Review: Long-acting β_2-agonists and inhaled corticosteroids reduce exacerbations in chronic obstructive pulmonary disease

Sin DD, McAlister FA, Man SF, Anthonisen NR. **Contemporary management of chronic obstructive pulmonary disease: scientific review.** JAMA. 2003;290:2301-12.

QUESTION

What are the effects of commonly used treatments for chronic obstructive pulmonary disease (COPD) on patient outcomes?

DATA SOURCES

Studies were identified by searching MEDLINE (1980 to 1 May 2002) and the Cochrane Database of Systematic Reviews, reviewing bibliographies of published articles, and contacting experts.

STUDY SELECTION AND ASSESSMENT

Studies were selected if they were English-language, randomized controlled trials (RCTs) with ≥ 3 months of follow-up in adults with COPD and assessed long-acting (LA) β_2-agonists (β_2As); LA inhaled anticholinergics (tiotropium); combined short-acting (SA) β_2As and SA anticholinergics; inhaled corticosteroids; combined inhaled corticosteroids and LAβ_2As; pulmonary rehabilitation (with ≥ 6-wk follow-up); long-term nocturnal noninvasive mechanical ventilation; domiciliary oxygen therapy; or disease management (any combination of patient education, enhanced follow-up, and self-management sessions). Analysis was restricted to RCTs with blinded {only drug interventions where placebo was possible}* ascertainment of outcomes, complete or near-complete {> 90%}* follow-up data, and well-balanced baseline characteristics in treatment and control groups.

OUTCOMES

COPD exacerbations and mortality.

MAIN RESULTS

The results are summarized in the Table.

CONCLUSION

In patients with chronic obstructive pulmonary disease, long-acting (LA) β_2-agonists (β_2As) and inhaled corticosteroids, with and without LAβ_2As, reduce exacerbations, but not mortality.

*Information provided by author.

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Summary of efficacy data for interventions for chronic obstructive pulmonary disease†

Comparisons	RRR/RRI (95% CI)	
	Exacerbation	Mortality
LAβ_2A vs placebo	RRR 21% (10 to 31)	RRR 24% (–48 to 61)‡
Tiotropium vs placebo	RRR 26% (11 to 38)	NA
Tiotropium vs LAβ_2A	RRR 7% (–8 to 20)‡	NA
Tiotropium vs ipratropium	RRR 22% (5 to 37)	NA
SAβ_2A + anticholinergic vs SAβ_2A	RRR 32% (9 to 49)	RRI 18% (–66 to 308)‡
SAβ_2A + anticholinergic vs ipratropium	RRI 4% (–35 to 68)‡	RRI 256% (–41 to 2053)‡
Inhaled corticosteroids vs placebo	RRR 24% (20 to 28)	RRR 22% (–5 to 42)‡
Inhaled corticosteroids + LAβ_2A vs placebo	RRR 30% (22 to 38)	RRR 48% (–34 to 80)‡
Inhaled corticosteroids + LAβ_2A vs LAβ_2A	RRR 20% (10 to 29)	NA
Inhaled corticosteroids + LAβ_2A vs inhaled corticosteroids	RRR 10% (–2 to 20)‡	NA
Pulmonary rehabilitation vs control (usual care, placebo, or education)	NA	RRR 10% (–24 to 35)‡
Supplemental oxygen vs usual care (patients with resting PaO_2 < 60 mm Hg sea level)	NA	RRR 39% (18 to 54)
Supplemental oxygen vs usual care (patients with resting PaO_2 ≥ 60 mm Hg sea level)	NA	RRI 16% (–15 to 58)‡
Disease management vs usual care	NA	RRR 37% (–4 to 62)‡

†SAβ_2A = short-acting β_2-agonist; LAβ_2A = long-acting β_2-agonist; NA = not assessed. Other abbreviations defined in Glossary; RRR, RRI, and CI calculated from data in article.
‡Not significant.

COMMENTARY

The review by Sin and colleagues covers a wide range of treatments for COPD. Breadth is achieved at the expense of detail, but the authors provide a useful overview. A major criticism of respiratory medicine has been the absence of large, long-term studies, unlike the field of cardiology.

In the controversial area of inhaled corticosteroid therapy for COPD, an attempt was made to rectify this paucity with several reasonably large studies that lasted ≥ 3 years. These studies provided some important answers, but still left unanswered questions. 2 meta-analyses (1, 2) published in 2003 found a slower decline in FEV_1 with inhaled corticosteroids compared with placebo, but the difference was < 10 mL/y, and the authors came to opposite conclusions on the importance of the finding. These meta-analyses included more studies than the review by Sin and colleagues, but the lack of available details makes comparisons difficult.

Recent studies of COPD have concentrated on clinically relevant outcomes, such as exacerbations, quality of life, and admissions, although definitions of exacerbations vary. LAβ_2As, tiotropium, and inhaled corticosteroids all reduce exacerbations by 20% to 30% relative to placebo. The added benefits of combination therapies on various endpoints are difficult to extricate and need further study. Corticosteroids seem to add to the effect of LAβ_2As. The results provide a good case for LAβ_2As or tiotropium in patients with more than mild COPD and inhaled corticosteroids in patients with more severe disease.

Good evidence exists on the benefits of rehabilitation in the short to medium term, although there is uncertainty on how to maintain the initial benefit, and many countries have difficulty providing adequate respiratory rehabilitation programs. Smoking cessation and long-term oxygen therapy are the only treatments that significantly improve the natural history and life expectancy of persons with COPD.

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References

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