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ScienceDirect

Neuromuscular Disorders 26 (2016) 47–55

www.elsevier.com/locate/nmd

Evaluation of muscle oxygenation by near infrared spectroscopy in patients with facioscapulohumeral muscular dystrophy

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Received 24 June 2015; received in revised form 1 October 2015; accepted 14 October 2015

Abstract

The purpose of the study was to determine muscle metabolism adaptation to exercise in facioscapulohumeral muscular dystrophy patients (FSHD) and to study the correlation with clinical functional status (6-min walk test).

8 FSHD patients and 15 age-matched healthy controls (Controls) performed two isokinetic constant-load knee extension exercises: (1) at 20% of their maximal extensors' peak torque (i.e. the same relative workload) and (2) at (20N·m) (the same absolute workload) for up to 4 min. All exercises consisted of rhythmic, voluntary, isokinetic, concentric contractions of the quadriceps femoris at 90°/s, whereas the flexion was performed passively at the same speed. Muscle oxygenation in the vastus lateralis was evaluated using near-infrared spectroscopy (NIRS).

The FSHD patients displayed a lower maximal peak torque than controls (−41%, $p < 0.05$). During the two-exercise modalities, deoxygenated haemoglobin (HHb) and total haemoglobin volume (tHb) were lower in the FSHD patients ($p < 0.05$). The initial muscle deoxygenation time delay was shorter in the control group (FSHD: 15.1 ± 4.1 s vs. controls: 10.4 ± 2.1 s, $p < 0.05$). Mean response time and maximal peak torque were both correlated with functional impairment (walking endurance).

The results suggest that FSHD patients present an impairment in their capacity to deliver or to use oxygen.

Keywords: Neuromuscular disease; Muscle oxygenation; Near-infrared spectroscopy; Exercise

1. Introduction

Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant inherited muscular dystrophy and affects about 1 in 20,000 people worldwide [1]. Symptoms may develop in early childhood but generally appear after adolescence. FSHD is characterised by a progressive asymmetric muscle weakness (due to fibre degeneration) in the facial muscles, shoulder girdle and arms [2]. In addition, muscle weakness develops in other areas and the lower limbs can be affected, leading to loss of mobility in 20% of patients. Potential complications include severe muscle weakness, wheelchair use and postural problems leading to a sedentary lifestyle. Hence, the ability of patients to perform physical activity is limited and contributes to a decreased quality of life [3,4]. Understanding the mechanisms involved in the physical weakness is thus a major issue.

The altered physical ability during exercise may result from a limited oxygen uptake within the active muscles in this population. Recent studies have shown an increased oxidative stress and mitochondrial dysfunction correlated to parameters of muscle function in patients affected by FSHD [5,6]. The impairment of one or more metabolic or mitochondrial pathways may result in an energy deficiency that could be a feature of muscle impairment. To investigate this hypothesis, near-infrared spectroscopy (NIRS) has been widely used for monitoring local muscle oxygenation in healthy subjects and in patients with various neuromuscular, metabolic, vascular or respiratory diseases [7–9]. More specifically in the field of neuromuscular disease, NIRS has been used almost exclusively to evaluate the muscular oxygen uptake capacity in patients with muscular metabolic disorders [10,11]. During an incremental exercise test, patients with muscular metabolic diseases display lower levels of deoxyhemoglobin (HHb) – perhaps as a result of a defect in oxygen uptake [7]. In patients

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http://dx.doi.org/10.1016/j.nmd.2015.10.004

0960-8966/

with myopathies, Quaresima et al. did not observe any difference in muscle oxygen levels and muscle blood volume when comparing children suffering from Duchenne muscular dystrophy and healthy children during treadmill exercise performed at the same absolute velocity [12,13]. Sander et al. observed similar levels of muscle deoxygenation in Duchenne muscular dystrophy patients and in healthy controls during a grip strength effort performed at the same relative resistance [14]. Using a 5-min isokinetic leg extension exercise trial, Allart et al. [8] reported that patients suffering from Becker muscle dystrophy (BMD) did not differ from their healthy counterparts in terms of peak HHb levels or blood volume. In contrast, the time course of the initial muscle de-oxygenation (as measured by NIRS) appeared to be faster in BMD patients and associated with disease severity and functional impairment. The authors suggested that it may have been due to the O_2 supply defect induced by the impaired vasodilation [8]. All together, these results suggest that muscular O_2 uptake disorders reported during exercise may appear very specific to the concerned myopathy: either characterised by impaired vasodilation (oxygen delivery) or limited by muscular metabolic alterations (O_2 consumption).

While FSHD is not known to be associated with impaired vasodilation, a better understanding of the mechanisms involved in the reduced physical ability of this population will be important in developing adapted training protocols. The objective of this study was to compare muscle oxygenation kinetics between FSHD patients and healthy subjects. We hypothesised that: (i) changes in muscle oxygenation during effort in FSHD patients will differ from their healthy counterparts and (ii) muscle oxygenation kinetics will reflect the functional capacity (distance covered during a 6-min walking test).

2. Patients and methods

2.1. Subjects

Eight male patients and fifteen age-matched healthy male controls were enrolled in this study between February and May 2014. Patients were medically followed-up in the referral centre for neuromuscular disease at Lille University Medical Center (Lille, France). The inclusion criteria included genetically confirmed FSHD, the ability to walk with or without a technical aid and a quadriceps strength rating of at least 4/5 according to Medical Research Council scale in at least one leg. Only male subjects were included in order to compare our results to our previous study conducted with patients affected by Becker muscular Dystrophy [8]. Control subjects had to be sedentary, i.e. less than one hour of physical activity per week. Subjects presenting local knee osteo-articular pain, other neurological disease, dyspnoea above 2 according to NYHA classification, cardiovascular contraindications for exercise or peripheral arterial vascular disease were excluded from the study. Written informed consent was obtained before participation. The study was performed in accordance with the Declaration of Helsinki.

Table 1
Anthropometric characteristics and extensor peak torque of the FSHD subjects and controls.

	Age (years)	Weight (kg)	Height (cm)	Peak torque (N.m)
FSHD group	36 ± 5	69 ± 5	172 ± 6	75 ± 21
Control group	38 ± 6	73 ± 6	176 ± 9	182 ± 54*

The values are expressed as mean ± SD.
* Significantly different between the FSH group and Control group ($p < 0.05$).

Anthropometric characteristics of patients and controls are presented in Table 1. FSHD symptoms lasted for 14 ± 8 years, the Brooke and Vignos functional scales were used to grade arm and leg function, respectively [15]. Five of 8 patients were scored either 1 or 2 for arm function (i.e. they were able to raise the arms and touch the hands together above the head) – and scored 1 in their legs (i.e. they were able to walk and climb stairs without assistance). The 3 other patients were scored 3 for the arm function (i.e. they were unable to raise the hands above the head but were able to raise an 8-oz glass of water to the mouth) and were scored 2 in the legs (i.e. they were able to walk and climb stairs with aid of railing).

2.2. Exercise protocol

Subjects performed exercise trials on a CON-TREX isokinetic dynamometer (MEDIMEX ®, Sainte Foy les Lyon, France) in knee mode. Subjects sat on the CON-TREX device with back reclined at 90° and were strapped according to the manufacturer's recommendations. The device was then calibrated according to manufacturer's instructions. The knee range of motion was set from 10 to 100° of flexion for all subjects and all assessments were made on the stronger leg. Exercise trials consisted in rhythmic, voluntary, isokinetic, concentric contractions of the quadriceps femoris at an angular velocity of 90°/s, whereas the flexion was performed passively at the same speed (Fig. 1).

Subjects were first familiarised with the experimental protocol by means of two practice runs of five submaximal repetitions, with a 30-s interval between runs. Maximal muscle

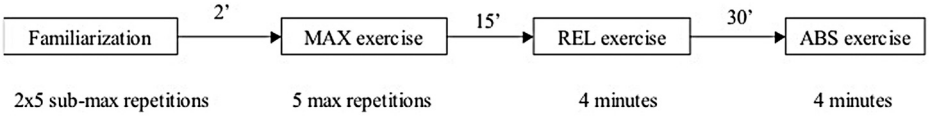

Fig. 1. Protocol design. MAX exercise: determination of the maximal peak torque; REL exercise: at the same relative load (20% of the maximal peak torque); ABS exercise: at the same absolute workload (20 N.m). The text under the boxes describes the exercise time or repetitions number and the text between the boxes indicates the rest period.