ICU MANAGEMENT & PRACTICE

ICU Volume 12 - Issue 4 - Winter 2012/2013 - Matrix Features

Therapeutic Hypothermia in the ICU: Indication, Sedation and Prognostication

Mild therapeutic hypothermia (TH) applied for 24 hours in the intensive care unit (ICU) is now recommended in comatose survivors of an outof- hospital cardiac arrest (OHCA), though some uncertainty around indication, clinical management and prognostication still remains. We will probably see this exciting field of intensive care further evolve in the coming years. The aim of this overview is to present some new information related to indications, sedation and prognostication in OHCA patients undergoing TH in the ICU.

Indications

The landmark studies of TH only included OHCA patients with a witnessed ventricular fibrillation (VF), and there has since been an ongoing discussion about whether the initial heart rhythm matters to the injured brain and how to secure widespread implementation of this simple and very effective therapy (Søreide and Sunde, 2008). In other words: Should TH be used indiscriminately and independently of initial heart rhythm and cause of cardiac arrest? From a pathophysiological point of view this makes sense, but due to the overall much worse prognosis in patients with non-shockable rhythms, many centres have been reluctant to cool such patients. Observational studies have provided conflicting results, but a recent systematic review (Kim et al. 2012) found that TH was associated with reduced inhospital mortality for adult patients resuscitated from non-shockable OHCA. Still, the authors cautioned that only a randomised controlled trial (RCT) could confirm the benefit of TH in patients with a non-shockable rhythm. The soon to be finished targeted temperature management RCT includes patients with non-shockable rhythms as a pre-specified subgroup (Nielsen N et al. 2012) and may therefore provide some answer to this question. Still, we foresee a discussion around indications for cooling in the ICU taking place for many years to come (Sunde K and Søreide E, 2011). Some issues to explore include: Should we cool older patients (Busch and Søreide 2011) than those included in the initial studies? What about patients with a non cardiac cause (like trauma, drowning, or hanging); should they also be cooled? In the ideal world, RCTs should be performed to answer these questions. However, in the real world, this may not be possible or even needed. If one accepts the notion that TH ameliorates reperfusion injuries in the brain with a very low risk of harm, no further proof of concept studies are needed. Instead, the focus should be on standardising and improving care provided from the scene of the cardiac arrest through to the hospital and further on through the rehabilitation phase. The impact of post-resuscitation care depends on the quality of care in the rest of the chain of survival. Hence, authors have suggested more use of a quality improvement study design (Sanders A 2011) and observational studies (Rea T and Dumas F 2012) in resuscitation science. More use of local quality improvement strategies (Kwok H and Rea T 2011) could improve community-based OHCA survival worldwide.

Sedation

TH requires sedation and analgaesia in order to provide patient comfort and blunt protective reflexes like shivering to increase endogenous heat production (Polderman K 2009). Animal studies have even suggested that sedation is a prerequisite for the neuroprotective effects of TH. Conversely, sedation may cause haemodynamic instability through vasodilatation and myocardial depression. Although required during the induction and maintenance phase of TH, sedation is frequently unwarranted after rewarming, during the phase of prognostication and weaning from mechanical ventilation. Hence, the sedative drugs used should have short duration of action, predictable metabolism during hypothermia, and acceptable haemodynamic side-effects.

In the original landmark trials, the patients were sedated with midazolam and fentanyl. These drugs continue to be the most widely used agents of sedation and analgesia, with and without neuromuscular blocking agents (Polderman K 2009). A recent study (Bjelland TW et al. 2012) found a reduction in total clearance of propofol, fentanyl and morphine during TH, but surprisingly the same was not found for midazolam. In a RCT, the same authors compared midazolam and fentanyl to a propofol/remifentanil-protocol (Bjelland T 2012b). They found a marked shortening of time from cessation of drug infusions to extubation in the group that could be extubated according to protocol. However, only 35 of the 60 patients included were considered eligible for termination of sedation within 72 hours after start of sedation. Further, the use of propofol and remifentanil resulted in increased haemodynamic instability.

Monitoring of sedation depth by spectral analysis may offer a method of reducing side-effects and detecting seizure activity masked by the administration of paralytic drugs. A protocol applying the BISmonitor for this purpose has been published (Chamorro C et al. 2010), but no clinical studies have evaluated this approach.

Ten years into the era of TH there is still a profound lack of data on the efficacy and safety of alternative sedation regimes. Worldwide, clinicians apply alternative protocols based on local experience and tradition. Most likely the ideal protocol does not exist. Sedation should be tailored to the individual patient, taking into account the degree of haemodynamic instability, severity of illness and predicted length of mechanical ventilation. An alternative approach would be to convert from longer acting sedatives to short acting sedatives at specific time points during TH, thereby promoting haemodynamic stability in the immediate post-arrest phase, while still reaping the benefits of shorter acting agents.

Prognostication

Before TH, prognostication in comatose post-cardiac arrest was pretty straightforward (Wijdicks EF et al, 2006). TH has definitely changed this,

as it alters the natural course of the recovery of hypoxic-ischemic encephalopathy and, as such, affects the prognosis. The sedative drugs used to facilitate cooling and mechanical ventilation also affect prognostication. Previously well-accepted clinical predictors of a dismal outcome are no longer valid (Rossetti AO et al. 2010; Oddo M and Rossetti AO, 2011; Bouwes A et al. 2012). Delayed awakening is observed more often. It has been shown that despite the widespread implementation of TH (Busch M and Søreide E 2008), clinical neurological examination and prehospital information still constitute the main part of prognostication data in such patients. Early prognostication without acknowledging the uncertainty of the used predictors may lead to withdrawal of life support and self-fulfilling prophecies (Perman SM et al. 2012; Bouwes A et al. 2012).

Somatosensory evoked potential (SSEP) has been considered the most reliable prognostic method in TH treated patients, with a false positive rate (FPR) of 0% for poor prognosis (not waking up) (Rossetti AO et al. 2010; Bouwes A et al. 2012). However, a recent study (Leithner et al. 2010) questioned the absolute negative predictive value of an absent bilateral SSEP N20 response. Electroencephalography (EEG) has also been comprehensively evaluated as a prognostic predictor after cardiac arrest (Oddo M and Rossetti AO. 2011). Some investigators have found a FPR of zero for unreactive EEG background activity in TH treated OHCA patients (Rossetti AO et al. 2010). Although the reported FPR=0 with specific SSEP and EEG findings is impressive, the remaining problem is the limited number of patients studied and resulting wide 95% confidence intervals (up to 10%). The predictive value of cranial computer tomography (CCT) and magnetic resonance imaging (MRI) in anoxic ischemic remain undetermined due to the small number of studied patients, the wide variety of tested parameters and the timing of examinations (Morrison LJ et al. 2010). Considering this, a multimodal, multi-specialty systematic approach to prognostication, which is employed no earlier than 72 hours after rewarming to normothermia and stop of sedation, has been suggested (Morrison LJ et al. 2010; Oddo M and Rossetti AO. 2011; Nolan JP et al. 2012). We think a team approach to prognostication will help us avoid overt misjudgements in the early acute phase. The roles and input of intensivists, cardiologists and neurologists in this respect need to be clarified. The multi-disciplinary approach, making use of advanced neurophysiological testing and imaging in the prognostication, is also an argument for more centralised care of post-cardiac arrest patients. Several authors have pointed towards this and other potential benefits of regionalised post-cardiac arrest care (Morrison LJ et al. 2010; Nolan JP et al. 2012).

Published on : Thu, 7 Mar 2013