



Hypothermia Therapy for Neonatal Hypoxic Ischemic Encephalopathy in the State of California

Bernardo Kracer, MD¹, Susan R. Hintz, MD, MS¹, Krisa P. Van Meurs, MD¹, and Henry C. Lee, MD, MS^{1,2}

Objective To characterize the implementation of hypothermia for neonatal hypoxic ischemic encephalopathy (HIE) in a population-based cohort.

Study design Using the California Perinatal Quality Care Collaborative and California Perinatal Transport System linked 2010-2012 datasets, we categorized infants ≥ 36 weeks' gestation with HIE as receiving hypothermia or normothermia. Sociodemographic and clinical factors were compared, and multivariable logistic regression was used to determine factors associated with hypothermia therapy.

Results There were 238 reported encephalopathy cases in 2010, 280 in 2011, and 311 in 2012. Hypothermia therapy use in newborns with HIE increased from 59% to 73% across the study period, mainly occurring in newborns with mild or moderate encephalopathy. A total of 36 centers provided hypothermia and cared for 94% of infants, with the remaining 6% being cared for at one of 25 other centers. Of the centers providing hypothermia, 12 centers performed hypothermia therapy to more than 20 patients during the 3-year study period, and 24 centers cared for < 20 patients receiving hypothermia. In-hospital mortality was 13%, which primarily was associated with the severity of encephalopathy.

Conclusions Our findings highlight an opportunity to explore practice-site variation and to develop quality improvement interventions to assure consistent evidence-based care of term infants with HIE and appropriate application of hypothermia therapy for eligible newborns. (*J Pediatr* 2014;165:267-73).

Neonatal hypoxic ischemic encephalopathy (HIE) has an incidence of 1.5 per 1000 live births.^{1,2} Randomized trials have demonstrated the benefit of hypothermia treatment initiated within 6 hours of life in patients with moderate-to-severe HIE on the outcome of death and/or moderate-to-severe neurodevelopmental impairment at 18 months of age.³⁻⁹ Reduction in the relative risk of death or neurodevelopmental impairment of 0.75 (95% CI, 0.68-0.83) and a number needed to treat of 7 (95% CI, 5-10)⁹⁻¹² have established hypothermia as the only effective treatment available.

When new medical therapies are introduced, treatment may not be uniformly applied to eligible infants, may change patterns of disparity in care, or may be applied to patient populations outside of those targeted in the original trial designs. There are limited studies documenting the treatment patterns, sociodemographic characteristics, and mortality rates of term infants with HIE during this era of implementation of therapeutic hypothermia. In the United Kingdom, the UK TOBY Cooling Registry has tracked implementation of hypothermia treatment for HIE since December 2006 before widespread implementation with the intention to audit uptake and implementation.^{13,14} Although they have observed a steady increase over time in registrations for patients treated with hypothermia, they did not collect data on patients with HIE who did not receive hypothermia.

In this population-based study we examined the sociodemographic and clinical characteristics of infants with HIE in California, characterized the use of hypothermia, and compared in-hospital outcomes of infants who received treatment with hypothermia vs those who did not.

Methods

We linked the California Perinatal Transport System and the California Perinatal Quality Care Collaborative (CPQCC) datasets. These quality improvement organizations provide benchmarks, site-specific data reports, and conduct performance improvement activities in perinatal care.¹⁵ The California Perinatal Transport System collects information from 53 transport systems in California and completes a neonatal data transport form for each transported infant. CPQCC collects maternal and neonatal data across 132 neonatal intensive care

From the ¹Department of Pediatrics, Division of Neonatal and Developmental Medicine, Stanford University School of Medicine and Lucile Packard Children's Hospital Stanford, Palo Alto, CA; and ²California Perinatal Quality Care Collaborative, Stanford, CA

Supported by the Department of Health and Human Services Health Resources and Services Administration Centers of Excellence (D34HP16047), from the National Institute of Health Developmental & Neonatal Biology Training Program (HD07249), the Cooperative Multi-center Neonatal Research Network Research Supplement (U10HD027880S1) to promote Diversity in Health-Related Research from the Eunice Kennedy Shriver National Institute of Child Health & Human Development (3U10HD02788019S1), and the Eunice Kennedy Shriver National Institute of Child Health & Human Development grant Number K23HD068400. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Eunice Kennedy Shriver National Institute of Child Health & Human Development. The authors declare no conflicts of interest.

0022-3476/\$ - see front matter. Copyright © 2014 Elsevier Inc. All rights reserved.

<http://dx.doi.org/10.1016/j.jpeds.2014.04.052>

CPQCC California Perinatal Quality Care Collaborative
HIE Hypoxic ischemic encephalopathy
NICU Neonatal intensive care unit

units (NICUs), representing greater than 90% of NICUs in California, and is estimated to cover greater than 95% of NICU admissions.

We examined the outcome of death before discharge by treatment-type hypothermia vs normothermia and risk factors, including the severity of HIE. We also examined the rates of hypothermia for centers by level of encephalopathy. Institutional review board approval was obtained from Stanford University Administrative Panel for the Protection of Human Subjects.

All CPQCC member hospitals participate in standardized data collection via a comprehensive, web-based data entry system.¹⁶ Training sessions promote accuracy and uniformity in data abstraction. Each record has range and logic checks at the time of data collection and closeout, with auditing of records with excessive missing data.

The CPQCC database collects data on infants younger than 28 days of age with a birth weight greater than 1500 g in the event of death, acute transfer, intubated and nonintubated ventilation with a back-up rate for greater than 4 continuous hours, culture-proven early bacterial sepsis, major surgery requiring general anesthesia, and readmission for hyperbilirubinemia greater than 25 mg/dL or requiring exchange transfusion.

Eligibility criteria were gestational age ≥ 36 weeks, birth weight ≥ 2000 g, a diagnosis of HIE, birth in the state of California between January 1, 2010, and December 31, 2012, admission to a CPQCC member NICU, and the absence of congenital anomalies.

HIE was defined in this study, based on the Vermont Oxford Network specifications,¹⁶ as occurring in infants with a gestational age ≥ 36 weeks, with recognized encephalopathy within 72 hours of birth, and 3 or more of the following: arterial cord pH less than 7.00, Apgar score at 5 minutes ≤ 5 , multiorgan system dysfunction, fetal distress on antepartum monitoring, brain imaging scan within 7 days of birth with diffuse or multifocal ischemia or cerebral edema, and/or abnormal electroencephalogram coupled with the absence of an infectious cause, congenital cerebral malformation, or inborn error of metabolism, which could explain the encephalopathy.

The encephalopathy level was categorized as mild, moderate, or severe based on the neurologic state of alert or hyper-alert (normal or exaggerated responsiveness), lethargy or mild stupor (diminished responsiveness), and deep coma or stupor (not arousable), respectively, during the first 7 postnatal days and ascertained by CPQCC coders after chart review. Regardless of the severity, a patient would have been noted to be encephalopathic in the first 72 hours to meet the definition of HIE.

The main outcome measure was the receipt of hypothermia, defined as an intervention in which head-cooling devices or body-cooling blankets and/or ice packs are used to reduce the core body temperature to 33-34°C for whole-body hypothermia or to 34-35°C for selective head hypothermia. Centers that provided hypothermia to at least one

patient during the study period were designated as cooling centers.

Treatment type was characterized by sociodemographic and clinical factors, delivery-room interventions, and respiratory management in the NICU. We assessed potential differences in receipt of hypothermia by the following characteristics: sex, race, ethnicity, prenatal care, maternal age, maternal hypertension, maternal diabetes, perinatal hemorrhage, chorioamnionitis, fetal distress, malpresentation, multiple birth, delivery mode, meconium stained amniotic fluid, birth weight, gestational age, Apgar scores, and early-onset sepsis. Fetal distress was defined based on the presence of documentation in the medical record of fetal distress, poor biophysical profile, or nonreassuring (abnormal) stress test on fetal monitoring or fetal status. Detailed definitions are available in the CPQCC data specification manual.¹⁶

Statistical Analyses

For bivariate comparisons, we used the χ^2 or Student *t* test. The dependent variables of hypothermia treatment and in-hospital death were assessed by stepwise multivariable logistic regression to determine independent risk factors, with estimation of ORs and 95% CIs. Sociodemographic, maternal, and neonatal clinical variables were considered in the models. For the multivariable model for in-hospital death, the main independent variable of interest was level of encephalopathy (mild, moderate, or severe). Records with missing data were incorporated into the crude analyses but were excluded from the regression models (1% of records). Analyses were performed using Stata/SE 13.0 (Stata-Corp, College Station, Texas). Because these were exploratory analyses, no corrections were made for multiple comparisons.

Results

Hypothermia Treatment

During the study period, there were 829 infants with HIE diagnosis and without congenital anomalies, with 238 (29%) neonatal HIE cases in 2010, 280 (34%) cases in 2011, and 311 (37%) cases in 2012. We observed an increase in the number of HIE cases, as well as hypothermia treatment during the study period, that occurred primarily in infants with mild or moderate HIE, with an 17% absolute rate increase in infants with mild HIE, 15% increase in infants with moderate HIE, and 12% increase in infants with severe HIE (Table 1).

There were no differences between the hypothermia vs normothermia groups in terms of sex, race and ethnicity, gestational hypertension, gestational diabetes, perinatal hemorrhage, chorioamnionitis, malpresentation, meconium stained amniotic fluid, fetal distress, birth weight, or gestational age. Maternal age was more advanced in the hypothermia group, which also had greater rates of prenatal care. The majority of infants were delivered via cesarean in both

Download English Version:

<https://daneshyari.com/en/article/4165076>

Download Persian Version:

<https://daneshyari.com/article/4165076>

[Daneshyari.com](https://daneshyari.com)