

Title:	Induced Hypothermia for Neuroprotection
Number:	CSC-10
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Source

This protocol is adapted primarily from the American Heart Association and the American Academy of Neurology guidelines statements on the treatment of patients with hypothermia after cardiac arrest.

Treatment Goals

Increased brain temperature exacerbates the neurological damage patients with neurologic injuries. Studies have demonstrated that lowering brain temperature, even by a few degrees, may reverse such injury. The goal of induced hypothermia is to avoid fever and, in some cases, to reduce body temperature to moderately (32-34 34° C) or mildly (34-36° C) hypothermic levels in selected patients with severe neurology injury. The induced hypothermia protocol may be implemented in any ICU. The assignment of patients to the appropriate ICUs should be based on the co-morbidities.

Inclusion Criteria

Patients who fulfill the following criteria should be considered at presentation for induced hypothermia:

1. Post-cardiac arrest
 - a. Within 6 hours of cardiac arrest (any non-perfusing rhythm: VT, VF, asystole, PEA). The time window may be extended to 12 hours at the discretion of the treating team.
 - b. Stable and perfusing cardiac rhythm and the ability to maintain a blood pressure with or without inotropes or vasopressors.
 - c. Comatose state, state, defined as: not following commands, no speech, no eye opening, and no purposeful movements to noxious stimuli. Posturing and other pathological movements are permissible.
2. Refractory intracranial hypertension
 - a. Refractory elevation of ICP despite hyperosmolar therapy and burst-suppression
3. Refractory fever
 - a. Refractory fever, defined as T > 38° C
 - b. Failure of acetaminophen 650 mg q 4 hours.

Relative Exclusion Criteria

Hypothermia impairs the coagulation cascade and suppresses the immune system. The following list contains several conditions should be considered before institution of hypothermia. These conditions may exclude some patients from induced hypothermia:

- 1) Major head trauma – If there is clinical suspicion for head injury with arrest, cooling should be temporarily interrupted to obtain a non-contrast head CT
- 2) Major surgery within prior 14 days
- 3) Systemic infection/sepsis with unstable vital signs
- 4) Known bleeding diathesis (e.g. thrombocytopenia, elevated INR, DIC, cryoglobulinemia, sickle cell disease, serum cold agglutinins)

The ultimate decision to induce hypothermia should be based on an assessment of the potential risks and benefits of hypothermia in each individual patient considering the complete clinical situation and co-morbidities.

Detailed Guidelines of Care

1) Initiating Cooling

Cooling must be initiated as rapidly as possible. In most cases, patients can be cooled initially with ice packs and then transitioned to the Arctic Sun system, though adequate cooling can be achieved with ice bags and cooling blankets alone.

Any of the methods of cooling, ice packs and cooling blankets or the Arctic Sun System, can be used to initiate cooling and should be started as soon as possible.

If iced saline has been started by EMS, complete infusion of the hanging bag, but do not start a new bag after the patient arrives. If ice packs have been placed on the patient, continue with ice packs and ensure placement on patient's groin, chest, axillae, and the side of the neck until the Arctic Sun system is initiated or target temperature is achieved.

- **Arctic Sun Cooling Device Method**
 - The Arctic Sun pads should be placed as soon as clinically feasible. Patients may be transitioned from ice packs/cooling blankets or initiated directly with the Arctic Sun.
 - The Arctic Sun machines and pads are stored in the NeuroICU, CCU and MICU.
 - After pads are placed, set the Arctic Sun to the desired temperature.
 - **Ensure two methods of measuring patient temperature.**
 - The Arctic Sun will adjust water temperature to maintain targeted patient temperature.
 - Remove ice packs after the Arctic Sun system has been initiated to prevent overcooling of the patient.
 - The Arctic Sun blankets are radiolucent and can be used during catheterization and radiologic procedures.
 - Defibrillator pads may be placed under the Arctic Sun gel pads. It is safe to defibrillate the patient with the Arctic Sun pads on the patient.

- **Ice Packs and Cooling Blankets Method**
 - Pack the groin, neck and axillae with ice bags.
 - Sandwich the patient between two standard cooling blankets.
 - Ensure two methods of measuring patient temperature.
 - Ice packs and standard cooling blankets should be used to achieve the goal temperature.
 - After the target temperature has been achieved, ice packs can be removed and cooling blankets used to maintain the target temperature.

2) ***Prevention and Management of Shivering***

Shivering reflects the body's homeostatic response to induced cooling. Shivering is uncomfortable and generates heat, thereby impairing the ability to achieve the target temperature.

Patients being cooled should receive sedation, low-dose analgesia, and in some cases, neuromuscular blockade to prevent shivering. The aggressiveness of shivering prevention and management should be escalated as needed.

I. Environmental interventions

- a. Counterwarming: after Arctic Sun pads are on, place Bair Hugger over the patient and set on low heat and ensure that distal extremities are covered under the Bair Hugger.

II. Sedation*

- a. A goal sedation level of RASS -4 to -5 must be present before initiating hypothermia and maintained during the entire hypothermia protocol
- b. Regardless, of RASS level, sedatives should be initiated in all patients as soon as the protocol is initiated
- c. Sedative agents
 - i. Propofol - First line sedative agent
 - ii. Midazolam – Use only if propofol is contra-indicated

III. Analgesia

- a. Patients should be on standing acetaminophen.
- b. Low-dose continuous infusions of opioids (fentanyl or hydromorphone) may be used.

IV. Other pharmacologic interventions

- a. Magnesium infusion: 2gm over 30 min followed by 1gm/hr infusion for a target serum level 3.0-4.5
- b. Buspirone 5 mg PO 2-3 times a day OR 7.5 mg PO twice a day; may increase the dosage by 5 mg/day every 2-3 days as needed (usual dose 20-30 mg/day 2-3 divided doses; maximum dose 60 mg/day)
- c. Meperidine intermittent IV push 12.5-50 mg as needed not to exceed 100 mg every 6 hours. Contraindicated in the setting of renal insufficiency (serum creatinine ≥ 1.5) or with the concomitant use of monoamine oxidase inhibitors (MAOI within the past 2 weeks)
- d. Dantrolene 50 mg PO 2-3 times a day; may increase the dosage by 25-75 mg/day every 2-3 days as needed; maximum dose 400mg a day.
- e. Dexmedetomidine 1 mcg/kg over 10 min. Maintenance infusion dose range is 0.2-0.7 mcg/kg/hr

- V. Neuromuscular blocking agents (NMBA)*
- a. NMBA are sometimes needed to suppress shivering and should be initiated with sedation and analgesia at the beginning of the protocol.
 - b. NMB should be titrated to reduce rigors and not complete neuromuscular blockade.
 - c. Never stop sedation and analgesic regimens while paralyzed.
 - d. NMB agents
 - i. Rocuronium 1mg/kg once
 - ii. Cisatracurium 0.15mg/kg bolus followed by infusion of 0-3 mcg/kg/min.

VI. Shivering scale could be used to quantitate its degree

- 0 - No shivering
- 1 - Episodic shivering for < 5min
- 2 - Sustained shivering for > 5 min
- 3 - Breakthrough shivering despite continuous infusions
- 4 - Refractory shivering, controlled by NMB only

***NB:** Hypothermia reduces clearance of sedatives and neuromuscular blockers by approximately 30%.

3) Monitoring and Supportive Therapy

I. Hemodynamics

- a. Heart rate
 - i. At initiation of hypothermia, tachycardia and hypertension may occur due to vasoconstriction as the patient attempts to conserve heat
 - ii. Bradycardia is associated with hypothermia and should be treated if accompanied by hemodynamic instability. There is no need to treat normotensive bradycardia.
 - iii. If significant dysrhythmia or hemodynamic instability develop, treat the patient with standard medical procedures. If the instability persists, cooling should be discontinued, and the patient should be re-warmed.
- b. Mean arterial pressure (MAP)
 - i. An arterial line should be placed for monitoring BP and obtaining blood specimens.
 - ii. Blood pressure pressures are often elevated in hypothermic patients because of peripheral vasoconstriction.
 - iii. A MAP goal of >90 mm Hg is preferred theoretically to improve cerebral perfusion. However, studies with lower MAP goals (65-100mm Hg) have shown benefit.
 1. A lower MAP goal (~75-80 mm Hg) may be used depending on the clinical scenario (e.g., anterior MI, depressed systolic function)
 - iv. Hypotension frequently occurs during re-warming.

- v. The decision to initiate and the choice of vasopressors should be determined according to the individual hemodynamic requirement of the patient.
- II. Intracranial pressure monitoring
- a. If cooling is being initiated to control ICP, invasive intracranial monitoring should be considered.
- III. Oxygenation
- a. Goal oxygenation saturation of 94-96% should be achieved. FiO₂ should be reduced as soon as possible to avoid prolonged oxygen saturations of 100% which may be harmful.
- IV. Ventilation
- a. Patients must be intubated with full ventilatory support for induced hypothermia.
 - b. Maintain normocarbia.
 - c. Avoid hyperventilation or hypoventilation.
 - d. Follow ventilator-associated pneumonia (VAP) bundle in all patients
- V. Bispectral Index (BIS) monitoring
- a. BIS should be recorded in patients receiving neuromuscular blocking agents
 - b. BIS levels are unreliable in hypothermia and should not be used to titrate the level of sedation or paralysis in patients undergoing induced hypothermia (IH). Typically, comatose patients who qualify for IH will have low BIS levels which should NOT prompt any change in sedation or NMBA. If the BIS level increases by 20 or is 60 or greater, it could signify increasing neurological activity and neurology should be consulted.
- VI. Laboratory assessment and electrolytes repletion
- a. Hypothermia induces diuresis and subsequent electrolyte wasting
 - i. Basic chemistries including K⁺, Mg⁺⁺, PO₄⁺⁺, Ca⁺⁺ should be monitored at least q 4 hours
 - ii. Potassium replacement
 - 1. Order low K⁺ scale
 - 2. Replete x to maintain levels >4.0 mEq/L
 - 3. No K⁺ repletion 6-8 hours before rewarming
 - 4. K⁺ levels may continue to be elevated hours past rewarming and require continued frequent electrolyte monitoring
 - b. Glucose control
 - i. Hyperglycemia is common after the initiation of induced hypothermia. The optimal blood glucose during induced hypothermia has not been determined. Caution must be taken to avoid hypoglycemia during the re-warming of the patient. Given these concerns, therapy does not need to be initiated unless the glucose is >200 mg/dl.
 - ii. Glucose monitoring recommendations
 - 1. Sites for blood glucose measurement: arterial line only
 - 2. Frequency of assessment

- a. Every hour while cooling
 - b. Every 30 minutes while rewarming
 - c. Every 30 minutes if glucose < 80 mg/dl at any time
 - iii. BHIP protocol may be used for glucose control with the following provisions
 1. Initiate BHIP when glucose is greater than 200 mg/dl.
 2. Do not exceed 50 units insulin/hour.
 3. During the rewarming phase, stop continuous intravenous insulin when glucose levels drop to less than 200 mg/dl, unless the patient has type 1 diabetes mellitus.
 4. If the patient has type 1 diabetes, during the rewarming phase, continue IV insulin at a rate of 0.5 units/hour.
 - VII. Seizures / myoclonus
 - a. Seizures and myoclonus are common following cardiac arrest and can worsen cerebral injury.
 - b. Continuous EEG monitoring is preferred during induced hypothermia particularly if myoclonus is observed or NMB is being used.
 - VIII. Miscellaneous
 - a. Patients should receive fibrinolysis, antiplatelet agents, or anticoagulants as deemed necessary.
 - b. Draw blood cultures 12 hours after the initiation of cooling. Infection will be masked during the cooling phase.
 - c. Skin care should be checked every two hours for burns caused by cold blankets.
 - d. Water temperature trends should be monitored in addition to core temperature.
- 4. Rewarming**
- I. Begin re-warming 24 hours after the initiation of cooling
 - a. This shift causes hypotension
 - b. Rewarming at a rate of 0.25-0.5° C (0.5-1° F) every hour.
 - c. Monitor the patient for hypotension related to rewarming as peripheral beds, which were once constricted, start to dilate.
 - II. When the patient's temperature is 37° C, discontinue the NMBA. Continue the sedation and analgesia.
 - a. Check the train-of-four (TOF) every hour. When TOF 4/4 response is achieved, wean the sedation.
 - III. The Arctic Sun pads may be left on the patient for the next 48 hours.

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