INPLASY

Effectiveness of Respiratory Muscle Training in Pompe Disease. A Systematic Review and Meta-Analysis

INPLASY202460094
doi: 10.37766/inplasy2024.6.0094
Received: 24 June 2024
Published: 24 June 2024

Lin, MY ; Hsu, PC.

Corresponding author:
Mu-Yun Lin

demorgan9864@gmail.com

Author Affiliation:
Taipei Veteran General Hospital.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Risk of bias assessment.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202460094

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 June 2024 and was last updated on 24 June 2024.

INTRODUCTION

Review question / Objective Patients : Pompe disease. Intervention: Inspiratory muscle training. Comparison : before respiratory muscle training versus after respiratory muscle training. Outcome : respiratory muscle strength, pulmonary function, functional capacity, quality of life.

Rationale Respiratory muscle training significantly increased respiratory muscle strength in many diseases like chronic kidney disease, heart failure, and pulmonary hypertension. Patients with Pompe diseases also present with respiratory muscle weakness despite the initiation of enzyme replacement therapy , so additional intervention of such as inspiratory muscle training may have positive effect on the cardiopulmonary function of this group of patients.

Condition being studied Pompe disease is a hereditary metabolic myopathy inherited in an autosomal recessive manner. Deficiency of the lysosomal enzyme acid alpha-glucosidase (GAA) leads to an accumulation of glycogen in skeletal, cardiac, and smooth myocytes, and causes weakness of the affected muscles, which often resulting in premature death. The clinical presentation of Pompe disease varies depending on factors such as the age of onset, the specific genetic mutations involved, and rate of disease progression. Pompe disease is categorized into two forms, known as infantile onset Pompe disease (IOPD), and late-onset Pompe disease (LOPD) by the residual GAA activity.
IOPD patients' symptoms typically manifest within the first few days to weeks after birth and include hypertrophic cardiomyopathy, reduced muscle tone, severe muscle weakness , and respiratory insufficiency7. Without adequate treatment,

cardiorespiratory failure can be fatal by the age of 24 months.
Limited treatment options exist for respiratory muscle weakness of Pompe disease. The introduction of enzyme replacement therapy (ERT) using alglucosidase alfa in 2006 (MyozymeTM) has significantly increased both overall and ventilator-free survival for children affected by IOPD. Respiratory muscle weakness can still endure in certain children with IOPD even after ERT. This weakness can lead to hypoventilation, diminished cough effectiveness, and reduced capacity for physical activity.
Individuals with LOPD typically have a more insidious course, they experience proximal muscle weakness that becomes evident around the age of 30. Respiratory weakness is frequently evident at the moment of diagnosis and when treatment is started. Generally, the inspiratory muscles are primarily affected.The weakness in the respiratory system leads to reduced airway clearance, impaired cough, sleep-disordered breathing, progressive respiratory insufficiency, and even acute or chronic respiratory failure.

METHODS

Search strategy
Search strategy of MEDLINE :
#1 : respiratory muscle training
#2 : inspiratory muscle training
#3: breathing training
#4: #1 OR #2 OR #3
#5 :Pompe disease
#6 :LOPD (Late onset Pompe disease)
#7 : IOPD (Infantile onset Pompe disease)
#8: #5 OR #6 OR #7
#9 : #4 AND #8.

Participant or population
Inclusion criteria:
1. diagnosis with LOPD or IOPD, determined by lack of GAA enzyme activity performed on skin fibroblasts
2. muscular weakness on pulmonary function tests
3. treated with ERT for at least one year before the beginning of the study.
Exclusion criteria : respiratory failure and lack treatment with ERT.

Intervention Respiratory muscle training(RMT) or inspiratory muscle training (IMT). inclusion criteria :
1. use devices like Threshold Inspiratory Muscle Trainer or other customized training devices that can adjust training intensity
2. training intensity is based on percentage of maximal inspiratory pressure or maximal expiratory pressure
Exclusion criteria :
1. does not use IMT trainer
2. only mentioned breathing exercise.

Comparator
Inclusion criteria:
1. sham RMT: individualized pressure-threshold equal to 15% of their MIP (for inspiratory training) and MEP (for expiratory training).
Exclusion criteria:
1. Did not use the same training device as the intervention group.

Study designs to be included 1. Randomized controlled trials 2. Nonrandomized uncontrolled intervention trial 3. Longitudinal observation study.

Eligibility criteria
Inclusion criteria:
1. RCT
-Randomize adults with LOPD 1:1 in blocks of weeks of RMT or sham-RMT.
-Participants and all researchers, except for the clinician providing RMT therapy, were blinded to group assignment.
2. Nonrandomized uncontrolled intervention trial
-Involves interventions of RMT or IMT
-Compares the functions before and after intervention
3. Longitudinal observation study
Exclusion criteria
1. Case report
2. Retrospective study.

Information sources MEDLINE, Embase.

Main outcome(s)
1. Respiratory muscle strength (maximal inspiratory pressure and maximum expiratory pressure)
– maximal inspiratory pressure measured from the residual volume
– maximal expiratory pressure measured at the total lung capacity

2. Pulmonary function (FVC, FEV1, FEV1/FVC)
– measured with spirometry in accordance with the ATS/ERS standards

3.Functional endurance (6 minute walk test)
-performed in accordance with the ATS guidelines

All measurements need to be taken by a technician who was blinded to the study.

Additional outcome(s) Questionnaire for quality of life.

Data management
Inclusion criteria
– complete measurement of the main outcomes, including standard deviation, mean change
– include more than 2 participants
data that will be obtained
– mean of each measurement, standard deviation, number of participant
All data extraction will be done by manual work and recorded in Excel.

Quality assessment / Risk of bias analysis NIH quality assessment tool for before-after (pre-post) studies will be used for risk of bias assessment.

Strategy of data synthesis
-Estimation of the intervention effect was performed by random-effects model and expressed as the difference before-after the intervention and compared between the intervention and control groups
-Mean differences (MD) were calculated with their respective 95% CI.
-Heterogeneity was analyzed using the χ^2 test with N-1 degrees of freedom, with an alpha of 0.05 as the threshold for statistical significance, and the I^2 test.
-We will use Comprehensive Meta-Analysis to perform meta-analysis.

Subgroup analysis We will divide participants into infantile-onset Pompe disease(IOPD) and late onset Pompe disease(LOPD).
The subgroup analysis is then done on IOPD and LOPD.

Sensitivity analysis We conducted a sensitivity analysis considering the studies reporting data on the maximal inspiratory pressure, maximal expiratory pressure, and 6 minute walk test in patients with Pompe diseases.

Language restriction English.

Country(ies) involved 1. Taipei Veteran General Hospital, Taiwan 2. West Garden Hospital, Taiwan.

Keywords Pompe disease ; respiratory muscle training ; respiratory muscle strength ; pulmonary function.

Dissemination plans We will submitt to a leading journal in either pediatrics or physical therapy. If the review warrant a change in clinical practice for Pompe disease, we will send a summary report to experts in the associated fields.

Contributions of each author
Author 1 - Mu-Yun Lin conceived and designed the work, collected the data, performed the analysis, and drafted the work.
Email: demorgan9864@gmail.com
Author 2 - Po-Cheng Hsu performed the analysis, gave substantial contributions to data acquisition and interpretation for the work, revised it critically for important intellectual content.
Email: myronrbman@gmail.com