Evidence Based Practice Critically Appraised Topic (CAT)

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Clinical Scenario:

62 year old male presents to the emergency department via private vehicle, with right sided hemi paresis, and garbled words. The patient is alert and his vital signs are stable. Patient's wife states that he was fine 30 minutes ago when she was talking to him at home. He requires a CT scan at the nearest facility to rule out of hemorrhagic stroke to determine if he is a candidate for TPA. He will be transferred via ground ambulance. Should the provider consider inducing hypothermia in this patient as a neuroprotective measure?

Clinical question:

Is there neuroprotective benefit of an induced hypothermia state in acute cerebral stroke patients, versus our current standard of normothermic care in the emergency department for the treatment of stoke?

Articles:

Hemmen, T., Lyden, P. (2007). Induced Hypothermia for Acute Stroke. Stroke journal of the American Heart Association. 38;794-799. DOI: 10.1161/01.STR.0000247920.15708.fa

Den Hertog H, van der Worp H, Tseng M, Dippel D. (2009). Cooling therapy for acute stroke. *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD001247. DOI: 10.1002/14651858.CD001247.pub2.

Critical Review of Study:

Hemmen & Lyden (2007) provided a grade C, level 5 review on the clinical implications of hypothermia research in stroke and technical and logistical issues associated with the application of hypothermia.

Den Hertog, van der Worp, Tseng and Dippel (2008) provided a grade A, level 1a evidence systematic review of cooling therapy for acute stroke patients. The purpose was to assess the improvement of outcomes when pharmacological and physical strategies reduced body or brain temperature in patients with acute stroke. The results included five pharmacological temperature reduction trials and three physical cooling trials from January 1998 to December 2007.

Results:

Hemmen & Lyden (2007) provided a review of the development of safer endovascular heat exchangers and novel antishivering protocols, which avoid sedation, makes the routine clinical use of hypothermia after stroke practical. Future studies will need to investigate the effect of hypothermia on clinical outcome, the safety in combination with thrombolysis, and its potential use in conjunction with other neuroprotective strategies.

In the systematic review by Den Hertog, et al., (2008) five studies including 423 participants were evaluated including patients over 18 years of age within 24 hours of a cerebral infarction or primary intracerebral hemorrhage. A pooled analysis of the temperature reduction trials showed no significant difference between active treatment and control in the proportion of patients who were dead or

dependent at final follow up (OR 0.9, 95% CI 0.6 to 1.4) There was no heterogeneity in the pharmacological reduction trials however there was high levels of heterogeneity between the two physical temperature reduction trials. Both pharmacological and physical temperature-lowering interventions were associated with a non-significant increase in the occurrence of infections.

Strength:

The strength of the research shows improved outcomes in animal studies when temperature is lowered. In humans temperature-lowering therapy has been proven effective in preventing death and dependency in patients who were resuscitated after cardiac arrest. In infants with hypoxic-ischemic encephalopathy, hypothermia of 33.5°C for 72 hours was safe, reduced fatality, and improved neurodevelopment outcome. These findings suggest that therapeutic hypothermia may also improve outcome in patients with acute stroke.

Implications for practice:

Hypothermia is one of the most promising neuroprotective therapies yet identified in preclinical studies. There is currently no evidence from randomized trials to support routine use of physical or pharmacological strategies to reduce temperature in patients with acute stroke. Large randomized clinical trials are needed to study the effect of such strategies. At this time The Intravascular Cooling in the Treatment of Stroke–Longer tPA Window (ICTuS-L) 12 study is currently under way and aims to test the combination of intravenous tissue plasminogen activator (tPA) and hypothermia. ICTuS-L is a phase I safety study.

I look forward to the results of future research in this area and the implications it may have in my practice.