Editorial

Getting hot under the collar: temperature and cerebral autoregulation

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Importance of temperature in critical illness

The brain is a thermodynamic machine and like many other machines, the brain needs an efficient cooling system to maintain optimal function. The human brain cooling system is important in both health and disease; having even been credited with allowing the rapid growth of the early hominid brain (1). Since Aristotle, heat has been considered an important modifiable factor in sick humans (2). However, it was not until the mid 20th century that the first formal studies of therapeutic decreases in temperature emerged in the United States (3). The last 20 years have seen a surge in interest in this relatively simple intervention. The rationale in the case of the brain is that decreasing temperature decreases the metabolic rate of the body tissues (including the brain), which therefore decreases the potential for a mismatch where oxygen demand exceeds supply. While a recent trial could not demonstrate a benefit of early therapeutic hypothermia after traumatic brain injury (4), targeted temperature has shown to reduce morbidity and mortality in other conditions such after cardiac arrest (5).

What's the problem with a little heat?

In general, the brain is warmer than blood temperature such that arterial blood circulation has a cooling effect on the brain parenchyma. In the context of a generalised fever, the increased temperature leads to an increase in metabolism by the Q_{10} or Arrhenius effect (6). In pathologies that decrease brain oxygen supply, increased local temperature can lead to increases in metabolism, flow, blood volume and therefore intracranial pressure (ICP). These principles seem to hold in clinical practice where hypothermia reliably decreases intracranial pressure and the development of fever leads to an increase in intracranial pressure (4,7). Severe increases in intracranial pressure can, in turn, lead to critical ischaemia in certain areas of the brain. While the effects of temperature on ICP are relatively well described, the effects of temperature on the stability of cerebral blood flow (CBF) to changes in cerebral perfusion pressure (CPP)—cerebral autoregulation—are less well studied.

Support for the use of cerebral autoregulation as a biomarker in critical brain injuries is emerging and encouraging. It can be easily monitored—both invasively and non-invasively, it is associated with patient outcome, and it can be used to define and refine treatment targets (8). Monitoring the response of brain vessels to spontaneous slow changes in blood pressure or perfusion pressure is the basic tenant of continuous cerebral autoregulation monitoring. Because it can be monitored continuously and is an indicator of brain vascular health, optimising it has become the focus of ongoing trials in acute brain injuries and cardiac surgery [reviewed in (9)].

Heat and cerebral autoregulation

In the article recently published in *Critical Care Medicine*, Adatia and colleagues investigated the effect of temperature on cerebral autoregulation as measured with near infrared spectroscopy (NIRS) (10). The authors found that increasing temperature was associated with a worsening of cerebral autoregulation. While aspects of this study confirm previous findings, the study does provide novel insight.

The study has several limitations—the modest sample size means that spurious relationships are possible as has been demonstrated in previously in the brain trauma population (11). Also, the site of temperature measurement is relevant—brain temperature can be up to 2 degrees warmer than tympanic or bladder temperature [reviewed in (6)] and therefore inferences about a threshold of temperature associated with disturbed autoregulation (reported as 38.6 degrees) should be treated with caution. Other important considerations are whether temperature measurements every 1–4 hours accurately reflect the dynamics of brain temperature and whether the rate of cooling or heating contribute the proposed relationship between temperature and cerebral autoregulation.

Similar to a previous study (12), a positive relationship between temperature and autoregulation (as estimated by the index COx) was found such that higher temperatures were associated with worse cerebral autoregulation. What could be reasons for this? Increased temperature in isolation leads to vasodilation (13) which in turn can lead to impaired vessel responsiveness as we see with hypercapnia. In addition, increased temperature has an effect on intracranial pressure (7), which, through a decreasing CPP could also lead to impaired cerebral autoregulation. *In vivo*, these effects may be in part counterbalanced by a temperature induced hyperventilation, hypocapnia and cerebral vasoconstriction (6). Importantly, this study controlled for changes in CO_2 which is a notable strength.

An important implication of this study is that when using cerebral autoregulation to define optimal blood pressures in critical illness, we would do well to consider physiological parameters that affect dynamic autoregulation apart from perfusion pressure. If our aim is to improve autoregulation, then, modifying BP represents just one avenue for intervention. In some patients, derangements of temperature, CO_2, or metabolism could be the major reason for impaired autoregulation, rather than a blood pressure *per se*.

Whether optimising the cooling system of our injured thermodynamic brains can lead to more efficient brain vessel function should be tested in upcoming trials. If proven successful, an interesting question arises; can we use autoregulation to help decide when to cool a brain injured patient?

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