Maternal Holding vs Oral Glucose Administration as Nonpharmacologic Analgesia in Newborns: A Functional Neuroimaging Study

Nonpharmacologic analgesia is administered in newborns using, for example, sweet solutions, breastfeeding, or maternal holding. Nonpharmacologic analgesia can decrease pain during minor procedures, such as a heel prick for blood sampling. From a neurophysiological standpoint, a previous study has demonstrated that, during a heel prick, oral glucose administration is associated with no significant cortical activation and therefore may interfere with the pain-associated response at the cortical level. Conversely, breastfeeding analgesia is associated with generalized cortical activation and may act by multisensory stimulation, possibly overwhelming the perception of pain.

We aimed to study the effect of 2 nonpharmacologic analgesic methods (administration of an oral glucose solution and maternal holding) on neonatal cortical activation during a heel prick. We tested the hypothesis that analgesia associated with maternal holding would differ from that associated with oral glucose administration and would be mediated by a difference in cortical activation.

Methods | The independent committee for bioethics of the Institute for Maternal and Child Health, Trieste, Italy, approved the study. Written informed consent was obtained from the parents. We enrolled 40 healthy newborns undergoing a heel prick for metabolic screening on their third day of life. Data were collected from November 1, 2013, through March 31, 2014. Assessment of cortical activation during the heel prick procedure was performed by multichannel near-infrared spectroscopy (ETG-100; Hitachi Medical, Ltd), which continuously monitors concentration changes in cortical hemoglobin from 24 channels. Eighteen near-infrared light emitters and detectors were positioned bilaterally above the parietal, midtemporal, and posterior frontal cortex (Figure 1). Newborns were randomly assigned to receive different nonpharmacologic analgesia. Twenty newborns were given 2 mL of oral glucose solution at a concentration of 20% two minutes before the heel prick, and blood sampling was performed with the newborn lying supine on a changing table. Twenty newborns were held by their mothers, beginning 2 minutes before the heel prick and throughout the procedure. Specifically, the mothers sat comfortably on a chair, kept their dressed newborn in their arms, and were not allowed to talk to him or her. An increase in the oxyhemoglobin (HbO₂) level during the heel prick was considered an estimation of pain. Instead, maternal holding (Figure 2) was associated with a bilateral activation of the left (channel 5: \( t_{18} = -3.837 \) \( P < .001 \); channel 7: \( t_{18} = -2.929 \) \( P = .008 \)) and right (channel 18: \( t_{18} = -3.136 \) \( P = .003 \)) somatosensory cortex and of the posteroinferior right frontal cortex (channel 22: \( t_{18} = -2.686 \) \( P = .008 \)). We found no difference in clinical pain expression between the 2 groups, as measured by the Neonatal Infant Pain Scale.

Discussion | As previously shown, no significant cortical activation was observed during a heel prick using oral glucose analgesia. Thus, the hypothesis that this compound may act by interfering with the cortical processing of pain is further supported. Conversely, maternal holding during the heel prick was associated with cortical activation, particularly in areas associated with the processing of somatic sensations and, in newborns, with affective responses (frontal cortex). We speculate that such analgesia may be mediated by multisensory

Figure 1. Schematic Representation of Placement of Near-Infrared Light Emitters and Detectors

Channels are indicated by their numbers. Optodes were located according to the International 10–20 System for electroencephalography and can be identified by standard letters and numbers. Cz indicates central; F3 and F4, superior frontal; P3 and P4, parietal; and T3 and T4, midtemporal.
stimulation in the context of an emotionally significant attachment relationship between the newborn and his or her mother.6

Stefano Bembich, PhD
Gabriele Cont, MD
Giulio Baldassi, BS
Jenny Bua, MD
Sergio Demarini, MD

Author Affiliations: Division of Neonatology, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy.

Corresponding Author: Sergio Demarini, MD, Division of Neonatology, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Via dell’Istria, 65, i-34137 Trieste, Italy (sergio.demarini@burlo.trieste.it).


Author Contributions: Drs Bembich and Demarini had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Bembich, Bua, Demarini.
Acquisition, analysis, or interpretation of data: Bembich, Cont, Baldassi.
Drafting of the manuscript: Bembich, Bua, Demarini.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Bembich.
Administrative, technical, or material support: Cont, Baldassi.
Study supervision: Demarini.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was supported by grant NR.50/11 from the Institute for Maternal and Child Health, IRCCS Burlo Garofolo.

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.


COMMENT & RESPONSE

Don’t Forget Palliative Patients

To the Editor We appreciate the Viewpoint by Dr Schechter recently published in *JAMA Pediatrics* on the hazards of indiscriminate use of opioids in children.1 He has made major contributions to pain management for children and his words deserve great respect. We accept that pediatricians have insufficient data about the effectiveness of opioids for chronic