ICU MANAGEMENT & PRACTICE

ICU Volume 8 - Issue 4 - Winter 2008/2009 - Hypothermia Series

Temperature Management in Stroke: Current and Future Options (R. Armonda)

Author

Col. Rocco A. Armonda, *MD*

Director Cerebrovascular Surgery & Interventional Neuroradiology,

Neurocritical Care National Capital Neurosurgery Consortium

Bethesda, Maryland, USA

rocco.armonda@med.navy.mil

rarmonda@hotmail.com

Introduction

The combination of enhanced care provided by stroke units combined with advanced temperature technology allows for a more precise control of a patient's temperature with ultimately improved clinical outcomes. Tem pe rature management has been an arduous, labour intensive process with traditional antipyretics and unregulated cutaneous cooling blankets. More recently the use of closed loop, self-regulating cutaneous hydrogel pads and endovascular cooling catheters have greatly improved the precision of temperature control and reduced the time and labour involved. Additional neuroendovascular and neurosurgical treatments have im proved the ability to revascularise ischae mic patients as well as decompress life-threatening infarcts. However, room for improvement exists with life-threatening reperfusion haemorrhages, functional limitations after decompressive surgery, and secondary infarct extension.

Goals of Stroke Care

The goals in stroke care include, when possible, reversing the clinical deficit, limiting the zone of injury, and reducing increased intracranial pressure in the face of a large infarct. Hypothermia combined with modern neurointerventional techniques, and when indicated, decompressive hemicraniectomy can achieve these goals. Although no randomised control trial combining hypothermia for stroke care has been performed, 9 feasibility studies with 215 patients have demonstrated promising results. These have been single- centred studies with a variation in the time of cooling from 4-75 hours as recently reviewed by Polderman in the Lancet and others combining induced hypothermia with hemicraniectomy (Pold er man 2008; Bardutzky and Schwab 2008; Oehm et al. 2006). This includes limiting secondary life-threatening oedema from severe middle cerebral artery infarcts. However, during the rewarming phase rebound intracranial pressure resulted in death in a third of patients (Georgiadia et al. 2002). This emphasises the need for precise, slow and controlled rewarming.

This suggests there is role for combined therapies as recently proposed by Dr. Juan Sahuquillo from the Department of Neurosurgery at Vall D'Hebron in Barcelona, Spain. In his pilot trial, Cool-Stroke, hypothermia was induced using endovascular cooling during the first 24 hours, with intracranial monitoring at 32-34°Celsius and was followed by hemicraniectomy in those patients who demonstrated >/= 5mm of midline shift during the subsequent days (Delgado et al. 2006). This proposed combination of treatments has several clinical and experimental supports. Meta-analysis of experimental data in stroke supports the role for 33°C to reduce infarct size. A dose-dependent relationship exists with response <35°C in infarct volume reduction (Van Der Worp et al. 2007).

Additional clinical support for this combined treatment has been reported by investigators in a safety trial of 25 patients with an improvement in functional outcomes when compared with hemicraniectomy alone. In Els' study, hemicraniectomy with hypothermia less than 35°C was applied with in 3 hours of a decompressive hemicraniectomy performed an average of 15 hours after presentation. Unlike other studies, no patients expired from intractable ICP during rewarming. No increased complications were noted in the hypothermia group and the overall mortality was lower than prior reports utilising hemicraniectomy or hypothermia alone. In addition to the early application of hemicraniectomy (14.9 +/- 5.6 hours) verses 24 hours in Georgiadias, 21 hours in Schwab, and 60 hours in Walz, mild hypothermia was applied (<35) vs. moderate (33°Celsius), with a rigorous standard ICU management. This included maintenance of corrected PaC02 36- 40, glucose 120-150, mean arterial pressure 90-110, central venous pressure 8-12. In the hypothermia group 10 of the 12 patients achieved hypothermia with the use of endovascular cooling catheters and two patients with surface cooling. Patients were cooled for 48 hours with achieving target temperature within 1.5- 3.5 hours, with continuous ear and oesophageal temperature monitoring. Controlled rewarming was performed no faster than one degree celsius/day. Hypothermia side-effects including pneumonia, electrolyte changes (q 2 hour labs), hypotension (MAP<80), and cardiac effects including bradycardia and arrhythmias were controlled. No immediate differences in outcome were noted. However at 6 months there was a trend for improved results in hypothermia treated patients compared to hemicraniectomy alone with a NIHSSS (10 +/- 1 and 11+/-3) and Barthal Index (81 +/- 14 vs. 70 +/- 17) (Els et al. 2006).

Fever Control

The ICU is the perfect setting to apply temperature management in stroke care. Up to 47% of stroke patients will have a persistent temperature >38.5°C. Preventing fever as an initial step is a major accomplishment in limiting secondary injury. A high correlation exists for poor outcome, prolonged length of stay, and decreased functional recovery directly related to a patient's fever burden. In a recent comprehensive meta-analysis fever was associated with increased mortality, intensive care unit stay, hospital length of stay and lower functional recovery (Greer et al. 2008; Ginsberg and Busto 1998). This relationship of poor outcome is also seen in SAH with fever burden and independently associated with poor outcome and mortality, as well as fever in ICH with duration of fever >37.5°C associated with poor outcome especially in the first 72 hours.

Current Treatment Advances

Current advances in intensive care medicine, temperature control technology, and neuroendovascular treatment of stroke have created a pivotal opportunity to improve stroke care and outcome. In the US, a rapidly aging population, an increase in stroke risk factors and more sedentary lifestyles have led to the continued rise of stroke occurrence. Technology has advanced to include improvements in controlled, closed loop systems, both invasive and non-invasive, which allow precise temperature reduction, control and rewarming. These drastic technological modifications allow the inclusion of patients with traumatic brain injury and stroke in temperature management treatments, where they were generally excluded the in the past. The first line of temperature intervention in the neurologically compromised patients is in decreasing fever burden. In Diringer's report of 296 patients from 13 neurocritical care centres (The Neurocritical Care Fever Reduction Trial Group) was a prospective, randomised, non-blinded study comparing endovascular cooling using the CoolGuard/Cool Line central line catheter (n=142) to traditional surface techniques (n=154). This included patients with subarachnoid haemorrhage (41%), intracerebral haemorrhage (23%), ischaemic infarction (13%), or traumatic brain injury (24%). Temperature was >38 degrees Celsius on two occasions or for >4 hours continuous, and required central venous access. He demonstrated a significant 64% reduction in fever burden (2.87 vs. 7.92°C-hrs) and no higher rate of complications when compared to the standard use of a central line catheter. No increased rates of antibiotics, infections, sedatives or narcotics were noted. (Diringer et al. 2004).

In selected patients revascularisation can be performed with either chemical or mechanical thrombolysis, however, resulting devastating reperfusion haemorrhage limits the application of revascularisation. The advantage of hypothermia in preserving the blood brain barrier and limiting the risk for reperfusion haemorrhage presents a unique combined advantage.

The role for combination treatment includes the use of hypothermia with both endovascular and open surgical techniques. Specifically, endovascular revascularisation with both chemical and mechanical thrombolysis allows the use of revascularisation with neuroprotection afforded with hypothermia. Additional intraoperative use of hypothermia during revascularisation with selected extracranial-intracranial bypass patient allows cerebral protection during the anastamosis. The benefits from hypothermia include decrease metabolic rate, decrease inflammatory cascade, decrease 02 free radicals, excitotoxic neurotransmitters, and limited programmed cell death. Microdialysis monitoring during induced hypothermia was comparable to the beneficial effect of decompressive hemicraniectomy in a recent clinical study (Berger et al. 2008).

The use of hypothermia should be considered a spectrum of temperature control, which included moderate, mild, and normothermia. Different levels of ischaemia/infarction may require a different depth of hypothermia. The use of temperature control including normothermia is also significant for the strong association of poor outcome in stroke and fever.

A range of temperature management strategies is available for acute ischaemia stroke and includes moderate hypothermia (32- 34°C), mild hypothermia (35°C), and maintenance of normothermia (</=37°C). The metabolic, electrolyte and hemodynamic changes associated with therapeutic hypothermia can be readily addressed in a modern ICU focused on stroke care and recovery. These changes are part of the expected side-effects associated with moderate hypothermia between 32-34°degrees Celsius and once managed enhance the neural recovery from injury and insult (Polderman 2004). This range of treatment options from normothermia to moderate hypothermia allows the tailored management for different stroke patients in different stages of their ischaemia.

Utilisation of Current Therapies

Recent large randomised studies have demonstrated improved neurological outcome after cardiac arrest. Significant acceptance and application has occurred in over 77% of Scandinavian countries with less than 25% application in most US centres (Polderman 2008). This is a problem not only with education, but changing healthcare implementation. Physicians tend to resist change. New techniques, procedures and standards progress slowly through medical circles due to this resistance. Overcoming institutions resistance requires coordinated leadership at many levels to include administration, nursing and physicians partici pation. Through far-forward thinking individuals these ideas of limiting secondary neural injury in the vulnerable ischaemic brain is both practical and achievable.

More advanced therapeutic neuroendovascular procedures have also been combined with temperature management in stroke. Additional protocols have been designed combining hypothermia with neuroprotecting agents to enhance recovery, protect the brain blood barrier, limiting reperfusion haemorrhage and cerebral oedema. These include the combination of both mechanical and chemical thrombolysis with endovascular cooling: ICTUS-L, ICTUS-C and Cool-Aid II. During Cool-Aid II target was achieved in 13/18 patients, 5 limited due to shivering side effects. Current protocols using selective palm and sole surface rewarming combined with Demerol, Magnesium, Dexmetomidine and sedation protocols has limited the occurrence of shivering (Mayer, Neurocritical Care).

Recent use of endovascular devices has been reported to decrease the time and labour to achieve target temperature in malignant MCA stroke.

In a series of 35 patients in over 5 years using an 8.5 French, 35 cm catheter (ICY, Alsius Corporation) closed-looped re gulated induced hypothermia at 33°C (32.1-33.6) was performed. Patients were kept at target temperature >72 hours with a slow rewarm not exceeding 0.1°C/hr (duration of cooling 85 +/- 10 hours). Patients were cooled 17+/-9 hours after onset of their stroke with target achieved in 2.7 +/-0.6 hours. Mortality was reduced with a 57% survival and mean Barthel index of 65 (40-85), Rankin Score of 2.9 (Bardutzky and Schwab 2008; Els et al. 2006; Geor -giadia et al. 2002). However, uncontrollable rebound ICP occurred in 11/35 patients resulting in death (Bar dutzky and Schwab 2008).

Future Options

A novel advanced therapy has also been proposed by researchers at Columbia University in New York and Xuan Wu Hospital, Capital Medical University in Beijing China. Drs. John Pile-Spellman and Feng Ling are examining the application of simultaneous intra-arterial selective rapid cerebrovascular cooling with cold saline injection during revascularisation and cerebral angiography (Chen et al. 2008). This robust study incorporates MR-imaging, which assesses local brain temperature and metabolism, transcranial dopplers, cerebral angiography with intra-arterial cooling and neuropsychological assessments. This protocol involves the use of selective short-term early brain cooling (33-35°C) to avoid reperfusion haemorrhagic transformation and systemic side effects while also utilising advanced neuroimaging techniques to measure brain temperature and metabolic effects. The neuroimaging techniques utilise MR spectroscopy (3T) as MR-Thermo metry and CBF measurements using cold saline as a contrast medium. They also plan to evaluate the neuropsychological effects of selective brain cooling on attention. Their proposal would utilise selective cerebral hypothermia as a bridging procedure prior to systemic hypothermia and as an adjunct to other neuroendovascular recanalisation techniques. Additionally, they would add a mean of anatomic localisation to measure different temperatures, metabolic rates and CBF in the brain whereby combining both physiologic and anatomic data in stroke management using selective hypothermia.

Conclusion

The future for hypothermia in stroke care will eventually lead to less invasive and more selective means of cooling the brain. Such techniques may include pharmacologic agents such as variations of H_2S, which induced hypothermia in laboratory animals mimicking hibernation. Combining this with other revascularisation techniques increases the therapeutic window for other neurovascular and surgical therapies to perform neuro-rescue. Future enhanced multi-modal monitoring of patients with stroke who are undergoing induced hypothermia will better elucidate the metabolic crisis and role for combined therapies in this ever increasing and vulnerable population.

Published on : Thu, 15 Aug 2013