european standards of care for newborn health

Topic Expert Group: **Medical care and clinical practice**

Postnatal management of newborn infants with hypoxic ischaemic encephalopathy (HIE)

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Target group
Term and near term infants with hypoxic ischaemic encephalopathy (HIE) and parents

User group
Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard
Newborn infants who have suffered from severe hypoxic-ischaemia receive early evaluation and appropriate postnatal management including therapeutic hypothermia and monitoring.

Rationale
The goal is to reduce long-term effects of hypoxic ischaemic brain injury. Moderate to severe perinatal asphyxia in term and near term infants is one of the most important causes of neonatal death and adverse motor and cognitive outcome, with an incidence of 2-20 per 1000 live born infants, depending in which part of the world they are born. (1) Until recently, therapy was limited to stabilisation of the newborn infant and treatment of hypoxic ischaemic encephalopathy (HIE) induced seizures. Reduction of the body temperature to 33.5°C is the only established therapy which has shown a decrease in adverse outcomes after perinatal asphyxia (death or substantial disability at 18 months of age) from about 66% for non-cooled infants to 50% in cooled infants. (2,3) Intensive research is ongoing to explore (pharmacological) neuroprotective interventions which could be used in addition to hypothermia to improve outcome. (4–7)

Benefits

Short-term benefits

- Reduced brain injury due to excitatory neurotransmitters and reactive oxygen species (8,9)
- Improved prognosis using stratified hypoxic ischaemic encephalopathy (HIE) severity, e.g. using neurophysiological monitoring (a-EEG (10–12) or EEG) (13) (see TEG Medical care & clinical practice)
- Reduced brain injury by early treatment of seizures (13,14)
- Reduced mortality (3)

Long-term benefits
- Improved neurocognitive outcome, increasing the rate of disability free outcome at 5 years (3,15) reduced health and societal costs (16), reduced

occurrence of epilepsy at 2 years (7), less severe cerebral palsy in survivors (15)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about the management and outcome of hypoxic ischaemic encephalopathy (HIE). (17–20)	A (Low quality) B (High quality) C (Moderate quality)	Patient information sheet
2. Parents receive counselling regarding the expected short- and long-term outcome and prognosis related to HIE prior to discharge by healthcare professionals. (20)	B (High quality) C (Moderate quality)	Clinical records
For healthcare professionals		
3. A unit guideline on management of HIE including criteria for hypothermia treatment is adhered to by all healthcare professionals.	B (High quality)	Guideline
4. Training in assessment and management of encephalopathic infants is attended by all responsible healthcare professionals. (21,22)	A (Moderate quality) B (High quality)	Training documentation
5. Moderate hypothermia treatment is started within 6 hours and continued for 72 hours after birth of eligible infants. (2,23)	A (High quality)	Audit report
For neonatal unit		
6. A unit guideline on management of HIE (22) including monitoring blood glucose, a-EEG, seizures (14), heart rate (24), oxygen saturation (25), PCO_2 (14,25), and blood pressure is available and regularly updated.	A (Moderate quality) B (High quality)	Guideline
7. Infants who require hypothermia treatment are managed in centres with documented expertise and experience including necessary transfer. (see TEG Birth & transfer)	B (Moderate quality)	Guideline

For hospital		
8. Training in assessment and management of encephalopathic infants is ensured.	B (High quality)	Training documentation
9. At designated units, cooling devices and monitoring equipment are available.	B (High quality)	Audit report
For health service		
10. A national guideline on management of HIE including criteria for hypothermia treatment is available and regularly updated.	B (High quality)	Guideline
11. Hypothermia treatment including documented follow-up at 2 years (e.g. Bayley III or similar) and necessary education is coordinated and organised.	B (High quality)	Audit report
12. Support services for families with infants with HIE are available.	B (High quality)	Audit report

Where to go – further development of care

Further development	**Grading of evidence**
For parents and family	
• Use routine health service and education data for long-term follow-up programmes.	B (Moderate quality)
For healthcare professionals	
N/A	
For neonatal unit	
• Develop regional training programmes on early assessment and management of hypoxic ischaemic encephalopathy (HIE).	B (High quality)
• Research on improved interventions, monitoring care and outcome predictors.	B (Moderate quality)
For hospital	
N/A	
For health service	
• Develop asphyxia registry service including outcome at 2 years. (14,18)	B (Moderate quality)

Getting started

Initial steps

For parents and family

- Parents are verbally informed by healthcare professionals about the management and outcome of hypoxic ischaemic encephalopathy (HIE) by healthcare professionals.

For healthcare professionals

- Attend training in assessment and management of encephalopathic infants.
- Join post-graduate education with respect to hypothermia and a-EEG or EEG monitoring and interpretation technique/knowledge.
- Develop appropriate neurodevelopmental follow-up expertise.

For neonatal unit

- Develop and implement a unit guideline on management of HIE including criteria for hypothermia treatment.
- Develop information material on management and outcome of HIE for parents.
- Provide appropriate devices and knowledge how to use device(s). (22)

For hospital

- Support healthcare professionals to participate in training assessment and management of encephalopathic infants.
- Provide appropriate budget and technical support for training and equipment.

For health service

- Develop and implement a national guideline on management of HIE including criteria for hypothermia treatment and follow-up.
- Recognise that therapies discussed in this statement are mandatory.

Description

Apart from the supportive therapies such as stabilisation of haemodynamics, support of respiration, monitoring of physiological parameters and metabolism (e.g. glucose metabolism, electrolytes, etc.) and treatment of seizures, moderate hypothermia (target; 33-34°C) should be initiated as soon as possible and not later than six hours after birth (within the so-called therapeutic window) and continued for 72 hours, with appropriate sedation and pain management. (2,23) It is important to anticipate the possible side effects of induced hypothermia; including thrombocytopenia; hypotension; arrhythmia/bradycardia and hearing loss. (3,26) If sepsis or infection is suspected, antibiotic treatment should be considered. Although beyond the scope of this topic, appropriate (brain) monitoring is mandatory. Depression of background amplitude on early amplitude-integrated EEG (a-EEG) or abnormal multi-channel EEG activity is an excellent indicator of severity, and can be used to stratify babies for therapeutic hypothermia. Continuous a-EEG/EEG monitoring is essential to detect electrographic seizures and the effect of anticonvulsant treatment. In addition, the use of near infrared spectroscopy-monitored cerebral oxygenation ($rScO_2$) can be useful to estimate severity. Proper documentation of brain injury, including serial neurological examination (cranial ultrasound; MRI, preferably with diffusion sequences) as well as biochemical markers in blood/serum or plasma is important to determine the prognosis in the first week of life. Be aware of the effect of hypothermia per se on biochemical markers (27–29) and physiological variables. (21) Systematic neurobehavioural testing and documentation at two years follow-up in

survivors (e.g. Bayley III (30) or Griffiths (31) as well as at early school age for long term, e.g. 5-8 years (see TEG Follow-up & continuing care). (18)

1. General measures (hemodynamic/respiratory stabilisation; treatment of convulsions; metabolic/electrolyte surveillance)
2. Moderate whole body hypothermia (33.5±0.5˚C)
3. Add-on therapies when such are proven effective in trials (e.g. pharmacology/noble gasses/repair with umbilical cord stem cells)

1 and 2 are established therapies and are standard clinical practice, 3 are experimental and are currently under clinical investigation.

Several phase II and III studies are underway for assessment as add-on therapies to be used with hypothermia, mostly pharmacological therapy (rhEPO; melatonin; allopurinol) and ventilation with noble gases (Xenon); Repair with stem cells (e.g. mesenchymal stem cells, autologous (UMBC cells) and allogeneic transplantation are being investigated). (4,13,32–34)

Source

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