FUNCTIONAL EVALUATION OF OXIDATIVE METABOLISM IN PATIENTS WITH METABOLIC MYOPATHIES

Grassi Bruno¹, Porcelli Simone¹, Marzorati Mauro², Lanfranconi Francesca¹, Vago Paola¹, Marconi Claudio², Morandi Lucia³
(University of Milano¹, Istituto Bioimmagini e Fisiologia Molecolare – CNR², Istituto Neurologico Carlo Besta³, Italy)

The aim was to evaluate two non-invasive methods of functional evaluation of skeletal muscle oxidative metabolism in patients with metabolic myopathies, such as mitochondrial myopathies (MM) and miophosphorylase deficiency (McArdle’s disease, McA). In these patients the impaired oxidative metabolism is the key pathophysiological mechanism of the disease and is responsible for the reduced exercise tolerance, which significantly contributes to the patients’ reduced quality of life.

Two variables were evaluated: 1) Skeletal muscle oxygenation indices during exercise, taken as an evaluation of the capacity of O2 extraction, and obtained by near-infrared spectroscopy (NIRS). 2) Kinetics of adjustment of O2 uptake (VO2) during the transition from rest to exercise. Experiments were conducted on 12 MM, 6 McA, 36 patients with reduced exercise tolerance or other signs/symptoms suggesting a metabolic myopathy but in whom muscle biopsy did not allow a diagnosis of any myopathy (patient-controls, P-CTRL), 20 healthy untrained controls (CTRL).

Maximal aerobic power (VO2peak), taken as an index of exercise tolerance, was significantly lower in MM (21.8±4.2 ml/kg/min; x±SE) and McA (18.8±3.3) than in P-CTRL (31.1±1.8) and CTRL (36.3±1.8). Also the values of the NIRS-derived index of O2 extraction (concentration changes in deoxygenated hemoglobin and myoglobin, Delta[deoxy(Hb+Mb)], expressed as a percentage of the maximal values obtained during transient limb ischemia) were significantly lower, at peak exercise, in MM (25.3±12.0 %) and McA (18.7±7.3) than in P-CTRL (62.4±3.9) and CTRL (71.3±3.9). Highly significant relationship was observed between Delta[deoxy(Hb+Mb)] peak and VO2 peak (r²=0.81). The data suggest that in MM and in McA the non-invasive determination by NIRS of a muscle oxygenation index such as Delta[deoxy(Hb+Mb)] peak allows to identify and quantify the impaired capacity of O2 extraction during exercise. VO2 kinetics were slower, as shown by the significantly higher time-constants, in MM (51.3±5.1 s) and McA (58.1±8.3) compared to P-CTRL (35.7±2.0) and CTRL (34.7±2.6). Slower VO2 kinetics indicate an impaired skeletal muscle oxidative metabolism. The time-constants of the VO2 kinetics were significantly related (r²=0.42) to the NIRS-derived index of impaired capacity of O2 extraction.

Conclusions. Both proposed methods of functional evaluation seem capable of identifying and quantifying the impairment of oxidative metabolism in MM and McA. The possibility to serially monitor such impairment by non-invasive tools should be of great interest for clinicians, who need an objective, quantitative and longitudinal evaluation of the impairment to be used in the follow-up of patients, as well as in the assessment of therapies or other interventions.

Keywords: Near Infrared Spectroscopy, Biomove session, Applied Physiology

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