Cochrane for Clinicians

Putting Evidence Into Practice

Inspiratory Muscle Training for Chronic Obstructive Pulmonary Disease

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Author disclosure: No relevant financial relationships.

Clinical Question

Is inspiratory muscle training alone or in combination with pulmonary rehabilitation effective for the treatment of chronic obstructive pulmonary disease (COPD)?

Evidence-Based Answer

Inspiratory muscle training improves symptoms, physical fitness, and quality of life in patients with COPD. When combined with pulmonary rehabilitation, inspiratory muscle training makes no difference compared with pulmonary rehabilitation alone.[1] (Strength of Recommendation: B, inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Primary care physicians treat approximately 80% of patients with COPD in the United States.[2] Pulmonary rehabilitation is an individualized, supervised program incorporating physiotherapy, nutritional and psychosocial care, and limb training. The Global Initiative for Chronic Obstructive Lung Disease guideline recommends pulmonary rehabilitation because it improves symptoms, exercise capacity, and quality of life across all grades of COPD severity. Inspiratory muscle training uses targeted exercises and devices to increase the strength and endurance of the diaphragm and intercostal muscles because weakness of inspiratory muscles is associated with dyspnea and respiratory failure in COPD.[3] Inspiratory muscle training is not typically included in pulmonary rehabilitation. The authors of the Cochrane review sought to determine if inspiratory muscle training alone or in combination with pulmonary rehabilitation can improve symptoms of COPD.

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, assistant medical editor.

A collection of Cochrane for Clinicians published in *AFP* is available at https://www.aafp.org/afp/cochrane.

CME This clinical content conforms to AAFP criteria for CME.
See CME Quiz on page 126.

This Cochrane review included 55 randomized controlled trials (RCTs) and 2,467 patients.[1] The studies were divided into two arms: pulmonary rehabilitation with inspiratory muscle training vs. pulmonary rehabilitation alone (22 RCTs; 1,446 participants) and inspiratory muscle training vs. control or sham (37 RCTs; 1,021 participants). The studies addressed pulmonary rehabilitation and inspiratory muscle training for interventions in COPD management. Participants were 44 years and older with stable COPD as diagnosed by the Global Initiative for Chronic Obstructive Lung Disease criteria.

Validated assessment tools were used to determine the effects on three primary outcomes: dyspnea, functional exercise capacity, and health-related quality of life. With these continuous data, the mean difference (MD) was used to analyze the size of the treatment effect: 0.2 represented a small effect, 0.5 was a medium effect, and 0.8 was a large effect. The tools used in the analysis for dyspnea were the Borg scale, the modified Medical Research Council dyspnea scale and the Baseline Dyspnea Index, and Transition Dyspnea Index. The measure for functional exercise capacity was the six-minute walk test, and the clinically significant measure for health-related quality of life was the COPD Assessment Test. The authors assessed the risk of bias in the included studies. Adverse effects were not reported.

When comparing inspiratory muscle training plus pulmonary rehabilitation to pulmonary rehabilitation alone, there was little to no difference in the scores of each of the three primary outcomes. However, inspiratory muscle training alone improved dyspnea compared with control or sham on the Baseline Dyspnea Index and Transition Dyspnea Index (MD = 2.98; 95% CI, 2.07 to 3.89; eight RCTs; 238 participants; very low-certainty evidence). Patients treated with inspiratory muscle training also demonstrated improvement in functional exercise capacity compared with control or sham, with an increase of 35.71 meters (95% CI, 25.68 to 45.74; 16 RCTs; 501 participants; moderate-certainty evidence) on the six-minute walk test. Inspiratory muscle training improved health-related quality of life (MD = –2.97; 95% CI, –3.85 to –2.10; two RCTs; 86 participants; moderate-certainty evidence) on the COPD Assessment Test, where any decrease in the test score represents a decrease in overall symptoms of COPD. The other assessments for health-related quality of life and inspiratory muscle strength found statistically significant improvement, but the clinical significance of these changes is questionable because of the risk of bias.

Limitations of the studies included heterogeneity in pulmonary rehabilitation and inspiratory muscle training

and the significant risk of bias within the included studies. Sources of bias were a lack of allocation concealment and a lack of blinding.

There are no guidelines recommending inspiratory muscle training in addition to pulmonary rehabilitation. This Cochrane review supports current respiratory society statements regarding pulmonary rehabilitation, which conclude that "[inspiratory muscle training] used in isolation does confer benefits across several outcome areas," but "its added benefit as an adjunct to exercise training in COPD is questionable."[4]

The practice recommendations in this activity are available at https://www.cochrane.org/CD013778.

The opinions and assertions expressed herein are those of the authors and are not to be construed as official or as reflecting the views of the U.S. Air Force, the U.S. Department of Defense, or the U.S. government.

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Effectiveness of Inhaled Corticosteroids for Acute Asthma Exacerbations

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Patient perspective by Helen Haskell

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Clinical Question

Does patient-initiated home management of asthma exacerbations with increased doses of inhaled corticosteroids (ICSs) reduce the need for further intervention compared with a daily maintenance dosage of an ICS among children and adults with mild to moderate persistent asthma?

Evidence-Based Answer

In this Cochrane review, patients with mild to moderate persistent asthma and symptoms consistent with an acute asthma exacerbation who are treated with increased doses of ICSs show no reduction in the need for further intervention with primarily systemic corticosteroids vs. patients treated with stable doses of ICSs. Similarly, increased doses of ICSs do not reduce unscheduled visits to physicians, acute care facilities, or emergency departments or hospital admissions compared with stable doses of ICSs.[1] (Strength of Recommendation: B, inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Asthma is a leading cause of morbidity and mortality related to chronic respiratory disease; it affects 272 million people worldwide.[2,3] Early recognition and management of asthma exacerbations are essential in reducing morbidity, mortality, and health care costs associated with asthma. Asthma action plans, which are written, patient-initiated, home management guidelines that describe maintenance therapy and steps for treatment escalation during an exacerbation, decrease the severity and duration of asthma exacerbations.[1] ICSs are a mainstay of asthma action plans, and the Global Initiative for Asthma (GINA) guideline recommends increased ICS dosing during an asthma exacerbation.[4]

The authors of the Cochrane review sought to determine the safety and effectiveness of increased ICS dosing as part of patient-initiated home management in children and adults with mild to moderate persistent asthma.[1] Asthma exacerbations required systemic corticosteroids or unscheduled medical attention, including unscheduled physician visits, urgent care and emergency department visits, and hospital admissions. The review included nine double-blinded, randomized controlled trials of participants with mild to moderate persistent asthma from North America, Europe, Australia, and New Zealand between 1998 and 2018; five trials included patients 15 years and older (n = 1,247), and four included children younger than 15 years (n = 676).[1] The primary outcome was treatment failure, defined as patients requiring rescue systemic corticosteroids. Secondary outcomes included unscheduled physician visits, urgent care and emergency department visits, hospital admissions, and exacerbation duration (i.e., time until symptom recovery, lung function recovery, or return to baseline $beta_1$ agonist use). Nonserious and serious adverse events, including hospitalization, prolongation of hospitalization, disability, fatality, or study withdrawal related to any adverse event, were considered secondary outcomes.[1,5]

Among children and adults with mild to moderate persistent asthma, action plans that instructed patients to increase their ICS dose at the onset of worsening asthma symptoms did not reduce asthma exacerbation severity or duration and, therefore, did not reduce the need for systemic corticosteroids. Unscheduled physician visits, visits to the emergency department, and hospitalizations were not reduced. Secondary outcomes, including serious and

nonserious adverse events associated with increased ICS dosing, could not be included or excluded due to a lack of clinical significance.[1]

These conclusions are limited by biases notable within the individual trials, including differences among studies about the patient's baseline ICS dose, how much the treatment dose of ICS increased, how adherent patients were to their asthma action plan before the trial, and what the patient's baseline asthma severity was.[1] Such biases result in wide CIs that limit the statistical validity and make the quality of data presented less helpful. Of note, study populations were limited to patients with mild to moderate persistent asthma; therefore, conclusions cannot be extended to patients with more severe asthma.

A notable 2018 nonblinded study, which was excluded from this Cochrane review, indicated that quadrupling the ICS dose may reduce systemic corticosteroid use or an unscheduled health care consultation for asthma over 12 months (incidence rate ratio = 0.82; 95% CI, 0.70 to 0.96), particularly among people with more severe asthma.[6] This review had several challenges, including the absence of a placebo control group, recruitment of a population not taking maintenance ICS, and a design that compared the relative effectiveness of two dosages of ICS as maintenance therapy. Further research is necessary.

Although the results of this Cochrane review suggest the use of stable ICS dosing during an exacerbation among patients with mild to moderate persistent asthma, the GINA guideline recommends increasing ICS use as part of patient-initiated asthma action plans during an acute exacerbation.[4] The GINA authors note that "little benefit may be seen from increasing maintenance doses of ICS when background adherence is high" but emphasize several studies that were outside the scope of this Cochrane review to create their guidance. Family physicians should be prepared to discuss the evidence in the updated GINA recommendations with patients who have mild to moderate asthma.

Patient Perspective

For patients and parents of children with asthma, a change in treatment can be unsettling. Especially because of the limitations noted by the Cochrane reviewers, it may be hard for patients to understand asthma recommendations and findings clearly. Patients should be reminded that medical recommendations are not set in stone but continually change and evolve.

One reason for the change in the GINA guidelines is research indicating that there is a greater risk than previously understood from short-acting beta agonists such as albuterol.[4] The many interactions and contraindications of the ICS/formoterol combination are barely discussed in the GINA update; however, they were the subject of U.S. Food and Drug Administration warnings until recently and are detailed on reliable patient information websites.[7-9] So, what is a patient to think? Effectiveness matters, but so does risk. The lesson seems to be that untreated asthma and its available treatments both entail a relatively high degree of risk. Altogether, it seems wise to recognize that there is substantial scope for professional and patient judgment and preference in the treatment of asthma exacerbations.

The practice recommendations in this activity are available at https://www.cochrane.org/CD007524.

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