What effect do inhaled steroids have on delaying the progression of COPD?

EVIDENCE-BASED ANSWER

The annual rate of decline in forced expiratory volume for 1 second (FEV₁) has been researchers' gold standard as an objective measure for progression of chronic obstructive pulmonary disease (COPD). Inhaled corticosteroids (ICS) do not consistently have a statistically significant impact on FEV₁ decline, and thus on the progression of COPD (strength of recommendation [SOR]: **B**, 2 conflicting meta-analyses and numerous conflicting randomized controlled trials). In those studies that did show improvements in FEV₁ decline, the change does not appear to be clinically significant (7.7 to 9.0 mL/year).

These findings do not take into account the potential impact of ICS on such patient oriented outcomes as exacerbation rates, quality of life, outpatient visits, hospitalization, and mortality.

EVIDENCE SUMMARY

No therapies are known to improve long-term lung function in COPD; the goal of disease-moderating therapy is therefore to *slow the rate* of decline compared with the expected rate. All of the studies reviewed used FEV_1 as an objective measure of whether ICS reduce this rate of decline in lung function.

Two recent meta-analyses evaluating medium- to high-dose ICS effects on FEV₁ decline provided conflicting results. One meta-analysis evaluated 8 controlled clinical trials lasting at least 2 years (n=3715) and found that, when compared with placebo, ICS significantly reduced the rate of FEV₁ decline by 7.7 mL/year (P=.02) and that *high-dose* ICS had a greater effect of 9.9 mL/year (P=.01).¹ Another metaanalysis of 6 randomized, placebo-controlled trials with a duration of at least 2 years (n=3571) found a nonsignificant trend in favor of ICS, It is imperative for FPs to emphasize the huge benefit of smoking cessation to all COPD patients

with a difference in FEV_1 decline of 5.31 mL/year (*P*=.08) between the ICS and placebo groups.²

The differences observed in these 2 metaanalyses may be explained by the authors using slightly different approximations to the standard error, applying slightly different statistical analytical methods, and using different inclusion criteria for trials. However, 5 of the trials in these reviews were the same. Both meta-analyses determined only rate of lung function decline and did not evaluate clinical outcomes.

A trial not included in the previously mentioned meta-analyses evaluated post-bronchodilator FEV₁ decline in 48 patients with *early* signs and symptoms of COPD for 2 years.³ Subjects were assigned to medium-dose fluticasone propionate or placebo. Early initiation of ICS treatment did not affect the progressive deterioration of lung function as no modifying effect on annual FEV₁ decline was observed, however, the study only had power to detect a 60-mL annual drop in FEV₁.

Meta-analyses and trials evaluating COPD progression have focused on a disease-oriented outcome (the rate of FEV_1 decline). However, patient-oriented outcomes such as exacerbation frequency, hospitalization, health-related quality of life, and mortality might be more important measures of successful therapy. Although such patient-oriented outcomes are not the focus of this review or the included meta-analyses, a few of the small randomized controlled trials included in these meta-analyses suggest that ICS may improve such patient-oriented outcomes. Notably, exacerbation rates significantly decreased by 25% (P=.026), and health status improved (P=.0043) among patients with moderate to severe COPD who were taking fluticasone compared with those taking placebo.⁴

Inhaled corticosteroids do not consistently have an impact on delaying the progression of COPD

In mild to moderate COPD, patients treated with triamcinolone had fewer respiratory symptoms (P=.005), fewer visits to a physician because of respiratory illness (P=.003), and improved airway reactivity (P=.02).⁵ Some systematic reviews and other randomized trials suggest that ICS have significant benefit on these patient outcomes.⁶

RECOMMENDATIONS FROM OTHERS

Scientists from the National Heart, Lung, and Blood Institute and the World Health Organization provided an update of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) in 2003.7 They reported that regular treatment with ICS does not modify the long-term decline of FEV_1 in patients with COPD. However, they recommended treatment with ICS for symptomatic COPD patients with an FEV_1 less than 50% of predicted (stage III: severe COPD and stage IV: very severe COPD) and repeated exacerbations (ie, 3 in the last 3 years). Guidelines from other countries also suggest that ICS do not affect the progression of COPD, but support the use of ICS for patients with severe COPD and repeated exacerbations.8-10

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■ CLINICAL COMMENTARY

Smoking cessation a huge benefit to all COPD patients

In adults aged more than 30 years old with COPD, the physiological abnormality is primarily an accelerated decline in the FEV_1 from the normal rate of about 30 mL per year to nearly 60 mL per year. In patients with COPD, smoking cessation is the only proven means to slow down the progression of the disease, with up to a sustained 50% reduction in the rate of lung-function decline.

Therefore, it is imperative for family physicians to underscore the magnitude of the benefit of smoking cessation to all COPD patients and to emphasize the current evidence that inhaled corticosteroid has a limited impact in delaying the progression of the disease.

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