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

It is imperative for FPs to emphasize the huge benefit of smoking cessation to all COPD patients

EVIDENCE-BASED ANSWER

The annual rate of decline in forced expiratory volume for 1 second (FEV_1) 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 FEV_1 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 FEV_1 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 FEV_1 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 FEV_1 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 meta-analysis of 6 randomized, placebo-controlled trials with a duration of at least 2 years (n=3571) found a nonsignificant trend in favor of ICS, 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 meta-analyses 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 FEV_1 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 FEV_1 decline was observed, however, the study only had power to detect a 60-mL annual drop in FEV_1.

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]

CONTINUED

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]

Laura Hansen, PharmD, James Havemann, MD, Martha Burroughs, MLS, University of Colorado Health Sciences Center, Denver

REFERENCES

1. Sutherland ER, Allmers H, Ayas NT, Venn AJ, Martin RJ. Inhaled corticosteroids reduce the progression of airflow limitation in chronic obstructive pulmonary disease: a meta-analysis. *Thorax* 2003; 58:937–941.
2. Highland KB, Strange C, Heffner JE. Long-term effects of inhaled corticosteroids on FEV1 in patients with chronic obstructive pulmonary disease. A meta-analysis. *Ann Intern Med* 2003; 138:969–973.
3. van Grunsven P, Schermer T, Akkermans R, et al. Short- and long-term efficacy of fluticasone propionate in subjects with early signs and symptoms of chronic obstructive pulmonary disease. Results of the DIMCA study. *Respir Med* 2003; 97:1303–1312.
4. Burge PS, Calverley PM, Jones PW, Spencer S, Anderson JA, Maslen TK. Randomised, double blind, placebo controlled study of fluticasone propionate in patients with moderate to severe chronic obstructive pulmonary disease: the ISOLDE trial. *BMJ* 2000; 320:1297–1303.
5. The Lung Health Study Research Group. Effect of inhaled triamcinolone on the decline in pulmonary function in chronic obstructive pulmonary disease. *N Engl J Med* 2000; 343:1902–1909.
6. Sin DD, McAlister FA, Man SF, Anthonisen NR. Contemporary management of chronic obstructive pulmonary disease: scientific review. *JAMA* 2003; 290:2301–2312.
7. Global initiative for chronic obstructive lung disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. NHLBI/WHO workshop report. Bethesda, National Heart, Lung and Blood Institute, April 2001; update of the management sections, GOLD website (www.goldcopd.com). Accessed April 3, 2004.
8. Chronic Obstructive Pulmonary Disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004; 59 Suppl 1:1–232.
9. McKenzie DK, Frith PA, Burdon JG, Town GI. The COPDX Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2003. *Med J Aust* 2003; 178 Suppl:S7–S39.
10. O'Donnell DE, Aaron S, Bourbeau J, et al. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease—2003. *Can Respir J* 2003; 10 Suppl A:11A–65A.

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.

Vincent Lo, MD, St. Elizabeth Family Medicine Residency Program, Utica, NY; SUNY Upstate Medical University, Syracuse

CONTINUED