Therapeutic hypothermia with intracorporeal temperature monitoring for hypoxic perinatal brain injury

Interventional procedures guidance
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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

1 Guidance

1.1 Current evidence on the safety and efficacy of therapeutic hypothermia with intracorporeal temperature monitoring for hypoxic perinatal brain injury is adequate to support the use of this procedure in carefully selected neonates

provided that normal arrangements are in place for clinical governance, consent and audit (See section 2.5.1 for comments on selection).

1.2 This procedure should only be carried out in units experienced in the care of severely ill neonates, by staff who have been specifically trained in the use of therapeutic hypothermia.

1.3 NICE encourages clinicians to enter details about all neonates undergoing this procedure into the UK TOBY cooling register. The register provides a suggested management algorithm. Submitting data to the register will contribute to the evidence on long-term follow-up and may lead to improvements in the management algorithm.

2 The procedure

2.1 Indications and current treatments

2.1.1 Hypoxic perinatal brain injury is caused by a decrease in the amount of oxygen supplied to an infant's brain close to the time of birth. Surviving infants may develop hypoxic-ischaemic encephalopathy and other organ damage, which can lead to severe, lifelong disability or death.

2.1.2 Hypoxic perinatal brain injury is characterised by fetal distress and is associated with acidosis. Diagnosis includes clinical examination, paired umbilical arterial and venous blood gas analysis and amplitude-integrated electroencephalography.

2.1.3 Hypoxic perinatal brain injury is traditionally treated with supportive care only, since no specific pharmacological agents or interventions have been shown to prevent the neuronal damage that perinatal hypoxia causes.

2.1.4 This procedure is usually carried out on infants with a gestational age of 36 weeks or more and this is reflected in the published literature.

2.2 Outline of the procedure

2.2.1 In therapeutic hypothermia the infant is cooled to between 33°C and 35°C, with the aim of preventing further neuronal loss in the days following the hypoxic injury.

2.2.2 Hypothermia is usually induced by cooling the whole body with a blanket or mattress (or sometimes by cooling the head only with a purpose-made cap). Intracorporeal temperature is continuously monitored, using a rectal or nasopharyngeal thermometer, as a proxy for brain temperature.

2.2.3 Treatment is started as soon as possible after diagnosis, usually within 6 hours of birth, and continued for approximately 72 hours. The infant is then slowly warmed to normal body temperature.

> Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the overview.

2.3 Efficacy

2.3.1 A systematic review of 10 randomised controlled trials (RCTs) (1320 infants in total) reported a lower risk of death in cooled infants (whole body or head) in the first 18 months of life than in infants treated by standard care (relative risk [RR] 0.78; 95% confidence interval [CI] 0.66 to 0.93) (follow-up not stated). In 3 of these RCTs with 18-month follow-up (767 infants in total) the combined risk of death and severe disability was significantly lower in cooled infants compared with infants treated by standard care (RR 0.81;95% CI 0.71 to 0.93) and cooling increased survival with normal neurological function compared with standard care (RR 1.53; 95% CI 1.22 to 1.93) at 18-month follow-up.

2.3.2 An RCT of 325 infants treated by whole body cooling or standard care reported survival without neurological abnormality in 44% (71/163) and 28% (45/162) of infants respectively at 18-month follow-up (RR 1.57; 95% CI 1.16 to 2.12). Among the surviving infants, there was a lower rate of cerebral palsy in those treated by cooling (28% [33/120] vs 41% [48/117]; RR 0.67; 95% CI 0.47 to 0.96).

2.3.3 An RCT of 234 infants treated by head cooling or standard care reported death or severe neurodevelopmental disability at 18-month follow-up in 55% (59/108) and 66% (73/110) of infants respectively (odds ratio 0.61; 95% CI 0.34 to 1.09). In the systematic review, the 3 RCTs with a total of 767 infants reported that the rates of severe disability and cerebral palsy in surviving infants were significantly lower in the cooled infants than infants treated by standard care at 18-month follow-up (RR 0.71; 95% CI 0.56 to 0.91 and RR 0.69; 95% CI 0.54 to 0.89, respectively).

2.3.4 The Specialist Advisers listed key efficacy outcomes as improvement in survival without neurological impairment, reduction in severe disability, improvement in Motor and Psychomotor Development Index scores and reduction in cerebral palsy.

2.4 Safety

2.4.1 An RCT of 208 infants reported a higher incidence of hypocalcaemia in cooled infants than in those treated by standard care (27% [28/102] and 19% [20/106] respectively; p values not reported).

2.4.2 In the RCT of 234 infants, 1 cooled infant (who died of other causes) had skin breakdown and local haemorrhage under the cooling cap. A case report described fat necrosis in an infant treated by whole body cooling using ice packs applied to the skin. At 9 months the infant had asymptomatic firm nodules with no calcification present. In another case report, an infant treated by whole body cooling using a water-filled mattress developed sclerema on the area of the back that was in contact with the cooling mattress at 3-week follow-up; this resolved without scarring after 3 months.

2.4.3 The Specialist Advisers considered theoretical or anecdotal adverse events to include metabolic disturbances, blood hyperviscosity syndrome, increased infections, and seizures during rewarming if it is carried out too quickly.

2.5 Other comments

2.5.1 The Committee noted the uncertainties and difficulties in selecting neonates for this procedure. Specifically, they noted the lack of evidence for using the procedure in neonates with less severe hypoxic brain injury, and the difficulties

in deciding not to use the procedure for neonates whose degree of brain injury or comorbidities are too severe to expect survival without severe neurological deficit.

3 Further information

Information for patients

NICE has produced information on this procedure for patients and carers ('Understanding NICE guidance'). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

4 About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a procedure. Funding decisions are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE interventional procedure guidance process.

We have produced a summary of this guidance for patients and carers. Information about the evidence it is based on is also available.

Changes since publication

4 January 2012: minor maintenance.

Your responsibility

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Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

Contact NICE

National Institute for Health and Clinical Excellence
Level 1A, City Tower, Piccadilly Plaza, Manchester M1 4BT

www.nice.org.uk
nice@nice.org.uk
0845 033 7780

Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

Accreditation