Pediatrics and Neonatology (2016) 57, 35—40

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.pediatr-neonatol.com

ORIGINAL ARTICLE

Serum Lactate, Brain Magnetic Resonance Imaging and Outcome of Neonatal Hypoxic Ischemic Encephalopathy after Therapeutic Hypothermia

Ming-Chou Chiang [a,b,c,*], Reyin Lien [a,b], Shih-Ming Chu [a,b], Peng-Hong Yang [a,b], Jainn-Jim Lin [c,d], Jen-Fu Hsu [a], Ren-Huei Fu [a], Kuang-Lin Lin [d]

[a] *Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital, Taoyuan, Taiwan*
[b] *Division of Respiratory Therapy, Chang Gung Memorial Hospital, Taoyuan, Taiwan*
[c] *Graduate Institute of Clinical Medical Sciences, Chang Gung University College of Medicine, Taoyuan, Taiwan*
[d] *Division of Pediatric Neurology, Department of Pediatrics, Chang Gung Memorial Hospital, Taoyuan, Taiwan*

Received Oct 28, 2014; received in revised form Jan 13, 2015; accepted Apr 1, 2015
Available online 27 May 2015

Key Words
biomarkers;
hypoxic ischemic encephalopathy;
lactate;
outcome;
therapeutic hypothermia

Background: Serum lactate was used to predict the severity and outcome of neonatal hypoxic ischemic encephalopathy (HIE) before the era of therapeutic hypothermia (TH). There is no report on neurodevelopment (ND) outcome of neonates with HIE treated with TH in Taiwan.
Methods: Between April 2011 and December 2012, newborn infants admitted to Chang Gung Memorial Hospital (CGMH), with gestational age $>$ 35 weeks and birth weight $\geq$ 1800 g, who had acute perinatal events, evidence of significant fetal compromise, and ongoing clinical encephalopathy were prospectively enrolled for TH. Whole body cooling method was used to maintain the affected neonate's esophageal temperature at 33.5 $\pm$ 0.5°C for 72 hours. Demographic data were recorded and hemogram, biochemical parameters, serum lactate, and creatine kinase (CK) were measured as well. Brain magnetic resonance imaging (MRI) was performed between 7 and 14 days of life. ND outcome of infants was evaluated by Bayley Scales of Infant Development, third edition (BSID-III) at 24 months of corrected age. Poor ND (PND) outcome was defined as infants surviving with either disability or ND delay.
Results: Seventeen patients were enrolled. Fifty-nine percent of babies (10/17) were born through cesarean section and 77% of babies (13/17) were transferred from outside hospitals. Six babies were moderate HIE and 11 babies were severe HIE. Among the 14 surviving patients,

* Corresponding author. Division of Neonatology, Department of Pediatrics, Chang Gung Memorial Hospital, 5—7, Fu-Shin Street, Guishan District, Taoyuan 33305, Taiwan.
E-mail address: newborntw@gmail.com (M.-C. Chiang).

http://dx.doi.org/10.1016/j.pedneo.2015.04.008

eight infants had PND outcome. There was no difference in demographic data between infants with and without PND. Serum level of lactate (mg/dL) after 72 hours of TH was higher (35.6 vs. 13.8, $p = 0.042$) in infants with PND. Neonates with abnormal brain MRI findings were also associated with PND ($p = 0.01$).

Conclusion: This is the first report on ND outcome of neonates with HIE treated with TH in Taiwan. Higher serum level of lactate following TH and abnormal results of brain MRI are associated with poor ND outcome.

1. Introduction

Perinatal asphyxia and neonatal hypoxic ischemic encephalopathy (HIE) are associated with high morbidity and mortality rates worldwide.[1,2] Current evidence and guidelines recommend that newly born infants born at or near term with evolving moderate to severe HIE should be offered therapeutic hypothermia (TH).[3–6] Used clinically, TH improves both survival and the neurologic outcomes of those who survive, but the effect is only modest.[7–10] Adjuvant therapies combined with TH are emerging and may improve the outcome of neonates with HIE.[11–13] Hence, it is important to study biomarkers of neonatal HIE which can be used to monitor severity of illness or therapeutic effects when discovering new therapies.

TH for neonatal HIE was introduced into Taiwan in 2010 and only 35.5% of moderate to severe HIE patients received TH between January 2010 and November 2011 in Taiwan.[14] To date, there are no neurodevelopment (ND) outcome data of neonates with HIE treated with TH in Taiwan. The aim of the study was to describe our experiences of TH in managing neonates with HIE and to report the ND outcome of affected infants. In addition, we collected and analyzed parameters and biochemical markers to discover factors associated with the ND outcome.

2. Materials and methods

This prospective study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (CGMH) and was conducted in the neonatal intensive care unit (NICU) at CGMH during the period between April 2011 and December 2012. CGMH is a medical center in the northern part of Taiwan which has approximately 3000–4000 deliveries annually and a level III NICU with 37 intensive care beds as well as 70 intermediate beds. CGMH has an active neonatal transport team and one sixth of the NICU admissions were through neonatal transport. Most of the outside hospitals are located within 30–60 minutes' drive from our hospital.

Newborn infants with gestational age > 35 weeks and birth weight ≥ 1800g, who were affected with moderate to severe HIE,[15] and met the criteria for TH were enrolled. Eligibility criteria were in accordance with the National Institute of Child Health and Human Development trial[7] with modification (Figure 1 and Table 1). In brief, affected infants should have acute perinatal events, evidence of significant fetal compromise, and ongoing clinical encephalopathy. The exclusion criteria in this study include major congenital anomaly, intracranial hemorrhage, availability of 1st hour blood gas with pH > 7.15 and base deficit <10, and refusal of therapy by family.

Once the infant fulfilled the criteria, TH would be commenced within 6 hours of life. Affected newborn infants were cooled by Blanketrol II (Hyper-Hypothermia System, Cincinnati Sub-Zero, Cincinnati, OH) to maintain their esophageal temperature at 33–34°C for 72 hours.[7] Patients would be sedated if they were shivering or became irritable. The patients then were rewarmed slowly (< 0.5°C/h) to 36.5°C. During the hypothermic period, vital signs were recorded every 30 minutes in the first 4 hours, every 60 minutes in 4–12 hours, and every 2 hours in the 12–72 hours. Hemograms, electrolytes, blood sugar, blood gas analysis, creatine kinase (CK), lactate, as well as liver and renal functions, were measured regularly.

Amplitude integrated electroencephalography was used to monitor seizures. Antiepileptic drugs would be prescribed if there was either a clinical or electrographic seizure. Brain ultrasonography was performed before TH to exclude intracranial hemorrhage and congenital anomalies, and brain magnetic resonance imaging (MRI) was performed between 7 and 14 days of age. Abnormal MRI findings were defined as the presence of abnormal signals of the posterior limb of the internal capsule, the basal ganglia, thalami, or watershed areas.

Bayley Scales of Infant Development, third edition (BSID-III) were used to assess ND outcome of surviving infants. Neurodevelopmental delay was defined as presence of any one of the following domains: cognitive scores < 85, language scores < 79, and motor scores < 85 at 24 months of corrected age. In this study, PND outcome was defined as surviving infants with one or more of the following: disability (cerebral palsy, bilateral blindness, or bilateral hearing loss) or delay (no disability but with lower BSID-III scores, defined as previous description).

Statistical analysis was performed with SPSS Statistics version 20 (IBM, Armonk, NY). Continuous variables were analyzed by Mann-Whitney U test and categorical variables were analyzed by Fisher's exact test. Data were presented as median (range). A p value < 0.05 indicated statistical significance.