Are Shorter Courses of Corticosteroids as Effective as Longer Courses in Acute Exacerbations of Chronic Obstructive Pulmonary Disease?

TAKE-HOME MESSAGE

In patients with acute chronic obstructive pulmonary disease exacerbation, short-term corticosteroids (<7 days) have similar rates of treatment failure, relapse, and medication adverse effects compared with longer-term corticosteroid therapy.

METHODS

DATA SOURCES

Authors identified trials from the Cochrane Airways Trials Register, CENTRAL, MEDLINE, and EMBASE; evaluated reference lists of included randomized controlled trials for additional studies; and searched ClinicalTrials.gov and the World Health Organization trial portal.

STUDY SELECTION

At least 2 authors assessed studies for relevance. Investigators included randomized controlled trials of adults with acute exacerbation of chronic obstructive pulmonary disease who were randomized to systemic corticosteroids for a short duration (ie, <7 days) or long duration (ie, >7 days). Included patients had severe to very severe chronic obstructive pulmonary disease (forced expiratory volume in 1 second 0.5 to 0.8 L or 25% to 33% of predicted). Investigators required that included studies standardize cointerventions across groups and excluded patients with asthma or other lung disease. Authors resolved disagreements

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Walters JAE, Tan DJ, White CJ, et al. Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease (review). *Cochrane Database Syst Rev.* 2018;3:CD006897.**

Jestin N. Carlson, MD, MS, and Alan Jones, MD, serve as editors of the SRS series.

Results

Difference in outcomes between patients treated with a short versus longer course of corticosteroids.

Outcome	No. of Studies (Patients)	Relative Effect, OR (95% CI)	Evidence Quality (GRADE)	Heterogeneity, I^2, %
Treatment failure	4 (457)	0.72 (0.36–1.46)	Moderate	0
Relapse	4 (478)	1.04 (0.70–1.56)	Moderate	0
Hyperglycemia	2 (345)	0.99 (0.64–1.53)	Moderate	0
Other adverse effects*	5 (503)	0.89 (0.46–1.69)	Low	0

OR, Odds ratio; *GRADE*, Grading of Recommendations Assessment, Development and Evaluation.

*Other adverse effects included gastrointestinal bleeding, gastroesophageal reflux, sleep disturbance, symptoms of congestive heart failure or ischemic heart disease, fracture, and depression.

Authors included 8 randomized controlled trials comprising 582 patients for qualitative analysis from 417 citations retrieved from their initial literature search. Of these, 5 randomized controlled trials met criteria for meta-analysis. The 8 included studies were parallel-group randomized controlled trials comparing

through consensus or discussion with a third author.

DATA EXTRACTION AND SYNTHESIS

Two investigators independently extracted data from included studies. Primary outcomes included treatment failure, relapse after therapy, and adverse drug effects. Authors analyzed continuous variables with mean differences and 95% confidence intervals (CIs) and standardized mean differences with 95% CIs for different scales of measurement. Investigators used Mantel-Haenszel odds ratios with 95% CIs for dichotomous outcomes. Authors used fixed-effect generic inverse variance outcomes for time-to-event outcomes. Investigators assessed heterogeneity with the I^2 statistic and χ^2 test. Two authors independently assessed risk of bias according to the *Cochrane Handbook for Systematic Reviews of Interventions*.[1]

systemic corticosteroids for short or longer duration in hospital settings. Study size varied from 21 to 314 patients, mean age was 65 to 73 years, and most patients were men (58% to 94% of included patients). Five studies used oral prednisolone only, and 3 used intravenous systemic corticosteroids. Length of therapy for short-duration groups included 3, 5, or 7 days, whereas longer-duration therapy lasted 10, 14, or 15 days. Studies were of good methodological quality, and most studies were at low risk of selection, performance, detection, and attrition bias, with some heterogeneity present in regard to inclusion criteria. Meta-analysis results suggest no difference in primary outcomes, including treatment failure, relapse, and drug adverse effects; or in secondary outcomes, including mortality, length of hospitalization, arterial blood gas components, lung function, and health-related quality of life (Table).

Commentary

Chronic obstructive pulmonary disease is characterized by persistent, often progressive, airflow obstruction, as well as chronic pulmonary inflammation.[2] Chronic obstructive pulmonary disease exacerbations result in increased mortality and worsening quality of life.[2-5] These exacerbations often require emergency department (ED) evaluation and management, with inciting causes typically including infection.[2,6,7] ED management includes addressing the underlying cause of exacerbation and decreasing airway obstruction and inflammation.[7,8] Corticosteroids may reduce systemic inflammation and airway edema, and literature suggests that systemic corticosteroids decrease treatment failure, decrease length of stay, and improve lung function in chronic obstructive pulmonary disease.[2,8,9] However, these medications have adverse drug effects that may increase with longer duration, frequency of exposure, and total dose of corticosteroid.[2]

The 2018 Global Initiative for Chronic Obstructive Lung Disease report recommends using corticosteroids for no longer than 5 to 7 days for acute chronic obstructive pulmonary disease exacerbation,[2] although other guidelines for corticosteroid therapy differ in regard to duration (7 to 14 days).[10,11] This current meta-analysis compared short-term systemic corticosteroids (<7 days) with longer-term duration (>7 days) in patients with severe or very severe chronic obstructive pulmonary disease, finding no difference in likelihood of treatment failure, risk of relapse, or adverse medication effects between short- and longer-term therapies. Secondary outcomes, including mortality, length of hospitalization, lung function, arterial blood gas components, symptom scores, and quality of life, also did not differ. Included studies were at low risk for selection, detection, and attrition bias.

Limitations of this meta-analysis include the need to exclude 3 studies because of unavailable data and small number of included patients in the meta-analysis. This small number of patients also precluded subgroup analyses. The meta-analysis authors included 5 studies not published as full articles and excluded 3 studies because of inability to obtain full data. Evaluating studies published as an abstract only is a significant limitation because it can be challenging to critically appraise their methodologies for sources of bias and quality. These studies may have had significant methodological flaws, which may in turn have precluded publication. Another important meta-analysis limitation is that studies did not include patients with mild or moderate chronic obstructive pulmonary disease; however, these patients are more likely to be discharged from the ED and therefore highly relevant to emergency medicine practice. Next, this meta-analysis also excluded patients requiring assisted ventilation (invasive and noninvasive). Also, there was limited information

about inclusion criteria. Finally, some variation existed in regard to route of systemic corticosteroids administration, with 2 studies using intravenous corticosteroids and 5 using oral corticosteroids.

This meta-analysis suggests that short-term systemic corticosteroids are sufficient for chronic obstructive pulmonary disease exacerbation. Further study is necessary in regard to patients with mild or moderate chronic obstructive pulmonary disease, and this meta-analysis emphasizes the need for studies to provide full results in publication.

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