EC Cardiology Editor's Column - 2019

Principles of Post-Cardiac Arrest Management and Therapeutic Hypothermia

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COLUMN ARTICLE

Abstract

Therapeutic approaches to be employed following achievement of the return of spontaneous circulation (ROSC) via measures included in advanced life support in patients with cardiac arrest (CA) have been updated substantially. The main goals of post-cardiac arrest management consist of elucidation of the causes of CA, minimizing cardiovascular and neurological damage and prevention of ischemia-reperfusion injury.

The utilization of "therapeutic hypothermia" (TH) is being used more widely. This approach is employed to treat hyperthermia and brain injury which have been closely linked to death in ROSC-achieved patients following CA, while mitigating demand for glucose and oxygen. Recent studies cited that results of early institution of TH with a target of 36ºC is comparable to 32 - 34ºC regarding improvement of neurological outcomes. The technique can be divided into three phases; induction, maintenance and rewarming. The usefulness of TH is controversial in the elderly, those with poor outcome and is contraindicated in those with hemodynamic instability.

Keywords: Cardiac Arrest; Return of Spontaneous Circulation; Post-Cardiac Arrest Management; Therapeutic Hypothermia

Principles of post-cardiac arrest management and therapeutic hypothermia

Post-cardiac arrest management (PCAM), includes all measures following achievement of the return of spontaneous circulation (ROSC) in patients with cardiac arrest (CA). These patients are not a homogeneous group; instead, they form a wide array of scenarios from a ROSC lasting for minutes followed by CA and death, to those discharged from hospital without any sequelae.

Main goals in the management consist of searching for the cause(s) of CA, minimizing cardiovascular and neurological damage and prevention of ischemia-reperfusion injury.

The most important threat to life is re-emergence of CA in the very first minutes following achievement of ROSC. Normalization of blood pressure, fluid replacement, and restoration of end-organ perfusion are the essential approaches to prevent secondary injury attributed to hypotension.

Mainstays in the evaluation following ROSC

Should ECG reveal ST elevation acute myocardial infarction (STEMI) the patient has to be transferred to emergency coronary angiography. It should be kept in mind that many of those patients without an obvious STEMI in the ECG would still have significant coronary lesions. Patients with ventricular dysrhythmias as the first detectable rhythms in collapse situation have the highest rate of coronary lesions. Therefore, those with pre-arrest chest pain or equivalent history of coronary syndromes and/or ventricular rhythms in the peri-arrest situations should be catheterized emergently, even if there is no marked STEMI on ECG.

Patients with prolonged QTc interval should be investigated for arrhythmias and electrolyte disorders. A high index of suspicion for pulmonary embolism is to be held in patients with acute right ventricular strain on ECG.

Point-of-care ultrasound/echocardiography will underline processes in the CA etiology. Great majority of patients with pericardial tamponade, massive pulmonary embolism, cardiogenic shock will be identified. Hypovolemic shock can be noted via changes in the size of vena cava inferior with systole and diastole. Bedside ultrasound will also be useful to highlight most cases with intraperitoneal hemorrhage, trauma, etc.

Non-contrast cranial computed tomography will disclose intracranial hemorrhage and other entities which can underlie CA as well. In large series of nontraumatic CA, around 4% of the sample were found to have cerebrovascular accidents precluding anticoagulant treatment [1]. Researchers noted that gray matter attenuation to white matter attenuation ratio was independently associated with survival and functional recovery. Survival rate approaches to zero as the gray-to-white matter ratio declines.

"Targeted Temperature Management" (TTM) or therapeutic hypothermia (TH) improve the functional and clinical outcome of these patients in the context of PCAM, although some controversial findings have also been published in the literature.

Applications of TH are known to be more beneficial in some specific clinical scenarios than the others. Patients resuscitated after out of hospital CA (OHCA) and ROSC instituted generally die from neurological damage in the long run [2]. The metabolic rate of the brain tissue falls around 10% with everyone ºC decline in the core temperature. This gave rise to widespread use of TH with the anticipation of mitigating the neurological injury triggered by CA.

TH can be applied patients with CA of unknown origin, or with cardiac or noncardiac origin. It is performed in patients of every age groups, although the net benefit in those older than 75 years of age is claimed to be controversial.

How to apply TH: TH can be classified in three phases: Induction, maintenance and rewarming (Table 1). The technique encompasses application of superficial pads, icepacks, immersion to cold water and instillation of cold water via intravenous lines [3].

When?	TH can be instituted immediately after all findings are documented following cardiac arrest.
Where?	• It can be applied in any suitable circumstances, i.e., in the field or in-hospital cardiac arrests, and. • In hospital settings, it can be used in the ED, operation room, or ICU as well.
How much?	Cooling is recommended to target 32 to 34ºC, while more recent studies found it comparable to results from 36ºC.
How?	• In the field, pads can be applied externally, without monitoring temperature and EEG waveforms. • In the hospital, different methods can be employed with continuous monitoring temperature and EEG waveforms.
Why?	• To prevent and treat hyperthermia and related brain injury • To minimize glucose and oxygen demand via decreased metabolic rate in patients with post-arrest condition and traumatic brain injuries, thereby increase sustainability of cellular life in vital organs.
Who?	The first healthcare provider who intervened to the patient in- or out of the hospital (nurse, paramedic, physician)

Table 1: 4W2H questions and checklist of hypothermia procedure.

Most researchers divide TH into three classes with regard to achieved temperature levels: mild (34.5°C - 36.5°C), moderate (34.5 - 32°C), marked (28 - 32°C) and deep hypothermia- (< 28°C) [4-6]. TH has been mostly used in OHCA and neonatal hypoxic and ischemic encephalopathy. Institution of mild TH following OHCA is associated with improved neurological outcomes [4,5]. In this regard, TH is recommended to be commenced in the early phase after CA.

TH in Trauma: The technique is also useful in the setting of trauma, especially in head injuries. It is more beneficial in those with severe head injury when compared to moderate-to-mild head injuries. The net benefit in these patients are thought to stem mostly from treatment of fever and prevention of relevant complications.

Many systematic reviews reported that the best results with mild TH had been noted after 48-hour maintenance, followed by slow rewarming [6,7]. In 2012, Sadaka., *et al.* performed a systematic review of findings derived from 13 randomised and 5 observational studies and concluded that intracranial pressures of all patients with head injuries could be reduced significantly after use of TH [8].

Peterson., *et al*. performed a meta-analysis of 8 studies and reported that TH procedure maintained longer than 48 hours was associated with a significant risk reduction for death (RR 0.51; 95% CI 0.33 - 0.79) and better neurological outcome (RR 1.91; 95% CI; 1.28 - 2.85) [7]. TH should be commenced as early as possible to minimize neurological damage.

Treatment of Hyperthermia after CA and ROSC: Hyperthermia following CA is an ominous sign to be treated emergently and definitely. Fever is known to cause a grave neurological outcome in these patients [4,5,9,10]. Cooling contribute in neurological improvement via taking intracranial pressure under control. Cold water infusion (4°C Ringer's lactate > 25 ml/kg) is one of the most effective methods in precipitating hypothermia [11]. Anti-fever measures such as cooling should be taken against all patients with ROSC after CA and serious neurological deficits [9,10].

Tokutomi., *et al*. reported in Japan, 2009 that patients cooled to 35°C had experienced safe reductions in intracranial pressures and the improvement was as favorable as those cooled to 33°C [12]. Another well-designed study compared cooling patients resuscitated from OHCA to 33°C vs. 36°C and cited death rates 50% and 48%, respectively, and therefore, cooling to 33°C failed to provide additional benefits [13].

In 2016, a joint statement from The Canadian Critical Care Society (CCCS) and other specialty organizations launched a recommendation to institute TH for all patients successfully resuscitated after CA and ROSC was documented [14]. While the recommendation for OHCA patients was strong, those with in-hospital CA were cited in a weak recommendation. Patients with recurrent ventricular fibrillation and/or tachycardia attacks should not be deprived of treatment with TH.

Contraindications: Physicians should beware of TH application in those patients with active, non-compressible foci of bleeding. It should be deferred in patients with hemodynamic unstability or shock states.

Adverse and untoward effects of TH

Tachycardia increased cardiac output and systemic vascular resistance is marked in the induction phase of TH, which result in augmented blood pressure readings. The most common untoward effects of TH include hypoglycemia (99%), shaking chills (84.6%), bradycardia (58.2%), electrolyte disorders (91.2%), acute kidney injury (52.8%), infections (48.4%), and bleeding disorders/acquired clotting deficiency (40%) [15].

Table 2 summarizes adverse effects which can be anticipated following TH [15,16].

	32°C - 35°C	**28°C - 32°C**	**< 28°C**
Vital signs	Increase in respiratory rate, pulse rate, blood pressure and cardiac output.	Decrease in respiratory rate, pulse rate, blood pressure and cardiac output.	Further decrease in all these variables. Apnea is anticipated below 24°C.
Cardiac - ECG	Prolonged PR, QRS, and QT intervals. Atrial fibrillation can be triggered below 33°C.	Increased risk for cardiac dysrhythmias. J (Osborn) waves, 1st. degree AV block.	Ventricular dysrhythmias. Asystole below 20°C
Neurological and metabolic changes	Hyperglycemia, hypoinsulinemia. markedly reduced brain metabolism.	Bilinçte ilerleyici bozulma, pupil dilatasyonu	Flattened EEG activity. Coma.
Renal- electrolytes	Unpredicted changes in electrolytes		
	Cold diuresis (+)		Reduced renal blood flow, oliguria (+)
Hematological	Coagulopathy (low platelet count, increased blood loss and transfusions with surgery) Hematocrit is elevated 2% for every 1°C reduction in core temperature.		
Gastrointestinal	Ileus, delayed gastric emptying, pancreatitis, gastric stress ulcers, disorders in liver functions		

Table 2: Side and adverse effects encountered with hypothermia.

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