Effects of controlled inspiratory muscle training in patients with COPD: a meta-analysis

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Authors' objectives
To assess the effectiveness of inspiratory muscle training (IMT) in patients with chronic obstructive pulmonary disease (COPD), and to determine which patient characteristics may influence its effectiveness.

Searching
MEDLINE (from 1966 to December 2000) and EMBASE (from 1988 to December 2000) and relevant references from peer-reviewed articles were searched; the search terms were stated. Studies written in a language other than English, German or Dutch were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies investigating the use of IMT at an intensity of greater than or equal to 30% maximum static inspiratory alveolar pressure (PImax) were eligible for inclusion. Two types of inspiratory muscle loading were used in the included studies: targeted resistive training (5 studies) and training with a threshold loading device (10 studies). In 6 studies IMT was added to general exercise reconditioning.

Participants included in the review
Studies with participants who had COPD were eligible for inclusion. The participants included in the treatment groups had a mean age of 63 (+/- 7) years (n=200), a mean height of 170 (+/- 8) cm (n=73), a mean weight of 70 (+/- 13) kg (n=97) and a mean body mass index of 25 (+/- 4) (n=65). The mean forced expiratory volume in one second was 43 (+/- 15%) (n=171), the mean forced residual capacity 148 (+/- 42%) (n=148), the mean PImax 71 (+/- 21%) (n=200) and the mean carbon dioxide tension in arterial blood 41 (+/- 6) mmHg (n=148).

Outcomes assessed in the review
Studies in which pulmonary function tests had been carried out and which reported outcomes for PImax, inspiratory muscle endurance, dyspnoea rating, 6- or 12-minute walking distance (6- or 12-MWD), and/or health-related quality of life were eligible for inclusion. The main outcomes included in the review were: inspiratory muscle strength (PImax), inspiratory muscle endurance (maximum voluntary ventilation in seconds or cmH2O), functional exercise capacity (6- or 12-MWD), laboratory exercise (capacity maximal oxygen consumption or capacity of maximal minute ventilation), and dyspnoea (Borg exercise-related and transitional dyspnoea index test). PImax was measured with maximal inspiratory mouth pressures from the percentage residual volume or FRC. One study used the sniff test to assess transdiaphragmatic pressure as a measure of inspiratory muscle strength.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The quality of the studies was assessed according to a modified version of the framework for methodological quality used by Smith et al. in a meta-analysis on the same topic (see Other Publications of Related Interest no.1). The areas assessed were randomisation, similarity of the groups, cointerventions, masking, outcome measures, compliance, exercise regime and follow-up. Two independent reviewers assessed study quality and agreement for each criterion was measured using a weighted kappa statistic. Any disagreements were resolved by consensus; where agreement could not be reached, a third reviewer made the decision.
**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Pulmonary function variables were presented as percentage predicted using normative data from Quanjer et al. (see Other Publications of Related Interest no.2). PImax was normalised using data from Rochester and Arora (see Other Publications of Related Interest no.3). Effect sizes for each study were calculated as the difference between the mean of the treatment group and the mean of the control group, divided by the pooled standard deviation of the post-treatment outcome measure of the treatment and control groups.

**Methods of synthesis**

How were the studies combined?
The effect sizes of the individual studies were weighted by sample size and then pooled using a fixed-effect model to produce a weighted summary effect size (SES). Where statistical heterogeneity was detected, a random-effects model was used. Where there were differences in the outcomes used in different studies, the studies were combined in a narrative.

How were differences between studies investigated?
The effect sizes for each outcome were assessed for statistical heterogeneity using the Q statistic. A sensitivity analysis weighted studies by quality, calculated by dividing the quality score of each individual study by the total possible score of 40, to assess the effects of quality on the results. Subgroup analyses were used to investigate studies in which IMT was used in addition to general exercise reconditioning, and to determine if the type of training device (threshold loading or flow-resistive loading) had an effect on the efficacy of IMT. Spearman rank correlation coefficients were calculated for baseline variables, and for improvements in inspiratory muscle strength and endurance in the treatment group, to assess any potential prognostic characteristics for the effectiveness of IMT. The number of studies needed to obtain a P-value of greater than 0.05 was calculated for each of the outcomes, in order to assess the effect of potential publication bias on the SES (Rosenthal file drawer method).

**Results of the review**
Fifteen RCTs with a total of 383 participants were included in the review.

Inter-observer agreement in the assessment of study quality had a median weighted kappa of 0.79. The total quality score for each study ranged from 12 to 31 out of a possible 40. The main problems with quality were poor descriptions of randomisation, no reporting of validity or reliability data for the outcome measures used, and a lack of blinding procedures.

The meta-analysis revealed a significant effect of IMT on inspiratory muscle strength (n=15; SES 0.56, 95% confidence interval, CI: 0.35, 0.77), inspiratory muscle endurance in seconds (n=7; SES 0.41, 95% CI: 0.14, 0.68), inspiratory muscle endurance in cmH2O (n=4; SES 1.16, 95% CI: 0.67, 0.15), Borg exercise-related dyspnoea (n=5; SES -0.55, 95% CI: -0.90, -0.19) and the traditional dyspnoea index test (n=2; SES 2.3, 95% CI: 1.44, 3.15). No statistically significant effects of IMT on functional or laboratory exercise capacity were found.

In the assessment of health-related quality of life, 2 studies found a significant improvement in both the control group and those receiving IMT, but no significant differences between the groups. Another 2 studies found no significant effect of IMT on health-related quality of life.

Baseline values for pulmonary function, inspiratory muscle strength and carbon dioxide tension in arterial blood were not found to be associated with improvements in inspiratory muscle strength or endurance.

The assessment of publication bias in the overall analysis showed that the number of studies needed to obtain a P-value of greater than 0.05 varied from 10 to 77 for outcomes that showed a statistically significant difference between the groups. Weighting studies for quality had little effect on the SES for all outcomes. No statistically significant heterogeneity between studies was found for the effect sizes in the overall analysis.
The subgroup analysis revealed no significant differences in inspiratory muscle strength or endurance between IMT using a threshold loading device or IMT using flow-resistive loading. The addition of IMT to general exercise reconditioning was found to have a significant effect on inspiratory muscle strength PImax (n=6; SES 0.47, 95% CI: 0.15, 0.79) and inspiratory muscle endurance in seconds (n=3; SES 0.55, 95% CI: 0.14, 0.97). Statistical heterogeneity was detected for the analysis of inspiratory muscle strength (n=6; chi-squared 13.28, P<0.05). Further subgrouping of the studies into those with and without inspiratory muscle weakness produced homogeneous groups. The group with inspiratory muscle weakness showed a statistically significant improvement in inspiratory muscle strength (n=3; chi-squared 8.81, P<0.01), whereas the group without inspiratory muscle weakness did not. Similar analyses with a random-effects model found neither group showed a significant improvement in inspiratory muscle strength, although the difference between the groups was still significant (P<0.05). There was no significant difference in functional exercise capacity between the groups.

**Authors' conclusions**
IMT can produce significant improvements in inspiratory muscle strength, inspiratory muscle endurance and dyspnoea, both at rest and during exercise. Functional exercise capacity did improve after IMT, but this change was not significant. Inspiratory muscle weakness was important in the effectiveness of IMT.

**CRD commentary**
The authors set out a clear objective at the beginning of the review, and the inclusion and exclusion criteria were defined clearly in terms of the participants, interventions, outcomes and study design. The search of two electronic databases was adequate, but since language was restricted to English, German and Dutch some relevant articles might have been missed. It was unclear how many reviewers selected the papers for inclusion and extracted the data; limiting these tasks to only one reviewer can increase the risk of introducing bias. Appropriate criteria were used to assess quality. Two independent reviewers performed the quality assessment, which helps to reduce bias.

The pooling of studies in a meta-analysis seemed appropriate, although a lack of information on the individual primary studies made this hard to assess. Some of the results did not seem to have been reported correctly (e.g. CIs not including the point estimate). The use of a qualitative synthesis for heterogeneous outcomes was sensible. Statistical heterogeneity was assessed for each of the meta-analyses and, where detected, subgroup analyses were used to investigate potential causes. However, the subgroup analyses included only small numbers of studies, which means that small treatment effects might have gone undetected. Methodological quality was assessed and found to have no effect on the results. This was generally a well-conducted review and the authors' conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that IMT was an important component of pulmonary rehabilitation programmes for people with COPD with inspiratory muscle weakness.

Research: The authors stated that studies that assess the effectiveness of IMT should select participants with COPD who have inspiratory muscle weakness.

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