Review: Regular inhaled short-acting β_2-agonists improve lung function in stable chronic obstructive pulmonary disease

Ram FS, Sestini P. **Regular inhaled short acting β_2 agonists for the management of stable chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis.** Thorax. 2003;58:580-4.

QUESTION

Is regular treatment with inhaled short-acting β_2-agonists (ISABAs) effective for stable chronic obstructive pulmonary disease (COPD)?

DATA SOURCES

Studies were identified by searching the Cochrane Collaboration trials register up to and including May 2002 and reviewing reference lists of review articles and retrieved studies.

STUDY SELECTION

Studies were selected if they were randomized, placebo-controlled trials (RCTs) of ISABAs given to patients with stable COPD for ≥ 7 days.

DATA EXTRACTION

Data were extracted on study duration, patient age, severity of COPD, concomitant medication, setting, type of ISABA, dose and delivery system, and use of a washout period. Individual study quality was assessed on the basis of allocation concealment. Outcomes included forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), peak expiratory flow rate (PEFR), breathlessness (7-point Likert scale), treatment failure, and patient preference.

MAIN RESULTS

13 crossover trials met the selection criteria (n = 237, age range 56 to 70 y). Patients were primarily men, and study duration ranged from 1 to 8 weeks. Drugs assessed were isoproterenol, terbutaline, and salbutamol; most were administered using pressurized metered-dose inhalers or other hand-held inhalers. Meta-analysis showed that patients who received ISABAs had improved postbronchodilator FEV_1, FVC, morning and evening PEFR, and breathlessness scores and fewer treatment failures compared with those who received placebo (Table). Patients preferred ISABAs to placebo (Table).

CONCLUSION

Regular inhaled short-acting β_2-agonists for ≥ 7 days improve postbronchodilator lung function and reduce breathlessness in patients with stable chronic obstructive pulmonary disease.

Source of funding: Netherlands Asthma Foundation.

For correspondence: Dr. F.S.F. Ram, National Collaborating Centre of Women and Children's Health, London, England, UK. E-mail fsfram@yahoo.co.uk.

Regular inhaled short-acting β_2-agonists for ≥ 7 days vs placebo for stable chronic obstructive pulmonary disease*

Outcomes at 1 to 8 wk	Number of trials (number of patients)	Weighted mean difference (95% CI)	
FEV_1 (L)†	6 (196)	0.14 (0.04 to 0.25)	
FVC (L)†	4 (116)	0.30 (0.02 to 0.58)	
Morning PEFR (L/min)†	{4 (124)}§	29.17 (0.25 to 58.09)	
Evening PEFR (L/min)†	{3 (86)}§	36.75 (2.56 to 70.94)	
		Standardized mean difference (CI)	
Breathlessness (100-mm visual analogue score)	4 {94}§	1.33 (1.01 to 1.65)	
		RRR (CI)	NNT (CI)‖
Treatment failure‡	5 (198)	51% (27 to 67)	{5 (3 to 9)}§
		RBI (CI)	NNT (CI)¶
Patient preference for β-agonists over placebo	4 (158)	{507% (198 to 1135)}§	{3 (2 to 3)}§

*FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; PEFR = peak expiratory flow rate. Other abbreviations defined in Glossary.
†Postbronchodilator; positive numbers favor β-agonists.
‡Treatment failure = number of dropouts because of worsening symptoms.
§Information provided by author.
‖Calculated from relative risk and control event rate in article.
¶Calculated from Peto odds ratio and control event rate in article.

COMMENTARY

COPD is defined as airflow limitation that is progressive, not fully reversible, and associated with an abnormal inflammatory response in the lungs (1). So why bother with a short-acting bronchodilator? Because it works. Research has recently caught up with clinical experience, and the view that airflow limitation in COPD is irreversible has been modified ever so slightly to "not fully reversible." Up to 50% of people with COPD will have an improvement in FEV_1 after using a β-agonist (2). Although the size of the response is less than in asthma (2), it still exists and is even more evident with sensitive testing (3).

The review by Ram and Sestini usefully quantifies these effects, showing that regular ISABA treatment leads to numbers needed to treat of 3 to 5 for symptom-based outcomes. Should we try to identify responders by their acute response to ISABAs? Don't bother. Patients can still be bronchodilated without improving FEV_1(3), and the FEV_1 response doesn't count for much anyway (4).

The drug and the delivery system, however, are important. Although longer-acting bronchodilators (β-agonists, anticholinergics, and oral agents) may improve efficacy and compliance, they are more expensive. This additional expense can only be justified when these treatments can be shown to reduce the costs associated with management of exacerbations. As for delivery systems, pressurized metered-dose inhalers are most cost-effective, and so we should resist the temptation to treat patients and their furniture with nebulized therapy in stable COPD (5). The review by Ram and Sestini supports regular bronchodilator use as standard therapy for COPD.

Peter G. Gibson, MBBS
John Hunter Hospital
Newcastle, New South Wales, Australia

References

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