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Original Article

Energy expenditure, body composition, and prevalence of metabolic disorders in patients with Duchenne muscular dystrophy

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ABSTRACT

Introduction: Duchenne muscular dystrophy (DMD) is a severe muscular disease characterized by progressive loss of functional muscle mass followed by changes in body composition.
Aim: To describe body composition, resting energy expenditure (REE), and metabolic disorders in DMD patients followed-up at a tertiary care center. To analyze the association with type of steroid and ambulatory status, and to compare obese DMD patients with patients with multifactorial obesity.
Population and methods: A prospective, observational, cross-sectional study was conducted. Anthropometric measurements were taken, evaluating body composition with bioelectrical impedance analysis (BIA), REE with indirect calorimetry, and biochemical parameters in all DMD patients seen between June 2013 and April 2014.
Results: 63 boys between 5.4 and 18.7 years of age were evaluated. Diagnosis of obesity ranged from 28% measuring body mass indexZ-score (BMIZ-score) to 70% using percentage of fat mass (%FM). Patients who had lost gait had a significantly higher %FM than those in whom gait was preserved (72% vs 46%, $p < 0.05$).
Insulin resistance was present in 29% associated with BMI Z-score and waist circumference and 40% had dyslipidemia associated with %FM, both of which were steroid independent. In obese DMD patients REE was lower than predicted and also lower than controls, and persist when dividing the patients into ambulators and non-ambulators.
Conclusions: A high prevalence of obesity was observed. BMI-Z-score underestimates the degree of FM. No correlation was found between steroid type and body composition or metabolic disorders. No differences were found in REE between ambulators and non-ambulators. Obese DMD patients have a lower REE than controls.

1. Introduction

Duchenne muscular dystrophy (DMD) is a severe neuromuscular disease of recessive X-linked inheritance caused by a mutation of the dystrophin gene (Xp21.2) and characterized by the progressive loss of functional muscle mass. This degenerative process starts at birth and progresses over the first two decades of life leading to gait loss, deterioration of respiratory muscles, and heart failure [1]. DMD is estimated to affect 2–3 each 10,000 live born boys.

In patients with DMD secondary effects of their disease are changes in body composition with increased total fat mass and decrease of lean mass resulting in less physical exercise, lower baseline resting energy expenditure (REE), and a risk of developing obesity [2] The main goal in the management of these patients is to try to preserve fat-free mass and avoid excessive weight gain.

Nevertheless, the methods to assess nutritional status may be imprecise [3] and measurement techniques applicable in the general population are inadequate in patients with this disorder [4], making it difficult to interpret markers to evaluate nutritional status [5]. These children often appear to have a normal weight according to their body mass index (BMI), but have excessive fat

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mass which is not observed because of these body composition changes.

Al together, this causes a risk of overestimating energy requirements leading to the development of obesity and secondary metabolic and non-metabolic complications, such as greater gait and passive motion difficulties, orthopedic alterations, and decreased autonomy further affecting quality of life [6].

Corticosteroid treatment has been shown to lead to initial improvement of muscle strength and reduce loss of muscle mass over time. The mechanism of action has not been elucidated; however, it has been suggested that steroids may suppress the inflammatory response and there is evidence that microfibers are replaced [7].

Although the prevalence of obesity is high in DMD, there are many studies about the associated metabolic risks or the use of steroids in the treatment of the disease, with controversial results.

In the multidisciplinary care for these patients nutritional status should be addressed from the moment of diagnosis.

Considering these data, we studied the body composition, baseline REE, and the presence of metabolic disorders in boys with DMD.

2. Main aim

The main aim of the study was: 1) to describe body composition, REE, and metabolic disorders in a series of patients with DMD in follow-up at our center; 2) determine body composition using biometric impedance analysis (BIA); 3) to compare body composition by type of steroid and ambulatory status and 4) to compare obese DMD patients with an age-matched group of patients with multifactorial obesity.

3. Methods

A prospective, descriptive, observational, and cross-sectional study was conducted. All children and adolescents with DMD in follow-up at Day Hospital of Hospital de Pediatría Juan P. Garrahan for management by the multidisciplinary team were consecutively enrolled in the study from June 2013 to April 2014.

The study was approved by the ethics committee of the hospital and informed consent was signed by all the participants.

Anthropometric variables were recorded: Weight was measured on a calibrated electronic stretcher scale to the nearest 100 g. In ambulatory patients height was measured using a wall-mounted altimeter to the nearest mm and in non-ambulatory patients, arm span be measured calculating the distance between the tips of the middle fingers with the arms maximally extended at shoulder level. Percentiles were calculated using the weight-for-age and length-for-age Charts 0–60 months of the World Health Organization (WHO) while after 61 months of age the Argentinean charts were used [8]. BMI was calculated as weight/height^2 and percentiles were computed based on WHO standards. Weight was classified as *low* in patients with a BMI < 5th percentile, *normal* if BMI was from the 5th to <85th percentile, *overweight* when BMI was from the 85th to <95th percentile, and *obese* when BMI was ≥95th percentile.

In ambulatory patients, waist circumference was measured with an inelastic measuring tape midway between the lowest rib and the iliac crest. Central obesity was defined as a waist circumference >90th percentile according to the reference values [9].

Arterial pressure was measured with a cuff covering 2/3 of the arm in a sitting position and after 10 min of rest. Percentiles were calculated according to the reference values of the TaskForce [10]. Arterial hypertension (AHT) was defined as systolic and/or diastolic hypertension of ≥95th percentile.

Presence of acanthosis was also recorded. Patients were classified as prepubertal or pubertal according to Tanner stage.

Serum glucose was measured using the glucose-oxidase method, insulin using radioimmunoassay (RIA) with a commercial kit, total cholesterol and triglycerides using the colorimetric method Color-CHOD-PAP, and HDL and LDL cholesterol using the CHOD-PAP method with heparin precipitation. Dyslipidemia was defined as: HDL < 40 mg% and/or triglycerides > 110 mg% [11]. Samples were taken after a 12-h fast in all cases.

Insulin resistance (IR) was estimated using the homeostatic model assessment (HOMA) method) [12] using the following formula:

Fasting insulin (μU/ml) x fasting glucose (mg/dl/18)/22.5.

IR defined as a HOMA value of ≥2.5 (>2 DS of the mean value in a control population) [13]. Patients were classified into three groups according to fasting glucose levels into *normal* < 100 mg/dl, *impaired fasting glucose*100–126 mg/dl, and *diabetes* > 126 mg/dl [14].

Body composition was determined with a single-frequency BIA device using the equation by Houtkooper et al:

Fat free mass = 0.61H2/R + 0.25 W + 1.31 [15]

To define %FM as pathological the 90th percentile of the reference values by McCarthy et al. [16] was used as a cutoff point.

Measurement of REE:

REE was calculated using indirect calorimetry, with a gas exchange analyzer to measure oxygen use and carbon dioxide production (CCM Express de MEDGRAPHICS; MGC Diagnostics Corporation, Saint Paul, MN, USA). The measurement was performed for 20 min after a 20-min rest. The Schofield formula [17] for predicted REE was used as a reference to categorize patients with a low or normal REE.

Energy expenditure was adjusted according to fat-free mass using the following formula: REE/kg fat-free mass [18,19].

Data on age at disease onset and disease type as well as steroid doses administered were collected.

4. Statistical analysis

A descriptive and analytical analysis was performed. First, the behavior of each variable was described and reported as mean and standard deviation for normal variables and as median and range for those with skewed distributions. Numerical and normal variables were analyzed using the Student's *t*-test and skewed variables with the Wilcoxon rank-log Test. Categorical variables were analyzed with the Chi2/Fisher test. Linear regression analysis was performed to determine the magnitude of correlation between different variables. A two-tailed test was performed and a $p < 0.05$ was considered statistically significant.

For the data analysis Stata 11.0 software (Data Analysis, Stata corporation 4905 Lakeway Drive College Station, Texas 77845 USA) was used.

5. Results

Overall, 63patients with DMD were evaluated. Mean age was 11.4 (5.4/18.7)years. All patients were boys, as expected because of the X-linked transmission of the disease. According to Tanner stage, 40% of the patients were prepubertal. Gait was preserved in 54% of the patients.

In this series of DMD patients, 83% was receiving steroid treatment (41% prednisone and 59% deflazacort), with a median of 4 years of treatment (0.2–11 years).

Summary and dispersion statistics of the demographic, anthropometric, and clinical variables are shown in Table 1.

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