Inhaled triamcinolone did not slow the decline in pulmonary function in patients with COPD

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 Dec 28;343:1902-9.

QUESTION

In patients with chronic obstructive pulmonary disease (COPD), does triamcinolone decrease the rate of decline in lung function or reduce symptoms, morbidity, or airway reactivity without adverse effects?

DESIGN

Randomized {allocation concealed*},† blinded (patients, clinicians, and outcome assessors),* placebo-controlled trial with mean follow-up of 40 months.

SETTING

10 centers in the United States and Canada.

PATIENTS

1347 patients were screened, and 1116 (mean age 56 y, 63% men) were studied. Inclusion criteria were age 40 to 69 years, presence of airflow obstruction, ratio of FEV_1 to forced vital capacity (FVC) < 0.7, and FEV_1 30% to 90% of predicted value. All patients were current smokers or had quit within the previous 2 years. Exclusion criteria were other serious medical conditions or use of bronchodilators or corticosteroids in the previous year. Follow-up range was 91% to 96%.

INTERVENTION

559 patients were allocated to triamcinolone given by metered-dose inhaler, 6 inhalations of 100 µg/inhalation twice daily (1200 µg/d). 557 patients were allocated to placebo inhalers.

MAIN OUTCOME MEASURES

Rate of decline in FEV_1 (progression of COPD). Secondary outcomes were respiratory symptoms, cause-specific morbidity and mortality, airway reactivity in response to methacholine, and general health-related quality of life (8 indicators).

MAIN RESULTS

The groups did not differ for decline in FEV_1 (mean decline was 44.2 mL/y in the triamcinolone group vs 47.0 mL/y in the placebo group, 95% CI for the difference −11 to 5.4 mL/y) or FVC; incidence of respiratory symptoms, except for less dyspnea and fewer new general breathing problems in the triamcinolone group; all-cause mortality (15 deaths in the triamcinolone group vs 19 in the placebo group, $P = 0.49$); general quality-of-life indicators, except for the mental health subscale, which showed worse scores at 36 months in the triamcinolone group; and adverse effects, except for more mouth irritation and a reduction in bone mineral density in the triamcinolone group. Patients in the triamcinolone group also had less airway reactivity at 9 and 33 months ($P = 0.02$ for both comparisons). Unscheduled physician visits were less frequent in the triamcinolone group (1.2 vs 2.1 visits per 100 person-y, $P = 0.03$) as were deaths from nonlung cancer (2 vs 10, $P = 0.02$).

CONCLUSION

Inhaled triamcinolone did not slow the decline in lung function in patients with chronic obstructive pulmonary disease, although airway reactivity was less, some symptoms were improved, and fewer unscheduled physician visits were made.

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*See Glossary.

†Information provided by author.

COMMENTARY

The study by the Lung Health Study Research Group (LHRG) of patients with mild COPD was 1 of several long-term studies to test the effect of inhaled corticosteroids (ICSs) on rate of decline of FEV_1 in COPD. All the studies were of similar design, but they were done in patients who had different degrees of severity of COPD and who were recruited from different settings. In terms of FEV_1 (the primary outcome), the studies were all consistent: The rate of decline was unaltered. However, FEV_1 reflects only 1 component of a complex chronic pathophysiologic process. In the trial by the LHRG, several clinical measures of disease activity were used as secondary outcomes, and consistency was found between these and related observations from the Inhaled Steroids in Obstructive Lung Disease (ISOLDE) trial (1), a similar study of ICSs in patients with moderate-to-severe COPD. Respiratory symptoms developed less frequently in the ICS group in the trial by LHRG, and deterioration in disease-specific, health-related quality of life was reduced in the ISOLDE study (1). Similarly, ICS-treated patients in the LSRG trial required fewer physician visits and had fewer exacerbations requiring medical therapy than those in the ISOLDE trial (1). Mechanisms responsible for the ICS effect in COPD are not clear, but this new study has made a notable contribution by showing improved bronchial hyperreactivity—a predictor of mortality (2). Concern over long-term ICS use exists, with a small reduction in bone mineral density in ICS-treated patients being reported, but it is difficult to assess its importance. The loss was detected only after 1 year of therapy. Older patients reported no excess of fractures after 3 years of ICS treatment (1).

Evidence from this study, combined with that from its predecessors, suggests that ICS may produce long-term symptomatic gain and a reduction in exacerbations and health resource use, but these drugs have no role in early or presymptomatic disease.

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References

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