NTS Clinical Guideline

Title:	Therapeutic hypothermia guideline		
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Introduction

A hypoxic-ischaemic insult occurring around the time of birth may result in an encephalopathic state characterised by the need for resuscitation at birth, neurological depression, seizures and electroencephalographic abnormalities. Perinatal asphyxia causing moderate or severe encephalopathy occurs in approximately 2/1000 births and may account for up to 30% of cases of cerebral palsy. Experimental studies show that mild therapeutic hypothermia has been shown to be a safe and effective treatment for neonatal encephalopathy.

Aim

The aim of intervention with hypothermia is to maintain rectal temperature of 33-34°C for 72 hours, commencing as soon as possible after resuscitation in eligible babies. Current protocols require cooling to begin within 6 hours of birth. To facilitate early cooling of babies born in hospitals without the facilities for therapeutic hypothermia, initiation of cooling can be delivered passively prior to the arrival of the neonatal transport team.

Subject group

The decision to treat infants with cooling remains the responsibility of the attending senior clinician. Infants who meet the following criteria may be considered for treatment with cooling:

- ≥36 weeks completed gestation
- evidence of perinatal asphyxia
- signs of encephalopathy

Contraindications

- conditions requiring immediate or imminent surgery
- other abnormalities indicative of a poor long term outcome

TOBY criteria

As early as possible after resuscitation and stabilisation the baby should be assessed according to TOBY criteria to see if therapeutic hypothermia is appropriate:

A. Infants ≥36 completed weeks gestation admitted to the neonatal unit with at least one of the following:

- Apgar score of ≤5 at 10 minutes after birth
- Continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth
- Acidosis within 60 minutes of birth (defined as any occurrence of umbilical cord, arterial or capillary pH <7.00)
- Base Deficit ≥ 16 mmol/L in umbilical cord or any blood sample (arterial, venous or capillary) within 60 minutes of birth

Infants that meet criteria A should be assessed for whether they meet the neurological abnormality entry criteria (B):

B. Seizures or moderate to severe encephalopathy, consisting of all the following:

- Altered state of consciousness (reduced response to stimulation or absent response to stimulation)

- Abnormal tone (focal or general hypotonia or flaccid)
- Abnormal primitive reflexes (weak or absent suck or Moro response)

If CFM available in referring unit, information from this may augment the assessment of encephalopathy.

Infants who meet criteria A and B may be considered for treatment with cooling. Babies with evidence of encephalopathy but not fulfilling criteria can be discussed with a cooling centre to establish whether cooling may still be appropriate. As soon as the decision is made to refer for cooling the referring unit should telephone the cooling centre and liaise with EBS and NTS.

Passive and active cooling

TARGET TEMPERATURE 33.0 - 34.0 °C RECTAL

Referral Unit's tasks:

- Documentation of both the admission and current temperature of the baby
- Ideally continuous rectal temperature monitoring, if not available axilla temperature should be **measured every 15 minutes**
- Turn off incubator (and the portholes opened if in a closed incubator)
- Baby naked apart from a nappy
- Baby's temperature must not fall below 33ºC
- Ice packs should not be used for cooling as these can result in severe hypothermia
- Active cooling techniques such as fans should not be implemented without rectal temperature monitoring to avoid overcooling

Transport team's tasks:

- Transport team should be dispatched as soon as they are available
- Prior to leaving check that all the equipment required is available in the ambulance
- En route set the transport incubator temperature at 28ºC, open the portholes to allow the incubator to cool down

On arrival at the referring unit:

- Clinical handover
- Start cooling log
- Immediately commence the baby on continuous rectal temperature monitoring (rectal temperature probe should be inserted 2-3cm and fixed to the skin using steristrips (if not possible, serial rectal temperature measurements should be taken)
- Incubator / ambient / rectal temperature readings should be documented every 15 minutes (e.g. in the cooling log)

Active cooling

- Needs to be commenced as soon as possible after arrival on the referring unit
- Cooling mattress needs to be prepared and placed under the baby
- Document the time when you start active cooling and when you reach target temperature
- Neurological assessment

- Whilst the baby is being stabilised and transferred, incubator / ambient / rectal temperature readings should continue to be documented every 15 minutes

aEEG assessment

- Must be recorded in all infants treated with cooling but cooling need **not** be delayed if unavailable or if there is a delay in initiation of CFM
- Is helpful to assess occurrence of seizures and monitor the severity of encephalopathy
- NTS team has to assess and print CFM trace if available. Background activity should be assessed and the presence of seizures identified

Seizures

- Needs to be guided by local protocols
- In general, symptomatic seizures or frequent (>3/hr) subclinical (EEG) seizures will be treated with anticonvulsants
- Cooling may affect the metabolism of several drugs, including anticonvulsants and sedatives, and toxic drug levels may occur even with normal doses
- 1st line anticonvulsant is phenobarbital (**20 mg/kg, followed by 10 mg/kg if seizure persists)**
- 2nd line is phenytoin **(18 mg/kg)**
- Midazolam **(50-100 mcg/kg)**, or clonazepam **(50 mcg/kg)** are commonly used if seizures persist. The dose should be adjusted according to response. See monograph if infusion is required.
- Lignocaine **(2 mg/kg)** is sometimes used as a further anticonvulsant, but should be avoided if phenytoin has previously been administered

Ventilation

- Infants treated with cooling may initially require mechanical ventilation
- Blood gases will guide ventilatory requirements

Cardiovascular support

- Alterations in heart rate and blood pressure are common during cooling. In general the heart rate is reduced and blood pressure increases with a reduction in body temperature
- Most infants with a rectal temperature of 33-34°C will have a heart rate around 100 bpm and a mean blood pressure greater than 40 mmHg
- A rapid rise in body temperature may cause hypotension by inducing peripheral vasodilatation
- Treatment with volume replacement and/or inotropes should be considered if the mean arterial blood pressure is less than 40 mmHg and evidence of poor perfusion
- A bolus of 10-20 ml/kg of normal saline should be given initially if clinically indicated
- If the blood pressure remains low, start dopamine 5-10 micrograms/kg/min, and/or dobutamine 5-10 micrograms/kg/min (if clinical assessment suggests poor cardiac function)

Analgesic and sedative therapy

- Cooling can be associated with stress.
- Signs of distress include tachycardia, facial grimacing and irritability. A heart rate consistently above 110 bpm in cooled infants suggests that the infant is distressed
- Ventilated infants may be sedated with intravenous morphine (10-20 mcg/kg/hr)
- Non-ventilated infants who appear distressed will also require sedative therapy, Morphine infusion at 5-10 mcg/kg/hr

Fluid Management

- Renal function is commonly impaired following severe perinatal asphyxia. The infant's weight, blood creatinine and electrolytes and urine output will guide fluid management
- Infants will require about 40-60 ml/kg/day. However infants in renal failure may require a more aggressive fluid restriction, e.g. 30 ml/kg/day. Boluses of 0.9% saline may be required to avoid hypovolaemia if diuresis occurs in the infant.

References

- Cooling on retrieval clinical guideline (2009) Cooling TOBY register
- Toby Protocol (2010) UK Toby Register, Clinicians handbook
- Strohm, B. and Azzopardi, D. Temperature control during therapeutic moderate whole-body hypothermia for neonatal encephalopathy.*Archives of Disease in Childhood - Fetal and Neonatal Edition* 2010; 95(5): F373-F375.