J Anesth (2000) 14:171–172

Journal of
Anesthesia

pH-Stat management is more appropriate during deep hypothermia, especially when circulatory arrest is added

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To the editor: Excitotoxicity [hyperactivation of N-methyl-D-aspartate (NMDA) receptors] and hypoxia have been identified as brain injury mechanisms of deep hypothermic circulatory arrest (DHCA) [1–3]. Their initial development during cooling induction prior to the arrest has been recognized but disregarded. Development of intracellular acidosis at 20°C, even without circulatory arrest [4], and post-DHCA functional impairment correlation with duration of the hypothermic perfusion prior to arrest [5] have been reported with alpha-stat management. Both facts further support our view: hypoxic metabolism (Bohr effect) caused by hypothermia and exacerbated by the hypocarbic alkalosis starts well before arrest.

Nature has used pH-stat mechanisms successfully to cope with hypothermia for millions of years [6]. This letter to the editor is written to incite reappraisal of the still unsolved issue, as evidenced by numerous facts that have been obtained with recent new technology but are being disregarded.

The proponents of alpha-stat have two major arguments: below 18°C the brain theoretically consumes mostly dissolved O_2 [7], and normothermic hypocarbia causes less cerebral embolization than normothermic hypercarbia [8].

Simply transposing the normothermic findings to the hypothermic state disregards the metabolic derangements caused by the Bohr effect, and the deleterious effects of alkalotic reperfusion on the activated NMDA receptors caused by the Bohr effect and by the arrest period of DHCA.

During the arrest period, there is no flow and therefore no chance of embolization, regardless of the pH management. However, if hypoxia had developed during cooling, the added arrest or embolic ischemia might be more detrimental than if the Bohr effect had been prevented by making O_2 available during cooling and rewarming with proper pH management, since patients do not go from 38° to 18°C or vice versa instantaneously.

The better postoperative neurologic outcome following deep hypothermic perfusion in infants with pH-stat than with alpha-stat management is known [9], and probably results from less hypoxia-induced excitotoxicity and minimization of NO generation than with alpha-stat strategies.

With the use of eucapnic or slightly hypercapnic ventilation (expired $[CO_2]$ of 5.1% to 5.7% providing pH of 7.23–7.1, $PaCO_2$ of 50–60 mmHg, and PaO_2 of 230–260 mmHg, uncorrected for temperature, equivalent to normoxic pH-stat hypothermic cardiopulmonary bypass), spinal cord function in rabbits after 1 h of ischemia was consistently preserved by surface-induced hypothermia to only 29.5°C [10], which is considered too high a temperature if 1 h of ischemia is to be protected with alpha-stat hypothermia [11].

Mild acidosis decreases Ca^{2+} influx, glutamate neurotoxicity, and neuronal injury from deprivation of oxygen and glucose by reducing the activation of NMDA receptors [12–15]. Alkalosis sensitizes neurons to ischemia and exacerbates excitotoxicity, potentiating reperfusion injury [15,16], which is the scenario with alpha-stat DHCA.

Eucapnic ventilation can usually be maintained with minimal changes in respiratory rate down to temperatures of 32°–33°C. The alpha-stat strategy might be preferable for temperatures >32°C, at which most coronary bypass operations are performed, but the pH-stat strategy is probably more physiologic for temperatures <32°C [10], regardless of whether conditions are normoxic or hyperoxic [17,18], particularly if circulatory arrest is being contemplated.

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Received: November 4, 1999 / Accepted: March 29, 2000