GUIDELINES FOR ASSESSMENT AND INITIATION OF THERAPEUTIC HYPOTHERMIA (COOLING) TREATMENT FOR MODERATE OR SEVERE HYPOXIC ISCHAEMIC ENCEPHALOPATHY

Saruntha Perera, Amit Gupta

AIMS OF THE GUIDELINE

• To ensure that babies with suspected HIE are appropriately assessed to see whether therapeutic hypothermia (cooling) is appropriate.
• To ensure that cooling is initiated in a safe and timely manner.
• To outline the care pathway for ongoing cooling treatment.

INTRODUCTION

Neonatal encephalopathy has an incidence of approximately 3/1000 births, with hypoxic ischaemic encephalopathy occurring in approximately 1.3-1.7/1000 and more specifically, moderate-severe HIE occurring in approximately 1.0-1.5/1000 live births in the UK.2,3 The risk of death or severe handicap in survivors of moderate or severe HIE is approximately 25 and 75% respectively3, and children without cerebral palsy or severe HIE is approximately 5% and 15%, respectively.4,5 Clinically significant adverse events attributed to cooling are uncommon and the benefits of therapeutic hypothermia outweigh the possible short-term adverse effects5.

Therapeutic hypothermia is now standard of care in selected neonates with HIE and is supported by NICE and BAPM.6

A recent Cochrane Review that included 11 trials on therapeutic hypothermia such as the UK total body cooling trial (TOBY) and US National Institute of Child Health and Human Development (NICHD) trial, confirmed that therapeutic hypothermia reduces death and disability at 18 months of age and improves neurodevelopmental outcomes in survivors with a number needed to treat for survival with normal neurological function at 18 months is 7 (95% CI 5-11)6, and 8 (95% CI 5-17)7, respectively. Recently published longer-term data at the age of 6-7 years by the TOBY and NICHD groups showed a benefit of therapeutic hypothermia for reduction of death and improvement of neurodevelopmental outcome up to school age.8,9 Clinically significant adverse events attributed to cooling are uncommon and the benefits of therapeutic hypothermia outweigh the possible short-term adverse effects5.

Current Practice

EVIDENCE FOR THERAPEUTIC HYPOTHERMIA

There is weak or unavailable evidence to guide cooling outside the above guidelines. There are circumstances where there may be theoretical benefits for cooling in certain other patients.10-14 Cooling in these circumstances should only be instigated following discussion with the cooling centre.

Examples would include:

• Infants who fulfil criteria A but only partially fulfil criteria B.

CONTRAINDICATIONS TO COOLING

There are no absolute contraindications to cooling infants who meet the criteria above except where there are other life-threatening congenital abnormalities present. Relative contra-indications include:

• Suspected significant haemorrhage or thrombosis (NB although hypothermia prolongs bleeding time, trials did not examine its effect).
Current Practice

GUIDELINES FOR ASSESSMENT AND INITIATION OF THERAPEUTIC HYPOTHERMIA (COOLING) TREATMENT FOR MODERATE OR SEVERE HYPOXIC ISCHAEMIC ENCEPHALOPATHY

Sarantha Perera¹, Amit Gupta¹

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INTRODUCTION

Neonatal encephalopathy has an incidence of approximately 3/1000 births, with hypoxic ischaemic encephalopathy occurring in approximately 1.3-1.7/1000 and more specifically, ischaemic encephalopathy occurring in approximately 3/1000 births, with hypoxic encephalopathy having an incidence of 2/1000 births1. Therapeutic hypothermia for reduction of death and improvement of neurodevelopmental outcome up to school age has been shown to be beneficial. Clinically significant adverse events attributed to cooling are uncommon and the benefits of therapeutic hypothermia outweigh the possible short-term adverse effects2.

Therapeutic hypothermia is now standard of care in selected neonates with HIE and is supported by NICE and BAPM3,4,5.

A recent Cochrane Review that included 11 trials on therapeutic hypothermia such as the UK total body cooling trial (TOBY) and US National Institute of Child Health and Human Development (NICHD) trial, confirmed that therapeutic hypothermia reduces death and disability at 18 months of age and improves neurodevelopmental outcomes in survivors with a number needed to treat for survival with normal neurological function at 18 months is 7 (95% CI 5-11) and 8 (95% CI 5-17), respectively. Recently published longer-term data at the age of 6-7 years by the TOBY and NICHD groups showed a benefit of therapeutic hypothermia for reduction of death and improvement of neurodevelopmental outcome up to school age4,5. Clinically significant adverse events attributed to cooling are uncommon and the benefits of therapeutic hypothermia outweigh the possible short-term adverse effects2.

Evidence for cooling outside the above guidelines is weak or unavailable. However, there are circumstances where there may be theoretical benefits for cooling in certain other patients6-14. Cooling in these circumstances should only be instigated following discussion with the cooling centre.

Examples would include:

• Infants who fulfil criteria A but only partially fulfil criteria B.

• Early prolonged or recurrent seizures (within 12 hours of birth).

• Infants who meet the criteria above except where there are other life-threatening congenital abnormalities present. Relative contra-indications include:

  • Suspected significant haemorrhage or thrombosis (NB although hypothermia prolongs bleeding time, trials did not examine these outcomes).

COOLING OUTSIDE TRIAL GUIDELINES

Evidence for cooling outside the above guidelines is weak or unavailable. However, there are circumstances where there may be theoretical benefits for cooling in certain other patients6-14. Cooling in these circumstances should only be instigated following discussion with the cooling centre.

Examples would include:

• Infants who fulfil criteria A+B but are between 6-12 hours old.

• Preterm infants, 33+5 weeks or more, who have suffered an acute asphyxia event and fulfil criteria A+B above.

• Acute postnatal collapse with a neurological examination consistent with a diagnosis of acute encephalopathy.

CONTRAINDICATIONS TO COOLING

There are no absolute contraindications to cooling infants who meet the criteria above except where there are other life-threatening congenital abnormalities present. Relative contra-indications include:

• Suspected significant haemorrhage or thrombosis (NB although hypothermia prolongs bleeding time, trials did not
demonstrate differences in complications related to abnormal clotting).

- Surgical conditions likely to be associated with significant blood loss.
- Severe PPHN - Cooling may produce adverse respiratory or cardiovascular effects. However, trials found no difference in the prevalence of PPHN between cooled patients and control groups.

**AMPLITUDE INTEGRATED EEG (aEEG) ASSESSMENT**

The aEEG (also known as Cerebral Function Monitor – CFM) is a single or dual channel time compressed and filtered EEG providing information on overall electrical activity in the brain.

- The amplitude integrated EEG (aEEG or CFM) must be recorded in all infants treated with cooling but cooling should not be delayed until the aEEG is initiated.
- A normal aEEG record indicates a high probability of normal outcome, and clinicians may consider that treatment with cooling is not required.
- Rewarming following active cooling may be considered if the clinical examination is normal and the CFM normalizes within the first 6 hours. However, ongoing neurological examination and CFM recording should occur during rewarming and if any signs of deterioration occur the patient should be re-cooled for the full 72 hours.

Apparent improvement of the aEEG AFTER 6 hours of age is NOT an indication for discontinuing cooling.

- A copy of the initial CFM traces should be sent with the baby to the cooling centre.
- IV anticonvulsant therapy may cause transient suppression of EEG activity. Ideally the aEEG should be performed before administering anticonvulsant therapy.

**VENTILATION**

- Most infants treated with cooling will initially require mechanical ventilation as a consequence of their encephalopathy/anticonvulsant medication.
- Ventilatory care should be managed according to local protocol
- Bolus doses of paralysis should be used if required rather than infusions to prevent drug accumulation.
- Blood gases will guide ventilatory requirements; particular care should be taken to ensure normocapnia. The infant’s temperature should be inputted into the blood gas machine so that the appropriate adjustment is performed.
- Ventilator gases should be warmed and humidified in the normal way.
- More frequent suctioning may be necessary as secretions tend to be more viscous when cold. Vary positioning 6 hourly, Chest physio as indicated.

**CARDIOVASCULAR SUPPORT**

- 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.
- Treatment with volume replacement and inotropes should be considered if the mean arterial blood pressure is less than 40 mmHg.

**SEPSIS**

- Antibiotic therapy may be given if clinically indicated. Gentamycin and other aminoglycosides should be avoided as there is a higher risk of toxicity

**SEIZURES**

- The management of seizures should be as usual
- In general, symptomatic seizures or frequent subclinical (>3/hr) seizures seen on aEEG/CFM should 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.

**REFERENCES**

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FLUID & ELECTROLYTE MANAGEMENT

- Renal function is commonly impaired following severe perinatal asphyxia and fluids should be restricted.

COAGULATION

- Send platelet count and clotting at the start of cooling. If there are clinical signs of increased bleeding tendency, treat babies with FFP without waiting for lab results.

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Key words: Incontinentia Pigmenti, new born, skin manifestations

INTRODUCTION:

Incontinentia pigmenti (IP) is a rare neuroectodermal dysplasia with an estimated incidence of 0.7 cases per 100,000 births. Up to date approximately 1,200 cases have been reported in scientific literature. IP has a multisystemic involvement where the skin manifestations are the hallmark and could be seen even at birth.

We present a baby girl with typical skin manifestations of IP seen at birth.

CASE REPORT:

A baby girl was born to healthy non-consanguineous parents at term via assisted vaginal delivery. Erythematous linear streaks and plaques of vesicular eruptions with hyperpigmentation arranged in a linear configuration, were mainly seen on the limbs and the trunk (Figure 1 & 2). Lesions were more pronounced on the flexor aspect of the lower limbs (Figure 2).

There was a history of premature rupture of membranes for 16 hours without other risk factors for sepsis. Baby was born with a birth weight of 3.08 kg (median to -1SD) with normal Apgar scores. Her length and occipitofrontal circumference were 50 cm (median) and 33 cm (-1SD) respectively. There was no scarring alopecia, nail dystrophy or skeletal abnormalities. Neurological examination including tone, reflexes, fontanelles and primitive reflexes were normal. Formal eye examination revealed abnormal palpebral and conjunctival dilated vessels with occasional pigmentation. No retinal vasculature abnormality, arteriovenous malformations or lens opacity were noted. A grade-2 ejection systolic murmur was found. Rest of the system examination was unremarkable.

She was the second born with a healthy developmentally normal female sibling. There weren’t any miscarriages or similar conditions, bulbous dermatosis, severe allergic reactions and neurological disorders in the family. Mother’s venereal disease screening was negative and she

Figure 1: Hyperpigmentation in a linear configuration on the trunk