Quantitative cerebral tissue oximetry in children with lower respiratory tract infections.

M. Lacerenza[1,&,*], V. Calcaterra[2,3,&], V. Rossi[2], S.Zanelli[2], M. Buttafava[1], M. P. Sormani [4,5], D. Contini[6], A. Torricelli[6,7] and G. Zuccotti[2,8]

[&] These authors contributed equally to this work

[1]PIONIRS s.r.l., 20124 Milano, Italy; [2]Pediatric Department, Buzzi Children's Hospital, 20154 Milano, Italy; [3]Pediatric and Adolescent Unit, Department of Internal Medicine, University of Pavia, 27100 Pavia, Italy; [4]Department of Health Sciences, University of Genoa, Genoa, Italy; [5]IRCCS Ospedale Policlinico San Martino, Genova, Italy; [6]Dipartimento di Fisica, Politecnico di Milano, 20133 Milano, Italy; [7]Istituto di Fotonica e Nanotecnologie, Consiglio Nazionale delle Ricerche, 20133 Milano, Italy; [8]Department of Biomedical and Clinical Science, University of Milan, 20157 Milano, Italy. *lacerenza@pionirs.com

Abstract: An observational study using Time-Domain Near-Infrared Spectroscopy was conducted to compare cerebral tissue oxygenation between healthy controls and children with lower respiratory tract infections (LRTIs). Cerebral tissue oxygenation was one of the predictors of LRTIs.

1. Introduction

The incidence of low respiratory tract infections (LRTIs) in childhood has decreased, thanks to improvements in immunization, nutrition, and socio-economic conditions. However, LRTIs remain the leading cause of mortality and morbidity in childhood [1]. In fact, lung damages are difficult to recover, therefore children are more susceptible to reinfection or multi-pathogen invasion, and more severe lung injuries [1]. Early identification and management of pediatric patients at risk for respiratory impairment are crucial for preserving long-term lung and brain health. However, determining the level of severity in a pediatric patient remains challenging due to the lack of high-level evidence and quantitative comprehensive data [1].

LRTIs contribute to hypoxia due to mechanisms such as impaired ventilation and ventilation-perfusion imbalances [2]. The brain's susceptibility to hypoxia underscores the importance of neuromonitoring to anticipate and mitigate potential complications.

Cerebral monitoring through Near-Infrared Spectroscopy (NIRS) is widely utilized in neonatal and pediatric intensive care units; however, its application in outpatient evaluations or routine health monitoring remains limited. Using time-domain (TD) NIRS, it is possible to noninvasively evaluate oxyhemoglobin concentrations (O_2Hb) and deoxyhemoglobin (HHb) at peripheral tissue and brain level providing greater accuracy and reproducibility of measurements [3] with low sensitivity to motion artifact and superficial tissue layers featuring better reliability of oximetry measurements. In particular, TD-NIRS has been used to study cerebral tissue oxygenation ($StO_2=O_2Hb/(O_2Hb+HHb)$) as a biomarker for brain physiological status.

The aim of this study was the assessment of cerebral StO_2 using a portable TD-NIRS tissue oximeter, in pediatric population with a concurrent LRTIs. Early identification of altered brain cortex StO_2 can potentially improve outcomes in these vulnerable patients, with the possibility to enable personalized treatments.

2. Methods

We conducted an observational case-control study with age and sex-matched groups (30 subjects for each group). Both patients and controls were enrolled among children (aged 0-18 years) admitted to the Pediatric Department of Buzzi Children's Hospital in Milan, Italy, from December 2023 to May 2024. Specifically, the cases were admitted because of concurrent LRTIs (pneumonia or bronchiolitis). After receiving information about the study, all participants or their caregivers provided written informed consent. The Ethics Committee Milano Area 1 approved the protocol (No. 0004021/2023). The study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2008.

We employed the NIRSBOX (PIONIRS S.r.l., Milan, Italy), a commercially available TD-NIRS device for research purposes. This system features two picosecond lasers operating at 685 nm and 830 nm, paired with a flexible, biocompatible probe ('Goccia' G5, PIONIRS S.r.l.) offering a 2.5 cm source-detector separation

The measurement of the tissue optical properties is non-invasive. The device provides continuous real-time monitoring of concentration of O_2Hb, HHb, total hemoglobin (tHb= O_2Hb +HHb) and StO_2. More details can be found in reference [3]. Data obtained by the NIRSBOX tissue oximeter were only recorded and not considered in therapeutic decisions.

The optical probe was manually held in place by the clinical operator during measurements in two locations: the left middle upper arm (below the deltoid region), and the left frontotemporal cortex (Fp1 of the 10/20 EEG system mapping). For each location, the protocol included five consecutive probe repositioning and for each repositioning the measurement lasted 5 s at 1 Hz acquisition frequency.

Demographic and physiological data were compared between LRTIs subjects and healthy controls. A multivariate logistic regression model was used to investigate the independent ability of each parameter to discriminate cases and controls. The model built was than evaluated using a confusion matrix, accuracy, specificity, and the area under the receiver operating characteristic curve (AUC).

3. Results and discussion

The demographic and physical characteristics of the two groups were comparable, with no significant differences observed, thereby reducing the potential for confounding factors Pediatric patients diagnosed with LRTIs exhibited elevated respiratory rates, reduced peripheral oxygen saturation (SpO_2, 97.1% vs 98.6%; p = 0.0003), and decreased cerebral tissue saturation (StO_2, 61.9% vs 65.3%; p = 0.001). Notably, no significant variations were observed in tissue oximetry parameters measured at the upper arm location. The multivariate analysis achieved an accuracy of 87%, including: respiratory rate, heart rate, StO2, SpO2, head circumference and height as regressors. Respiratory Rate and cerebral StO_2 emerged as the strongest predictors, while SpO_2 retained moderate significance, the other variables showed p-values < 0.05.

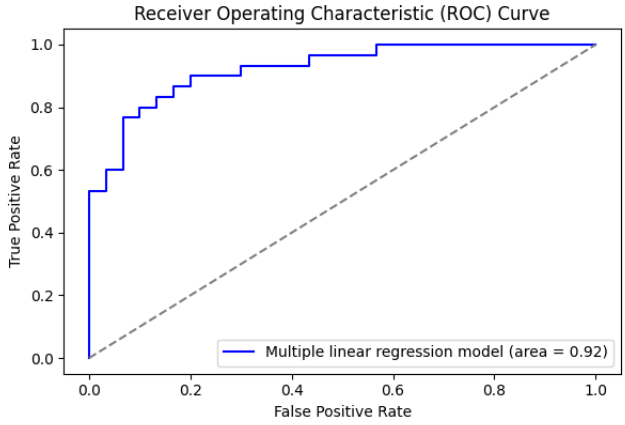

Figure 1: Receiver Operating Characteristic (ROC) curve resulting form the multiple linear regression model.

4. Conclusions

This investigation underscores the distinction in cerebral StO_2 levels between pediatric LRTI cases and healthy controls. Integrating cerebral StO_2 into a multivariate logistic regression model improved diagnostic accuracy from 80% to 87%, surpassing the performance of traditional clinical parameters alone. . Interestingly, hematocrit levels and peripheral tissue saturation are not significant predictors for distinguishing LRTIs from controls. These findings show the potential value of integrating cerebral StO_2 metrics into management of pediatric patient with respiratory infections.

[1] Guo, J. et al., “Lower Respiratory Tract Infections in Early Childhood,” The Lancet 2023, **402**, 2194–2195.
[2] Bhutta, B. et al. *Hypoxia* Book available online: https://www.ncbi.nlm.nih.gov/books/NBK482316/ (accessed on 29 July 2024).
[3] Calcaterra, V. et al., “Reference Values for Cerebral and Peripheral Tissue Oximetry in Children: A Clinical TD-NIRS Study,” Acta Paediatr. 2024, apa.17459.