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DO SLOW AND SMALL OXYGEN CHANGES AFFECT THE CEREBRAL CYTOCHROME OXIDASE REDOX STATE MEASURED BY NEAR-INFRARED SPECTROSCOPY?

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1. INTRODUCTION

Cytochrome oxidase ($CytO_2$), an enzyme of the mitochondrial electron transport chain, is responsible for the majority of cellular oxygen consumption. The change of the redox state of the CuA center of the $CytO_2$ can be detected by near infrared spectroscopy (NIRS). NIRS techniques make it possible to non-invasively measure quantitative changes in $CytO_2$ concentration[1,2]. As cellular oxygen levels are well above the saturating concentration, it might be expected that $CytO_2$, in vivo, would have a very low level of reduction and would be insensitive to small changes in oxygen supply during normoxia. From isolated mitochondria Km is 0.01 kPa[3] and the critical PaO_2 0.9kPa[4], therefore changes in $CytO_2$ redox state are only expected to occur in severe hypoxia. However, in vivo studies with optical spectrophotometry have not confirmed these hypotheses. In adult subjects the $CytO_2$ redox state is altered by changing the arterial oxygen saturation (SaO_2)[5], which may be explained by the concept that some cells are always at the verge of compromised oxygenation, because cells have different distances to the nearest blood vessel. In contrast, neonatal studies on the influence of changes in SaO_2 did not reveal any reproducible and systematic correlation of SaO_2 and $CytO_2$ redox state[6]. Therefore the importance of measurements of $CytO_2$ is very controversial and direct validations of the data have not yet been performed[7].

The aim of this study was to evaluate changes of cerebral $CytO_2$ redox state, induced by slow and small changes in SaO_2, and to investigate the influence of different algorithms to calculate changes in $CytO_2$ concentration.

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2. METHODS

During the first two days of life, in 22 mechanically ventilated preterm neonates (mean gestational age 30.4±3.4weeks, birth weight of 1539±706g) a minimum of 6 slow O_2 changes (ΔSaO_2>1.5%) was achieved by altering the inspired O_2 fraction (Fig. 1). The infants were asleep. SaO_2 was measured by pulse oxymetry (Hellige SMK132 or Nellcor N-200) on the right hand and kept between 85 and 95%. The pCO_2, measured by continuous transcutaneous CO_2-monitoring (Hellige, Germany), was constant during the whole procedure. Arterial blood pressure was monitored (Hellige SMK 132, Germany) via an intra-aortic catheter. Cerebral parameters were measured by a Critikon 2020 Cerebral RedOx Monitor at four wavelengths at 776.5, 819.0, 871.4 and 908.7nm. Neonatal blood contains fetal hemoglobin with a higher O_2 affinity than adult hemoglobin. This leads to a lower pO_2 in neonatal tissue.

Critikon algorithm: The goal of the Critikon algorithm is to determine cerebral concentrations of hemoglobin without the influence of the superficial layers, which is achieved using a multi-distance approach and a coupling compensation system. The algorithm is described in detail in the literature[8]. The absorption spectra were taken from the literature: hemoglobin[9], $CytO_2$[10].

UCL algorithm: If only the signal from detector at 37mm is analyzed, the Critikon instrument is technically equivalent to systems such as the Hamamatsu (Japan) NIRO 500 (wavelengths: 775, 810, 870, 904nm), and NIRO 300 (wavelengths: 775, 807, 850, 913nm) or the Critikon 2001 (UK). The algorithm corresponds to the UCL4 algorithm[11] and implements the absorption spectra supplied by Hamamatsu.

The data were averaged over 10s. The beginning and end of an O_2 change was identified by looking at the SaO_2 trace only.

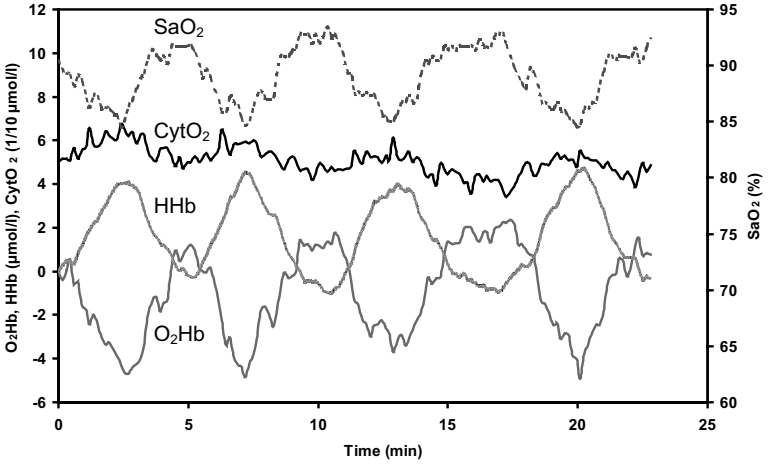

Figure 1. Typical slow oxygen changes. Arterial oxygen saturation (SaO_2), oxyhemoglobin (O_2Hb), deoxyhemoglobin (HHb) and cytochrome ($CytO_2$).

A program was used to calculate the difference between the beginning and end, and the mean for SaO_2, O_2Hb, HHb, tHb = O_2Hb+HHb, $CytO_2$, heart rate, blood pressure, and pCO_2. Variables were examined using bivariate linear regression analysis (SPSS, NJ,