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Research Article

Inspiratory Muscle Training in Patients with Steinert's Disease: is there a Beneficial Role?

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Abstract

Steinert's disease is an autosomal dominant systemic neuromuscular disease. Patients have weakened respiratory muscles strength and function, leading to pneumonia and respiratory failure, the most important causes of morbidity and mortality. Inspiratory muscle training is a safe adjunctive therapy which may increase strength and endurance of respiratory muscles. Despite the reported benefits, inspiratory muscle training remains understudied in patients with neuromuscular disorders. We conducted a single-center prospective study, with a simplified three-month duration protocol of inspiratory muscle training. The cohort included patients with Steinert's disease and decreased maximal inspiratory pressure. The training was individually tailored and progressive. The main outcome was maximal inspiratory pressure. Our secondary outcomes included maximal expiratory pressure, peak-cough flow and compliance to the training. After three months of training, we found significant improvements in pulmonary muscle function. Our protocol might have a potential role delaying the expected respiratory complications of the disease. Nevertheless, larger prospective studies are required to validate the long-term clinical benefits of our results.

Keywords: Dystrophy; Inspiratory; Muscle; Rehabilitation; Steinert's disease; Training

Abbreviations: ATS/ERS: American Thoracic Society/ European Respiratory Society; IMT: Inspiratory muscle training; MEP: maximal expiratory pressure; MIP, maximal inspiratory pressure; NMD(s): Neuromuscular disease(s); PCF: peak cough flow; SD: Steinert's disease; SAM: Sistema de Apoio ao Médico

Introduction

Neuromuscular Diseases (NMDs) typically impair respiratory muscles function and strength, increasing the risk of lung atelectasis, hypoxemia and low quality of life [1,2]. Steinert's disease (SD), or myotonic dystrophy type 1, is an autosomal dominant NMD [2,3-5]. It has a prevalence of 0.5-18.1 per 100000 individuals, and is considered the most common muscular dystrophy [6]. SD occurs due to increased CTG triplet expansion in the DMPK gene, which encodes the DM-protein kinase. Generally, the number of repetitions and age of onset correlates with the severity of the disease [7,8]. It can manifest at any age, however it is commonly diagnosed at adulthood, between the second and fourth decades of life [6,8,9]. Patients typically have myotonia as the initial symptom, involving specific muscles of the forearm, hand, tongue and jaw, which can improve with muscle activity ("Warm-Up Phenomenon") [9]. They may also develop cardiac arrythmias, cataracts, sleep disturbances, impaired diaphragm and respiratory function, leading to increased morbidity and mortality [2-4,7,9]. The pattern of clinical manifestations may vary significantly [9]. The main causes of death are pneumonia and respiratory failure [2,3,5]. The disease course is usually slowly progressive, nevertheless, rapid deterioration may occur [7]. Currently, there are no approved disease-modifying treatments available [6,9]. Therefore, the best management implies a multidisciplinary approach that helps preserving the quality of life and prevent further complications of the disease [7,9].

Inspiratory Muscle Training (IMT) is a safe approach, which may increase strength and endurance of respiratory muscles of patients with NMD [2,5,10-14]. The American Thoracic Society/ European Respiratory Society (ATS/ERS) recommends adding IMT to the rehabilitation of patients with suspected or confirmed respiratory muscle weakness [15]. There are three main IMT methods, including resistive loading, threshold loading and normocapnic hyperpnea, but insufficient data to recommend

one type over the other [15,16]. The inspiratory muscle strength correlates with exercise capacity and, therefore, IMT may have an important role in the multidisciplinary care of such patients [12,13]. Wanke et al. reported benefits of this training in patients with Duchenne muscular dystrophy [17]. In subjects with muscular dystrophy and heart failure, the respiratory muscle weakness contributes to the worsening of the condition, but IMT may improve symptoms of dyspnea [13]. Theoretically, any improvement in respiratory muscle function might potentially delay the onset of pulmonary complications in these patients [18,19]. Despite the reported benefits, studies of IMT in SD still lack in the literature and the effects in morbidity and mortality remain unknown [1,2,5,13,19]. In this study, we developed a novel and simplified protocol of IMT and assessed its benefits in a cohort of patients with SD.

Materials and Methods

Subjects Selection

We analyzed all adult patients with NMD, followed in pulmonology or neurology consultations, who underwent MIP assessment between 2017 and 2019. Only patients with SD and decreased maximal inspiratory pressure (MIP <60cmH_2O) [20], who accepted to participate in the study, were selected to include our cohort. Accordingly with the training device cautions and recommendations, we decided to exclude all patients with prior pneumothorax, severe lung emphysema, rib fractures, marked osteoporosis, pulmonary hypertension, uncontrolled asthma, low perception of dyspnea, ear disturbances, diastolic cardiac failure or worsening of symptoms after IMT. We also excluded subjects incapable of performing the training.

Study Protocol

We conducted a single-center prospective study and developed a novel training protocol, with three-month duration and single-daily sessions. This protocol is simplified compared with other studies [12], in order to assure safety, efficacy and compliance to the training. Similarly to prior investigations [2], we did not include a control group, due to the limited number of participants. The training was individually tailored to the participants capacity. It started with low resistances, at 20% of baseline MIP, 2 sets of 20 repetitions, and progressed up to 3 sets of 12 repetitions, at 50% of baseline MIP (Table 1). We used an interval-based training strategy with one-minute resting between sets, to prevent dyspnea. When a subject referred significant facility or difficulty performing the training, the physician would adjust the training to higher or lower resistances, respectively. Therefore, patients completed the study training at different resistance levels, at their own best capacity.

Resistance	Repetitions	Sets	Rest	Frequency
20% Baseline MIP	20	2	1 min	Once daily
30% Baseline MIP	12	3	1 min	Once daily
40% Baseline MIP	12	3	1 min	Once daily
50% Baseline MIP	12	3	1 min	Once daily
Abbreviations: MIP, maximal inspiratory pressure; min, minute.				

Table 1: Training progression protocol.

The first session occurred under medical supervision. Subjects were monitored for symptoms and vital signs changes (heart and breathing rates, blood pressure, peripheral oxygen saturation), at the beginning and ending of training. Subjects had monthly follow-up hospital appointments, and training intensity was gradually increased at the consultation, according with their tolerance and symptoms. We used modified Borg scale to monitor the level of dyspnea, tolerance, and to adjust the training intensity [21]. Our goal was to select an intensity that would maintain Borg scale between 2 (slight) and 4 (somewhat severe) [22]. All participants were asked to keep a training journal, to register training compliance and breathlessness level (using modified Borg scale) at the end of each set. They were encouraged to maintain a honest registry and to report the training only when it was performed. In each follow-up appointment, patients brought their journal, so that exercise tolerance could be assessed. Only the physician was responsible for adjusting the threshold resistance of the device.

Training Device

We used Powerbreathe Medic Classic devices to perform the IMT (Figure 1). The Powerbreathe is a light-weight portable device that offers an adjustable threshold load up to 90 cmH_2O. The adequate technique for each repetition requires performing a fast maximal inspiration against the defined threshold load, followed by a slow passive expiration. Users should assure a good mouth sealing around the mouthpiece, the use of a nose clip and should maintain normal breathing rates (10-20 cycles per minute). All devices were provided by Vivisol for the sole purpose of conducting this study, with no conflict of interests to declare.

Figure 1: PowerBreathe Medic Classic device.

Assessment Measures

We collected all clinical data using the institutional clinical software Sistema de Apoio ao Médico (SAM) and SClínico. The cohort baseline characterization included age, gender and clinical relevant parameters such as NMD diagnosis, pathological background and treatment. We assessed pulmonary function parameters including MIP, maximal expiratory pressure (MEP) and peak cough flow (PCF). These parameters were collected at the beginning of the protocol and reassessed after completing three months of training, for comparison.

MIP and MEP measurements were performed in the pulmonary function laboratory by two cardiopulmonologist technicians using a plethysmograph (MasterScreen Body from Jaeger). Patients remained in the sitting position during the procedure and used a nose clip. After explanation of the procedure, three measurements were performed. The higher result was selected for the study. PCF was assessed with a portable peak flow meter, and the procedure was conducted by the physician. After a detailed explanation, participants performed three coughing maneuvers in the sitting position, using a nose clip and assuring adequate mouth sealing. The higher value was selected for the study. Every pulmonary function measurements, procedures, devices and professionals were the same during the study, in order to minimize possible bias.

Outcomes

- Main outcome was MIP.
- Secondary outcomes included MEP and PCF. Compliance to training was also assessed.
- Respiratory infections was not an outcome, since the cohort had no prior reported infections.

Data Analysis

Data analysis was made with IBM SPSS Statistics v23. We used mean (± standard deviation), median (± interquartile range) and valid percentages to characterize the variables. We used Wilcoxon tests to compare the MIP, MEP and PCF assessments, due to the non-parametric distribution of the variables. A p-value of 0.05 or less was considered as statistically significant. Statistical power was calculated with 95% confidence interval. Training compliance was calculated based on the ratio of training sessions performed/prescribed. We have not considered the subjects who abandoned the protocol or were lost to follow-up (it is unknown if they continued the training at home).

Ethics Approval

This study has been approved by the Hospital Ethics Commission, Administrative Council and Medicine Department. Each patient signed an informed consent form before enrolling in the study.

Results

Cohort Characteristics

We analyzed a population of 113 patients with NMD, who underwent pulmonary function assessment between 2017 and 2019. After selecting patients with SD and decreased MIP, with no exclusion criteria, a total of 9 patients was eligible to be enrolled in the study (Table 2). There was 6 men and 3 women in the cohort. Mean age was 48±11 years (35-66 years) and median MIP was 29.78±31.62 cmH_2O (16-57 cmH_2O). Unfortunately, 2 participants abandoned the study, and other 2 were lost to follow-up due to the current COVID-19 pandemic.

Characteristics	Results
Total of Patients, n (%)	9 (100)
Females	3 (33.3)
Age (years), mean±SD	48±11
Sleep Disorders, n (%)	

Obstructive Sleep Apnea	5 (71.4)
Central Sleep Apnea	1 (14.3)
Ventilatory Support, n (%)	
BPAP	3 (33.3)
CPAP	1 (11.1)
APAP	1 (11.1)
Cough Assist	0 (0)
Compliant patients	4 (80)
Physiotherapy, n (%)	4 (44.4)

Abbreviations: SD: standard deviation; BPAP: bilevel positive airway pressure; CPAP: continuous positive airway pressure; APAP: automatic positive airway pressure.

Table 2: Patients baseline characteristics.

Training Progression

All participants started training with low resistances, at 20% of baseline MIP, with a median of 6±6 cmH_2O (3-12 cmH_2O). At the end of the protocol, median training resistance was 14.5±13 cmH_2O (7-25 cmH_2O), which represents 50±13% of baseline MIP (Table 3).

Variables	Baseline	3 Months	p Value	Cohen's d	Power
IMT Resistance (cmH_2O), median±IQR	6±6	14.5±13	-	-	-
IMT Resistance (% bMIP), median±IQR	20	50±13	-	-	-
Respiratory Function, median±IQR					
MIP (cmH_2O)	29.78±31.62	41±27.65	0.043	0.355	0.243
MEP (cmH_2O)	33.35±23.11	44.47±11.38	0.08	0.481	0.359
PCF (L/min)	300±120	430±385	0.144	1.083	0.891
Compliance rate (%), median±IQR	-	98.96±5.5	-	-	-

Abbreviations: IMT, inspiratory muscle training; IQR, interquartile range; bMIP, baseline maximal inspiratory pressure; MEP, maximal expiratory pressure; PCF, peak cough flow.

Table 3: Patients results after 3 months of inspiratory muscle training.

Outcomes

We found a statistically significant improvement of MIP with 3 months of IMT (Table 3). Median MIP progressed from 29.78±31.62 to 41±27.65 cmH_2O (p=0.043). We also found improvements in MEP (p=0.08) and PCF (p=0.144). Compliance to training was almost complete (98.96±5.5%).

Training Safety

This training protocol was safe and had no significant adverse outcomes reported. Some participants referred a slight occasional dizziness at the beginning of training, which was dependent of the high inspiratory rate during the performance. It was easily corrected during consultation and self-limited. Vital signs remained relatively unchanged during the supervised sessions.

Discussion

IMT has shown benefits in the rehabilitation of patients with NMD, although more research is required [1,2,5-7]. In this study, only patients with SD were included. We developed an IMT protocol with once-daily sessions, simplified compared with other studies [8], to preserve muscle recovery, efficacy and compliance. To our knowledge, this is a novel protocol which reported improvements in respiratory muscle function of patients with SD.

Theoretically, our protocol might potentially have a role

delaying the expected respiratory outcomes of SD, and, therefore, might be considered to integrate their multidisciplinary care. Our major limitations were the small cohort size and the lack of a control group, which may influence our results and conclusions. Gender-specific differences were not assessed due to the small cohort size. Although the best protocol is not clearly defined, our training duration might be considered a limitation, since previous studies included greater periods [2,10,19]. Areas of future research should include the long-term assessment of the clinical benefits achieved with this protocol.

Conclusions

IMT may have benefits in patients with SD, improving respiratory muscles function such as MIP. It might potentially have a role in the prevention of respiratory complications associated with the disease. Nevertheless, larger prospective studies are required to validate the long-term clinical benefits of our results.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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