Provision of therapeutic hypothermia during neonatal transport

Therapeutic hypothermia is an accepted and indeed expected treatment for term infants with hypoxic ischaemic encephalopathy. As initiation of this treatment is time critical neonatal transport services must be able to both initiate and continue cooling safely during the transport episode. This article describes the experience of the Scottish Neonatal Transport service in providing cooling during transport.

Anne P Mitchell
RGN, RM, ANNP Nurse Consultant, Scottish Neonatal Transport Service
anne.p.mitchell@luht.scot.nhs.uk

Ewen D Johnston
MBCHB, MRCPCH, Specialist Registrar Neonatology, Neonatal Unit, Simpson Centre for Reproductive Health, Royal Infirmary, Edinburgh

Keywords

therapeutic hypothermia; cooling; passive cooling; active cooling; servo-controlled cooling; neonatal transport

Key points

Mitchell A.P, Johnston E.D. Provision of therapeutic hypothermia during neonatal transport. *Infant* 2011; 7(3): 79-82.

1. Therapeutic hypothermia is an effective but time-critical treatment for hypoxic ischaemic encephalopathy.
2. Passive, active and servo-controlled cooling can be undertaken safely during transport.

Neonatal transport can be a challenging process, with the safe provision of therapeutic hypothermia during transfer the most recent therapy to stimulate discussion and be implemented. Transport teams have traditionally focused on the avoidance of hypothermia and subsequent cold stress during transfer, to an extent that hyperthermia is as often an issue as hypothermia in the management of infants being moved between hospitals[1]. Therapeutic hypothermia therefore involves a complete change in approach to thermal care for some infants.

Therapeutic hypothermia is an effective but time-critical treatment for moderate to severe hypoxic ischaemic encephalopathy (HIE) in term infants (≥36 weeks' gestation) and is accepted as a standard of care throughout the UK[2]. Several randomised controlled trials have shown therapeutic hypothermia to be effective in reducing the risk of death or severe disability at the age of 18-22 months[3].

Mechanism of cerebral injury due to hypoxia-ischaemia

Fifty percent of brain metabolism is used to provide energy for the ion pumps in neural cell membranes. During hypoxia-ischaemia, energy levels fall and neural membranes depolarise, allowing a rapid influx of sodium and water into the cells, resulting in cell swelling and cell death[4]. However, neural injury does not cease when the hypoxic-ischaemic insult has resolved and energy levels have returned to normal. There is a latent phase representing a limited window of opportunity in which to decrease or even prevent a further cascade of inflammatory events.

Some hours after the initial insult, energy levels begin to fall again and excitatory neurotransmitters are released from neural membranes which result in a cascade of processes causing further cell death. There is release of cytokines, free radicals and neurotransmitters which damage the cell skeleton and membrane.

Time dependency of therapeutic hypothermia

Prolonged, moderate hypothermia decreases cerebral injury and has been found to be related to subsequent improved neurological outcome[3]. One of the key factors in efficacy is the time between the hypoxic ischaemic insult and the initiation of hypothermia. Maximum benefit has been shown to be obtained when cooling is started as soon as possible postnatally, but within six hours of birth[5]. The TOBY trial data suggest that cooling within four hours of life has most benefit[6]. Anderson et al[7] raise the point that for some infants the insult may have started some time before birth and that the postnatal therapeutic window for initiating effective treatment might be considerably less than six hours.

Not all infants who could benefit from therapeutic hypothermia are born in centres equipped to provide this treatment. Transfer to a centre where cooling is provided can delay initiation of treatment, potentially beyond the therapeutic window. Distance, road conditions, weather, transport team response times and the need for further stabilisation of the baby all impact on the time taken to arrive in a cooling centre. In Scotland distances travelled may be from as little as 15 to over 200 miles, and in order to reach island communities a flight will be required.

Passive cooling methods	Active cooling methods
Stop active warming Turn off overhead heater (or reduce servo setting to 34°C) but monitor temperature closely Nurse in open cot rather than incubator If incubator is the only option: – turn off and open portholes. – nurse naked on an open nappy – no sheepskin, no nesting – no hat	***Adjuncts*** Cool gel pack (fridge) Chemical cold pack Cool bean bag (fridge) Fan ***Mechanical*** Servo-controlled Non servo-controlled

TABLE 1 Passive and active cooling methods to reduce a baby's core temperature.

Cooling at referring units and during transport

Early implementers of therapeutic hypothermia very quickly realised the need for this therapy to be in progress during transfer. Fairchild et al[8] in Virginia, USA, published data on four year's experience in transferring infants who required cooling. Eighty percent of the infants who undergo therapeutic hypothermia in this unit are born remote from the cooling centre. The team have established a teaching programme for referring units in order to initiate cooling and optimise cooling care in referring units. Most cooling is started passively in the referring unit and continued actively by the transport team (**TABLE 1**).

The Virginia service states that passive cooling in referring units is effective as a means of providing initial cooling, however it is acknowledged that while most infants attain goal temperatures, some need active adjuncts to cool effectively while others, cooled passively, are overcooled (32%). Active cooling is discouraged in the Virginia area for most referring units[8].

Hallberg et al[9] reviewed the time from birth to the start of cooling within cooling centres in Sweden and subsequently evaluated the feasibility of initiating passive cooling at referring centres and during transport. Infants cooled passively were to have their rectal temperatures monitored either continuously or every 15 minutes. Despite requesting strict temperature monitoring, a significant number of infants (33%) arrived at the cooling centres with rectal temperatures below the designated therapeutic hypothermic range. Several of these infants did not receive rectal temperature monitoring before or during transport.

Hallberg et al[9] conclude that while passive induction of hypothermia is achievable and allows an earlier start to therapeutic hypothermia, there are substantial risks associated with unintended excessive cooling. Infants who had been excessively cooled were also found to have increased morbidity and mortality rates[9]. This could reflect that excessive passive/active cooling is detrimental to the infant, however asphyxiated infants are known to naturally cool faster than healthy infants[10,11] and increased morbidity may be a reflection of the severity of hypoxia already affecting the infant. Continuous monitoring of core temperature is recommended by Hallberg when carrying out any form of cooling.

Most authors, including Erecinska and Thoresen, consider cooling below 33-34°C to be unsafe[12]. Compagnoni[13] however has investigated cooling to 30°C and shown no adverse effects. Compagnoni's study recruited 39 infants; 10 cooled to between 32 and 34°C, 18 to between 30 and 33°C and the remaining 11 randomised to routine care. Both cooled groups showed better outcomes than the non-cooled infants, but there seemed to be little difference between the two cooled groups. This is a small study which would need multicentre replication before implementation.

Kendall et al[14] implemented passive cooling both before and during transfer of patients moved by the London Neonatal Transfer Service. The guidelines developed for the TOBY trial[15] meant that infants could be cooled prior to arrival in the designated cooling centres for that area. Due to journey times, 69% of these infants would not have reached the target rectal temperatures prior to six hours of age if cooling had not been initiated prior to transfer. With the benefit of cooling during transport 67% of infants transferred were within the target temperature range on arrival in the cooling centre. Despite strict guidelines, none of the referring units had measured a rectal temperature prior to the arrival of the transport team. Eleven percent (4) of the infants were overcooled and some were difficult to rewarm to within the therapeutic range. Active cooling of any kind without rectal temperature monitoring is discouraged due to the risk of subtherapeutic hypothermia by this group.

Monitoring body temperature

Variations between skin, axilla and rectal temperature monitoring were examined by Kendall et al[14]. Skin temperature readings did not correlate well with rectal temperature readings. Axilla temperature monitoring, although not identical, did reflect rectal temperatures more closely. In units unable to provide continuous rectal monitoring this finding would allow continuous axilla monitoring to be undertaken, providing a trend in temperature, with intermittent rectal temperatures to supplement these readings. A previous study by Hissinck[16] found poor correlation between axilla and rectal temperatures; however the infants in that study were in the normothermic range. The authors state that appropriate positioning of the temperature probe in the axilla is essential to achieve good correlation with rectal temperatures[16].

Guidelines for pre-transport cooling

Passive cooling of infants with HIE is now being undertaken safely during transfer in the UK[15]. Eighty six percent of infants in Scotland who were cooled prior to or during transfer would not have had cooling initiated before six hours of age had cooling not been undertaken during the transport episode. This is not because there was an extended transport stabilisation episode period required but simply due to delays in referral and travel time.

Guidelines for referring units need to reflect the wide variety of units that may request a transfer; from a tertiary unit which can provide cooling but may not have an available cot, to community midwifery units that may only have a few births per year and that have limited resources to monitor a sick infant.

Teaching has always been an integral

FIGURE 1 Interior of ambulance with cooling unit *in situ.*

part of the role of the Scottish Neonatal Transport Service (SNTS) which offers courses suitable for staff in transport/ tertiary care or working in a more isolated setting. This established relationship has allowed SNTS to introduce therapeutic hypothermia across the country; designing guidelines for pre-transport care, referral pathways and teaching aimed at appropriate levels for referring units. The SNTS has worked in tandem with the Scottish Cooling Group to establish therapeutic hypothermia as a treatment across Scotland, which is available to any infant who may benefit.

Some level two units and tertiary units not providing cooling have quickly become comfortable with the provision of passive cooling to 34.5°C prior to the transport team's arrival with support from the receiving consultant. Other units do not feel that they can monitor and control this process closely and thus how cool an infant will be before arrival of the team varies. However in all cases it is recommended that active warming should be stopped and that the asphyxiated infant should not be nursed in an incubator if an open cot is available. All units in the South East of Scotland have been provided with clear referral guidelines and guidance as to pre-transport care. Through the SNTS and the Scottish Cooling Group these have been disseminated across Scotland and made easily accessible in each potential referring unit. The precise method chosen to implement therapeutic hypothermia is less of a concern than the need to focus on staff training and patient safety[3].

Implementation of rectal monitoring

In South East Scotland there are no community maternity units, therefore it has been fairly simple to liaise with each potential referring unit to ensure that the means to monitor rectal temperature continuously is available. All units use the same rectal probes as the transport team and have purchased connecting cables to link probes to the existing monitors. Only one monitor type did not accept the standard connection cable but this was easily overcome with the purchase of a small, inexpensive adaptor. These simple measures ensure that rectal monitoring is utilised during passive cooling with the added advantage that the probe does not need to be replaced either on the arrival of the team, or at the receiving unit.

Concerns regarding overcooling

Initially there was great anxiety among transport staff around the potential to overcool infants and therefore during transport infants were only cooled to between 34°C and 34.5°C to avoid subtherapeutic hypothermia. There have been no infants with temperatures recorded below 33°C therefore the target rectal temperature is now 34°C.

If active cooling is required once the team arrives, cool covered gel packs, chemical cold packs or cool bean bag positioning aids can be used. When using these adjuncts it must be remembered not to fully cover the infant with packs in order to still allow heat loss. When cooling any infant the team must have the ability to rewarm the infant if needed – either by increasing the ambient incubator temperature or other means, such as clothing the baby or activating a heated mattress and laying it near the baby (not directly under). Overcooling is a very real risk and transport staff should monitor temperature trends closely, pre-empting overcooling by removing adjuncts before the attainment of goal temperature. The standard team composition for retrieval of a sick infant is two staff, however a third person to monitor temperature alone can be very helpful when stabilising and transferring an asphyxiated infant being cooled by non servo-controlled means.

Practice which may counteract cooling

Securing an infant's endotracheal tube (ETT) in South East Scotland is done using hats, ties and holders. Although ideally the infants requiring therapeutic hypothermia would not wear hats, it was felt that altering ETT fixation at the same time as introducing a new therapy was likely to add to staff anxiety. Therefore currently infants are transported with the usual fixation and the fixation is then changed to exclude the hat once the baby is admitted to the cooling centre. It is acknowledged that while this has not impacted on the ability to cool the whole body, it may have decreased the ability to locally cool the head surface.

Initial concerns were also raised as to the potential detrimental effects of using heated, humidified gases during ventilation, however this has not adversely affected the ability to cool an infant effectively.

Servo-controlled cooling

Hallberg[9] suggests that fluctuations in an infant's temperature may impact on the effectiveness of therapeutic hypothermia. The current literature supporting cooling on transport, by either passive or active means, reflects significant variations in temperature readings even when within the therapeutic range.

SNTS has the benefit of dedicated ambulances, therefore the South East

Scotland team investigated the possibility of providing servo-controlled cooling during transport which offers much improved control over the range of temperature fluctuation. The regional NNU had already purchased two CritiCool™ devices to provide servo-controlled therapeutic hypothermia and allowed the transport team access to one of these. As with all equipment carried in an ambulance the issues of weight, fixation, staff safety and power requirements all had to be considered. The South-East Scotland SNTS team working closely with the Scottish Ambulance Service (SAS) and ParAid (Birmingham, UK) developed a system to provide servo-controlled therapeutic hypothermia during transport. The system was designed to encompass current safety standards; the wheels supplied with the device were removed and it was mounted in a wheeled cage, which was secured firmly into the ambulance using the same system used to secure incubators (**FIGURES 1 AND 2**). The SAS tested this for stability under progressive driving conditions and ParAid undertook computerised crash simulation calculations.

The power requirements were reviewed by the SAS and deemed suitable for use in the ambulance. The CritiCool™ device has no in-built battery power supply, which initially caused concern regarding temperature control during transfer from the nursery to the ambulance. However experience has shown that the time taken from nursery to ambulance, even allowing for a brief visit in labour ward to see the infant's mother, does not cause fluctuations in temperature control. CritiCool™ have developed extra long tubing to reach the incubator from the cooling machine without causing a trip or infection control hazard (another option is to join two lengths of tubing together).

Utilising servo control from the point of transport team arrival, throughout the transport episode and at the receiving cooling centre minimises temperature fluctuations and allows the team to concentrate on provision of all aspects of stabilisation and intensive care more easily. This is an ideal means of cooling but currently requires a dedicated vehicle and instant access to a servo-controlled means of cooling that can be secured safely in the ambulance. This is not yet possible in a front line ambulance, during flight or for MRI, therefore transport teams need to be familiar with the provision of both passive and active cooling with adjuncts, as well as considering their ability to provide servo-controlled cooling during transport.

FIGURE 2 Servo-controlled cooling unit mounted in a wheeled cage and secured within the ambulance.

Conclusion

Therapeutic hypothermia is now an integral part of neonatal care provision for infants who have had either a moderate or severe hypoxic ischaemic insult. Effective hypothermia is considered to have started once the infant's rectal temperature is sustained below 34°C, even if this is prior to arrival at a cooling centre. Initiation of cooling, either by the transport service or in referring units, will be necessary in many instances to ensure that this treatment is commenced before six hours of age. Therapeutic hypothermia can safely be provided during transport whether the team uses passive or active means including servo control.

Acknowledgement

The authors would like to thank Dr Julie-Clare Becher, Consultant Neonatologist, NNU Simpson Centre for Reproductive Health, Royal Infirmary, Edinburgh for her input into the article.

References

1. **Bowman E.D., Roy N.** Control of temperature during newborn transport: An old problem with new difficulties. *J Paediatrics Child Health* 1997;33: 398-401.
2. **BAPM**. *Position Statement on Therapeutic Cooling for Neonatal Encephalopathy* July 2010 Available at www.bapm.org/publications/ (Accessed Jan 31 2011).
3. **Edwards A.D., Brocklehurst P., Gunn A.J. et al.** Neurological outcomes at 18 months of age after moderate ypothermia for perinatal hypoxic ischaemic encephalopathy: synthesis and meta-analysis of trial data. *BMJ* 2010;340-63.
4. **Thoresen M.** Cooling the newborn after asphyxia – physiological and experimental back ground and its clinical use. *Semin Neonatology* 2000;5:61-73.
5. **Jacobs S., Hunt R., Tarnow-Mordi W. et al.** Cooling for newborns with hypoxic ischaemic encephalopathy. *Cochrane Database Systematic Rev* 2007 4;CD003311.
6. **Azzopardi D.V., Strohm B., Edwards A.D. et al.** The TOBY Study Group. Moderate hypothermia to treat perinatal asphyxial encephalopathy. *New Engl J Med* 2009;361:1349-58.
7. **Anderson M.E., Longhofer T.A., Phillips W., McRay D.E.** Passive cooling to initiate hypothermia for transported encephalopathic newborns. *J Perinatol* 2007;27:592-93.
8. **Fairchild K. Sokora D., Scott J., Zanelli S.** Therapeutic hypothermia on neonatal transport: 4 year experience in a single NICU. *J Perinatol* 2009;30:1-6.
9. **Hallberg B., Olson L., Bartocci M. et al.** Passive induction of hypothermia during transport of asphyxiated infants. *Acta Paediatrica* 2009;98: 942-46.
10. **Burnard E.D., Cross K.W.** Rectal temperature in the newborn after birth asphyxia. *BMJ* 1958;2:1197-99.
11. **Bruk K.** Temperature regulation in the newborn infant. *Biol Neonate* 1961;3:65-121.
12. **Erecinska M., Thoresen M., Silver I.A.** Effects of hypothermia on energy metabolism in mammalian central nervous system. *J Cerebral Blood Flow Metabolism* 2003;23:513-30.
13. **Compagnoni G., Bottura C., Cavallaro G.et al.** Safety of deep hypothermia in treating neonatal asphyxia. *Neonatology* 2008;93:230-35.
14. **Kendall G.S., Kapetanakis A., Ratnavel, N. et al.** Passive cooling for initiation of therapeutic hypothermia in neonatal encephalopathy. *Arch Dis Child, Fetal Neonatal Ed* 2010;f1-5.
15. **National Perinatal Epidemiology Unit**. United Kingdom 2008 Available at: http://www.npeu.ox.ac.uk/tobyregister (Accessed January 12, 2011).
16. **Hissink Muller P.C.E., van Berkel L.H., de Beaufort A.J.** Axillary and rectal temperature measurements poorly agree in newborn infants. *Neonatology* 2008; 94:31-34.