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Therapeutic Hypothermia Following Cardiac Arrest

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Incidence

According to the Sudden Cardiac Arrest Foundation (2014), each year, 424,000 people in the U.S. (more than 1,000/day) experience EMS-assessed out-of-hospital non-traumatic sudden cardiac arrest. This is roughly equivalent to the number of people who die from Alzheimers' disease, assault with firearms, breast cancer, cervical cancer, colorectal cancer, diabetes, HIV, house fires, motor vehicle accidents, prostate cancer and suicides *combined* (Sudden Cardiac Arrest Foundation, 2014).

It is estimated that the likelihood of surviving an out-of-hospital cardiac arrest (OHCA) to hospital discharge can be as low as 6% to 8% (Williams, Calder, Cocchi & Donnino, 2013). Additionally an estimated 200,000 hospitalized patients are treated for cardiac arrest annually. Adult inpatient cardiac arrest mortality rates have been historically high at 67% to 71% despite advancement in resuscitation care (Williams et al., 2013).

History

The following is a historical timeline for the use of therapeutic hypothermia (TH) as described by Varnon and Acosta (2008):

- Documented in 1803, Russians used a method of resuscitation that involved covering patients with snow hoping for return of spontaneous circulation (ROSC);
- In 1813, TH was used in an effort to preserve injured limbs and for its numbing effects during amputations;
- In 1937, Dr. Terry Fay "cooled" a patient to 32˚C for 24 hours to attempt to prevent cancer cells from multiplying;
- In 1953, animal studies revealed heart and brain benefits of TH during cardiac surgery;
- A direct link between body temperature and intracranial pressure and brain volume was documented in 1955. It was confirmed that TH reduced cerebral oxygen consumption, blood flow and metabolic rate in an animal brain;
- By 1959, TH was used by neurosurgeons for head and spinal cord injuries as well as cardiac surgery;
- Between 1960 and 1990, the use of TH decreased due to possible complications;
- In 2002, the American Heart Association recommended TH as a treatment modality OHCA comatose victims of cardiac arrest.

Pathophysiology

Hypoxic-ischemic Brain Injury

The pathophysiology of brain injury following cardiac arrest is extremely complex. Due to the high metabolic demand, the brain is very susceptible to damage from deprivation of blood supply (Busl & Greer, 2010). Hypoperfusion to the brain initiates a cascade of events including (a) neuronal hyperexcitability-excitotoxicity; (b) disrupted calcium hemostasis; (c) oxidative stress and free radical formation; (d) blood-brain barrier dysfunction; (e) microvascular injury; (f) abnormal protease cascade; (g) cell death pathway signaling; and (h) postischemic inflammation (Williams et at., 2013).

The initial injury happens at the time of insult but there may be continued damage after circulation and oxygenation are reestablished (Busl & Greer, 2010). Table 1 and Table 2 briefly describe the complex pathophysiological changes leading to cell damage following cardiac arrest and subsequent hypoxic-ischemic brain injury, as described by Busl and Greer (2010).

Table 1
Biochemical mechanisms in hypoxic-ischemic brain injury

Mechanism	Immediate Effect	Result
Anoxic Depolarization	↓ extracellular sodium	
	↓ extracellular calcium	Activation of
	↑ intracellular calcium	calcium-dependent processes
ATP Depletion	Local acidosis	Generalized acidosis, cell damage, edema
Glutamate Release	Excitotoxic activation of enzymes	Neuronal tissue breakdown
Free Radical formation, Nitric Oxide production		Cell breakdown

Table 2
Functional cell changes in hypoxic-ischemic injury

Underlying Functional Problem	Result
Mitochondrial Damage	Lack of energy repletion
Cytoskeletal Damage	Inability to maintain cell structure
Glutamate Receptor Activation	Immediate early gene up-regulation
	Heat shock protein production

Therapeutic Hypothermia (TH)

Therapeutic hypothermia is the only intervention shown to improve neurological outcomes following cardiac arrest (Lantry, Dezman, & Hirshon, 2012). As described by Lantry, Dezman, and Hirshon (2012), hypothermia is subdivided into four stages: (1) mild hypothermia (32-35˚C) with physiological responses such as shivering and vasoconstriction; (2) moderate hypothermia (28-32˚C) marked by violent shivering, severe confusion, delirium and memory loss; (3) severe hypothermia (20-28˚C); and (4) profound hypothermia (less than 20˚C) both defined by cardiac dysrhythmias, shallow breathing and a progressive decline in consciousness that leads to death.

Therapeutic hypothermia is characterized by mild hypothermia (32˚C to 34˚C). The body should be cooled to a core temperature of as soon as possible after ROSC. According to Sahuquillo & Vilalta (2007), the neuroprotective properties of TH are multifactorial and can include the following:

i. Reduction in brain metabolic rate – all the energy-producing pathways in the brain including the cerebral metabolic rate for glucose, oxygen and lactate are reduced 2-4x by a 10°C decrease in temperature;

ii. Effects on cerebral brain flow – the reduction in cerebral metabolic rate for oxygen results in a reduction of cerebral brain flow;

iii. Reduction in critical threshold of oxygen delivery – by significantly lowering critical oxygen delivery with TH, the injured brain seems to be more tolerate of reduced levels of oxygen delivery without shifting to anaerobic metabolism;

iv. Calcium antagonist – intracellular calcium overload has been associated with ischemia and neuronal death;

v. Blockade of excitatory neurotransmitters – TH has been shown to reduce or block these excitotoxic neurotransmitters, such as glutamate, released by injured tissues that can lead to brain damage;

vi. Decrease in edema formation – modulates the detrimental effects of injury on the blood brain barrier (BBB) by attenuating the increased permeability following injury and reduce protein passage into the brain, thus reducing edema ;

vii. Modulation of inflammatory response – TH significantly reduces mediators of inflammatory cascades such as cytokines IL-6, IL-10, TNFα;

viii. Neuroprotection of white matter – TH causes more profound neuroprotection than any known neuroprotective drug by protecting not only neuronal cell bodies but axons as well.

Importance for Nursing

Eligibility Criteria

Table 3 describes the eligibility criteria for therapeutic hypothermia (Malhotra, Dhama, Kumar, & Jain, 2013).

Table 3
Eligibility Criteria for Therapeutic Hypothermia

Inclusion	Exclusion
Initial rhythm of ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT)	Admission temperature <32˚C
≤60 minutes from collapse to ROSC	Evidence of neurological response to commands after resuscitation
Systolic blood pressure (SBP) >90 mmHg (or MAP >60 mmHg) with no more than one vasopressor	Cardiac arrest related to trauma Major head injury Systemic infection/sepsis
Unconscious after successful ROSC with Glasgow Coma Scale ≤8 <6 h from ROSC	Recent major surgery (within 14 days) Comatose state prior to cardiac arrest/coma from other causes
	Persistent hypotension (SBP <90 mmHg, MAP <60 mmHg) despite one vasopressor for >30 minutes after ROSC
	Persistent hypoxemia SaO_2 (arterial oxygen saturation) <85% after ROSC despite mechanical ventilation
	Pre-existing coagulopathy or bleeding
	"Do Not Resuscitate" or "Do Not Intubate" code status or terminal illness prior to cardiac arrest

Initiation and Management

During the induction phase, the goal is to reach the target core temperature of 32-34˚C as quickly as possible. A cooling rate of 1°C/h will reach a target temperature of 33°C in roughly 4 hours and is generally recommended (Alshimemeri, 2014).

Patient monitoring should include:

- electrocardiogram,
- fluid balance,
- invasive blood pressure measurement and
- core body temperature measurement.

Also, ongoing monitoring of lab values including

- complete blood count,
- platelet/coagulation,
- electrolytes, and
- arterial blood gas (Malhotra et al., 2013).

Changes in body temperature leads to shifting of electrolytes in and out of the cell causing electrolyte abnormalities and risk for arrhythmias, therefor replacement should be administered during the induction phase and should be discontinued during rewarming (Malhotra et al., 2013).

Sedatives, such as benzodiazepines, Propofol or short-acting narcotics, are used to reduce cerebral metabolism and with TH acts to reduce central nervous system (CNS) oxygen consumption (Malhotra et al., 2013).

Shivering is common and can be managed with narcotics such as Fentanyl or a neuromuscular blockade if severe and impairs cooling (Malhotra et al., 2013).

Invasive blood pressure and fluid balance monitoring is important due to hypotension and profuse diuresis that can result from TH (Malhotra et al., 2013).

Importance for Nursing

Complications

Table 4 briefly lists the possible adverse effects of therapeutic hypothermia as described by Malhotra et al. (2013).

Table 4
Adverse Effects

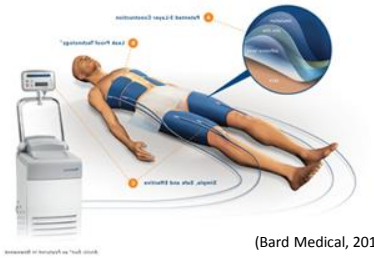
Organ System	Abnormality
Renal	Hypokalemia
	Hypomagnesemia
	Hypocalcemia, hypophosphatemia
Endocrine	Hyper/Hypoglycemia
Cardiovascular	Myocardial depression
	Increased systemic vascular resistance (SVR)
	Hypovolemia
	Repolarization abnormalities
	Bradyarrhythmias
	Ventricular arrhythmias
Gastrointestinal	Impaired gut motility/ileus
	Hepatic dysfunction
	Stress ulcer
	Elevated serum amylase
Respiratory	Respiratory alkalosis
	Reduced secretion clearance/cough
Hematological	Impaired platelet function
	Coagulopathy
	Hemoconcentration
Immunologic	Neutropenia
	Anti-inflammation
Pharmacokinetics	Reduced clearance of sedatives and neuromuscular blockers
Integumentary	Poor wound healing

Conclusion

New methods of resuscitation and multidisciplinary goal-directed for post-cardiac arrest patients has led to improved outcomes and a decrease in morbidity and mortality (Williams et al., 2013).

The timing of the onset of cardiac arrest, start of CPR, ROSC, hospital arrival, initiation of TH, reaching target temperature and rewarming are all important factors in determining the post-arrest outcome (Shinada et al., 2013).

European research reported by Nielsen et al., 2009 revealed over a period of 4 years, half of 986 TH-treated OHCA patients survived and over >90% having good neurological outcomes at long-term follow-up. Therapeutic hypothermia has shown significant results that can greatly impact the outcome of such a devastating pathophysiological injury.



(Bard Medical, 2012)

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