

Review: Little if any advantage exists for using regular vs as-needed inhaled short-acting β_2 -agonists in asthma

Walters EH, Walters J. Inhaled short acting beta2-agonist use in asthma: regular vs as needed treatment. *Cochrane Database Syst Rev.* 2000;(4):CD001285 (latest version 7 Aug 1999).

QUESTION

In patients with asthma, how effective and safe is regular use of inhaled short-acting β_2 -agonists compared with as-needed use?

DATA SOURCES

Studies were identified by using the Cochrane Airways Group "Asthma and Wheez* RCT" register, reviewing the bibliographies of existing trials, and contacting trial authors and pharmaceutical companies.

STUDY SELECTION

Studies were selected if they were randomized controlled trials in which patients with asthma in the experimental group received short-acting β_2 -agonists regularly along with an inhaled bronchodilator for relief of symptoms and patients in the control group used an inhaled bronchodilator for as-needed rescue use only.

DATA EXTRACTION

Data were extracted on patient characteristics, study design, and the following main outcome measures: asthma control and pulmonary function, airway reactivity and quality of life, and rate of exacerbations.

MAIN RESULTS

32 trials met the selection criteria and had evaluable data for 31 outcomes. Little or no statistical difference existed between the treatment groups for most outcomes (including forced vital capacity, maximum midexpiratory flow, symptom scores, quality of life, use of rescue bronchodilator, exacerbation rates, early asthmatic response to inhaled allergen, and exercise challenge). In crossover studies involving 437 patients, evening peak expiratory flow was better with regular treatment (weighted mean difference [WMD] 13.1 L/min, 95% CI 1.9 to 24.3). However, in

crossover studies involving 303 patients, FEV₁ was better with as-needed treatment (WMD 157 mL, CI 123 to 192), and the results from 7 crossover studies showed lower airway reactivity with as-needed treatment (standardized mean difference 0.83, CI 0.53 to 1.12). In all cases, parallel group studies showed no statistical difference.

CONCLUSION

In patients with asthma, little if any advantage exists in regular use of inhaled short-acting β_2 -agonists.

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For correspondence: Professor E. H. Walters, Department of Respiratory Medicine, Alfred Hospital, Commercial Road, Prahan, Victoria, Australia. FAX 61-3-9276-3434. ■

COMMENTARY

Questions about the safety of short-acting inhaled β_2 -agonists for treating asthma arose during the 1960s and again during the 1980s. Observational studies indicated that regular use of these agents might have caused an increase in asthma mortality. That suggestion engendered heated debate and served as a rationale for numerous clinical trials. Walters and Walters have provided a careful systematic review of these many trials. They conclude that regular use of short-acting β_2 -agonists neither causes much harm nor confers much benefit over as-needed use. From considerations of cost and convenience, it makes sense that we should prescribe these agents on an as-needed basis only.

This conclusion will have little effect on current practice for 2 reasons. First, most current treatment guidelines already recommend that short-acting β_2 -agonists be reserved for as-needed use. Second, long-acting inhaled β_2 -agonists have largely supplanted short-acting β_2 -agonists for most patients who have anything more than the mildest forms of asthma. A long-acting β_2 -agonist given twice daily to patients with persistent asthma symptoms is clearly superior to a short-acting β_2 -agonist given 4 times daily (1). We may presume that

a long-acting β_2 -agonist would show the same advantage if control patients were given a short-acting β_2 -agonist on an as-needed basis only. No substantive safety issues have emerged from use of long-acting β_2 -agonists (2), so it appears that the short-acting β_2 -agonists will be relegated mostly to occasional "rescue" therapy.

One seeming inconsistency remains. If a long-acting β_2 -agonist confers more sustained bronchodilation and better clinical outcomes than does regular use of a short-acting β_2 -agonist, why does regular use of the short-acting β_2 -agonist not confer greater benefit than less frequent use of the same drug? The answer to that question is not immediately obvious to this observer.

*Dennis E. Niewoehner, MD
Veterans Affairs Medical Center
Minneapolis, Minnesota, USA*

References

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