

## The Hierarchy of Evidence

**The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynyk and Fineout-Overholt (2011).**

- I** Evidence obtained from a systematic review of all relevant randomised control trials.
- II** Evidence obtained from at least one well designed randomised control trial.
- III** Evidence obtained from well-designed controlled trials without randomisation.
- IV** Evidence obtained from well designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case- series
- V** Evidence obtained from systematic reviews of descriptive and qualitative studies
- VI** Evidence obtained from single descriptive and qualitative studies
- VII** Expert opinion from clinicians, authorities and/or reports of expert committees or based on physiology

Reference <i>(include title, author, journal title, year of publication, volume and issue, pages)</i>	Evidence level (I-VII)	Key findings, outcomes or recommendations
<p>Jacobs S.E., Berg M., Hunt R., Tarnow Mordt W.O., Inder T.E., Davis P.G. (2013). Cooling for newborns with hypoxic ischemic encephalopathy. Cochrane Database Systematic Review. 31 (1)</p>	<p>I</p>	<ul style="list-style-type: none"> <li>- Beneficial in term and late preterm infants with HIE</li> <li>- Reduces mortality without increase in major disabilities in survivors</li> <li>- Benefits outweigh the short term adverse effects</li> <li>- Should be instituted in all term/ late preterm infants showing moderate to severe HIE before 6 hours of age</li> <li>- - Four trials reported the effect of hypothermia on the presence of pulmonary hypertension of the newborn (Shankaran 2002; Eicher 2005; NICHD Study 2005; TOBY Study 2009). Meta-analysis of the four trials showed no significant effect of hypothermia on PPHN of the newborn and therefore it should not be considered as contraindication for therapeutic hypothermia.</li> </ul>

<p>Mosalli, R. (2012) <i>Whole Body Cooling for Infants with Hypoxic Ischemic Encephalopathy</i>. Journal of Clinical Neonatology. 1 (2). 101-106.</p>	<p>I</p>	<ul style="list-style-type: none"> <li>- Pressure area care: Change the position every 6 h during care: flat- supine, right or left side to avoid pressure sores on cold edematous skin.</li> <li>- Fluid Restriction- 40-60mls/kg/day.</li> <li>- Sedation: For ventilated babies, the following should be followed: Give a loading dose of morphine. Then start an infusion at a rate of 10-20mck/kg/min. Consider early weaning after 12 h. At 48 h, discontinuation of morphine should be considered to reduce the risk of accumulation and toxicity. Morphine should be made up in 10% dextrose to avoid hypoglycemia.</li> </ul>
<p>Murray, D. M., O'Connor, C. M., Ryan, A. C., Korotchikova, I., Boylan, G. B. (2016) <i>Early EEG Grade and Outcome at 5 Years After Mild Neonatal Hypoxic Ischemic Encephalopathy</i>. PEDIATRICS. 138 (4)</p>	<p>IV</p>	<ul style="list-style-type: none"> <li>- Survivors of untreated mild HIE, graded clinically or by early EEG have higher rates of disability than their peers and have cognitive outcomes similar to that of children with moderate encephalopathy in an uncooled HIE cohort.</li> </ul>

<p>Laptook et al, (2017) <i>Effect of Therapeutic Hypothermia Initiated After 6 Hours of Age on Death or Disability Among Newborns With Hypoxic-Ischemic Encephalopathy A Randomized Clinical Trial</i>. American Medical Association. 318 (16).</p>		<ul style="list-style-type: none"><li>- Therapeutic Hypothermia initiated at 6 to 24 hours after birth may have benefit but there is uncertainty in its effectiveness. Further research is required to explore the effectiveness of TH in infants &gt;6 hours of age.</li><li>- The results of this trial should not change the priority of early identification of infants with hypoxic-ischemic encephalopathy and initiation of hypothermia at less than 6 hours.</li></ul>
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