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TECHNICAL INNOVATION

Can induced hypothermia be assured during brain MRI in neonates with hypoxic-ischemic encephalopathy?

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Abstract Until now, brain MRIs in asphyxiated neonates who are receiving therapeutic hypothermia have been performed after treatment is complete. However, there is increasing interest in utilizing early brain MRI while hypothermia is still being provided to rapidly understand the degree of brain injury and possibly refine neuroprotective strategies. This study was designed to assess whether therapeutic hypothermia can be maintained while performing a brain MRI. Twenty MRI scans were obtained in 12 asphyxiated neonates while they were treated with hypothermia. The median difference between esophageal temperature on NICU departure and return was 0.1°C (range: −0.8 to 0.8°C). We found that therapeutic hypothermia can be safely and reproducibly maintained during a brain MRI. Hypothermia treatment should not prevent obtaining an early brain MRI if clinically indicated.

Keywords Hypoxic-ischemic encephalopathy · Newborn · Perinatal asphyxia · Hypothermia · MRI

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Introduction

Induced hypothermia is a treatment for neonatal hypoxic-ischemic encephalopathy (HIE) with an accumulating safety and efficacy profile [1–6]. Currently, brain MRI is routinely performed on 4- to 7-day-old neonates receiving therapeutic hypothermia [7–9]. This timing falls in the convenient window after induced hypothermia is complete and before transfer to another care center. This timing is also based on the idea that induced hypothermia might delay the appearance of brain injury and that early imaging while the asphyxiated newborn is treated with hypothermia might not capture the full extent of brain injury [10]. However, there is increasing interest in brain MRI during the first 3 days of life while hypothermia treatment is still being provided to rapidly understand the degree of brain injury, to screen for risks of complications exacerbated by induced hypothermia (e.g., intracranial hemorrhage) and to refine neuroprotective strategies [11–13]. Such early neuroimaging would need to be performed while assuring maintenance of the hypothermia. This study was designed to assess whether hypothermia treatment for asphyxiated neonates can be maintained safely and reproducibly while performing brain MRIs.

Description

We conducted a prospective cohort study of consecutive term neonates with HIE admitted to the neonatal intensive care unit (NICU) who met the criteria for induced hypothermia [2, 3, 5, 6]. Eligible neonates received whole-body cooling to a goal esophageal temperature of 33.5°C with an acceptable range of 32.5–34.5°C per NICU guidelines adapted from Shankaran et al. [3]. Induced hypothermia was initiated by

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6 h of life, continued for 72 h (unless contraindications developed, such as significant hemorrhages or thromboses in the setting of a clinical coagulopathy), and then followed by a slow rewarming [3]. As part of the research protocol [14], sequential MRI studies were planned to clarify the evolution of brain injury during the first month of life and to compare the results of early versus late imaging in this patient population. Each enrolled neonate clinically stable enough to safely tolerate the study underwent one or two early brain MRIs during the first 3 days after birth while receiving the hypothermia treatment. Then they underwent one to two late MRI scans, including a third scan at 8–13 days of age and a fourth at 1 month of age. MRI scans were performed using a 3-T Siemens Magnetom Trio (Siemens Medical Solutions, Erlangen, Germany) with a 32-channel head coil preferentially [15], but otherwise with a standard 12-channel head coil. Each MRI study included anatomical T1- and T2-W imaging, diffusion-weighted imaging, spectroscopy and perfusion-weighted imaging. The protocol was approved by the Institutional Review Board and parental consent was obtained.

Induced hypothermia was continued during the early brain MRI scans (Fig. 1). During the 3-day hypothermia treatment, neonates were maintained on the Gelli-Roll® hypothermia blanket and Blanketrol® III hypothermia system (Cincinnati Sub-Zero Products Inc., Cincinnati, OH, USA) on the radiant warmer with the heat source off. During transport to MRI, the hypothermia system was unplugged while the neonate remained on the hypothermia blanket. Upon arrival to the MRI receiving area, the hypothermia system was plugged back in to maintain the temperature of the hypothermia blanket while the neonate was in the MRI scanner. Neither the hypothermia blanket nor the hypothermia unit is MRI-compatible, therefore they had to remain outside the MRI suite. Neonates were wrapped with one or two thin blankets and placed on a Vac-Fix® MRI-compatible pillow (Bionix, Toledo, OH, USA) containing small polystyrene spheres, which had been stored for 1 h prior to the exam in a 4°C refrigerator and carried the MRI table. The blankets and pillow were kept dry to avoid injury at the site of skin contact. Ears were covered with earmuffs to reduce noise exposure. The MRI-incompatible esophageal probe was removed and an MRI-compatible temperature probe was attached to continuously monitor skin temperature during the MRI exam. The strategy was to add or remove a blanket if the temperature dropped or increased more that 1°C compared to the baseline skin temperature just before MRI. Supportive therapies, including mechanical ventilation, vasoactive infusions and sedation, were maintained throughout the study per current clinical practice. Additional sedation was administered only if deemed clinically necessary and was rarely required. Once the neonate was placed in the MRI scanner, the air in the MRI-compatible pillow was removed by suction to mold the shape of the pillow to the infant's head and body and further reduce motion artifacts. At the end of the MRI study, the neonate was removed from the MRI-compatible pillow and blankets, placed back on the hypothermia blanket and brought back to the NICU. Time and esophageal temperature were measured at the times of NICU departure and return.

Complete imaging and data were available for 20 MRI studies in 12 term asphyxiated neonates treated with induced hypothermia. No adverse events were recorded. The median difference between esophageal temperature on NICU departure and on return was 0.1°C (Fig. 2), with a range of −0.8 to 0.8°C, remaining in the acceptable range of 32.5–34.5°C for all scans except four. Of note, in the patients in whom temperature was outside the acceptable range (first scan for patients 2, 3, 5 and 8), the temperature was already inadvertently out of range before NICU departure, and temperature was readjusted after the MRI. Also of note, skin temperature measured by the MRI-compatible temperature probe remained stable throughout all studies.

The median duration of the total transport from NICU departure to return was 1.9 h (Fig. 2), with a range of 1.3–2.6 h. This included the transport time to and from the MRI area, the time to prepare and transfer the neonate into the MRI scanner and then back into the incubator on the cooling blanket, and the MRI scan time. The MRI scan time was approximately 1 h.

As described in another communication [14], brain injuries were already visible on these early MRI scans in some of the asphyxiated neonates while they were still being treated with induced hypothermia (Fig. 3). No significant motion artifacts were present.

Discussion

For practical reasons, performing brain MRIs is more convenient after induced hypothermia is complete. However, it should not be delayed if an early MRI might be of significant clinical value, for example if there is suspicion of a complication that might be exacerbated by induced hypothermia (e.g., intracranial hemorrhage). We found that therapeutic hypothermia with a goal core temperature of 33.5°C and an acceptable range of 32.5–34.5°C can be safely and reproducibly maintained during an MRI in term asphyxiated neonates. Hypothermia treatment should not prevent obtaining early brain imaging, as hypothermia can be maintained safely during the entire process.

The optimal timing is unknown for brain imaging of term asphyxiated neonates treated with induced hypothermia to accurately define their brain injuries and

Fig. 1 Procedure for performing brain MRI in neonates with hypoxic-ischemic encephalopathy treated with induced hypothermia. **a-b** During hypothermia treatment, neonates are maintained on the hypothermia blanket and hypothermia system in the incubator with the canopy up and the heat source off. During the whole treatment, neonates are monitored by amplitude-integrated electroencephalogram. **c** Materials: an MRI-compatible pillow containing small polystyrene spheres and one to two thin blankets, stored for a few hours prior to the exam in a 4°C fridge, as well as earmuffs and complete MRI-compatible cardiovascular monitoring. **d-h** Neonates are wrapped with blankets and placed on the MRI-compatible pillow. Ears are covered with earmuffs. The MRI-incompatible esophageal probe is removed. Complete MRI-compatible cardiovascular monitoring is placed. **i-k** When the neonate is in place in the MRI scanner, the air in the MRI-compatible pillow is suctioned, and imaging process starts

predict their neurological function [11–13]. Before induced hypothermia was widely offered, the second or third day of life was considered ideal to understand early potential brain injury [16, 17]. However, it has been hypothesized that induced hypothermia might delay the appearance of brain injury and that early imaging while the asphyxiated newborn is treated with hypothermia might not capture the full extent of brain injury [10]. In our feasibility study, we found that MRI scans obtained at 2–3 days of age during hypothermia still seem to predict later brain injuries in asphyxiated newborns and that the brain injuries identified during this early time appear to represent irreversible changes [14]. The late brain imaging studies did not reveal any brain injuries that were not seen earlier, but also did not show that the brain injuries, if present, were underestimated on these early scans [14]. Larger studies would be useful to determine whether early MRIs obtained during hypothermia treatment might allow

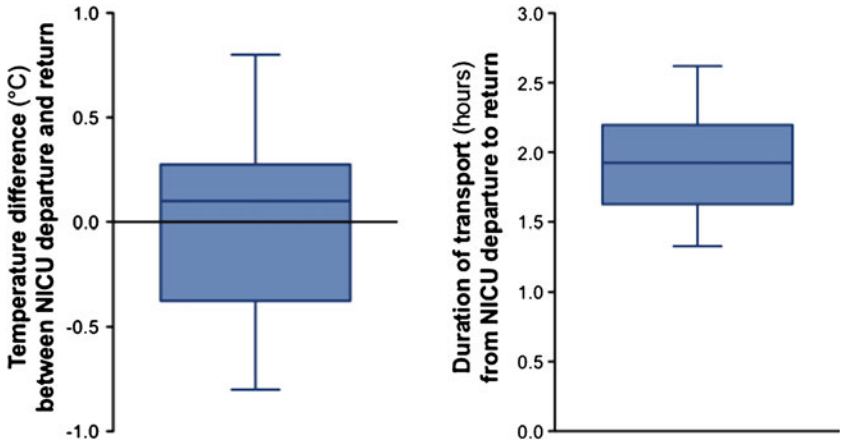

Fig. 2 Duration of total transport and difference between esophageal temperature on NICU departure and return in term asphyxiated newborns treated with induced hypothermia who were undergoing brain MRI. Box and whisker plots (median, 25th and 75th percentiles, minimum and maximum) representation

the refinement of induced hypothermia or suggest the addition of other neuroprotective strategies for preventing further brain injury. In the meantime, in clinical settings where only one brain imaging exam might be obtained, it is certainly reasonable to delay the exam to the second week after delivery, when the lesions are clearly visible on conventional imaging [14].

Median duration of the total transport from NICU departure to NICU return was nearly 2 h. One contribution to our successful maintenance of hypothermia during this prolonged period was our team approach. This team included a neuroradiologist and MRI technician [18] as well as a neonatologist or a neonatal nurse practitioner, NICU nurse and a respiratory therapist, who cared exclusively for the neonate from NICU departure to return. The team was trained in critical neonatal transport to MRI and was aware of the details of providing care for asphyxiated neonates treated with induced hypothermia. Collaboration between neonatology and neuroradiology was focused on minimizing the time outside the NICU. The imaging protocol included all the essential MRI sequences to evaluate brain injury in term asphyxiated neonates (including high spatial resolution T1- and T2-weighted imaging, diffusion-weighted imaging, spectroscopy and perfusion-weighted imaging) [19] while avoiding prolonged time in the MRI scanner, preferably completing the exam in less than 1 h.

In conclusion, therapeutic hypothermia can be safely and reproducibly maintained during brain MRI in term asphyxiated neonates. This treatment should not prevent obtaining an early brain MRI if it is thought to be of important clinical value. Additional studies are needed in neonates to determine the full prognostic value of early imaging during hypothermia treatment.

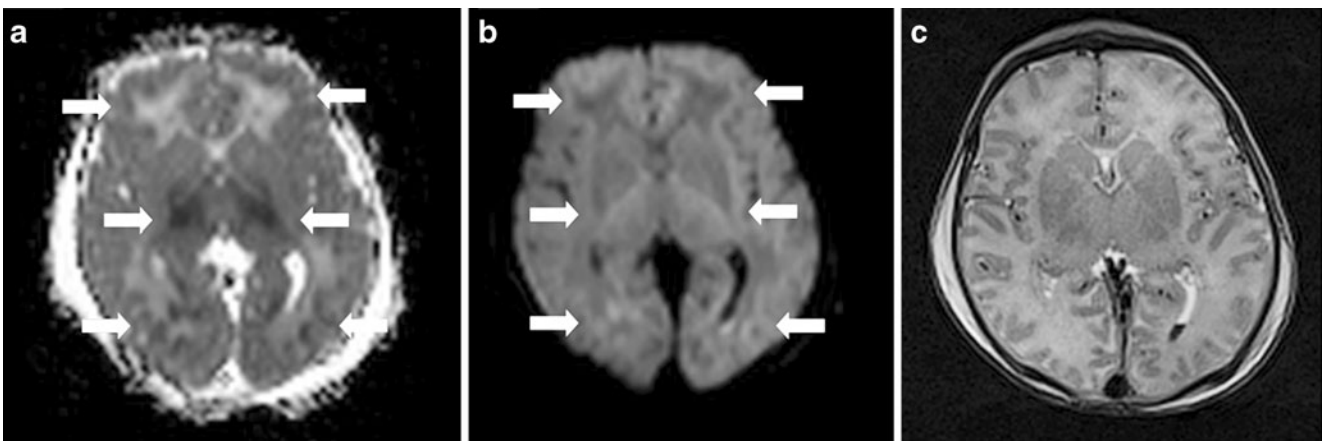

Fig. 3 Brain MRI performed on a 2-day-old newborn demonstrates total cortical injury pattern while he is still receiving therapeutic hypothermia. **a** ADC map. **b** DWI image. **c** T2-weighted imaging. Clear diffusion abnormalities are present in the cortex, white matter and basal ganglia of this newborn as seen on ADC map and DWI images (*arrows*), while findings are not so evident on concomitant T2-W imaging

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Conflicts of interest No conflict of interest. The mention of specific vendors for equipment is solely reflective of equipment usage in our unit. We do not receive any financial or other compensation from any of the vendors mentioned in this review. We realize that there are other vendors who manufacture MR-compatible equipment.

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