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Review

Inspiratory muscle training for children and adolescents with neuromuscular diseases: A systematic review

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Abstract

Patients with neuromuscular diseases are at risk of morbidity and mortality due to respiratory compromise caused by respiratory muscle weakness. A systematic review was performed using pre-specified search strategies to determine the safety of inspiratory muscle training (IMT) and whether it has an impact on inspiratory muscle strength and endurance, exercise capacity, pulmonary function, dyspnoea and health-related quality of life. Randomised, quasi-randomised, cross-over and clinical controlled trials were included if they assessed the use of an external IMT device compared to no, sham/placebo, or alternative IMT treatment in children aged 5–18 years with neuromuscular diseases. Seven full-text articles and two on-going trials (n = 168) were included. Most studies used threshold IMT devices over a medium to long-term period, and none reported any adverse events. Studies differed regarding intensity, repetitions, frequency, rest intervals and duration of IMT. Six studies reported no significant improvement in pulmonary function tests following IMT. Two comparable studies reported significant improvement in inspiratory muscle endurance and four studies reported significantly greater improvement in inspiratory muscle strength in experimental groups. The latter was confirmed in a meta-analysis of two comparable studies (overall effect $p < 0.00001$). Other outcome measures could not be pooled. There is currently insufficient evidence to guide clinical IMT practice, owing to the limited number of included studies; small sample sizes; data heterogeneity; and risk of bias amongst included studies. Large sample randomised controlled trials are needed to determine safety and efficacy of IMT in paediatric and adolescent patients with neuromuscular diseases.

Keywords: Inspiratory muscle training; Paediatric; Adolescent; Neuromuscular diseases

1. Introduction

"Neuromuscular diseases" (NMDs) can be defined as a group of disorders that include pathology of the muscle, neuromuscular junction, peripheral nerves and motor neurons [1]. One out of 3500 individuals can suffer from a disabling NMD that can either present in childhood or at a later stage [2,3]. Patients with NMDs are at a high risk of morbidity and mortality due to acute respiratory infections and chronic respiratory compromise caused primarily by diaphragmatic and intercostal muscle weakness [4–6]. The diaphragm is the strongest of the inspiratory muscles. Weakness or dysfunction of the inspiratory musculature leads to severe respiratory complications such as decreased lung volumes (for example, vital capacity (VC)), altered and ineffective breathing, decreased thoracic and shoulder mobility, decreased chest expansion and alveolar ventilation, poor secretion clearance and, finally chronic respiratory insufficiency and respiratory failure which can lead to premature death [7–11]. In many cases it is more a case of cough insufficiency rather than hypoventilation that causes the morbidity and mortality amongst patients with NMDs [12].

Some studies have suggested that respiratory muscle training may be useful in improving and/or preserving respiratory function; delay the onset of serious respiratory complications; prolong patient's lives and improve the health-related quality of life (HRQoL) in paediatric and adolescent patients with NMDs [13–17], but study results are limited and conflicting. Despite the limited evidence for the use of inspiratory muscle training (IMT) in patients with NMDs, recent observational studies conducted in Chile and Brazil, mainly amongst people with Duchenne Muscular Dystrophy (DMD), have suggested positive results [18–20]. IMT could be considered as an adjunct in patients presenting with respiratory muscle weakness [21,22],

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but is not fully endorsed by the American Thoracic Society due to safety concerns [16]. Further research, especially on the long-term outcomes of IMT, is therefore recommended.

The use of IMT in patients with NMDs remains controversial. Some studies have shown promising results, especially if commenced early in the course of the disease [7,11,14,15,23–27]. However, patients with different levels of respiratory muscle weakness might react differently to respiratory muscle training intervention [13]. Furthermore, the review by Ho and colleagues expressed concern regarding the limited efficacy of standardised respiratory muscle training in NMDs. They suggest that training programmes should be individualised and reviewed regularly as the condition progresses [13].

In the case of DMD, the protective mechanism of nitric oxide release in an exercising muscle might be defective, which increases the risk of muscle damage during exercise [16,28]. Therefore, when implementing muscle strengthening programmes in this subpopulation, caution should be taken to not overexert patients during training. Another concern is that whilst IMT might improve/preserve respiratory function, it could also accelerate fatigue of weakened muscles and cause muscle damage due to overwork of the muscles [15].

There are currently no systematic reviews or clear guidelines regarding indications, methods of application, and contra-indications to the use of IMT in children and adolescents with NMDs. Therefore, the purpose of this review was to determine the safety of IMT and its efficacy with regard to improving inspiratory muscle strength and endurance, exercise capacity, pulmonary function, dyspnoea and HRQoL in paediatric and adolescent patients (5–18 years) living with NMDs.

2. Methods

This review was based on the Cochrane methodology for systematic reviews [29] and was registered with Prospero in September 2014 (CRD42014013875).

2.1. Search strategy

During October to November 2014, fifteen online databases were searched from inception for randomised controlled trials, quasi-randomised controlled trials, clinical controlled trials, cross-over trials, and on-going studies, using pre-specified search strategies. The databases included were Africa-Wide Information, CENTRAL (Cochrane Central Register of Controlled Trials), CINAHL (Cumulative Index to Nursing and Allied Health Literature), Cochrane Neuromuscular Disease Group Specialized Register, Medline, PEDro, Pubmed, Respiratory Care Journal, Sabinet, Scopus and Science Direct. Furthermore Clinicaltrials.gov, PACTR (Pan African Clinical Trials Registry), SANCTR (The South African National Clinical Trial Register) as well as the WHO International Clinical Trials Registry (ICTRP) were searched for on-going trials. The search strategy included specific keywords which were based on those NMDs more commonly seen amongst paediatric and adolescent patients (for example, DMD). Patients included were children and adolescents 5–18 years old with confirmed diagnoses of NMDs.

IMT was defined as training/intervention targeted at improving the muscle strength and endurance of inspiratory muscles (diaphragm, intercostal muscles) or delaying respiratory regression in NMD patients by making use of an external device with either a flow/resistive/threshold load in ventilated and non-ventilated patients. Studies that investigated IMT used as therapy, either at hospital, home or an institution during the acute, sub-acute and chronic stages were included. The researchers compared the use of an external IMT device (threshold, resistive or flow) with either control/no treatment or sham/placebo/standard care or an alternative method of IMT in ventilated and non-ventilated paediatric and adolescent NMD patients (5–18 years old). Studies that assessed both IMT and expiratory muscle training were included in order for the reviewers to analyse the IMT component. There were no language restrictions on the searches in order to limit language bias. Language experts were consulted for articles in languages other than Afrikaans or English.

Recent publications and reports, including grey literature (internal reports, conference abstracts and proceedings) were screened in order to minimise publication bias. Experts and specialists in the field, colleagues as well as device manufacturers and funders were contacted for any other unpublished data or results not found via electronic database searching. The reference lists of all included studies were hand-searched to ensure that all relevant, additional studies and data were included.

2.2. Outcome measures

The primary outcome measures assessed in this review were frequency or rate of hospitalisations, respiratory infections (based on the need for antibiotics) as well as any adverse events related to the intervention such as disease progression, desaturation, cardiac failure, muscle fatigue and muscle fibre damage, hyperinflation, and barotrauma such as a pneumothorax. The secondary outcome measures assessed were pulmonary function tests (e.g. VC, Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), Total Lung Capacity (TLC) and multiple gas washout techniques); cough efficacy (measured by Peak Expiratory Cough Flow (PECF)); vital signs (including heart rate (HR), respiratory rate (RR), arterial blood gases (ABG)); diaphragmatic changes (measured with ultrasound); measures of inspiratory muscle strength (maximal inspiratory pressure (MIP), maximal inspiratory capacity (MIC), sniff nasal inspiratory pressure (SNIP), transdiaphragmatic pressure (Pdi)); and endurance (maximal voluntary ventilation (MVV)) as well as HRQoL measured by any validated instrument.

2.3. Selection of studies

Databases were searched by the primary researcher (AH) and relevant studies were identified (title and abstract). Two reviewers (AH, LC) independently reviewed the search results to determine eligibility for inclusion and findings were compared.

Two reviewers (AH, BM) independently extracted data from the included studies with a pre-structured data extraction form. Information was collected on participants (demographic data,