Targeted Temperature Regulation

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INTRODUCTION

Definition

Targeted temperature regulation or management refers to the regulation of core body temperature to maintain normothermia, prevent fever or to induce hypothermia. In this document, hypothermia refers to core temperature <35°C, normothermia refers to core temperature 35°C to <37.5°C and fever/hyperthermia refers to temperatures >37.5°C.

Effect of temperature on brain injury

The three main temperature dependent pathological processes that hypothermia acts on are ischemic brain injury, reperfusion injury and secondary brain damage (1). Hypothermia reduces the metabolic rate by 5-7% for every 1°C reduction in temperature. In doing so, hypothermia reduces the formation of lactate, other waste products of anaerobic respiration, excitatory neurotransmitters such as glutamate as well as free radical oxygen species that develop during reperfusion injury and contribute to the progression of ischemic cerebral cell death. Hypothermia also suppresses the inflammatory cascade and the production of inflammatory cytokines that occurs following global ischemia and reperfusion.

Role of temperature regulation in neuroprotection

While the use of hypothermia to improve outcomes in pediatric patients with or at risk of neurological injury remains under investigation, the avoidance of fever and maintenance of normothermia is an important neuroprotective strategy for these populations.

Well before the pathophysiology of therapeutic hypothermia was elucidated, its benefits have been anecdotally appreciated. Hippocrates, (circa 450 B.C.) advised packing wounded soldiers in snow (2). In 1943, Temple Fay published his observation that patients with traumatic brain injury (TBI) had better outcomes when their temperature was lowered from 38.3°C to 32.7°C. More recently, Bernard et al (3) described significant improvements in short and long term survival and neurological outcomes in adults who remained comatose despite return of sustained circulation after out of hospital cardiac arrest. Yet the same benefit of hypothermia has not been established in children with in-hospital or out of hospital cardiac arrest (4, 5) (6), or those with traumatic brain injury (7, 8).

The physiological basis of the neuroprotective effects of hypothermia has resulted in an ongoing search for the right formula for therapeutic hypothermia. The degree and duration of hypothermia, rate of rewarming, and the appropriate patient population who may benefit from this treatment remain under hopeful investigation [eg. the multicenter Pediatric Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients (P-ICECAP) trial (NCT05376267)].

CHAPTER TARGETED TEMPERATURE REGULATION

INDICATIONS AND EXCLUSIONS

Indications include but are not limited to:

- Post cardiac arrest
- Severe traumatic brain injury
- Severe encephalitis
- Status epilepticus
- Refractory intracranial hypertension

Exclusion: Perinatal hypoxic ischemic encephalopathy as separate guidelines exist for this patient population

GENERAL PRINCIPLES

Temperature Regulation Targets

For the majority of patients who require neuroprotection, the goal should be to maintain normothermia, or low normal temperatures within the range 35-36° C. For these patients, avoidance of fever and maintaining temperature <37.5°C is of utmost importance. Patients should receive optimized dosing of antipyretics in addition to early initiation of Blanketrol®, a servo regulated temperature regulation blanket used in our unit.

Temperatures as low as 33°C is referred as mild hypothermia. Moderate hypothermia is temperature in the range of 28–32°C and deep hypothermia is temperature <28°C. Certain patient groups, such as those with refractory intracranial hypertension or refractory status epilepticus for whom lower temperature goals (as low as 32°C) may be instituted after multidisciplinary discussions and careful consideration of risks and benefits. Patients who are cooled to temperatures <35°C are at risk of complications and require close monitoring and anticipatory management.

Contraindications to Therapeutic Hypothermia

Contraindications to therapeutic hypothermia (2) include uncontrolled bleeding, haemorrhagic stroke, GCS>8, uncontrolled hemodynamically unstable rhythms, cardiac arrest due to trauma. Relative contraindications: (2) include thrombocytopenia (<50,000) coagulopathy, prolonged cardiac arrest (<60 minutes) and refractory hypotension despite vasopressor support.

Complications of Therapeutic Hypothermia

Complications are more likely to occur with moderate hypothermia. Patients may experience cold diuresis, pulmonary hypertension, cardiac arrythmias (particularly if <33° C), myocardial dysfunction, coagulopathy, electrolyte abnormalities (hypokalemia) or thyroid hormone dysregulation.

TEMPERATURE REGULATION PROCEDURE

Stages of Temperature Regulation

Temperature regulation has three stages: cooling to target temperature, maintenance of target temperature, (typically for at least 72 hours), followed by re-warming. Guidance

regarding initiation and management of Blanketrol® during these phases, rate of cooling and rewarming are detailed in the pathways attached.

Targeted temperature regulation using servo regulated cooling blankets such as **Blanketrol®** should be accompanied with core temperature monitoring (rectal or oesophageal). Rectal temperature monitoring is usually practised in our unit. If this is not possible, efforts should be made to obtain oesophageal probes for core temperature regulation.

Cooling and Maintenance of Target Temperature

There are no contraindications to rapidly cooling the patient down to reach target temperatures. However shivering should be anticipated and prevented. During the maintenance of target temperatures, patients require continuous monitoring of core temperatures and routine monitoring of skin for thermal burns.

Rewarming

Rewarming should not exceed the rate of 0.5 to 1° C every 24 hours. Rapid rewarming may negate the benefits of therapeutic hypothermia. However, in the event of significant complications of hypothermia, it may be prudent to rewarm the patient more quickly. The complications of rapid rewarming (raised intracranial pressure, hyperkalemia, cardiac arrythmias) must then be balanced against the complications of hypothermia. If intracranial pressure rises during rewarming, it may be necessary to optimize other measures to manage ICP first before rewarming is initiated and to consider whether a longer duration of temperature regulation is required for adequate ICP control.

MANAGEMENT OF SHIVERING

Shivering thermogenesis is the primary means of heat production during hypothermia. In response to hypothermia, rhythmic contraction of skeletal muscles results in heat generation. This is expected and is not a complication of treatment. However, if observed, shivering should be actively prevented with deep sedation and muscle relaxants if necessary as it will counter the goals of targeted temperature management.

RECOMMENDED MONITORING DURING THERAPEUTIC HYPOTHERMIA

Patients should have continuous cardiac and central venous pressure monitoring. If the indication for temperature regulation is intracranial hypertension, intracranial pressure monitoring should be used. Indwelling urinary catheter should be used to monitor for cold diuresis.

Blood investigations that may require monitoring include FBC, PT/PTT/INR, renal panel, calcium, magnesium, phosphate, NT pro-BNP, creatine kinase, CK-MB, Troponin I, serum glucose, lactate and thyroid function tests. The need and frequency of these tests should be at the discretion of the treating physician based on the patient's clinical condition and associated or anticipated complications.

During hypothermia, pharmacokinetic parameters may change, resulting in drug and metabolite accumulation in the plasma resulting from impaired clearance (9). Drug doses may need to be adjusted, especially for drugs with a low therapeutic index (9).

REFERENCES

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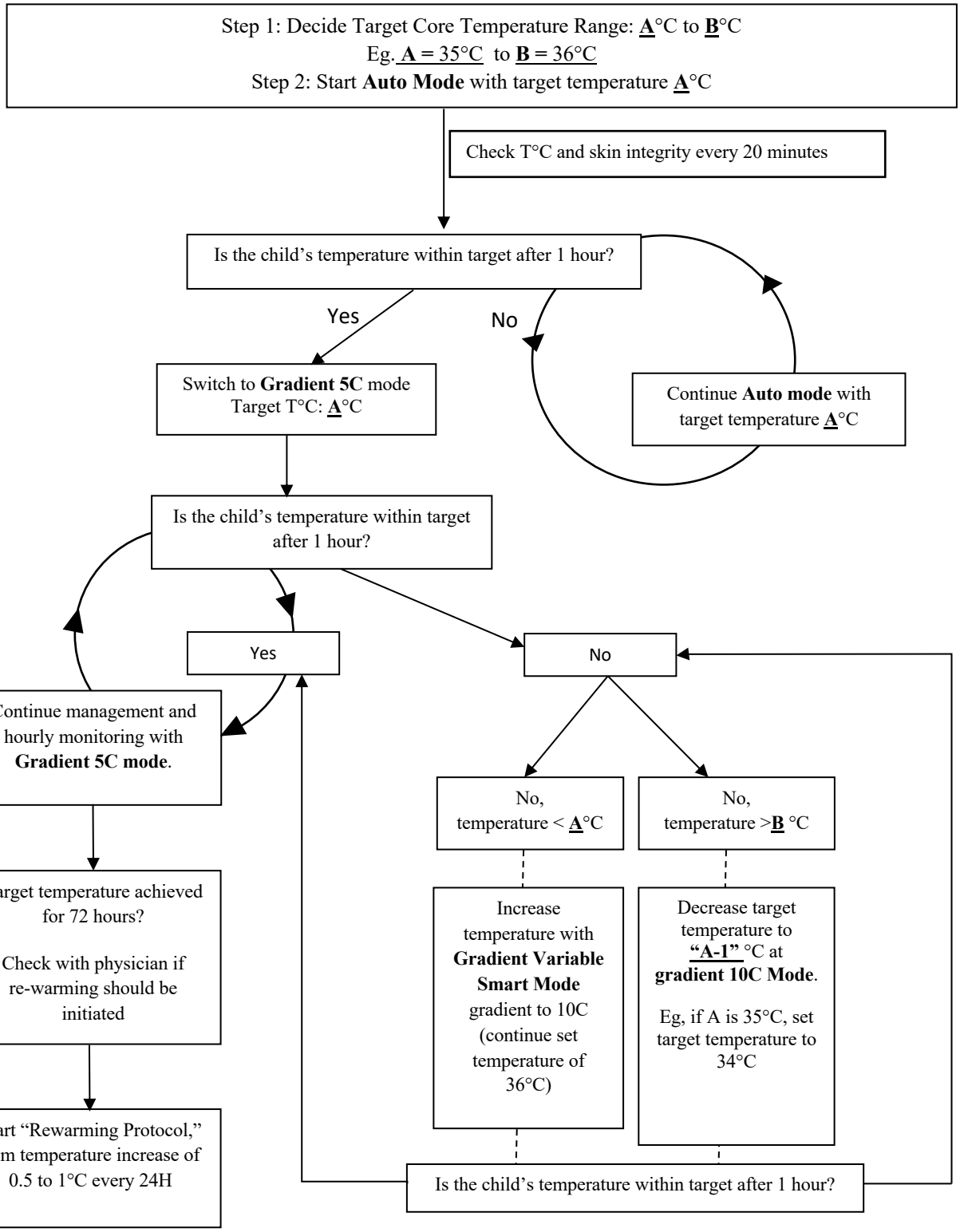
Targeted Temperature Management

COOLING PROTOCOL (BLANKETROL)

Please see Targeted Temperature Management Protocol for Inclusion Criteria and Further Details



Warning!

- Extended use of Blanketrol with exceeding temperatures of 40 °C water temperature can cause tissue damage and burns
- Check patients' temperature and skin integrity of areas in contact with blanket every 20 minutes during initiation.

Precautions:

- Monitor for shivering when cooling rapidly. If shivering occurs, immediately discuss with physician for optimization of sedation /neuromuscular blockade to prevent shivering.
- There is no contraindication to rapidly cool patients

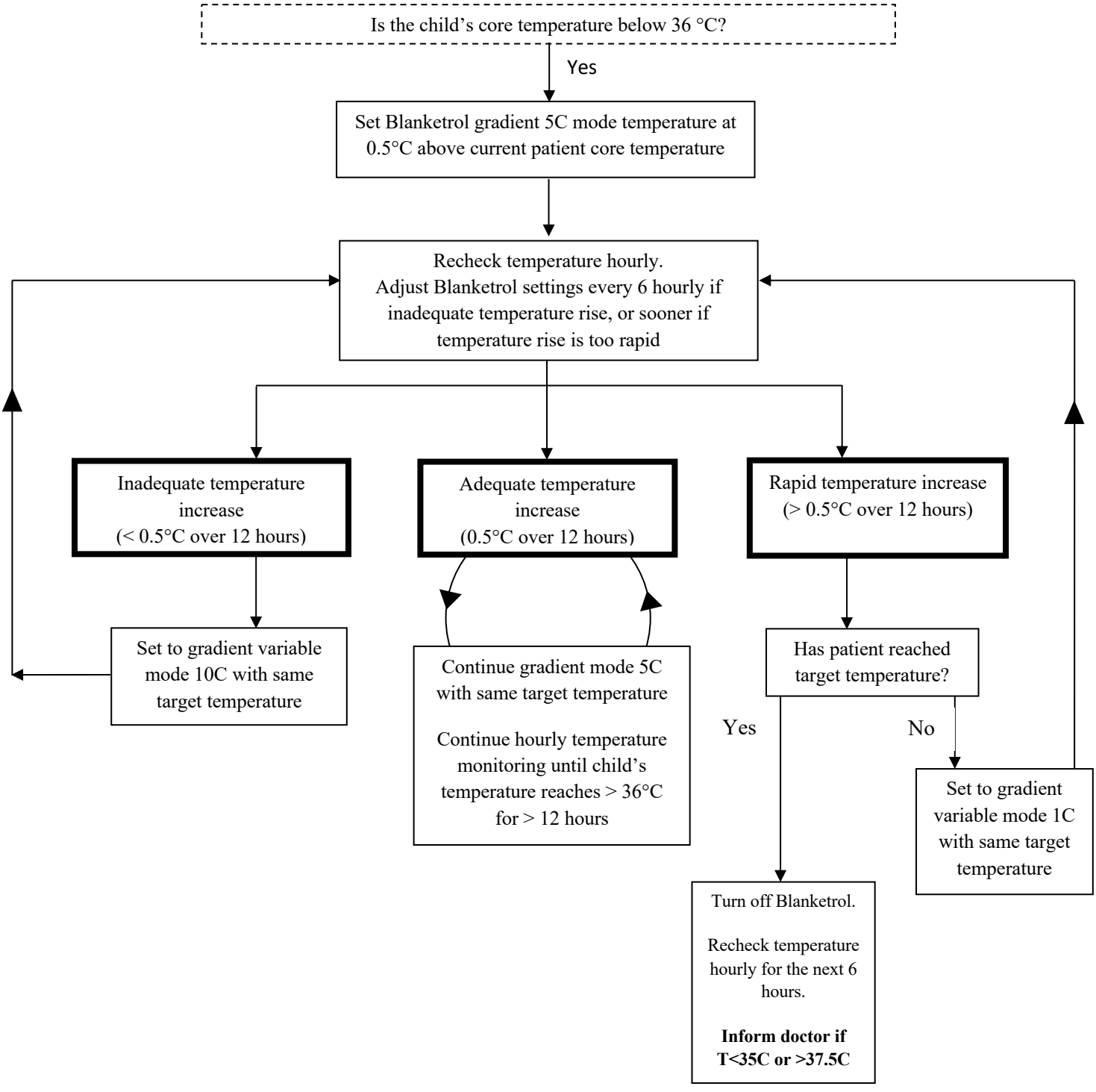
**For any Blanketrol malfunction or technical issues, refer to Blanketrol manual to troubleshoot machine

Targeted Temperature Management

RE-WARMING PROTOCOL (BLANKETROL)

Please see Targeted Temperature Management Protocol for Inclusion Criteria and Further Details

Goal: To rewarm patient's core temperature to ≥36°C
Target rate of temperature rise: 0.5°C to 1.0°C every 12 hours
This rate should not be exceeded as rapid re-warming can cause increase in ICP and negate the beneficial effects of targeted temperature management.



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