.

**Hyperthermia in acute stroke**

During the first several days after stroke, a fever or subfebrile temperature develops in up to 50% of patients[13]. Stroke itself as well as superimposed infection is one of the major causes of poststroke hyperthermia. Numerous animal experiments of stroke showed that hyperthermia during or immediately after ischemia aggravates neuronal injury by accentuating various biochemical and inflammatory ischemic mechanisms within ischemic penumbra[14,15]. Furthermore, even delayed hyperthermia worsens ischemic injury which means that postischemic brain is abnormally sensitive to the effects of temperature elevation[15]. Studies in human also showed association of elevated temperature with poor outcome in patients with acute stroke. Poststroke hyperthermia was demonstrated to be an independent poor prognostic factor in several retrospective studies and was associated with a significant increase in morbidity and mortality in a recent meta-analysis[13,15]. Although superimposed infection is one of the causes of hyperthermia, infection itself, at least within first several days, does not seem to be related to poor outcome[14]. However, as is the issue of poststroke hyperglycemia, it is not clear whether hyperthermia influences stroke severity or vice versa and the timing of hyperthermia seems to be important. Boysen et al[16]. reported that stroke severity determines body temperature as a significant rise in body temperature occurred hours after onset in major stroke, while Castillo et al[17]. reported that body temperature within the first 24 hours from onset was independently associated with poor prognosis and larger infarct volume. Therefore, it would be safe to say that poststroke hyperthermia seems to be an event both induced by and inducing neuronal injury. For the management of poststroke hyperthermia, no specific and effective treatment has been developed, especially for the stroke induced central hyperthermia. Recently, use of paracetamol (6 g/day) in acute ischemic stroke patients showed a small but rapid and potentially worthwhile reduction of 0.3 ºC in body temperature[18]. Although there are still no clinical data about the usefulness of normalizing temperature with antipyretics, recommendations have been made to counteract any incipient fever in acute stroke patients with antipyretics and antibiotics where appropriate [2,15].

**Conclusion**

Elevation of blood glucose and body temperature is quite common in patients with acute stroke. Numerous animal stroke experiments have demonstrated that hyperglycemia and hyperthermia can accentuate the neuronal injury. The association of these physiologic parameters with stroke outcome has been reported also in many clinical studies. Despite the lack of conclusive evidences on the clinical usefulness of normalizing these parameters, it is highly recommended to maintain normoglycemia and normothermia with use of appropriate manners.

**REFERENCES**

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