Fever in the Neuro ICU: Current Prevention Methods are Inadequate

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Introduction

Trauma, subarachnoid hemorrhage (SAH), cerebrovascular occlusive disease, and spontaneous intracranial hemorrhage (ICH) all can cause significant brain injury. It is increasingly clear that two distinct phases of injury result in the ultimate neurologic dysfunction suffered by the patient. The first phase involves direct physical damage to the brain tissue, either from the percussive effects of trauma to the head, or compression and tearing of brain tissue from an enlarging blood clot. The second phase, often called secondary brain injury, is due to a variety of metabolic and physiologic processes intitiated by regional cerebral ischemia. These processes include breakdown of the blood-brain barrier, disruption of cerebral auto regulatory mechanisms, the accumulation of toxic extracellular levels of excitatory amino acids and free radicals, the cellular inflammatory response and regional hyperthermia. Ultimately, the result of secondary injury is cytotoxic and vasogenic edema, elevated intracranial pressure and cell death. A mismatch of blood flow and metabolism is a likely underlying abnormality responsible for secondary brain injury, though it is clear that both abnormal hypermetabolism, as well as ischemia itself, are worsened in the face of hyperthermia.

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The Interrelation of Temperature and Secondary Brain Injury

Fever is Harmful

In patients with spontaneous intracerebral hemorrhage, Schwartz, et al. have documented a significant association between the duration of fever (>37.5˚ C) and poor outcomes for 196 patients surviving for the first 72 hours after their hemorrhage. A significant increase in morbidity and mortality associated with fever after a patient has suffered a stroke was found in a metaanalysis of 3,790 patients. Finally prevention of fever in 20 patients with middle cerebral artery infarcts has been shown to provide better control of critically elevated intracranial pressure and better than expected outcomes.

Deep Brain Temperature is Often Higher than Body Temperature

Using an external ventricular drainage catheter that contains a microthermistor, the direct measurement of deep brain temperature was studied in eight patients with severe TBI for five days to determine how well rectal and bladder (or core) temperatures correlate with brain temperatures. Based on some 30,000 minute-by-minute observations, we found a frequent disparity between core temperature and brain temperatures, which ranged from .1 to as high as 2°C difference. *Differences were greatest when the core temperatures were above 38°C.* On several occasions we recorded rectal temperatures of 38 or 39°C while the deep brain temperature was 40 to 41°C. These findings have led us to change our protocol in the neurotrauma ICU. In the past, we began treatment for fever when rectal temperatures exceeded 38.5°C. Currently, we begin treatment of fever when rectal temperature exceeds 37.5°C in order to be sure that we are adequately treating presumed higher brain temperatures.

Lowering Patient Temperature Has Therapeutic Benefits

The intentional cooling of patients with severe Traumatic Brain Injury (TBI) as a therapeutic option was first reported by Temple Fay in the 1930's. During the next 20 years or so, others also reported its use for TBI patients and all of these investigators suggested a possible benefit, though none of these studies were prospective randomized clinical trials. In the late 1980's there was a resurgence of interest in this treatment when it was demonstrated that cooling to as little as 32°C might be effective. This was an important observation since it was clear that cooling below 30°C was associated with an increased risk for cardiac arrhythmias. During the last 10 years, numerous clinical studies have been conducted investigating the efficacy of therapeutic moderate hypothermia for severe TBI. Those studies consistently find a 20-30% reduction in cerebral blood flow, possible decrease in cerebral blood volume, increase in tissue pO2, and preservation of ATP stores with the use of this treatment. In addition, seven clinical studies of patients with TBI and one study of patients with stroke have found a significant reduction of intracranial pressure with the use of hypothermia to as little as 34°C. The clinical studies also have found that hypothermia causes significant suppression of interleukin 1-β (IL-1β) and glutamate in the ventricular cerebral spinal fluid. A prospective randomized trial of 82 patients with severe TBI published in 1997 found a two-fold increase in the number of patients achieving mild or no disability at six months after injury if they were cooled to 32-33°C for 24 hours after injury as compared to a similar group of TBI patients that were treated without the use of therapeutic hypothermia. Clinical studies of the use of therapeutic moderate hypothermia for the treatment of brain injury may have found benefit of this treatment not only because of a lower than normal temperature during the early period after injury, *but also by assuring that hyperthermia was avoided in that group*.

Fever in the Neurosurgical Intensive Care Unit

It has long been the impression of neurosurgeons that fever is very common in critically ill neurosurgical patients. Febrile episodes may occur as the result of pulmonary problems such as atelectasis or pneumonia, urinary tract infections or deep venous thrombosis. Fever in a neurosurgical patient also can be the result of hypothalamic dysfunction or SAH, either of which can cause an increase in IL-1β levels. It also is well known that the longer the patient resides in the ICU, the more likely they will have one or more febrile episodes. In order to prospectively quantify the occurrence of fever we studied 428 consecutive patients admitted to our neurovascular or neurotrauma ICUs from January through June 1997.

Thirty-four percent of these patients had cerebrovascular accidents, 13% had aneurysmal SAH, and 32% had TBI as their primary diagnoses. Rectal temperatures were obtained every 2 to 4 hours and a febrile episode was defined as a rectal temperature that exceeded 38.5°C. Febrile episodes (>38.5°C) were aggressively managed in our ICUs with the use of external cooling blankets, acetaminophen and, in particularly refractory cases, nasogastric ice water lavage. In this study, we found that 46.7% of the patients had at least one febrile episode, and there were a total of 946 febrile episodes recorded for the population as a whole. There was no apparent correlation with the diagnoses, though there was a very strong correlation with the length of stay in the ICU. Thus, those patients staying less than 24 hours had only a 15.5% incidence of febrile episodes, while those hospitalized for greater than 14 days had a 92.6% incidence. It was clear from this study that *fever is an even more common problem than we had anticipated, despite aggressive conventional methods of fever management*.

Conventional Fever Management Methods Are Inadequate

Conventional treatment for fever in the ICU can best be described as "reactive". That is the patient is hospitalized in the ICU and rectal or bladder temperatures are monitored. When the temperature exceeds a predefined threshold, the nurse begins standard treatment for the fever. This may involve administration of acetaminophen or other antipyretics either orally or rectally. This treatment, however, may take 30 minutes to an hour or so to show maximum benefit. In addition, surface cooling techniques are employed, most commonly the use of one or more cooling blankets applied over the torso and abdomen of the patient. There is controversy, however, about the effectiveness of this technique for managing fever as a study by Lenhardt et. al. shows that actively cooling the skin surface causes thermoregulatory vasoconstriction in the periphery thereby decreasing cutaneous heat loss. Additionally, a similar study shows that such external cooling may cause the patient to shiver contributing to a 35-40% increase in oxygen consumption, metabolic demand and associated elevations in body temperature further limiting the effectiveness of cooling blankets as a method of controlling fever. When fever is particularly refractory, internal lavage of the stomach is often used with ice-saline solution. This, however, requires the primary nurse to stand by the bedside for extended periods of time manually infusing and draining the saline solution from the nasogastric tube. In addition to the relative "labor intensive" aspects of these treatments, it can be seen from our study of 428 patients that *these methods are often not effective in preventing fever*.

Intravascular Technology for Fever Management Holds Promise

An alternative to conventional methods of fever management may be an intravascular approach to fever management. We recently completed a phase-one trial with Duke University, Graffagnino et. al., using intravascular cooling technology in 20 patients with Subarachnoid Hemorrhage (SAH), Intracerebral Hemorrhage (ICH), Traumatic Brain Injury (TBI), and Stroke. The patients were followed for seven days after the onset of their disease. Ten of the patients had intravascular cooling with the CoolLine™ catheter and 10 had their fever controlled with the conventional methods described above. That study revealed that those patients whose temperature were controlled with the CoolLine™ intravascular device had a fever in excess of 37.9°C less than half of the time of a similar group of patients treated with only conventional fever management methods. There were no significant complications associated with the use of the CoolLine™ intravascular cooling catheter and the management of fever was *significantly less labor intensive from a nursing standpoint*.

"Patients treated with CoolLine™ had a fever in excess of 37.9˚C less than half the time and the management was significantly less labor intensive."

Conclusions

Fever above 38°C that occurs in patients with acute neurosurgical diseases appears to worsen secondary brain injury and presumably ultimate neurologic outcomes. Laboratory investigations are quite clear regarding the adverse effects of fever in terms not only of functional outcomes but also histologic and neurochemical injury. Several preliminary clinical studies also suggest worsened neurologic outcome in patients who are febrile compared to those who are not. Unfortunately, however, a large prospective study of 428 patients with acute neurosurgical diseases has shown that fever is extraordinarily common during the first seven days after SAH, Stroke, ICH and TBI. The ability to eliminate fever in most of these patients during the first five to seven days after their injury would seem desirable. Based on a phase-one trial, it appears that intravascular cooling is a promising new method for avoiding fever in the neurosurgical ICU.

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