

EBEM Commentator

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Are Corticosteroids
Effective in Acute
Exacerbations of Chronic
Obstructive Pulmonary
Disease?

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SYSTEMATIC REVIEW
SOURCE

This is a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the Cochrane Database of Systematic Reviews and a commentary by an emergency physician knowledgeable in the subject area.

The source for this systematic review abstract is: Wood-Baker R, Walters EH, Gibson P. Oral corticosteroids for acute exacerbations of chronic obstructive pulmonary disease (Cochrane Review). In: *The Cochrane Library*. Issue 1. Oxford, United Kingdom: Update Software; 2003.

The *Annals'* EBEM editors helped prepare the abstract of this Cochrane systematic review as well as the Evidence-Based Medicine Teaching Points.

OBJECTIVE

To determine whether corticosteroid therapy is of benefit in the treatment of patients with acute exacerbations of chronic obstructive pulmonary disease.

DATA SOURCES

Studies were identified by searching the Cochrane Airways Review Group chronic obstructive pulmonary disease randomized controls trial register and MEDLINE. The reviewers also wrote to study authors and searched bibliographies of relevant articles.

STUDY SELECTION

Studies were included if they were randomized controlled trials comparing systemic (oral or parenteral) corticosteroids with placebo in adults with chronic obstructive pulmonary disease with recent functional deterioration. Studies enrolling patients with acute asthma were excluded.

DATA EXTRACTION

Two reviewers independently selected trials for inclusion in the review and evaluated study quality. One reviewer extracted data, which

were sent to the authors for verification. Where author contact was unsuccessful, a second reviewer extracted data. Odds ratios (ORs) and weighted mean differences or standardized mean differences with 95% confidence intervals (CIs) are reported.

MAIN RESULTS

Seven trials that involved more than 600 adult patients were included. Two of the studies were published in abstract form only. Four studies looked specifically at patients admitted to hospital, 2 involved emergency department (ED) patients, and 1 examined outpatients. Outcomes reported varied, and few were common to all studies. The most commonly reported outcome, the forced expiratory volume in one second (FEV₁) between 6 and 72 hours after treatment, showed a significant treatment benefit for corticosteroids (weighted mean difference 120 mL [95% CI 5 to 190 mL]). There were also significantly fewer treatment failures in patients treated with corticosteroids; however, the number of trials reporting this outcome was small, and there was significant heterogeneity between them. There was an increased likelihood of an adverse drug reaction with corticosteroid treatment.

CONCLUSIONS

Corticosteroids increase the rate of lung function improvement during the first 72 hours after an exacerbation of chronic obstructive pulmonary disease, but at an increased risk of an adverse drug reaction. There is no evidence that the benefit is maintained after 72 hours, and no clear benefit on other outcomes.

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COMMENTARY: CLINICAL IMPLICATIONS

Despite the frequency of chronic obstructive pulmonary disease exacerbations, only a small number of studies have addressed the use of corticosteroids, and significant controversy remains regarding their use in acute chronic obstructive pulmonary disease. Recent studies suggest ED patients are prescribed corticosteroids (65%) more often than antibiotics (30%) at discharge, and clinical practice guidelines often recommend corticosteroids.¹

This systematic review searched for the best available evidence regarding the use of systemic corticosteroids in the treatment of chronic obstructive pulmonary disease. The review included studies with patients from a variety of settings (admitted patients, ED patients, and outpatients), with a wide range of severity. The outcomes reported in the studies were diverse, and there was significant heterogeneity between the studies for several outcomes, which limited the amount of data available for pooled analyses. The primary analysis demonstrated a small benefit of corticosteroids in FEV₁ at 72 hours, but this benefit was of questionable clinical importance and was offset by an increase in side effects attributed to the medications. There was no demonstrated benefit of corticosteroids on forced vital capacity (FVC) at 72 hours, or on "late" FEV₁ or FVC. There were no demonstrated differences for other out-

comes, including mortality, quality of life, and exercise tolerance.

Does this mean emergency physicians should abandon the use of corticosteroids in patients with chronic obstructive pulmonary disease? Perhaps not. Despite the solid techniques used in this meta-analysis, we should be cautious applying these results to our ED patients. The wide variety of patients in this meta-analysis may not be representative of the typical ED patient with chronic obstructive pulmonary disease, and a relatively small number of patients contributed data to each outcome. In addition, the primary outcome of improvement in FEV₁ may not measure differences that are important to physicians (who might prefer to decrease ED relapse or mortality) or patients (for whom quality of life might be most important). Of particular note, treatment failure, which combined ED relapse and repeat hospitalization, was a secondary outcome for this study. Despite the fact that there was significant statistical heterogeneity for this outcome, the overall effect showed a marked benefit of corticosteroids (OR for relapse 0.50), and 4 of the 5 studies appear to point toward a benefit of corticosteroids. Subgroup analyses are risky in meta-analyses, but one wonders if certain patients (eg, those with more severe exacerbations) may derive more benefit from corticosteroids.

So the debate continues: who, if any, of our patients with chronic obstructive pulmonary disease should receive steroids in the ED? Unfortunately, this meta-analysis does not really answer our question—yet. This systematic review should be due for an update soon (the Cochrane Library aims to have the reviews updated every year²), and

research is ongoing in this area. More studies, with standardized outcomes, are needed to clarify the issue.

TAKE HOME MESSAGE

There is insufficient evidence to draw firm conclusions regarding the use of corticosteroids in the acute treatment of chronic obstructive pulmonary disease. Although most current guidelines recommend corticosteroids and their use is common, the evidence is strongest for admitted patients. More studies are needed to clarify the role of corticosteroids in the ED setting, especially for those patients discharged from the ED with an exacerbation of chronic obstructive pulmonary disease.

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EVIDENCE-BASED MEDICINE TEACHING POINTS

Blinding. Blinding (or masking) in randomized controlled trials indicates that the group assignment (eg, to treatment or control) is kept a secret. A number of different groups involved in a study may be blinded: study participants, health care providers, study investigators, data collectors, data analysts, data interpretation, and those writing up the study report. Blinding is performed to attempt to minimize bias from a number of sources.

Blinding may decrease bias in a number of ways. First, blinding attempts to minimize any placebo effect of a therapy, and compliance

with treatment and use of concurrent therapies may also be affected by unblinding. Second, blinding of clinicians aims to minimize performance bias, which is the differential treatment of patients because of the knowledge of whether they are receiving active treatment.

Unblinded data collectors could distort trial results by differing intensity of questioning or examination for treatment effect or side effects because of their knowledge of treatment allocation (detection bias). Data collectors may also record outcomes differently based on knowledge of which treatment the patient is receiving. Unblinded data analysts and authors can further introduce bias by decisions on which outcomes to analyze or report, decisions regarding patient exclusions and withdrawals, and their interpretation of the data.

Despite the attention paid to the importance of blinding, little is known about the true effect of blinding on the various groups. The placebo effect was described as early as 1955, but the true size of its effect is still unclear.³ Few studies have looked at the effect of blinding on trial results. Those who have examined this question have looked at the influence of reporting of double blinding on trial results, and they have had conflicting results.⁴

In addition, a recent study has called into question the reporting and interpretation of blinding. Although conventional descriptions of blinding have included the use of the terms "single," "double," and "triple" blinding, the authors demonstrated a wide variability in interpretation of these terms by both clinicians and textbooks. Instead, they recommend including descriptions of which groups were unaware of treatment

allocation, which is consistent with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.⁴

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