Con: Topical Head Cooling Should Not Be Used During Deep Hypothermic Circulatory Arrest

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UNQUESTIONABLY, SIGNIFICANT DEGREES of hypothermia are neuroprotective. No more dramatic examples of this are the anecdotal reports of accidental near drowning in which cold-water immersion and the hypothermia that followed allowed for dramatic survival despite long periods without oxygen.[1-3] In cases of aortic arch surgery requiring deep hypothermic circulatory arrest (DHCA), hypothermia is similarly clinically neuroprotective. In these situations, the circulation to the brain can be stopped for an hour or more, often with few significant long-term effects. The suspended animation afforded by DHCA allows life-saving procedures that would have otherwise been impossible.

The mechanisms responsible for the neuroprotective effect of hypothermia are multiple and occur at both cellular and molecular levels.[4] Hypothermia has a well-defined and measurable effect on cerebral metabolism, reducing the cellular requirements for oxygen by 6% to 7% per degree Celsius.[5] However, it has other, likely just as relevant, neuroprotective effects that are mediated by nonmetabolic mechanisms. For example, in the ischemic brain, mild-to-moderate hypothermia has been shown to attenuate the release of glutamate, thus reducing the detrimental molecular events initiated by the excitotoxic effects of excessive N-methyl-D-aspartate activation.[6] In addition, calcium influx is reduced by hypothermia as is the activation of calcium-dependent enzymes associated with various cellular destructive pathways.[7] Other effects of hypothermia include the slowing of the onset of neuronal depolarization (ie, the terminal electrical event when ionic gradients across cellular membranes are lost),[8] hastening of the recovery of protein synthesis,[9] the reduction in membrane-bound protein kinase C activity,[10] and the suppression of nitric oxide synthase activity.[11] The cerebral inflammatory response, measured by microglial activation,[12] also is attenuated by hypothermia, as is the reduction of the formation of reactive oxygen species.[13] It is likely that several or all of these effects in combination constitute the multimodal neuroprotective effects afforded by hypothermia.

Although experimental demonstrations of hypothermic neuroprotection are well established, clinical examples have been relatively few.[14-17] The demonstration of any neuroprotection from the levels of hypothermia typically used during cardiopulmonary bypass for coronary artery bypass graft surgery or valve surgery has been difficult. This has been complicated by issues related to defining appropriate temperature monitoring sites and those related to rewarming strategies.[18-22] Although mild-to-moderate degrees of hypothermia have been used throughout the course of conventional cardiac surgery, for aortic arch surgery, in which blood flow is interrupted to the cerebral vessels for periods of variable duration, deep hypothermia (herein arbitrarily defined by a temperature of $<22^{\circ}C$) has been the mainstay for neuroprotection. During DHCA, numerous modalities have been used to maintain the brain at a temperature at which cellular destruction from ischemia can be attenuated.

With the philosophic desire to "do all that you can do" to protect the brain, topical head cooling with various ice preparations frequently has been used during DHCA surgery despite the absence of any direct clinical data suggesting any benefit. Although many centers use this routinely, many do not, thus highlighting the clinical equipoise as to the utility of this technique. When deciding whether to use topical head cooling, its potential benefit (largely based on theoretical efficacy) must be weighed against its potential harmful effects. Importantly, when deciding whether to institute an unproven therapy, clinicians must first consider the fundamental dictum of primum non nocere (ie, to "first do no harm").

Topical cooling has been instituted by a number of different methods, from near submersion of the head in an ice slurry to the topical application of ice contained within plastic bags. Other specially designed water-cooled caps also have been used. However performed, it is logistically impossible to completely surround the cranium with cooled material, and most of the current methods remain cumbersome. In addition, topical application of ice bags or the near immersion of the head in an ice bath makes the application of other cerebral monitoring devices, independently beneficial to the brain themselves, challenging. Both multichannel as well as single-channel electroencephalographic monitoring and near-infrared spectroscopic (NIRS) cerebral oximetry monitors have been used during DHCA cases and are critical to the management of these patients.[23-25] Anything that interferes with these monitors has the potential to be detrimental to these patients. Ice has the potential to dislodge electroencephalographic electrodes and impair the adhesive of the NIRS optode and sensor arrays. Poorly applied NIRS sensors can lead to inaccurate readings resulting in falsely reassuring data. In addition, the topical application of heavy ice bags may lead to pressure on the eyes, which theoretically could be injurious by increasing ophthalmic pressure with subsequent reductions in retinal blood flow and ischemia. Although there are no known reported cases of blindness from ischemic retinopathy directly attributed to this, it remains a theoretic concern. The topical application

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of ice also could lead to frostbite caused by a combination of the hypothermic injury coupled with the pressure effects on the skin beneath the ice bags that reduce cutaneous blood flow.

The current experimental data examining the efficacy of topical cooling are mixed at best, with some data suggesting benefit, but other data suggesting a detrimental effect. For example, Pokela et al[26] showed that, in a study of pigs undergoing 75 minutes of DHCA (at 20°), animals that received topical head cooling with ice packs were no better in their histopathologic scores than those without topical cooling. Furthermore, cerebral microdialysis (allowing direct sampling of cerebrospinal fluid) analysis revealed a worse brain lactate:glucose ratio, suggesting the potential for less favorable brain metabolic indices.

Thus, with many potential harmful effects and no direct evidence that topical cooling has any meaningful benefit, using this technique routinely is highly questionable. Admittedly, the absence of any direct benefit is caused partly by the paucity of any randomized controlled trial in this area. Part of the reason for this is the relatively few numbers of DHCA cases that occur, making a large multicenter trial the only reasonable means to examine this. Because of interinstitutional differences as well as other logistic difficulties, a trial such as this is unlikely ever to be conducted. As a result, other lines of evidence must be used to search for any potential benefit to topical cooling. However, whether extrapolating any benefit attributable to topical cooling from other clinical paradigms reasonably should be done is debatable.

When considering the nonsurgical data examining the potential efficacy of topical cooling, it is important to discriminate between adult and pediatric populations. There is some indirect evidence that in pediatric patients, for example, in whom the cranium is very thin, there is the potential for the substantive transmission of thermal energy across the skull. Studies in the perinatal asphyxia literature do suggest that topical cooling may have some benefits although there is no direct evidence from any pediatric cardiac surgery studies. Mild-to-moderate hypothermia has been reported in several studies of neonatal hypoxic-ischemic encephalopathy. One trial (N = 238) focused on infants presenting with perinatal asphyxia in whom hypothermia (33.5°C) was instituted within 6 hours of birth and maintained for 72 hours after which a slow passive rewarming occurred.[27] Neurodevelopmental outcomes assessed at 18 to 22 months of age showed that the combined endpoints of death or moderate/severe disability were much improved compared with conventional normothermia therapy. Importantly, hypothermia did not appear to increase the incidence of severe disability in the survivors, a clinical situation that clearly would be disadvantageous. A second study, the Total Body Hypothermia for Neonatal Encephalopathy trial, was a randomized trial that also examined term infants with asphyxial encephalopathy. In this study (N = 325), infants were randomized to either a group cooled for 72 hours or a noncooled control group. The assessment of survivors at 18 months similarly showed an improvement in overall neurologic outcomes. Studies continue to determine if these benefits are maintained over an even longer time period. Although there is a wealth of experimental data outlining the beneficial mechanisms and degree to which hypothermia could protect the brain, caution and balance should be used when considering these clinical applications of hypothermia. Extrapolating these beneficial results in neonatal asphyxia to other surgical settings of potential brain injury is, at best, weakly supported.

One of the most important considerations in the decision to use topical cooling is whether it realistically can be expected to have any meaningful effect on the actual induction or maintenance of cerebral hypothermia. Thermodynamically, in order for topical cooling to be effective, enough thermal energy needs to transit across the cranium (ie, energy in the form of heat needs to flow down a gradient from the relatively warmer brain toward the surrounding topically cooled area). The transmission of thermal energy is dependent on the thermoconductivity of the skull and its encompassing tissues, the temperature gradient that exists between the brain and the surrounding environment, and the amount of conductive surface contact. It is difficult to measure the actual amount of heat from the brain itself that can be lost to the environment, but computer models have shown that the skull is a relatively poor conductor of thermal energy.[28,29] This has two important consequences. First, a very large gradient must exist in order for the heat to be driven down this gradient. It is unlikely that the temperature of the ice bags is sufficiently low to allow much further heat energy to move from the brain that has already been cooled during bypass. Secondly, with the average operating room temperature at around 18° to 19°C (and oftentimes cooler) and a brain temperature of 14° to 16°C (temperatures routinely used for DHCA), it is unlikely that the reverse process of passive rewarming of the brain after the onset of DHCA can occur. Even if a sufficient temperature gradient was present, with the relatively small amount of actual skin contact to serve as a conductive surface, conductive heat transfer cannot be a major factor.

The use of any topical head cooling also must be put in the context of the current expanding use of selective antegrade cerebral perfusion (SACP).[30] As a result, the true duration of cerebral circulatory arrest becomes increasingly smaller. Therefore, even if there was a potential benefit to topical cooling, it is increasingly unlikely to show any meaningful effect because of the diminishing returns related to the use of SACP. Furthermore, some surgical groups are using much higher temperature DHCA targets because of the ability to provide the low-flow perfusion of SACP.[31-33] With this, the temperature gradients between the brain and surrounding environment are substantially reduced, largely eliminating any passive rewarming. It is clear that the relevance of topical cooling in the setting of SACP is being lost. In summary, the absence of any definitive data suggesting a benefit to topical head cooling, its potential for significant adverse effects, the cumbersome logistics associated with it, the computer modeling showing poor heat transfer, and its diminished relevance using SACP, topical head cooling should not be used routinely during cardiac surgery.

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