Brain temperatures during therapeutic hypothermia of birth asphyxia are significantly different in patients with poor outcome versus patients with mild to moderate injury

Stefan Bluml[1,2], Tai-Wei Wu[3,4], Ashok Panigrahy[1,5], John P Grimm[1], Marvin D Nelson[1], Thomas G Perkins[6], Jonathan Chia[6], and Jessica L Wisnowski[1,5]

[1]Children's Hospital Los Angeles/USC, Los Angeles, CA, United States, [2]Rudi Schulte Research Institute, Santa Barbara, CA, United States, [3]Neonatology, Children's Hospital Los Angeles/USC, CA, United States, [4]Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan, [5]Children's Hospital of Pittsburgh, Pittsburgh, PA, United States, [6]Philips Healthcare, Cleveland, OH, United States

Introduction:

Hypoxic-ischemic encephalopathy (HIE) affects approximately 1-6 per 1000 live births in the United States. Therapeutic hypothermia (TH) aims to lower brain temperature to prevent secondary energy failure. However, newborn brain temperature during TH is unknown as generally rectal temperatures are monitored. The goal of this study was to measure brain temperatures and to determine whether the impact of cooling was different in the brains of patients with poor outcome when compared with patients with minor or moderate HIE.

Methods:

A brain phantom was developed to derive a calibration curve for the calculation of brain temperature based on chemical shift differences between the water peak and metabolites in MR spectroscopy. Patients admitted for TH were enrolled and assigned as moderate (M) HIE or severe (S) HIE based on Sarnat staging. All studies were carried-out on a clinical 3T system (Philips Healthcare, Best, The Netherlands). MR examinations were performed during and after TH. For all patients, rectal temperatures were continuously monitored. For studies during TH, cooling was maintained throughout the MR examinations. MR spectra of basal ganglia (BG), thalamus (Thal) and parietal grey matter (GM) were acquired using a single voxel PRESS sequence (TR=2s, TE = 35ms; 128 averages). iNMR software (Mestrelab Research, Molfetta, Italy) was used to determine the chemical shifts. Temperature measurements in the BG, Thal, and GM were averaged for this preliminary report.

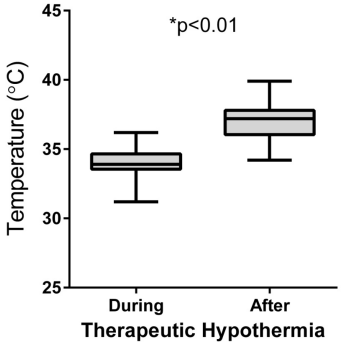

Fig. 1: *Average brain temperatures during and after TH with all patient data were pooled.*

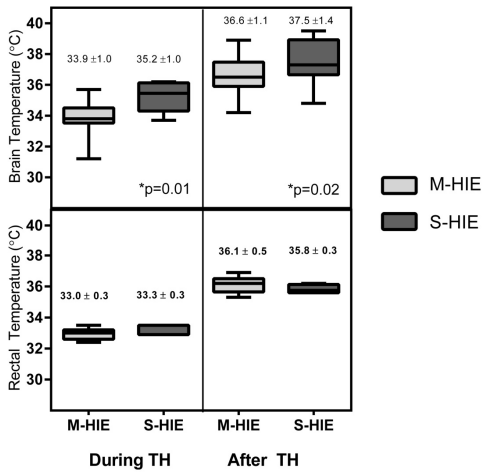

Fig. 2: *Brain and rectal temperatures in S-HIE and M-HIE during and after TH. Whereas rectal temperatures in these two groups were not different, significantly less cooling of the brains was observed in patients that were classified as S-HIE.*

Results:

Eighteen patients (14 M-HIE, 4 S-HIE) were enrolled. Overall, brain temperatures were significantly lower ($p<0.01$) during TH (34.0 ± 1.1°C) than after TH (37.0 ± 1.3°C) (**Fig. 1**) while mean rectal temperature during and after TH was 33.1 ± 0.3°C and 36.1 ± 0.5°C, respectively. Absolute brain temperatures in S-HIE were significantly higher than in M-HIE during (35.3 ± 1 °C vs. 33.9 ± 1°C) and after TH (37.5 ± 1.4°C vs. 36.6 ± 1.1°C) (**Fig. 2**). The brain-rectal temperature gradient was also significantly greater in S-HIE compared to M-HIE during (2.1 ± 1.2 °C vs. 0.8 ± 1°C) and after TH (1.7 ± 1.2°C vs. 0.5 ± 1.1°C).

Discussion:

TH lowered brain temperatures in all subjects. However, patients with S-HIE had significantly higher brain temperature than those with moderate HIE. It thus may be necessary to perform direct brain temperature measurements in individual patients to ascertain that the targeted level of cooling has been achieved. However, it is unclear whether effective lowering of brain temperature by TH would indeed result in better neurological outcomes.

Acknowledgment: Rudi Schulte Research Institute, Gerber foundation, K23NS063371, 1UL1RR031986, and P50NS019632.