Is alpha-stat management still justified for deep hypothermic circulatory arrest in adults?

To the Editor:

We read with great interest the article titled "Neuro-psychologic Outcome After Deep Hypothermic Circulatory Arrest in Adults," by Reich and associates (J Thorac Cardio-vasc Surg 199;117:156-63). The authors are to be congratulated for the timely and careful evaluation of deep hypothermic circulatory arrest (DHCA) as a means to protect the central nervous system (CNS) in adults after alpha-stat blood gas management.

Although alpha-stat blood gas management during perfusion hypothermia is widely accepted as the standard, pH-stat management is more physiologic, as observed phylogenically in nature. We would like to bring a few points to the attention of the readership:

The observed limit of 25 minutes as the dividing line between patients with and without sequelae seems to us too short, considering the rather low esophageal temperature of 12°C to 15°C. We¹ studied a rabbit model of spinal cord ischemia for 60 minutes during surface-induced hypothermia managed according to pH-stat strategies. We observed that gross neurologic function can be consistently preserved at an esophageal temperature of 29.5°C. Even though CNS areas involved with neuropsychologic functions might be more vulnerable to ischemia than the spinal cord, the discrepancy seems to be out of proportion. Perfusion hypothermia for 60 minutes at 20°C under alpha-stat management *without circulatory arrest* followed by rewarming causes derangements in glucose use and decreased blood flow, which were attributed to rewarming² but more likely were triggered by the hypothermia per se.³ Such alterations may cause injury if long-lasting or severe enough, such as when circulatory arrest is superimposed. Whether pH-stat management would prevent those changes from occurring is not known, but the following observations are noteworthy:

1. Although the major argument for using alpha-stat management during hypothermic perfusion in adults has been to avoid the so-called "luxury perfusion" of pH-stat strategies and the consequent increased likelihood of microembolization, pH-stat management for DHCA in children has been found to result in better neurologic outcome than alpha-stat strategies.⁴ There are no reasons to believe that the outcome would be physiologically or metabolically any different in adults.

2. The shift of the oxyhemoglobin dissociation curve to the left induced by the hypothermia-induced alkalosis is aggravated by the alpha-stat management. The increased affinity of hemoglobin to oxygen results in impairment of oxygen delivery, rendering the tissues hypoxic or anoxic despite adequate blood PO_2 .

3. Alpha-stat management will result in extracellular alkalinity that has been found to exacerbate excitotoxic neuronal injury by sensitizing neurons to ischemic injury and to potentiate reperfusion injury.⁵

4. On the contrary, mild acidosis, which may be obtained by pH-stat management, decreases Ca^{++} influx by reducing

N-methyl-D-aspartate receptor activation, glutamate neurotoxicity, and oxygen-glucose deprivation neuronal injury in cortical cultures,⁶ as well as hippocampal neurons.⁷

5. In their study, all patients were given methylprednisolone (30 mg · kg⁻¹) before undergoing DHCA. Although protective effects of methylprednisolone (30 mg · kg⁻¹) given before ischemia were reported in 1983,⁸ 2 years later Sapolsky and Pulsinelli reported that even 10 mg · kg⁻¹ of cortisone (glucocorticoids) potentiates ischemic injury to neurons.⁹ To what extent and in which direction the methylprednisolone worked in patients undergoing DHCA is unknown. However, the possibility that the detrimental effect was the dominant effect cannot be ruled out when other conditions are taken into consideration simultaneously.

An equally careful prospective study using pH-stat management may result in longer than the 25-minute dividing time limits observed with alpha-stat strategies or may decrease the relative role of age as a risk factor. The long-debated issue of which blood gas management protocol is preferable during hypothermic perfusion needs to be resolved.

Tadaomi-A. Miyamoto, MD
Research Department
Kokura Memorial Hospital
Kitakyushu, Japan
Koho-J. Miyamoto, MD, PhD
Assistant Professor
II Department of Physiology
University of the Ryukyus
School of Medicine
Okinawa, Japan

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12/8/100286*Reply to the Editor:*

We wish to thank Miyamoto and Miyamoto for their thoughtful letter in response to our recent publication regarding neuropsychologic outcome after deep hypothermic circulatory arrest (DHCA). In their discussion of the controversy of pH-stat versus alpha-stat blood gas management, they raised several important issues and ideas for future investigation.

There are several potential explanations for the association between DHCA of more than 25 minutes' duration and late neuropsychologic dysfunction in our study. Although we can-

not rule out alpha-stat management, we believe that factors such as longer cerebral ischemia, more complex aortic repairs, and more advanced atheromatous disease in elderly patients were more likely causes. Additionally, the extrapolation of animal models of neuronal protection to the clinical scenario of adult aortic reconstruction is problematic.

We have no immediate plans to use pH-stat blood gas management in patients undergoing DHCA for aortic reconstruction. We firmly believe, however, that improved modalities of cerebral protection will arise eventually from experimental models and clinical investigation, including the important contributions of Miyamoto and Miyamoto, among others.

David L. Reich, MD
Professor of Anesthesiology
Mount Sinai School of Medicine
One Gustave L. Levy Place
New York, NY 10029-6574

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