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ORIGINAL ARTICLE

Characterization of the physical capacity in children of the Chilean National Program of Cystic Fibrosis

Caracterización de la capacidad física en niños del Programa Nacional de Fibrosis Quística de Chile

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Abstract

Introduction: Cystic fibrosis (CF) is an inherited, progressive, multisystem disease. Better physical capacity may slow disease progression, thus improving prognosis and survival. The objective of this research was to evaluate the physical capacity of children admitted to the National CF Program of the Metropolitan Region, Chile. **Patients and Method**: A multicenter, cross-sectional study design was used. The inclusion criteria were children aged 6 to 12 years enrolled in the National CF Program; Tanner sexual maturity stage I, no respiratory exacerbations in the last 30 days, and no musculoskeletal pathologies. The maximum aerobic capacity was assessed through the peak oxygen uptake (VO_2peak) and determined with an incremental protocol in a magnetic cycle ergometer connected to an ergo-spirometer with which, at the same time, respiratory gases, oxygen consumption and carbon dioxide production values every 30 seconds, anaerobic threshold, and maximum workload were analyzed. The values of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC ratio, and forced expiratory flows between 25% and 75% of vital capacity were assessed through ergo-spirometry. At the beginning of the ergo-spirometry,

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arterial oxygen saturation, respiratory rate, heart rate, blood pressure, tidal volume and the perception of lower extremity fatigue and dyspnea were recorded using the modified Borg scale. The test lasted approximately 10 minutes. **Results:** The clinical records of 43 children collected from six health centers were reviewed. Out of these, 29 children met inclusion criteria, and 23 were recruited. Two children were unable to participate, reducing the final subject group to 21 (13 males, 8 females). The mean age was 8.8 ± 2 years; weight 30.5 ± 10.9 kg; height 1.32 ± 0.11 m; and body mass index 17.1 ± 3.5 (z-score 0.01 ± 1.34). More than half of the children (61%) had normal weight. The obtained VO_2peak was 43.7 ± 6.5 ml/min/kg (106.7 ± 19.8% of the predictive values). Only 10% of the children had values lower than those predicted by sex and age. No correlations were found between VO_2peak and anthropometric and pulmonary function variables. **Conclusion:** Most of the evaluated children (90%) had physical capacity similar to healthy subjects by sex and age.

Introduction

Cystic Fibrosis (CF) is an inherited, autosomal recessive disease caused by a mutation of the gene encoding for cystic fibrosis transmembrane conductance regulator (CFTR)[1]. Currently, there are more than 1,900 CFTR mutations worldwide and about 2/3 of the cases correspond to the delta F508 mutation[1]. In Chile, this mutation represents less than 40% of all cases[2].

This pathology generates different alterations in different organs, mainly in the lungs and at the gastrointestinal level[3] causing, in many cases, consequences that affect the quality of life and survival of these patients, who thanks to advances in the development of new treatments, mainly pharmacological, have improved the prognosis of this disease[4, 5].

Physical activity and exercise are widely accepted as part of therapeutic strategies in the management of CF[6-8] being a fundamental part of the growth and development of children[9]. There are several ways to objectively measure physical fitness, the gold standard is the maximal oxygen uptake (VO_2max) through an incremental exercise test on a cycle ergometer or a treadmill.[10-12].

The VO_2max during maximum exercise is a prognostic marker in CF[13, 14]. Compared to healthy subjects, children with CF show a reduction in the maximum exercise performance and the respiratory function, malnutrition and intrinsic skeletal muscle abnormalities[15, 16]. Another factor affecting VO_2max, in addition to the eventual alteration of gas exchange caused by the base disease, is the decreased efficiency of the mitochondrial Adenosine Triphosphate (ATP) synthesis or abnormalities of the myofibrillar mechanisms[17].

In Chile, CF is under the regime of explicit health guarantees (GES) which guarantee coverage in access, quality, terms and financial protection for patients with this disease. For this reason, each patient in the program is monitored by a pediatric pulmonologist who confirms the diagnosis and guides the treatment; however, aspects related to physical fitness are included but are not part of the basic group of benefits[18].

Subjects with CF are characterized by a low level of moderate to vigorous physical activity[19, 20]. Nixon et al noted that the total time used for physical activity by children with CF is similar to that used by healthy children, but the latter did vigorous physical activity for longer[19]. The objective of this study is to determine the maximum physical fitness, evaluated through VO-2max, in children from the Metropolitan Region included in the National Cystic Fibrosis Program of the Ministry of Health of Chile.

Patients and Method

Design

A cross-sectional descriptive study was conducted on children included in the National Cystic Fibrosis Program who live in the Metropolitan Region.

Inclusion criteria were children with a confirmed diagnosis of cystic fibrosis, age between 6 and 12 years, stage I in the Tanner classification, signed parental consent and children's assent.

The exclusion criteria were 1-Second forced expiratory volume (FEV1) <35% of the predicted volume, respiratory exacerbation in the last month, skeletal muscle injury in the two months before the protocol or subjects who have participated in physical training programs in the last six months.

This study was approved by the Ethics Committee of the Southern Metropolitan Health Service, Ministry of Health of Chile, approval letter n° 2886/2013.

Anthropometric variables

Weight and height were obtained with a precision scale with a measuring rod (SECA 225 Hamburg, Germany). In addition, the body mass index (BMI) was calculated and classified according to nutritional status.

Physical Fitness

Maximum aerobic capacity was evaluated through VO_2max using the protocol of Godfrey et al[21]. A magnetic cyclo ergometer connected to an ergo-spirometer (Oxycon Pro, Jaeger, Würzburg, Germany) was used to carry out the protocol, with which the respiratory gases were analyzed in parallel: oxygen consumption and carbon dioxide production values every 30 seconds, anaerobic threshold, maximum working load (Wmax). The values were expressed as absolute value and percentage of the reference value[22]. The equipment was calibrated before each use.

Pulmonary Function

It was evaluated through the ergo-spirometer which shows the values of forced vital capacity (FVC), FEV1, ratio FEV1/FVC, and forced expiratory flows between 25 and 75% (FEV_{25-75}) of vital capacity. The obtained values were expressed as an absolute value and as a percentage of the reference value[23]. The equipment was calibrated before each use.

Protocol. Patients were called randomly. They were asked to arrive in the morning at the evaluation center for the cardiopulmonary test. The previous indications were no food four hours before the test, no exercise 24 hours before the test, no food or energy drinks 24 hours before the test.

In the ergo-spirometer, the following were recorded at the beginning: arterial oxygen saturation (SPO_2), respiratory rate (RR), heart rate (HR), arterial pressure (AP), tidal volume (TV), and the perception of lower extremity fatigue and dyspnea was consulted through the modified Borg scale.

Before starting the incremental exercise test, patients performed a three-minute warm-up with a load of 10 watts. Loads of 10, 15 and 20 watts/min were used in children with a height of <125 cm, between 125 cm and 150 cm, and >150 cm respectively. The test lasted 10 minutes approximately. Each child was told to make the maximum effort by asking him or her to maintain a cadence of about 60 revolutions/min. During the entire test and 5 minutes after finish it, the following were recorded: HR, SPO_2, RR, AP, TV, fatigue of the lower extremities and sensation of dyspnea. Measurements in which children achieved at least two test completion criteria were considered satisfactory[24, 25]. At the same time, the HR was monitored throughout the test every five seconds through a heart monitor (Polar R810, Kempele, Finland).

Statistical analysis

Descriptive statistics were expressed in mean ± standard deviation for continuous variables and in frequencies for categorical variables. Shapiro Wilk test was applied for the evaluation of normality. The Pearson or Spearman correlation was used to determine the correlation of the variables. All calculations were made with the SPSS Statistics software version 23.0 (IBM, Armonk, NY, USA).

Results

The clinical records of the 43 children from the National CF Program registered in March 2014, who were controlled at the six centers participating in the study, were reviewed. Out of the total number, 29 children met the inclusion criteria, of which 23 finally agreed to participate. Two of the children could not meet the criteria for completing the protocol (Figure 1). The sample consisted of 21 children (13 men and 8 women) with an average age of 8.8 ± 2 years; height of 1.32 ± 0.11 m; weight of 30.5 ± 10.9 kg; Body Mass Index of 17.1 ± 3.5 (z-score 0.01 ± 1.34) (Table 1). 61% of the patients were eutrophic, 14.3% were underweight, 14.3% were at risk of obesity and 9.4% were obese. Depending on the type of ventilatory impairment, the following were classified: normal 38.1%, minimal obstructive 33.3%, mild obstructive 4.8%, moderate obstructive 9.5%, advanced obstructive 4.8%, and restrictive 9.5%. The sample had an FVC of 89.1 ± 18.2 %; FEV1 of 82.1 ± 19.7 % and the FEV1/FVC ratio of

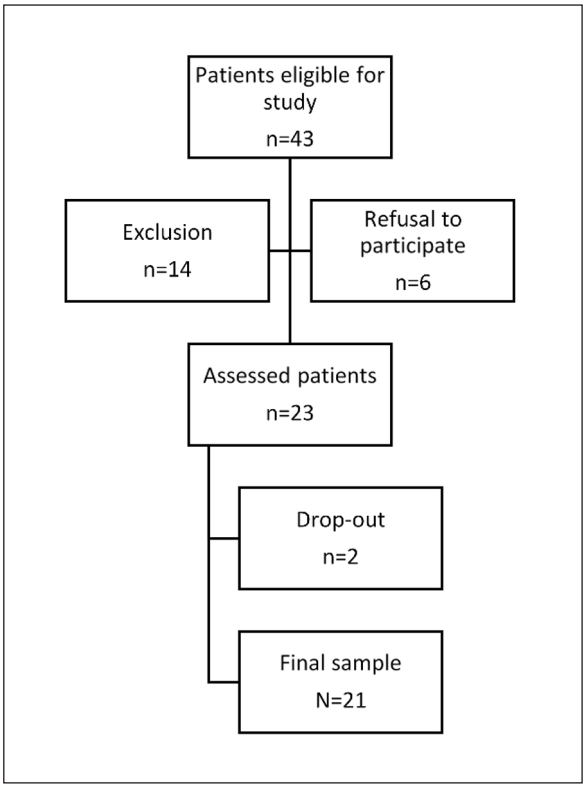

Figure 1. Flow Chart of patient selection and exclusion.

80.5 ± 8.7 %. The obtained VO_2max was 43.7 ± 6.5 ml/Kg/min (106.7 ± 19.8% of the predicted value). The obtained ventilatory threshold values were 83.5 ± 9.4 %. The maximum working load was 80.4 ± 20.5 watts (96.7±24% of the reference value) (Table 2). There was no correlation between the evaluated variables.

13 of the patients had normal VO_2max and eight decreased VO_2max, only significant differences were found in BMI ($p<0.05$) and weight ($p<0.05$).

Table 1. Descriptive statistics of the population

Variable	
Sex (Male/Female)	13/8
Age (years)	8.8 ± 2.0
Weight (Kilograms)	30.5 ± 10.9
Height (centimeters)	132 ± 10.9
BMI	17.1 ± 3.5
FVC (ml)	1915 ± 650
FVC%	89.1 ± 18.2
FEV1 (ml)	1540 ± 526
FEV1%	82.1 ± 19.7
FEV1/FVC (%)	80.5 ± 8.7
FEF25-75	1.48 ± 0.79

BMI: Body mass index; FVC: Forced vital capacity; FEV1: Forced expiratory volume during the first second; FEF25-75: Forced expiratory flows between 25 to 75%.

Table 2. Physical Capacity variables of the population

Variable	
VO2peak (ml/Kg/min)	43.7 ± 6.5
VO2peak (% predicted value)	106.7 ± 19.8%
Ventilatory threshold (% predicted value)	83.5 ± 9.4
Wmax (Watts)	80.4 ± 20.5
Wmax (% predicted value)	96.7 ± 24

VO2peak: peak oxygen consumption; Wmax: maximum working load.

Discussion

90% of the children participating in the study present values of VO_2max similar to healthy subjects, according to gender and age.

Our results are consistent with those observed by Kilbride et al, who demonstrated that physical fitness, assessed through VO_2max, in pre-pubertal children with CF has no significant differences with healthy children of similar characteristics[26]. This is confirmed by the fact that the mean VO_2 of our sample was 107% of the predicted value.

It has been shown that maximum working capacity (Wmax) assessed through a cyclo ergometer is a valid test for measuring physical fitness in children with CF[27, 28]. Kent et al, assessed the reliability of this parameter using an incremental test using the Godfrey protocol in children between six and 11 years of age obtaining maximum loads of 76.2 watts corresponding to about 90% of the reference value[29]. Although our study did not evaluate reliability, using the same protocol, the values were similar, reaching about 80 watts (96% of the reference value), which reinforces that this protocol is feasible to perform in a young population and with similar results.

Mc Loughlin et al[30] studied ten subjects with CF and ten controls to compare the lactic threshold assessed directly and through the ventilatory threshold (VT) during an incremental ergo-spirometry test. The results concluded that the VT significantly overestimates the lactic threshold in subjects with CF due to a delay in the elimination of carbon dioxide during exercise. This could explain the high VT values obtained by our study group (83%).

According to our results, children with CF and stage I in the Tanner classification do not show a linear relationship between the deterioration of their lung function and the deterioration of their maximum physical fitness. Thus 90% of our sample has a VO_2max within the expected ranges and instead, only 38% have normal lung function.

In children with CF, there are early alterations in the respiratory system [31] that appear early in pulmonary function measured by spirometry. Probably, in early stages of the disease, the ventilatory reserve allows delaying systemic manifestations. This is why our results, along with those of Kilbride et al, show differences in lung function, but not in physical fitness compared to healthy children. In contrast, studies that have included children with different stages of sexual maturation show a deterioration in the lung function and physical fitness compared to healthy children.[13, 32].

At prepubertal level, physical fitness is clearly aerobic and there are few differences between genders.[33]. As sexual characteristics appear, these differences will accentuate with a higher capacity, both aerobic and anaerobic, in favor of males[33].

Although in our study there is no linear relationship between physical fitness and lung function, the literature shows that high levels of physical activity contribute to slowing the deterioration in lung function[34]. Schneiderman et al$_{34}$, evaluated physical activity in 212 children with CF over nine years, finding that the lung function has a greater decline in those children who

have less physical activity than estimated for their age and anthropometric characteristics. Therefore, if one of the main objectives of treatment is to minimize the fall of FEV1, physical training should be incorporated as a fundamental pillar of the treatment of CF patients. For the above, it is a priority to characterize the physical fitness at an early age, incorporating the measurement of VO_2max among the routine evaluations in CF throughout life[35, 36].

Although at stage I of Tanner classification, the differences are not as marked as at later stages, the fat-free mass, which is one of the determinants of maximum exercise capacity, was not evaluated. Another limitation is the number of subjects recruited. However, it is a rare disease in our country.

In conclusion, 90% of the children participating in the study present values of maximum physical fitness similar to healthy subjects according to gender and age. As this is a progressive disease, studies are needed to determine whether this pattern is repeated at older ages with greater respiratory involvement or long-term follow-up of children from very early ages.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

This project received funding from the Andres Bello University to carry out the oxygen consumption tests. The institution did not influence the design of the study; nor in the collection, analysis or interpretation of data; nor in the preparation, revision or approval of the manuscript.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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