Therapeutic hypothermia may enhance reperfusion in acute ischemic stroke

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Acute ischemic stroke is a leading cause of death and disability throughout the developed world. Although early vascular reperfusion has been shown to improve clinical outcomes, fewer than 5% of patients with acute ischemic stroke actually receive thrombolytic therapy. The challenge of thrombolytic therapy is rapidly shrinking recovery of brain tissue coupled with increasing vulnerability to reperfusion injury. The result, a narrow time window, has proved to be the stumbling block in wider dissemination of this treatment. Conceivably, coadministration of a "tissue protectant" could enhance the effectiveness of thrombolysis while expanding the time window and reducing the risks of reperfusion.

A promising candidate to serve this purpose is hypothermia. A wealth of animal experiments demonstrated that hypothermia, or simply fever prevention, diminishes ischemic damage with transient occlusion followed by reperfusion. In models of permanent occlusion, reduction of infarct size was less impressive. In transient models, hypothermia was most effective when administered during the period of vascular occlusion (intra-ischemic) or immediately after vascular reperfusion (postischemic). According to these models, hypothermia is efficacious in concert with reperfusion in only a narrow time window. Some investigations suggest that lengthy periods of hypothermia enhance the benefit of its early postischemic induction, even in permanent occlusion models. Consequently, in patients with acute stroke, therapeutic hypothermia will more likely confer benefit in conjunction with early vascular reperfusion and when applied over prolonged time periods.

The use of antipyretic agents alone has not been shown to effectively reduce core temperature after stroke, although post-stroke fever can be inhibited. Therapeutic mild to moderate hypothermia can be achieved by surface cooling (external cooling) or by using intravenous counter-current heat exchange (endovascular cooling). Other modalities, such as localized hypothermia, are being developed. Limitations of external cooling are almost invariably associated with imprecise timing and continuation of the hypothermic effect. With endovascular cooling, heat is directly removed from or added to the thermal core, thus bypassing the heat sink and insulating effects of peripheral tissues. Several early open and controlled studies have shown that endovascular cooling is safe and can effectively manage core temperatures in the mild to moderate hypothermic range.

This lecture will review key experimental and clinical studies to advance the understanding of mechanisms by which hypothermia may enhance stroke outcomes and how these insights may help to translate the benefits of hypothermia from bench to bedside.

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