

Overview of the use of Therapeutic Hypothermia in Patients Resuscitated from Cardiac Arrest



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Introduction

Neurologic injury is the most common cause of death in patients with out-of-hospital cardiac arrest (OHCA) and contributes to the mortality of in-hospital cardiac arrest (CPJM). In the recent years, therapeutic hypothermia (TH) has become the treatment of choice for survivors of OHCA to mitigate the damage. TH is launched to be a remedy against high mortality rate of major adverse cardiac events. Besides adult OHCA, the procedure is undertaken essentially in the treatment of neonatal hypoxic-ischemic encephalopathy (HIE). This article is written to review the rationale regarding the procedure carried out following OHCA and enlighten the untoward effects attributed to TH in the emergency setting.

Why is it Utilized so Commonly?

Following the successful resuscitation, TH is thought to decrease neurologic reperfusion injury by reducing cerebral oxygen consumption and biochemical damage [1]. Via a variety of mechanisms, TH affects several pathways concurrently to decrease death rate of the brain cell in OHCA. As far as cell death mechanisms after cardiac arrest, apoptosis can be slowed down by TH affecting both caspase-dependent and caspase-independent cellular mechanisms. In addition, certain cold shock proteins can augment cell survival by inhibiting apoptosis specifically during cooling [2]. To restore energy stores in the brain tissue, proper resuscitation is essential. A reduction in cerebral metabolism at hypothermia may explain why hypothermia can protect brain cells in ischaemic circumstances [3]. It was demonstrated empirically that brain glucose turnover is decreased by 5% for every degree the temperature is lowered [4]. Assuming a direct correlation between metabolism and neuroprotection, cooling to 33°C, for example, should result in a one-fifth reduction in cellular destruction [2,5].

It is also performed to provide neuroprotection during certain types of surgery and after serious events (e.g., subarachnoid hemorrhage) that threatens the brain. The specific mechanisms of hypothermic neuroprotection are not yet clear, partly because TH suppresses a myriad of potential injurious factors. Recently, some researches indicated that TH can improve survival and favorable neurological outcome in post-resuscitation patients regardless of the initial rhythm [6]. Furthermore, international consensus groups and committees recommended TH for adults with an initial shockable rhythm at a constant temperature between 32°C and 36°C for at least 24 hours [7]. Dumas et al. [8] reported that five-year survival following resuscitation from OHCA was 78% among those treated with percutaneous coronary intervention (PCI) compared with 54% among those not receiving PCI and 77% among those treated with TH compared with 60% among those not receiving TH [8]. It is interesting that TH is comparable to PCI after such huge amount of experience in long years and millions of patients with PCI in reducing mortality risk in the long run.

How is it used?

TH has been historically classified into: mild (34.5-36.5°C), moderate (34.5-32°C), marked (28-32°C) and profound hypothermia (<28°C) [5,6]. The administration of 'mild TH' has been shown to improve neurological outcomes and can prevent severe brain damage after OHCA [1,9]. Induced hypothermia is evaluated in three steps: induction, maintenance and rewarming, and each phase produces several changes in normal physiology. Hypothermia induction should be started as soon as possible to minimize neurologic damage. Infusing cold fluids, e.g., Ringer's lactate >25 ml/kg at 4°C, is the easiest and most effective method for inducing hypothermia [10]. Mild cooling was shown to be beneficial without many of the feared side effects. Both survivors

of arrest by itself and with the addition of TH procedure increase risk of complications from the hypothermia [11].

Any cons?

TH is not free of side or untoward effects. Reductions in body temperature affects almost all biological processes. Therefore, TH can cause serious complications. Although many respond to standard measures, some may end up with important morbidity and mortality. MacLaren et al. compared the incidences of adverse events and predictors of good versus poor neurological recovery after TH in a review of medical records of 91 patients who received TH for ≥ 6 hours [12]. They reported that common adverse events were hypoglycemia (99%), shivering (84.6%), bradycardia (58.2%), electrolyte abnormalities (up to 91.2%), acute kidney injury (52.8%), infection (48.4%), and coagulopathy (40.7%). TH is reported to cause an increase in insulin resistance and a reduction in insulin levels which result in hyperglycemia. The frequencies of meningitis, pneumonia and wound infections were also augmented. Hypothermia was also reportedly associated with increased blood loss and transfusions. Hypokalaemia, hypomagnesaemia, hypophosphatemia, hypo- and hyperglycaemia and some other electrolyte disorders were encountered during the procedure. TH can also trigger mild metabolic acidosis.

Effects on Inflammatory Response

The synthesis, release and uptake of certain catecholamines and neurotransmitters are inhibited by TH [13,14]. Inhibition of glutamate and dopamine, for example, prevents probable damage to the tissues [15,16], while blood-brain barrier is maintained with TH [17]. TH also helps protection of adenosine triphosphate stores [18]. Post-arrest patients have a modest systemic inflammatory response compared to healthy controls, associated with lower HLA-DR expression and attenuated immune response to Gram-negative and Gram-positive antigens [19]. Inhibition of the exaggerated systemic inflammatory response syndrome is thought to be one of the mechanisms through which TH can mitigate the harmful effects of ischemia-reperfusion. In a swine model of cardiac arrest, TH reduced expression of pro-inflammatory cytokines within the brain [20].

Conclusion

TH is viewed as a life-saving maneuver in patients with OHCA. The adverse and untoward effects should be taken into account and balanced with expected benefits.

Conflict of Interest

None.

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