Temperature Management

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Per-Olof Grände and Peter Reinstrup

Recommendations

Level I

Active cooling to subnormal temperature in traumatic brain injury (TBI) patients does not improve outcome.

Level II

There is support for the avoidance of high fever, but no support for active cooling.

Level III

Level III studies support the use of active cooling in TBI patients, a conclusion not supported from Level I or II studies. Paracetamol can be used to reduce fever in TBI patients.

68.1 Overview

Body temperature can be measured at different sites where rectal temperature is the classical standard position for body core measurement. Other sites have been vagina, bladder, ear, oral and oesophagus. Measurement of brain temperature with a temperature probe inserted in the brain (positioned in the parenchyma or in a ventricle) has shown that brain temperature is only slightly higher (≈ 0.3 °C) than body core temperature in spite of the much higher metabolism of the brain (Mellergård and Nordström 1991). The high blood flow to the brain will counteract a difference between body core temperature and brain temperature. Normal rectal temperature is 36.7 ± 0.7 °C.

Based on experimental and clinical studies, there is a general view that high fever is detrimental to TBI patients (Thompson et al. 2003). An important goal in the treatment of these patients has therefore been to prevent or reduce fever. So far, we lack evidence-based consensus regarding how to reduce temperature in TBI patients. Fever can be reduced pharmacologically by affecting the hypothalamic thermostat or by active cooling of the patient. During the last 15 years, it has also been suggested that active cooling to subnormal temperatures (32–34 °C) should be beneficial due to its well-known neuroprotective effect, as demonstrated in animal studies after brain ischaemia and also in humans after near drowning in cold water and after active cooling following heart resuscitation (Polderman 2008; Grände et al. 2009; Sandestig et al. 2014). There was no improved outcome, however, in a recent randomised heart resuscitation hypothermia study

P.-O. Grände (✉) · P. Reinstrup
Department of Anaesthesia and Intensive Care, Lund University and Lund University Hospital, Lund, Sweden
e-mail: per-olof.grande@med.lu.se; peter.reinstrup@med.lu.se

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in the group treated with active cooling down to 33 °C compared to a temperature of 36 °C (Nielsen et al. 2013). The fact that hypothermia decreases an increased intracranial pressure has also been taken as an indication for beneficial effect of hypothermia in head trauma patients (Polderman 2008; Andrews et al. 2015).

The mechanisms behind the suggested hypothermia-induced neuroprotection are not clarified, but the reduced neuronal metabolism, reduced inflammatory response, reduction in toxic substances such as glutamate and a scavenging effect are discussed to be involved. It was therefore believed that active cooling should be beneficial in TBI patients. In this chapter, we give recommendations on how and when temperature should be reduced and the goal temperature in TBI patients, based on the results of the most recent studies and current knowledge in this field. It is concluded that active cooling is associated with side effects and that we lack support for its use in TBI patients, and it can therefore not be recommended (see below).

Tips, Tricks and Pitfalls

- Avoid active cooling in TBI patients.
- Too high body temperature can be reduced by affecting the thermostat pharmacologically with paracetamol (1 g × 2–4 p.o.). A persistent life-threatening high fever above 39 °C can be reduced with one bolus dose of methylprednisolone (Solu-Medrol) (0.25–0.5 g i.v.).
- Normothermia is the optimal temperature.

68.2 Background

68.2.1 Active Cooling of the TBI Patient

There have been many studies on TBI patients that have analysed the effect of active cooling to normal and subnormal temperatures on outcome. Cooling of the whole body (systemic cooling) has been used in most studies so far.

Local cooling of the brain has been discussed to reduce complications of systemic cooling, such as pulmonary complications and coagulation disturbances. Selective brain cooling can be obtained by a cooling cap or by intranasal cooling with circulating cold water via a tubing/balloon system inserted into the nose. Local cooling, especially with an intranasal cooling technique, so far has had difficulty in reducing brain temperature, and additional technical development is necessary before it can be recommended (Springborg et al. 2013).

In spite of the fact that reduction of fever by active cooling to a normal temperature or lower has been used in clinical practice in TBI patients for decades, there have been no randomised or larger studies confirming any beneficial effect of this therapeutic measure on outcome. Several smaller studies have suggested that there is improved outcome with active cooling (Marion et al. 1997; Adelson et al. 2005), but, as mentioned, the best trials on children and adults could not confirm such an effect (Clifton et al. 2001, 2011; Hutchison et al. 2008). The well-known hypothermia-induced reduction in ICP most likely is an effect of hypothermia-induced vasoconstriction with a simultaneous decrease in cerebral blood flow and blood volume. The ICP effect of hypothermia to 33–35 °C on outcome in TBI patients starting with an ICP above 20 mmHg was recently analysed in a large multicentre European randomised study (Andrews et al. 2015). As expected, they found that ICP decreased with hypothermia, but there was no improvement in outcome, and the study was interrupted in advance due to signs of adverse effects.

A comprehensive analysis of the best studies supported the view that active cooling to subnormal temperatures has no beneficial effect on outcome in TBI patients; instead, these studies indicated that active cooling even worsens outcome. This conclusion was supported by a recent Cochrane analysis (Sydenham et al. 2009). Thus, we still lack any support for the view that treatment of a severe head injury with or without fever and with or without a raised ICP by active cooling to normal or subnormal temperature is beneficial. Thus, at this stage, active cooling systemically or locally cannot be recommended as a general

therapy or a therapy to reduce temperature or ICP in TBI patients.

There are some specific characteristics that may explain why the well-established neuroprotective effect of active cooling does not improve outcome in TBI patients (Grände et al. 2009; Sandestig et al. 2014). Active systemic or local cooling always means a difference between the body or brain temperature and the temperature stipulated by the hypothalamic thermostat. This difference creates a pronounced metabolic stress with the purpose of restoring body temperature to the level before cooling, resulting in an increase in plasma catecholamines. Muscle shivering is a visible component of this stress response, but the increase in stress and catecholamine release most likely is present without shivering. There is a great risk that the increased catecholamine concentration after active cooling will further reduce the already compromised circulation of the penumbra zone. There is also a risk that ventilatory adjustment to the hypothermia-induced lower metabolism is not performed, leading to a condition corresponding to hyperventilation, resulting in worse perfusion of the penumbra zone. Hypothermia also means a lower blood pressure, resulting in more frequent use of vasopressors, which may not only reduce perfusion of the penumbra zone, but also increase the risk of development of ARDS (Robertson et al. 1999) and loss of plasma volume to the interstitium (Dubniks et al. 2007; Nygren et al. 2010). Finally, reduction of the body temperature to subnormal values may induce coagulation disturbances and increase the volumes of contusional bleedings (Rundgren and Engström 2008).

68.2.2 Pharmacological Reduction of Fever

From a physiological point of view, fever should be treated by adjusting the hypothalamic thermostat. Several types of new temperature-reducing substances have been tested experimentally, but so far none of these substances can be used clinically due to severe side effects. This means that at the moment, paracetamol and steroids are the only temperature-reducing substances affecting the hypothalamic thermostat available in clinical practice. Paracetamol can be used to reduce fever, but it reduces temperature by only about 0.5 °C in acceptable doses. In higher doses, it has side effects in terms of inhibition of the endogenous production of prostacyclin, and it has toxic effects on the liver.

Steroids (e.g. methylprednisolone) effectively reduce fever by affecting the hypothalamic temperature centre. A randomised study on TBI patients (the CRASH study), including both moderately injured and more severely injured patients (GCS <14), analysed the effect of routine use methylprednisolone (Edwards et al. 2005). It showed worse outcome in TBI patients given steroids. Note that steroids were given in a very high dose of more than 20 g for 2 days in that study and were used independently of fever or not and independently of the severity of the head injury. The results of the CRASH study support the conclusion that corticosteroids in high doses should not be used in the treatment of moderate and severe head injury and especially not for several days. This does not mean, however, that the fever-reducing effect of just one bolus dose of methylprednisolone at the relatively low dose of 0.25–0.5 g to an adult with a severe TBI cannot be used to reduce a life-threatening high fever. Such a dose may significantly reduce fever for up to 2 days, and the beneficial fever-reducing effect most likely overrides the potential adverse effects shown by the 20–30 times larger doses in the CRASH study and the well-known adverse effect of a very high fever. A subsequent increase in blood glucose can be controlled by insulin.

68.3 Specific Paediatric Concerns

The highest-quality randomised trials performed for the adult and the paediatric population have not shown any beneficial effects of active cooling following TBI (Clifton et al. 2001, 2011). The best paediatric study performed so far (Hutchison et al. 2008) strongly indicated that hypothermia even worsens outcome. This means that according to our present knowledge, active hypothermia should not be used in the paediatric population.

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