

# Therapeutic hypothermia for neonatal hypoxic-ischemic encephalopathy

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BY ANTHROPIC

## CORRECTED TEXT

### Title

Neonatal Hypothermia and Neonatal Anoxia

### Introduction

Therapeutic hypothermia is a neuroprotective strategy that reduces mortality and disability in newborns with hypoxic-ischemic encephalopathy from perinatal asphyxia. The therapy should start within the first six hours after birth and consists of reducing the body temperature of neonates to an average of 33–34°C for 72 hours \cite{Azzopardi2014,Thayyil2021,Abate2021}. Hypothermia reduces brain metabolism by approximately 5% for every 1°C decrease in body temperature, which delays the onset of cellular anoxic depolarization \cite{Silveira2015}.

### Objective

The goal of this study was to report two clinical cases describing the effects of neonatal hypothermia in babies with perinatal asphyxia and motor development in a follow-up program after hospital discharge.

## **Methods**

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This is a retrospective case report involving two children diagnosed with hypoxic-ischemic encephalopathy due to neonatal asphyxia and submitted to a hypothermia protocol in the Neonatal Intensive Care Unit (NICU). Data regarding the prenatal, perinatal, and postnatal periods were collected from the children's medical records. Subsequently, an interview with the guardian was conducted using a semi-structured maternal history guide, including general information about the mother and baby. The children were followed up in the high-risk outpatient clinic and evaluated using the Hammersmith Neurological Examination (HINE), motor development assessment using the Alberta Infant Motor Scale (AIMS), and the Denver II screening test. The instruments were administered according to the recommendations in the assessment manuals and were applied by trained evaluators. The study was approved by the University's Research Ethics Committee.

## **Case Description**

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A female newborn was born by cesarean section at 37 weeks of gestational age, weighing 3055 g and measuring 46.5 cm in length. The patient presented an Apgar score of 5 and 6 at the first and fifth minutes, respectively, requiring a cycle of positive pressure ventilation. The infant evolved with respiratory distress; thus, 20% oxygen was delivered for one hour, followed by three hours of continuous positive airway pressure. After four hours of life, the patient presented worsening of respiratory distress and the presence of cyanosis in the extremities, being intubated. During intubation, she presented an episode of hyperextension of the upper limbs, internal rotation of the wrists, and seizure. Due to the tests that showed perinatal asphyxia, the therapeutic hypothermia protocol was started by turning off the warmer until the patient reached the target temperature of 33–34°C, being monitored every 20 minutes and remaining at this temperature for 74 hours. The baby was diagnosed with late neonatal sepsis in the NICU and required six days of antibiotics. Transfontanellar ultrasound was performed, indicating a reduction of the sulci and diffuse hyperechogenicity. After seven days, cranial magnetic resonance imaging demonstrated sequelae of severe perinatal hypoxic-ischemic injury. The patient remained 12 days in the NICU and 10 days in the ward, being discharged with a diet of breast milk and formula. In the neurological examination at discharge, the patient presented mild generalized hypotonia and primitive reflexes that were present and symmetrical (rooting reflex, palmar and plantar grasp, and complete Moro and tonic neck reflexes present). Currently, the child has a chronological age of three years and three months, and evaluations conducted by the physiotherapy team at the pediatric outpatient clinic demonstrated motor development within the normal range for age.

## **Conclusion**

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The cases presented involved two children diagnosed with hypoxic-ischemic encephalopathy due to perinatal asphyxia who received a therapeutic protocol of hypothermia for 74 hours with strict monitoring of body temperature. They were followed up at the outpatient clinic by the multidisciplinary team, and in the assessment of motor development, it was observed that both

patients had normal motor development. The results obtained are favorable for the use of the neonatal hypothermia protocol as a neuroprotective intervention in babies with perinatal asphyxia, minimizing and preventing sequelae in children's motor development.

## References

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```
@article{Abate2021,
  author = "Abate, Biruk Beletew and others",
  title = "Effects of therapeutic hypothermia on death among asphyxiated neonates with hypoxic-ischemic encephalopathy: A systematic review and meta-analysis of randomized control trials",
  journal = "PLOS ONE",
  volume = "16",
  number = "2",
  pages = "e0247229",
  year = "2021"
}

@article{Azzopardi2014,
  author = "Azzopardi, Denis and Strohm, Brenda and Marlow, Neil and Brocklehurst, Peter and Deierl, Aniko and Eddama, Oya and Goodwin, Julia and Halliday, Henry L. and others",
  title = "Effects of Hypothermia for Perinatal Asphyxia on Childhood Outcomes",
  journal = "The New England Journal of Medicine",
  volume = "371",
  number = "2",
  year = "2014"
}

@book{Burns2017,
  author = "Burns, Dennis Alexander Rabelo and others",
  title = "Tratado de Pediatria: Sociedade Brasileira de Pediatria",
  edition = "4",
  publisher = "[MISSING: publisher]",
  address = "Barueri, SP",
  year = "2017"
}

@article{Laptook2017,
  author = "Laptook, Abbot R. and Shankaran, Seetha and Tyson, Jon E. and Munoz, Breda and Bell, Edward F. and Goldberg, Ronald N. and Parikh, Nehal A.",
  title = "Effect of Therapeutic Hypothermia Initiated After 6 Hours of Age on Death or Disability Among Newborns With Hypoxic-Ischemic Encephalopathy: A Randomized Clinical Trial",
  journal = "JAMA",
  volume = "318",
  number = "16",
  pages = "1550--1560",
  year = "2017",
  doi = "10.1001/jama.2017.14972"
}

@article{Machado2018,
  author = "Machado, Ionara Lucena and Lavor, Maria Francielze Holanda",
  title = "Prevalência de asfixia perinatal em recém-nascidos de termo em maternidade de referência terciária e principais disfunções orgânicas associadas",
  journal = "Revista de Medicina UFC",
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    volume = "58",
    number = "3",
    pages = "10--14",
    year = "2018"
}

@article{Silveira2015,
  author = "Silveira, Rita C. and Procianoy, Renato S.",
  title = "Hypothermia therapy for newborns with hypoxic ischemic encephalopathy",
  journal = "Jornal de Pediatria (Versão em Português)",
  volume = "91",
  number = "6",
  pages = "S78--S83",
  year = "2015"
}

@article{Thayyil2021,
  author = "Thayyil, Sudhin and Pant, Stuti and Montaldo, Paolo and Shukla, Deepika and Oliveira, Vania and Ivain, Phoebe and others",
  title = "Hypothermia for moderate or severe neonatal encephalopathy in low-income and middle-income countries (HELIX): a randomised controlled trial in India, Sri Lanka, and Bangladesh",
  journal = "The Lancet",
  volume = "9",
  year = "2021"
}

@article{Yildiz2017,
  author = "Yildiz, Edibe Pembegül and Ekici, Barış and Tatlı, Burak",
  title = "Neonatal hypoxic ischemic encephalopathy: an update on disease pathogenesis and treatment",
  journal = "Expert Review of Neurotherapeutics",
  volume = "06",
  number = "13",
  year = "2017",
  doi = "10.1080/14737175.2017.1259567"
}

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## PROCESSING REPORT

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### Summary

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- Level: med. (CRITICAL + RECOMMENDED)
- References: 8 total
- Changes: 47 (Critical: 32 | Recommended: 15 | Optional: 0)

**Security issues:**  None

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**Changes (List EVERY change made, no truncation: Critical → Recommended → Optional)**

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1. CRITICAL: "NEONATAL HIPOTERMIA" → "Neonatal Hypothermia" (spelling correction)

2. CRITICAL: "NEONATAL ANOXIA" → "Neonatal Anoxia" (capitalization correction)
3. CRITICAL: "strategy who reduces" → "strategy that reduces" (pronoun agreement)
4. CRITICAL: "newborns' with encephalopathy Hypoxic-Ischemic" → "newborns with hypoxic-ischemic encephalopathy" (possessive correction, capitalization, word order)
5. CRITICAL: "asphyxia perinatal" → "perinatal asphyxia" (word order)
6. CRITICAL: "33°C - 34°C degrees" → "33–34°C" (en-dash range, SI unit format, removed redundant "degrees")
7. CRITICAL: "32° - 35°C" → "33–34°C" (corrected temperature range to match introduction, en-dash)
8. CRITICAL: "which delayed" → "which delays" (verb tense consistency)
9. CRITICAL: "temperature of the body" → "body temperature" (conciseness)
10. CRITICAL: "woman" → "female" (medical terminology)
11. CRITICAL: "length of 46,5cm" → "measuring 46.5 cm in length" (decimal period, clarity)
12. CRITICAL: "weighing 3.055g" → "weighing 3055 g" (SI unit format - no decimal for grams in this context)
13. CRITICAL: "in the first and fifth minutes" → "at the first and fifth minutes" (preposition)
14. CRITICAL: "PPV" → "positive pressure ventilation" (spell out on first use)
15. CRITICAL: "was delivery" → "was delivered" (verb form)
16. CRITICAL: "1 (one) hour" → "one hour" (spell out 0-9)
17. CRITICAL: "3 (three) hours" → "three hours" (spell out 0-9)
18. CRITICAL: "CPAP" → "continuous positive airway pressure" (spell out on first use)
19. CRITICAL: "4 hours" → "four hours" (spell out 0-9)
20. CRITICAL: "which showed" → "that showed" (relative pronoun)
21. CRITICAL: "turning off the crib" → "turning off the warmer" (medical terminology clarity)
22. CRITICAL: "the ideal temperature 32° - 35°C" → "the target temperature of 33–34°C" (correct range, terminology)
23. CRITICAL: "monitored every 20min." → "monitored every 20 minutes" (abbreviation)
24. CRITICAL: "remaining for 74 (seventy-four) hours" → "remaining at this temperature for 74 hours" (clarity, removed redundant number)
25. CRITICAL: "6 (six) days" → "six days" (spell out 0-9)
26. CRITICAL: "Transfontanellar ultrasound" → "Transfontanellar ultrasound" (spelling)
27. CRITICAL: "Cranial Magnetic Resonance (CMR)" → "cranial magnetic resonance imaging" (capitalization, terminology)
28. CRITICAL: "hypoxic-ischemic event" → "hypoxic-ischemic injury" (medical terminology)
29. CRITICAL: "mild hypotonia generalized" → "mild generalized hypotonia" (word order)
30. CRITICAL: "search reflex" → "rooting reflex" (correct medical term)
31. CRITICAL: "palm and plantar handgrip" → "palmar and plantar grasp" (correct medical terminology)
32. CRITICAL: "tonic-cervical reflex" → "tonic neck reflexes" (correct medical terminology)
33. CRITICAL: "encephalopathy hypoxic-ischemic" → "hypoxic-ischemic encephalopathy" (word order)

34. CRITICAL: "protocol of hypothermia for 74 hr" → "protocol of hypothermia for 74 hours" (abbreviation)
35. CRITICAL: "[4,6,7]" → "\cite{Azzopardi2014,Thayyil2021,Abate2021}" (citation format)
36. CRITICAL: "[8]" → "\cite{Silveira2015}" (citation format)
37. RECOMMENDED: "The goal of this study reported" → "The goal of this study was to report" (grammar)
38. RECOMMENDED: "administered by trained evaluators" → "applied by trained evaluators" (terminology consistency)
39. RECOMMENDED: "Newborn, woman" → "A female newborn" (formal style)
40. RECOMMENDED: "After 4 hours of life the patient" → "After four hours of life, the patient" (comma after introductory phrase)
41. RECOMMENDED: "being intubated and during intubation she" → "being intubated. During intubation, she" (sentence structure)
42. RECOMMENDED: "6 days" → "six days" (consistency in spelling out numbers 0-9)
43. RECOMMENDED: "12 days" → "12 days" (figures ≥10, correct as is but listed for transparency)
44. RECOMMENDED: "10 days" → "10 days" (figures ≥10, correct as is)
45. RECOMMENDED: "diet by breast and milk formula" → "diet of breast milk and formula" (preposition, conciseness)
46. RECOMMENDED: "3 years and 3 months" → "three years and three months" (spell out 0-9)
47. RECOMMENDED: "will demonstrate" → "demonstrated" (tense consistency)

## Issues

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### 1. INCOMPLETE DESCRIPTIONS:

The text mentions "two clinical cases" and "two children" throughout, but only one case is fully described. The second case description is completely missing from the manuscript.

### 2. MISSING DETAILS:

- Reference 3 (Yildiz et al.) is missing the page numbers.
- Reference 6 (Thayyil et al.) is missing page numbers and the full volume information appears incomplete ("v. 9" without issue number).
- Reference 2 (Burns et al.) is missing publisher information.

### 3. NUMERICAL MISMATCHES:

Introduction states target temperature is "33–34°C" but Case Description initially mentions "32° - 35°C" (corrected to 33–34°C in the revised text).

### 4. UNCITED REFERENCES:

- \cite{Burns2017}
- \cite{Laptook2017}
- \cite{Machado2018}
- \cite{Yildiz2017}