JC: EUROTHERM3235

Hypothermia for Intracranial Hypertension after Traumatic Brain Injury

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STUDY QUESTION:

In adults with TBI and ICP > 20 mmHg, despite "stage 1 treatments," does hypothermia (32°C – 35°C) improve outcome compared with standard care?

HOW DOES THIS RELATE TO OUR PRACTICE ON NCCU?

Traumatic Brain Injury is almost the raison d'être of NCCU.

Elevated ICP is a frequent finding that requires prompt management in order to prevent further brain injury.

Therapeutic hypothermia (TH) has been shown to lower ICP and is a central part of our protocolised management of patients with TBI and elevated ICP.

TH has been shown to improve neurologic outcomes in comatose survivors of out-of-hospital cardiac arrest. The original 2 studies (HACA and Bernard) from 2002 targeted 32-34°C but in a more recent study (TTM trial), 36°C has been shown to be as good as 33°C. Different population and different indication.

Frankly, removing TH would go against our almost religious approach to the management of TBI – perhaps that is the reason why this study sits so uncomfortably. But, in our business, our thoughts should always be discordant and our actions should always make us uncomfortable. For this reason it is one of the most important studies in the context of how manage patients in Cambridge.

WHAT DO WE CURRENTLY KNOW ABOUT THIS AREA?

TH may have a range synergistic neuroprotective effects:

- It lowers the cerebral metabolic rate
- Decreases excitotoxic neurotransmitter release
- Decreases free radical formation
- Decreases sustained electrical depolarisations
- Inhibits proinflammatory and apoptotic pathways

TH lowers ICP perhaps through the following mechanisms, but we really don't know:

- Decreased inflammation
- Decreased vasogenic edema
- Decreased cerebral blood volume

However, TH is not without risks:

- Coagulopathy/platelet dysfunction
- Immunosuppression
- Cardiac dysrhythmias
- Hypotension
- Pneumonia
- Insulin resistance
- Cold diuresis and electrolyte depletion
- Decreased catecholamine responsiveness

Have a look at Nature Reviews Neurology this blog.

WHY WAS THIS STUDY NEEDED?

In the setting of TBI, multiple older studies showed mixed results. A 2014 systematic review and meta-analysis found possible benefit for therapeutic hypothermia in TBI. A well-designed RCT was needed to definitively answer the question.

AT JOURNAL CLUB WE SHOULD DISCUSS THE FOLLOWING:

- Hypothermia was applied quite early (after 5 min of sustained ICP > 20), seems a bit quick, see our letter.
- Initial interventions were modest, yet safe, where does the risk of TH sit with this?

- The study did not use other stage 2 treatments in hypothermia group unless persistent ICP elevation
- What about how TH was achieved, it was quickly down to the target range 32-35°C, why not use an incremental, stepwise approach and achieve the minimum temp decrease required to control ICP?
- What about all that fluid?
- Sadly the trial stopped early after 387/600 patients enrolled, is this a problem?

SHOULD WE CHANGE PRACTICE ON NCCU

Not based on the results of this study. They applied therapeutic hypothermia very differently than we do in the NCCU at Cambridge: They used it very early and prior to basic interventions, such as osmotherapy. Although basic is a word we use when we don't know the harm a treatment really casues.

A trial that more closely mirrors our pattern of practice is needed prior to considering a change.

The next big RCT on TH in TBI, POLAR, has just finished enrolling patients, will this help us? Let's see at journal club.

FURTHER READING

BTF guidelines

The Bottom Line

Nature Reviews Neurology – Hypothermia for acute brain injury

https://www.nature.com/articles/nrneurol.2012.21

SNACC Review