Oral montelukast was better than inhaled salmeterol for reducing exercise-induced bronchoconstriction in adults with asthma

Edelman JM, Turpin JA, Bronsky EA, et al., for the Exercise Study Group. **Oral montelukast compared with inhaled salmeterol to prevent exercise-induced bronchoconstriction.** Ann Intern Med. 2000 Jan 18;132:97-104.

QUESTION

Is oral montelukast as effective as inhaled salmeterol for prevention of exercise-induced bronchoconstriction (EIB) in adults with asthma?

DESIGN

8-week, randomized {allocation concealed*}†, blinded {patients, clinicians, outcome assessors, statisticians},*† controlled trial.

SETTING

17 asthma treatment centers in the United States.

PATIENTS

191 patients who were 15 to 45 years of age (mean age 26 y, 52% men), had a history of chronic asthma, had an $FEV_1 \geq 65\%$ of the predicted value at rest, and had a decrease in $FEV_1 \geq 20\%$ after a standardized exercise challenge on 2 occasions during baseline measurement. Exclusion criteria were upper respiratory infection or exacerbation of asthma that had required emergency care in the previous month or hospitalization for asthma in the previous 3 months. Follow-up at 8 weeks was 93%.

INTERVENTION

After a 2-week period of placebo, 97 patients were allocated to oral montelukast, 10-mg tablet once in the evening for 8 weeks, and 94 were allocated to inhaled salmeterol, 2 puffs of 50-μg aerosol formulation twice daily for 8 weeks.

MAIN OUTCOME MEASURES

Main outcome was change from baseline in the maximal percentage decrease in FEV_1 after a standardized exercise challenge at 8 weeks. Other outcomes included maximal percentage decrease in FEV_1 at 1 to 3 days and 4 weeks, the need for rescue medication during or after exercise, and adverse events and laboratory abnormalities.

MAIN RESULTS

Analysis was by intention to treat. Within 3 days of initiation of therapy, both groups improved in the maximal percentage decrease in FEV_1 after exercise; this improvement was maintained at 4 weeks and 8 weeks in patients who received montelukast but not in patients who received salmeterol ($P = 0.015$ at 4 wk and $P = 0.002$ at 8 wk). At any time, fewer patients who received montelukast required rescue doses of β-agonist after exercise challenge than did patients who received salmeterol (26% vs 40%, $P = 0.04$). The groups did not differ for frequency of clinical or laboratory adverse events.

CONCLUSION

Oral montelukast reduced exercise-induced bronchoconstriction in adults with asthma more than did inhaled salmeterol at 8 weeks of therapy.

Source of funding: Merck and Company, Inc.

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*See Glossary.

†Data provided by author.

COMMENTARY

Airway hyperresponsiveness to exercise and response to therapy are important and quantifiable indexes of asthma control. Currently, montelukast does not have an approved indication in the United States for the management of EIB. Previous investigation has shown that at 12 weeks montelukast therapy offered greater protection against EIB than did placebo (1). Edelman and colleagues expand our understanding of the role of montelukast by comparing it with an inhaled bronchodilator rather than with placebo.

Several issues deserve mention. First, this trial evaluated and compared the protective effects of montelukast and salmeterol at the end of their dosing intervals. Whether comparable protection against EIB exists earlier in the dosing cycle was not studied. Second, the effect of montelukast in patients with more severe chronic asthma was not investigated. These points aside, this study shows that montelukast had a durable effect in reducing the magnitude of the bronchoconstuctive response to provocative exercise challenge.

What should the practitioner take from these results? For patients with mild asthma and near-normal baseline lung function, the prescriber must weigh the potential benefit and burden (cost, convenience, and safety) of using a long-term drug, such as montelukast, against those of an as-needed inhaled β-agonist for the prophylaxis or management of EIB. These findings also suggest that the protective effect of salmeterol in EIB decreases after long-term administration. This finding is consistent with those of other studies of salmeterol and other long-acting inhaled β-agonists (2).

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References

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2. **Lipworth B, Tan S, Devlin M, et al.** Effects of treatment with formoterol on bronchoprotection against methacholine. Am J Med. 1998;104:431-8.

