**Korean Hypothermia Network Post-Cardiac Arrest Care Manual**

Section 3. Temperature control

1. Prevention and treatment of hyperthermia

* During the first 72 hours after return of spontaneous circulation (ROSC), prevent hyperthermia by monitoring proper core temperature and in case it develops, actively control it by using antipyretics or cooling devices.
* If necessary, acetaminophen can be administered via a nasogastric tube every 6 hours.
* In hyperthermia develops, bolus inject acetaminophen, aspirin, or ketorolac, and then actively control by using cooling devices.

2. Targeted temperature management (TTM)

1) Preparation before TTM induction.

a) Indication and contraindication of TTM:

* Regardless of initial rhythm, the patients who do not show meaningful responses to verbal commands after ROSC continuing for more than 20 minutes are suggested for TTM. In case of cardiac arrest due to trauma, severe sepsis, poor cognition or poor neurological condition before cardiac arrest, pregnant women, arrhythmia that does not respond to treatment or coronary vasospasm, a refractory shock that does not respond to fluid or vasopressors, and active bleeding or thrombolytic use, therapeutic hypothermia are relatively contraindicated, and thus TTM should be determined by an expert. However, TTM is contraindicated for the patients with terminal illness before cardiac arrest, those with a Do-Not-Attempt-Resuscitation (DNAR) order, and others with other etiologies for coma.
* For the patients who are suggested for TTM, measure the initial core temperature, and when it is less than 32°C, rewarm passively with the target temperature range (32–36°C), and then maintain for 24 hours and gradually rewarm (0.25–0.5°C/h). If the initial temperature is 32–36°C, do not use induction methods such as using cold fluid, but use proper cooling equipment to maintain the target temperature for 24 hours and then slowly rewarm. If the initial temperature exceeds 36°C, actively induce cooling to the target range by combining various cooling methods and then maintain it target range for 24 hours, and slowly rewarm.
* After reaching the normal core temperature (36.5–37°C), it needs to be maintained up to 72 hours after ROSC.

b) Ancillary tests and procedures before cooling induction:

* Perform initial neurological examination immediately after ROSC.
* Perform 12-lead electrocardiography (ECG) and arterial blood gas analysis (if possible, include electrolytes and lactate).
* Measure blood glucose level.
* Perform initial blood tests (CBC, Routine blood chemistry with cardiac biomarkers, PT/PTT/INR, u-hCG [for pregnant female], if possible, include S-100, NSE).
* Perform initial blood, urine, and sputum cultures.
* Perform initial chest radiograph.
* If possible, perform initial transthoracic echocardiography.
* When the blood pressure is stabilized, perform a brain computed tomography scan and rule out intracranial hemorrhage.
* Check levels of electrolytes (K, Mg, P, iCa) in the initial blood test, and start correction if they are below the normal range.
* Insert a urethral catheter and nasogastric tube.
* Insert an arterial catheter early.
* Insert a central venous catheter.

2) TTM induction and maintenance.

a) Target temperature and target induction time:

* Perform TTM induction as soon as the decision is made.
* Set the target temperature at 32–36°C, which is an acceptable range.

b) Ancillary tests and procedures during TTM induction:

* Perform arterial blood gas analysis (if possible, include electrolytes and lactate) every hour, optimize oxygenation and ventilation status, and monitor changes of electrolyte level.
* Measure blood glucose level every hour, and maintain a target range of 144–180 mg/dL.
* Induce TTM quickly by using various cooling methods.
* To prevent frostbite, covering the hands and feet with a towel can be helpful to reduce the shivering threshold.

c) Medications to be administered during TTM induction:

* When starting the TTM induction, inject a sedative (midazolam, lorazepam, or propofol) and analgesic (fentanyl or remifentanyl) bolus to reduce temperature control responses and then continue the intravenous infusion.
* In case hypothermia is induced by cold IV fluid, administer a sedative and analgesic as soon as possible.
* Before TTM induction, inject a long-acting neuromuscular blocking agent (vecuronium or pancronium) bolus following sedative and analgesic injection, and then if necessary, administer continuous infusion of a relatively short-lasting neuromuscular blocking agent (cisatracurium or rocuronium).
* To prevent shivering and control, the following drugs can be used:
  + Buspirone, 30 mg with 8-hour intervals via the nasogastric tube.
  + Meperidine, 25 mg IV bolus injection (except when accompanied by renal failure and oliguria; seizure disorder history; patients who are taking MAO inhibitor, buspirone, or SSRI; and pregnant women in the third trimester).
  + Magnesium, 2 g IV infusion.
* When continuous infusion of a neuromuscular blocking agent is planned, apply an available neuromonitoring method (e.g., continuous electroencephalogram).
* Acetaminophen can be administered every 6 hours by a nasogastric tube.
* To prevent stress ulcers, infuse a H2 blocker and coating agent every 6 hours via a nasogastric tube.

d) Duration of TTM maintenance:

* After reaching the target temperature range (32–36°C), maintain for 24 hours.

e) Ancillary tests during hypothermia maintenance:

* Perform arterial blood gas analysis (include electrolytes and lactate) every 6 hours.
* Measure blood glucose level every 4 hours, and maintain a target range of 144–180 mg/dL.
* Perform follow-up blood tests every 6, 12, and 24 hours after ROSC (CBC, routine blood chemistry with cardiac biomarkers, CRP, PT/PTT/INR, urinalysis).
* Perform follow-up 12-lead ECG and chest radiography every 6, 12, and 24 hours after ROSC.
* Perform follow-up cultures 24 and 48 hours after ROSC (blood/urine/sputum).

f) Medications to be administered during maintenance:

* Adjust insulin infusion volume according to a local protocol to maintain blood glucose levels at 144–180 mg/dL.
* Acetaminophen can be administered every 6 hours by a nasogastric tube.
* To prevent stress ulcers, infuse a H2 blocker and coating agent via a nasogastric tube every 6 hours.
* Stop potassium-containing fluids 8 hours before rewarming.

g) Discontinuation of TTM induction and maintenance:

* Consider discontinuation of cooling during TTM induction and maintenance period in case of the following situation:
  + Active severe hemorrhage.
  + Persistent arrhythmia causing hemodynamic instability.
  + Refractory shock.
* In case of refractory shock, consider additional treatments such as ECMO or IABP.

h) TTM induction and maintenance, combination method 1 (cold fluid + ice packs):

* Record the starting time of the induction and methods.
* Set the monitor to temperature alarm.
* Rapidly infuse 30 mL/kg of 4°C normal saline or Ringer’s fluid via a peripheral IV line or femoral vein by using a pressure bag for 30 minutes with caution of pulmonary edema.
* In case prominent pulmonary edema or heart failure is accompanied, avoid rapid infusion of cold fluid.
* Fill up a large-size plastic bag with ice and cold water (1:1), cover it with a pillow case, and then place it in the head, neck, both arm pit, and the groin of the patient.
* When additional manpower is available, perform the internal cooling method also at the same time (e.g., bladder or gastric lavage with cold water).
* Once the core temperature reaches the target temperature, stop the rapid infusion of cold fluid.
* Replace the ice pack every 1 hour or in shorter intervals.
* If the target temperature is 32–34°C, when the core temperature falls towards 32°C, remove the ice packs, and when the temperature rises up to 34°C, re-apply the ice packs.
* Be careful of leakage from the ice packs, and carefully observe the skin condition where the ice packs are applied.

i) TTM induction and maintenance, combination method 2 (cold fluid + surface cooling device):

* Record the starting time of induction and methods.
* Set the monitor to temperature alarm.
* Rapidly infuse 30 mL/kg of 4°C normal saline or Ringer’s fluid via a peripheral IV line or femoral vein by using a pressure bag for 30 minutes with caution of pulmonary edema.
* In case prominent pulmonary edema or heart failure is accompanied, avoid rapid infusion of cold fluid.
* If the target temperature is 32–34°C, once the core temperature reaches 34°C, stop the rapid infusion of cold fluid.
* For the cooling equipment that requires a blanket, cover the patient’s front and back, but make sure the blanket directly touches the patient’s body, and check the skin every 2 hours.
* For ArcticSun, attach pads in the proper size well on the recommended areas and connect with the device.
* Refer to the User’s manual for detailed setting methods for each equipment suitable for induction and induction stage.
* When additional manpower is available, perform an internal cooling method also at the same time (e.g., bladder or gastric lavage with cold water).

j) TTM induction and maintenance, combination method 3 (cold fluid + endovascular cooling):

* Record the starting time of induction and methods.
* Set the monitor to temperature alarm.
* Rapidly infuse 30 mL/kg of 4°C normal saline or Ringer’s fluid via peripheral IV line or femoral vein by using a pressure bag for 30 minutes with caution of pulmonary edema.
* In case prominent pulmonary edema or heart failure is accompanied, avoid rapid infusion of cold fluid.
* If target temperature is 32–34°C, once the core temperature reaches 34°C, stop the rapid infusion of cold fluid.
* When additional manpower is available, combine with internal cooling method at the same time (e.g., bladder or gastric lavage with cold water).
* While the equipment is being primed, insert the endovascular catheter into the femoral or subclavian vein.
* Once the catheter is properly positioned, connect it with the tubing set of the start-up kit, set the target temperature, and start maximum cooling.

k) TTM induction and maintenance, core temperature monitoring and recording.

* During TTM induction and maintenance, continuously monitor the two core temperatures if possible (esophagus and bladder; esophagus and rectal, or bladder and pulmonary artery; and pulmonary artery and rectal).
* Record the core temperature every 30 minutes during TTM induction.
* Record the core temperature every 1 hour during TTM maintenance.

3) Rewarming and treatment after re-warming:

* Start rewarming 24 hours after reaching the target temperature range (32–36°C).
* Set the rewarming speed at 0.25–0.5°C/hour.
* In case the device has an automated feedback system, set it at the rewarming mode, and set the rewarming speed at 0.25–0.5°C/hour.
* If there is no automated feedback system, be careful when setting the temperature, make sure it does not rewarm too quickly, and reset it often.
* Refer to the user’s manual of each company for detailed setting methods per device.
* Maintain the existing sedative, analgesic, or neuromuscular blocker up to 35°C.
* In case of shivering, the following medications can be used:
  + Buspirone, 30 mg via a nasogastric tube.
  + Meperidine, 25 mg bolus injection (except when accompanied by renal failure and oliguria; seizure disorder history; patients who are taking MAO inhibitor, buspirone, or SSRI; and pregnant women in the third trimester).
  + Vecuronium, 0.1 mg/kg bolus injection.
* Hypotension can develop due to vasodilation; observe vital sign changes, and record it every hour.
* Increase in CO2 production is expected; thus, properly changing the mechanical ventilation setting is needed.
* Continuously monitor two core temperatures if possible (esophagus and bladder; esophageal and rectal, or bladder and pulmonary artery; pulmonary artery and rectal).
* Record core temperature every 30 minutes.
* During or after rewarming, perform neurological examination.
* Perform arterial blood gas analysis (if possible, include electrolytes and lactate) every hour, optimize oxygenation and ventilation, and observe changes in electrolyte levels.
* Measure blood glucose level every hour, and keep the target range at 144–180 mg/dL.
* Perform follow-up 12-lead ECG, chest x-ray, and blood test every 48 and 72 hours after ROSC (CBC, routine blood chemistry with cardiac biomarkers, CRP, PT/PTT/INR, urinalysis) and perform follow-up cultures (blood/urine/sputum culture).
* To prevent stress ulcers, infuse a H2 blocker and coating agent via a nasogastric tube every 6 hours.
* When the blood glucose level drops below 144 mg/dL, stop the insulin infusion.
* If the target temperature is 32–34°C, once the core temperature reaches 35°C, stop the neuromuscular blocker first, and maintain the sedative and analgesic.
* If the target temperature is 32–34°C, once the core temperature reaches 36°C, stop the sedative and reduce or maintain analgesic.
* After discontinuing the neuromuscular blocker and sedative, check the patient’s cognition or movement.
* After rewarming and after reaching normal temperature, record the core temperature every hour and maintain a normal temperature up to 72 hours after ROSC.
* To prevent rebound hyperthermia, acetaminophen can be administered every 6 hours via a nasogastric tube.