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Review article

EVALUATION OF INTRA-MUSCLAR OXYGENATION DURING EXERCISE IN HUMANS

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Abstract
Near infrared spectroscopy (NIRS) has been frequently used to assess intra-muscular oxygenation past few decades. In recent years, refinement of NIRS hardware and algorithms used to convert changes in optical absorption to changes in concentration improved the validity of oxygenated haemoglobin (HbO_2), deoxyhaemoglobin (Hb), myoglobin (Mb) and the oxidised copper compound of cytochrome aa_3, (cyt aa_3) measurements. Subsequently, the use of NIRS to study the muscle oxygenation profiles during various types of exercise and to monitor differences in oxygenation levels in patients under various pathological conditions is being increased. It would be thought-provoking to combine future muscle studies with MRS and/or electromyography techniques to improve the understanding of intramuscular oxygenation.

KEY WORDS: Near infrared spectroscopy, muscle oxygenation.

İNSANLARDA EGZERSİZ SIRASINDA KAS İÇİ OKSİJENLENMENİN DEĞERLENDİRİLMESİ

Özet
Geçtiğimiz birkaç on-yıldan beri kas-içi oksijenlenmeyi değerlendirmede "near infrared spektroscopy" (NIRS) yöntemi sıklıkla kullanılmaktadır. Son yıllarda NIRS cihazlarının ve bunlarda kullanılan optik absorbsiyon değişikliklerini konsantrasyon farklarına çeviren algoritmaların gittikçe gelişmesi oksijenlenmiş hemoglobin (HbO_2), oksijensiz hemoglobin (Hb), miyoglobin (Mb) ve okside bakır bileşiği olan sitoktom aa_3, (cyt aa_3) ölçümlerinin güvenilirliğini arttırmıştır. Böylece NIRS farklı egzersiz tiplerinde kas içi oksijenlenme profillerini ortaya koymanın yanı sıra değişik patolojik bozuklukları olan hastalarda oksijenlenme düzeylerini gözlemede kullanılması giderek artmaktadır. Gelecekteki kas çalışmalarında NIRS ile beraber MRS veya elektromiyografi tekniklerini birleştirmek kas içi oksijenlenmenin anlaşılmasını geliştirmede yeni çarpıcı düşüncelerin oluşmasına yol açabilir.

ANAHTAR KELiMELER: Near infrared spectroscopy, kas oksijenizasyonu.

Introduction

In human body, muscle cell is a the leading oxygen consumer during aerobic energy production process i.e. oxidative metabolism. The extraction of O_2 from blood by muscle cells and the blood flow dictate the rate of O_2 utilization ($QO0_2$). Near infrared spectrophotometry (NIRS) provides a relatively new technology capable of continuous non-invasive monitoring of changes in tissue (O_2 stores and O_2 availability at the cellular level) (Piantadosi et al., 1986; Hampson et al., 1987; Jöbsis-Vanderviliet et al., 1988). It works on the fact that biological tissues are relatively transparent to light of the near infrared region of the spectrum (wavelength between 700-l000 nm) and therefore NIRS can be used to measure muscle oxygenation up to 8 cm of tissue (Wilson et al., 1989; Chance et al., 1992). Light in the visible region (wavelength between 450-700nm), on the other hand, is strongly absorbed in tissue and therefore fails to penetrate more than approximately 1 cm of tissue.

In biological tissues, there are compounds whose absorption of light is oxygenation-status dependent. Such compounds in muscle tissue are oxygenated haemoglobin (HbO_2), deoxyhaemoglobin (Hb), myoglobin (Mb) and the oxidised copper compound of cytochrome aa_3, (cyt aa_3, the terminal member of the mitochondrial cytochrome chain). Information can be obtained about the oxygenation state of the tissue by determining the concentration of these variables. The near infra-red (NIR) absorption characteristics of the tissue therefore give information about the presence of these compounds within it.

The absorbence of deoxygenated Hb peaks at a wavelength of 760 nm, while that of oxygenated Hb is highest at 850 nm. The isobestic point for the oxygenated and deoxygenated forms of Hb occurs at 798 nm (Chance et al., 1992; Mancini et al., 1994). Since the near infrared absorption spectrum of Mb overlaps with that of Hb, changes in tissue saturation monitored at 760 nm and 850 nm are attributed to the desaturation of both Hb and Mb (De Blasi et al., 1993). Studies on isolated muscle preparations have indicated that approximately 65%-75% of the deoxygenation observed during exercise is due to the release of oxygen by Hb, while the balance is due to that released by Mb (Wilson et al., 1989; Chance et al., 1992).

In practice, absorption at several different wavelengths is measured and an algorithm is used to convert changes in optical absorption to changes in concentration (Seiyama et al., 1988; Wilson et al., 1989). In doing so, it is possible to display the changes occurred in the concentrations of different variables of interest (e.g. HbO_2, Hb, HbT-total hemoglobin-, representative response are presented in Figure 1) during experiment graphically, and, an event marker allows specific points (e.g. onset or end of exercise and MVC, etc) to be recorded for future reference.

The reliability and validity of NIRS technology in evaluating muscle oxygenation levels during exercise has been established (Wilson et al., 1989; Mancini et al., 1994; Sako et al., 2001). One of the limitations of NIRS is that oxygen uptake in intact human muscle (mVO_2) cannot be calculated because the effective path length of the NIRS signal cannot be readily quantified (Mancini et al., 1994). However, this technique can provide important information about the profile of muscle oxygenation during exercise and recovery. Furthermore, it enables us to better understand the physiological factors influencing exercise performance when used in combination with cardiorespiratory and metabolic measurements.

A number of scientists have therefore used NIRS to study the muscle oxygenation profiles during incremental and square-wave exercise in various forms, such as cycling (Wilson et al., 1989; Chance et al., 1992; Mancini et al 1994; Belardinelli et al 1995a; 1995b; Matsui et al., 1995; Costes et al., 1996; Bhambhani et al., 1997; 1998; 2001), rowing (Chance et al., 1992), arm cranking (Jensen-Urstad et al., 1995; Ogata et al., 2002) and speed skating (Rundell et al., 1997). In addition, the acute changes in muscle oxygenation that occur during isotonic grip exercise (Hamaoka et al., 1996; Kutsuzawa et al., 2001), upper extremity weight-lifting exercise (Tamaki et al., 1994) and isometric contractions of the forearm (Hampson and Piantodosi, 1988; De Blasi et al., 1993; Murthy et al. 1997) and knee extension exercise (Sahlin, 1992; Quarisema et al., 2001) have been documented. In clinical studies this technique has been used to establish differences in respiratory muscle (Mancini et al., 1991) and working muscle (Wilson et al., 1989; Matsui et al., 1995) oxygenation levels between healthy subjects and patients with heart failure . It seems, therefore, that NIRS can be a useful tool in the evaluation of exercise performance.

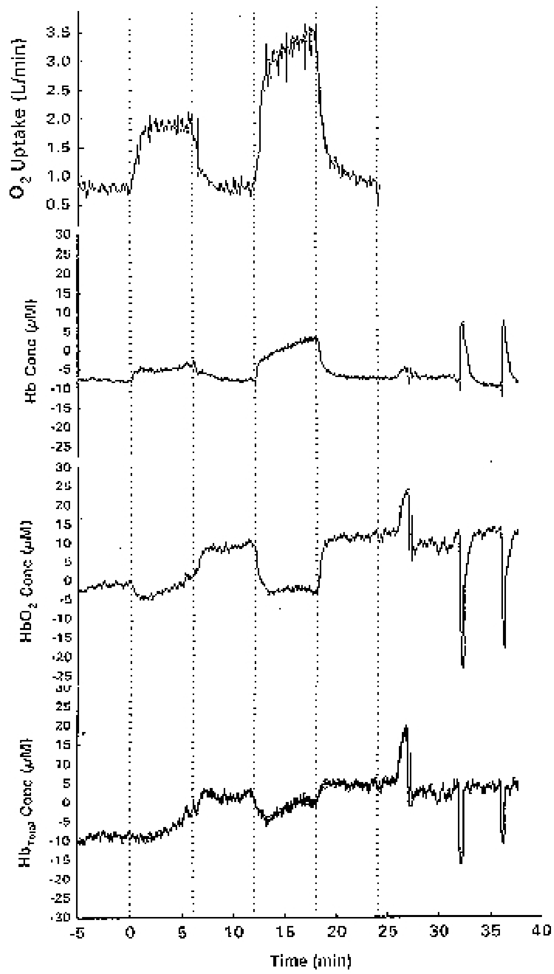

Figure 1. The comparison of VO_2, Hb, HbO_2 and HbT profiles during moderate and very heavy constant-load exercise.

Muscle oxygenation profiles during sub- and supra-θ_l exercise

Several experiments have been performed using the NIRS technique during muscular exercise in humans in order to gather some information as to what is occurring within the muscle at varying workloads. An extensive analysis of the oxygen supply and demand in near maximal exercise has been performed by Chance et al. (1992), with the aim of understanding the post exercise responses in terms of repaying the energy cost incurred. They presented data regarding the changes in deoxygenation profile and blood flow as the work rate increased, and the signals from different muscles were compared simultaneously.

Wilson et al. (1989) examined the oxygenation levels in the vastus lateralis muscle during an incremental work test on a cycle ergometer comparing healthy controls against patients with heart failure. They examined the metabolic exercise responses with respect to oxygenation in a group of patients suffering severe exercise intolerance due to their pathological condition. They were able to demonstrate that both patients and controls had similar levels of Hb desaturation when reached exhaustion, but the heart failure patients reached this level sooner than the controls.

To use NIRS technique efficiently for observing the intramuscular oxygenation changes during exercise, it is important to combine it with the breath by breath gas exchange analysis technique. Combining both techniques, Kawaguchi et al. (2001) reported that kinetics of peripheral muscle oxygenation reflect systemic VO_2. Belardinelli et al. (1995a) examined the desaturation response of the vastus lateralis muscle during four periods of steady state cycling at four different work rates. They tested if there was any evidence to support the hypothesis that the slow component of oxygen uptake at heavy work rates is related to the progressive desaturation of haemoglobin, facilitated partly by the Bohr effect consequent to the muscular lactic acidosis. The group was able to demonstrate a decrease in oxygen saturation that occurred gradually in proportion to the increasing work rate. Additionally, at sub-θ_L work rates the level reached a minimum and stayed either constant or began to return to baseline. However, the level of desaturation continued to fall throughout the period of exercise at supra-θ_L work rates. In conclusion, these results were considered consistent with the hypothesis by the group.

Belardinelli et al. (1995b) also studied the intramuscular oxygenation response profile of incremental exercise test. They particularly studied the lactate threshold (θ_L), testing whether any relation between intramuscular oxygenation profile and the θ_L exists. Therefore, they investigated the hypothesis that lactic acidosis causes a shift in the haemoglobin dissociation curve and is closely related to such a break point in this curve. The lactate threshold was estimated by a V-slope plot and the time at which the θ_L occurred was analysed for significant events in the desaturation of the vastus lateralis muscle. As discussed, one limitation of NIRS work is that without a specific experiment to determine the differential path-length the results are not quantitative, and thus cannot be compared between individuals. As a result of this the group scaled all NIRS results to the maximum and minimum readings that they recorded. From this experiment the group were able to show that with progressive increase in work rate the level of oxygenation within the muscle decreased. Significantly, they were able to show that the desaturation curve consisted of two components, with an increase in the rate of desaturation occurring very slightly before the detection of the θ_L at the mouth. They proposed that this accelerated desaturation marks the onset of the lactic acidosis.

Bhambhani et al. (1997) reported evidence for significant changes in the NIRS signal at the lactate threshold. They designed a study, using NIRS and breath by breath analysis, in which subjects performed incremental exercise tests where the same rate of increment was used in each experiment. This is in contrast to the study of Belardinelli et al. (1995b) in which different rates of incrementation had been used. The group demonstrated four phases of oxygenation in an incremental exercise test, with the notable absence in about half of their experiments, of the components that Belardinelli et al. (1995b) have reported. The group also argued that at the onset of exercise there is a transitional increase in the signal for oxygen saturation, attributable to an increase in the blood supply to the working muscles. However, as the exercise progresses the blood pool in the vastus lateralis muscle begins to become increasingly desaturated, until it reaches a minimal level, at or near exhaustion. Critically, these investigators state that as the level of saturation falls after an initial increase, it is the point at which it crosses its baseline level that is significant “crossing point” – although it is not clear what this actually represents physiologically. The lactate threshold was estimated by a computer, using the V slope method and the group has shown that the θ_L occurs at or just after the point where the near infra-red signal crosses the baseline.

Chance et al. (1992) and Matsui et al. (1995) also have documented the NIRS trend exercise as a four-phase response. They reported in phase I, there was an immediate, rapid increase in absorbency from the resting baseline values at the onset of zero load exercise, implying an increase in muscle oxygenation relative to this level. In phase II there was a steady decline in tissue absorbency that continues beyond the resting baseline value as the power increased, suggesting a decrease in muscle oxygenation relative to this value. In phase III, absorbency readings tend to level off with increasing power output until VO_{2max} is attained. In phase IV (during recovery), there was a very rapid increase in the absorbency that extends above the maximum values observed in phase I. This response, which has been attributed to hyperaemia (Chance et al., 1992), tends to level off after the first 2-3 minutes into the recovery phase.

The results of all these experiments are encouraging as they show the potential of NIRS to present a non-invasive method for detecting a number of events in exercise testing as long as the appropriate device is chosen to evaluate the intramuscular oxygenation profile. However, these studies used the "Runman" which provides a single output estimate of the near infra-red assessment: it is not possible, for example, using this device to detect the influence of the increase in blood volume *per se* on the oxygenation profile (Chance et al., 1992; MacDonald et al., 1999). It is advisible, therefore, to choose a NIRO 500 (Hamamatsu) device, which enables to monitor continuously the deoxyhaemoglobin, oxyhaemoglobin and total haemoglobin concentrations in the interrogation field of the muscle throughout the experiment.

Conclusion

Interestingly, almost all of the above studies concentrated on lower extremities, exclusively on vastus lateralis. It is generally assumed that only leg muscles are working and the upper extremities are resting during leg exercise cycling. To date, there is only a few study focused on the upper extremity oxygenation profile during leg exercise cycling (e.g. Özyener et al., 1999). Hence, the "resting" situation of the upper extremities remains to be demonstrated. Especially, any extra work done by the upper body could contribute to the emergence of the VO_2 slow component and provide important insight into the energetics of muscle.

It is salient to note, therefore, that NIRS could play an important role to enhance scientific understanding of oxidative metabolism in healthy muscle as well as the pathological effects on damaged muscle tissue. To combine future muscle studies with MRS and/or electromyography techniques could provide valuable insights into muscle energetics and mechanisms coupling intramuscular oxygenation with pulmonary oxygen uptake.

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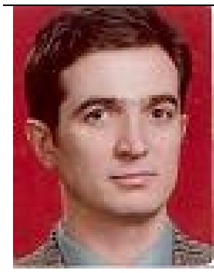

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