See related article, pages 199–203

Does Hyperglycemia Contribute to Secondary Injury in Subarachnoid Hemorrhage?

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Central nervous system injury has been classified as primary and secondary. The most common primary injuries include trauma, ischemic stroke, intracranial hemorrhage, brain neoplasms, and subarachnoid hemorrhage (SAH). Secondary injuries may follow the primary injury and potentially treated. The implications of this report may be important because hyperglycemia can be easily diagnosed at the patients’ bedside and potentially treated.

We have known for several years of a potential association between hyperglycemia and worsening outcome in animal models of cerebral ischemia. Such association was not initially evident in humans experiencing ischemic stroke. In fact, it was first believed that hyperglycemia represented a stress response to stroke without any impact on clinical outcome. Since then, several observational studies have reported on the independent association between persistent hyperglycemia and increased mortality or reduced functional recovery in patients with various primary injuries including ischemic stroke, intracerebral hemorrhage, and trauma.

Possible mechanisms that have been proposed linking hyperglycemia with worse clinical outcome include the following: worsening of tissue acidosis facilitating extension of infarction; production of reactive oxygen species; suppression of neuronal survival signals; endothelial damage; deleterious effects on macrophage or neutrophil function; and axonal dysfunction and degeneration.

The most important aspect of the report by Frontera et al is that in patients with SAH persistent hyperglycemia may be associated with increased length of stay, medical and neurological complications, and death or severe disability. Does this mean that tight blood-glucose control will improve outcome in all patients with SAH? The answer will have to wait until evidence from needed clinical trials becomes available. However, we have clinical trial evidence to support the use of intensive insulin therapy in critically ill patients. Such intensive therapy leads to reduced in-hospital mortality, blood stream infections, acute renal failure, days of mechanical ventilation, and critical-illness polyneuropathy. It has been suggested that control of glucose levels rather than the amount of exogenous insulin account for the beneficial effects of intensive insulin therapy. One small study has reported on the effect of intensive insulin therapy on the prevention of secondary brain insults in a group of patients with various intracerebral processes including SAH. Patients were randomized to intensive insulin therapy versus conventional approach. The authors found that intensive insulin therapy prevented secondary injury to both central and peripheral nervous systems as evidenced by lower intracranial pressures, fewer seizures, reduced incidence of critical illness polyneuropathy, and better long-term rehabilitation results. Glucose/insulin infusions have been reported for glucose modulation after ischemic stroke and SAH. Preliminary reports indicate that the treatment regimen is safe. We await the results of well-conducted randomized trials to determine with certainty whether tight blood-glucose control has an important role in the prevention of secondary injuries of patients with ischemic stroke and SAH.

References


**Key Words:** acute stroke | brain infarction | hyperglycemia | intracranial hemorrhage | neuroprotection | outcomes | subarachnoid hemorrhage
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