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Editorial

Therapeutic hypothermia for hypoxic-ischemic encephalopathy in neonates: To cool or not to cool ?

Thirunavukkarasu Arun Babu[1], Vishnu Ballambattu Bhat[2]*

[1]*Dept. of Pediatrics, All India Institute of Medical Sciences (AIIMS), Mangalagiri, Andhra Pradesh, India*
[2]*Dept. of Pediatrics, Aarupadai Veedu Medical College and Hospital, Vinayaka Mission's Research Foundation-DU, Puducherry, India*

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Hypoxic-ischemic encephalopathy (HIE) in neonates is a critical condition resulting from insufficient blood flow and/or oxygen to the brain around the time of birth. This can lead to severe long-term neurological impairments or even death. In the quest to mitigate the devastating impacts of HIE, therapeutic hypothermia (TH), which involves cooling the whole body of the neonate, has emerged as a vital intervention associated with improved short-term morbidity, mortality, and long-term neurodevelopmental outcomes in term and late preterm babies.[1] Though it has become the standard of care during the last decade for neonates with HIE in developed countries, considerable doubts pertaining to its efficacy still exist, especially in low- and middle-income country (LMIC) settings.[1–3] This article aims to review the currently available evidence to understand the efficacy and safety of TH for neonates with HIE.

TH involves lowering a newborn's body temperature to around 33-34°C for 72 hours shortly after birth. The theoretical foundation of this treatment lies in reducing the metabolic rate of the brain, thereby slowing the cascade of biochemical events that lead to neuronal injury after oxygen deprivation. Numerous randomized controlled trials (RCTs) and subsequent meta-analyses provide robust evidence in favour of TH.[1] Landmark studies such as the NICHD trial, the TOBY trial, and others have demonstrated significant reductions in death and disability among neonates treated with hypothermia compared to standard care.[4–6] Few trials, including the recently published HELIX trial, have cast doubts regarding the efficacy of TH in LMIC settings. The HELIX trial, in particular, created a huge uproar among the scientific community due to serious questions regarding the merits of the study methodology, interpretation of the data, and the biased perspective of the authors.[6,7] The Cochrane review, which aggregated data from multiple RCTs, concluded that therapeutic hypothermia reduces the risk of death or major neurodevelopmental disability at 18 months of age, even in LMIC.[1] A recently published meta-analysis, including pooled data from 2,926 patients from various RCTs, concluded that TH reduces neurologic disability and cerebral palsy, but its effect on short-term and long-term mortality was uncertain.[6]

* *Corresponding author*.
E-mail address: drvishnubhat@yahoo.com (V. B. Bhat).

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Follow-up studies on children who underwent TH as neonates show improved cognitive and motor outcomes. These children are less likely to suffer from severe cerebral palsy, blindness, or severe intellectual impairment. This long-term data strengthens the argument for the widespread adoption of cooling therapy in appropriate clinical settings.[1,6,8] The efficacy of TH is closely tied to the timing of its initiation. Evidence suggests that cooling is most beneficial when started within six hours of birth. Additionally, the therapy is typically reserved for neonates with moderate to severe HIE, as those with mild HIE often recover without intervention, and those with severe HIE might not benefit significantly.[1]

While generally considered safe, TH is not without potential risks. Complications such as arrhythmias, coagulopathies, and infections have been reported. Therefore, continuous monitoring and a well-equipped neonatal intensive care unit (NICU) are essential to manage any adverse effects promptly. Implementing TH requires significant resources, including specialized equipment and trained personnel. In low-resource settings, where such infrastructure might be lacking, the feasibility and practicality of cooling therapy become major concerns.[9] Research is ongoing to explore less resource-intensive methods and to extend the benefits of hypothermia to a broader population.

While the current evidence solidly backs the use of TH for neonates with moderate to severe HIE, ongoing research continues to refine this intervention. Studies are exploring optimal cooling temperatures, durations, and the potential benefits of adjunct therapies.[1,6,10] Additionally, investigations into the genetic and molecular underpinnings of HIE may offer new targets for therapy, potentially enhancing the effectiveness of cooling or providing alternative treatments.

In the debate of "to cool or not to cool," the scales tip favorably towards cooling for neonates with moderate to severe HIE, even in LMIC settings. The currently available negative evidence against TH is not strong enough to recommend stopping its use in HIE babies. The available evidence clearly underscores significant benefits in reducing mortality and long-term neurological impairments. However, it is crucial to balance these benefits with considerations of safety, resource availability, and the specific circumstances of each neonate. As research progresses, the medical fraternity must remain vigilant, ensuring that the implementation of TH is both evidence-based and adaptable to evolving insights. Ultimately, the goal remains clear: to give every newborn the best possible start in life, minimizing the impact of HIE on their future, and TH is unequivocally the best tool we have in our armamentarium at present.

1. Conflict of Interest

None.

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Author biography

Thirunavukkarasu Arun Babu, Professor and Head

Vishnu Ballambattu Bhat, Adviser

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