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Review

Near-infrared spectroscopy: Applications in neonates

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S U M M A R Y

Near-infrared spectroscopy (NIRS) offers non-invasive, in-vivo, real-time monitoring of tissue oxygenation. Changes in regional tissue oxygenation as detected by NIRS may reflect the delicate balance between oxygen delivery and consumption. Originally used predominantly to assess cerebral oxygenation and perfusion perioperatively during cardiac and neurosurgery, and following head trauma, NIRS has gained widespread popularity in many clinical settings in all age groups including neonates. However, more studies are required to establish the ability of NIRS monitoring to improve patient outcomes, especially in neonates. This review provides a comprehensive description of the use of NIRS in neonates.

1. Introduction

Adequate tissue oxygenation is a prerequisite for aerobic metabolism [1]. Occult regional dysoxia associated with ischemia–reperfusion is a major contributor to morbidity and mortality in critically ill patients, with both subnormal and supranormal tissue oxygenation being detrimental. End-organ perfusion and oxygenation is indirectly monitored by means of systemic blood pressure, heart rate, arterial oxygen saturation, hemoglobin concentration, and mixed venous oxygen saturation (SvO_2). Direct, non-invasive, real-time assessment of tissue oxygenation is desirable in critically ill neonates. In 1999, a workshop convened by the NICHD and NINDS recommended that near-infrared spectroscopy (NIRS) can be used to conveniently quantitate cerebral oxygenation continuously at the bedside without the risk associated with traditional invasive studies [2]. NIRS has the potential to monitor regional oxygen saturation (RSO_2) in multiple organs, with cerebral ($cRSO_2$), renal ($rRSO_2$), and splanchnic ($sRSO_2$) oxygenation being the most frequently monitored in neonates [3]. This article provides a brief synopsis of the principles of NIRS and clinical applications in neonates.

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2. Principles of near-infrared spectroscopy

NIRS, introduced in 1977 as a technology that is capable of continuous non-invasive monitoring of oxygenation in living tissue, is based on the transparency of biological tissue to light in the near-infrared spectrum (700–1000 nm wavelength) and its differential absorption by chromophores including hemoglobin, myoglobin, and cytochrome aa3 [4–8]. Light absorption by hemoglobin is an order of magnitude greater than that of cytochrome aa3. NIRS devices use NIR light at wavelengths of maximal absorption for the relevant chromophores, generally 700–850 nm, where the absorption spectra of oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) are maximally separated with minimal overlap with that of water (980 nm) [8] (Fig. 1).

Early NIRS devices used two wavelengths, limiting their use to the measurement of two chromophores, O_2Hb and HHb [8]. The addition of more wavelengths, through additional light sources that emit light at discrete wavelengths, or by broadband spectroscopy systems, improves accuracy. One of the most commonly used NIRS devices, IN Vivo Optical Spectroscopy (INVOS) System [Covidien, Dublin, Ireland (formerly Somanetics, Troy, MI, USA)], has a light-emitting diode (LED) that emits NIR light of two wavelengths (730 and 810 nm), and two optodes to receive the scattered light (Fig. 2) [7]. The proximal or shallow detector receives a signal from the peripheral tissue and the distal or deep detector receives a signal from the peripheral and deep tissues; by subtracting the proximal from the distal value, tissue-specific RSO_2 at a depth of about 1–2 cm is obtained [9]. Because the tissue microcirculation contains arterial, venous, and capillary components, RSO_2

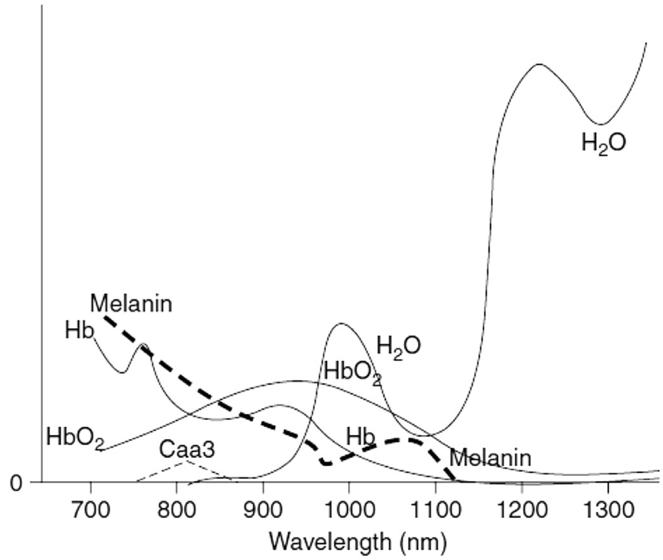

Fig. 1. Absorption spectra for oxygenated hemoglobin (HbO_2), deoxygenated hemoglobin (Hb), Caa3, melanin, and water (H_2O) over wavelengths in NIR range. Note the relatively low peak for Caa3. Commercial cerebral NIRS devices currently utilize wavelengths in the 700–850 nm range to maximize separation between Hb and HbO_2. The presence of melanin as found in human hair can significantly attenuate Hb, HbO_2, and Caa3 signals. (Reproduced with permission by Oxford University Press from: Murkin JM, Arango M. Near-infrared spectroscopy as an index of brain and tissue oxygenation. Br J Anaesth 2009;103 Suppl 1:i3–13.)

represents a 'weighted average', with approximately 75–85% of the signal originating from venules. As opposed to pulse-oximeters which subtract out non-pulsatile flow, NIRS devices focus on the total light signal [10]. Accordingly, pulse oximetry provides measurement of arterial oxygen saturation (SO_2) reflecting only oxygen supply to tissue, whereas NIRS-measured RSO_2 reflects the balance of local tissue oxygen supply and demand. Thus, NIRS is considered complementary to pulse oximetry.

A modification of the Beer–Lambert law ($A = \alpha BdC + G$) describes the relationship between the absorption of NIR light and the absorbing chromophore's concentration in tissue, where A is the attenuation measured in units of optical density, α is the specific absorption coefficient of the chromophore at a particular wavelength (L/μmol/cm), B is the differential pathlength factor (DPF), d is the distance between NIRS optodes (cm), C is the concentration of the chromophore in the tissue (mmol/L), and G is an additive term that represents the scattering losses of NIR light as it passes through the tissue. All coefficients in the equation, except for the DPF, are known constants or can be measured. Difficulty in determination of DPF and its variation between subjects has been a major obstacle to standardization of NIRS parameters across subjects and the clinical application of NIRS [10]. Consequently, NIR spectrometers commonly used in clinical practice avoid the need to estimate optical path-length by measuring only the ratio of O_2Hb to HHb, rather than their absolute concentrations. Because the change in the intensity of the reflected light depends on the O_2Hb to HHb ratio, an oxyhemoglobin saturation can be derived:

$$RSO_2 = \frac{HbO_2}{(HbO_2 + HHb)}$$

Fractional tissue oxygen extraction (FTOE), a measure for the amount of oxygen extracted by the tissue, can be computed from RSO_2 and arterial oxygen saturation (SO_2) thus: [$FTOE = (SO_2 - RSO_2)/SO_2$] [11]. Regional FTOE gives an estimate of the balance between local oxygen delivery and consumption [6].

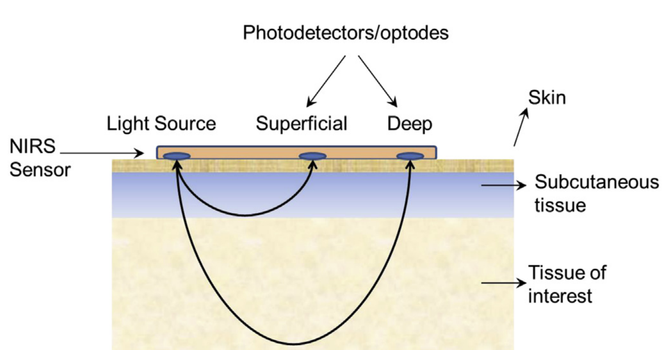

Fig. 2. IN Vivo Optical Spectroscopy (INVOS) System (Covidien).

3. Devices

In recent years, NIRS has evolved from an experimental tool to a clinical monitoring device with broad potential use [1]. Improvements in design have resulted in smaller, cheaper, resilient monitors without the need for calibration and improved user interfaces. Specialized mini-probes are available for neonates.

NIRS monitors are available from different manufacturers (Table 1) [1,8,10,12,13]. The INVOS oximeter was the first to be approved by the US Food and Drug Administration in the 1990s, reinvigorating clinical interest in NIRS. It is the most common oximeter in clinical use today. It utilizes two LED sources and two photodetectors (described above). In contrast, the Fore-Sight cerebral oximeter (CAS Medical Systems, Branford, CT, USA) uses a four-wavelength (690, 779, 808, and 850 nm) laser source and two photodiode detectors 1.25 and 4 cm from the source, providing an absolute measurement of RSO_2. The Nonin Equanox 7600 (Nonin Medical Inc., Plymouth, MN, USA), utilizes four LEDs (730, 760, 810, and 880 nm) in a dual-emitter/dual-detector sensor. Some manufacturers are combining NIRS and other technology into devices with multimodal capability [8]. Using a combination of NIR light and ultrasound, CerOx (Ornim Medical Ltd, Lod, Israel) provides assessment of brain oxygenation and blood flow.

Existing devices incorporate the same technology but with differences in the number and absolute value of wavelengths, as well as in computational algorithms to translate measured changes in light attenuation to a physiologic measure such as changes in O_2Hb and HHb concentrations and RSO_2. Thus, comparing devices from different manufacturers can be difficult. In a bench study to evaluate test–retest variability of NIRS-measured $cRSO_2$ using the INVOS 5100 and the NIRO 300 cerebral oximeters in anaesthetized children [14], a wide range of values were obtained with poor agreement between the devices. Similarly, a comparison of peripheral muscle RSO_2 ($pRSO_2$) in adults using three NIRS oximeters showed significant pair-wise differences in median values, repeatability, and/or dynamic measurements [12]. Highly significant differences have also been reported between $cRSO_2$ readings obtained with different probes [15]. The large range of RSO_2 values obtained with different sensors and oximeters in otherwise healthy subjects makes it difficult to define a normal range of $cRSO_2$ and has limited widespread clinical implementation [14]. When RSO_2 is used for trend monitoring, the reproducibility of measurement is less important; but good reproducibility is paramount if RSO_2 is to be used as a spot measurement or if the monitoring is started when the patient status is uncertain, e.g. on admission to critical care.