Daily corticosteroids were not better than as-needed corticosteroids in mild persistent asthma

Boushey HA, Sorkness CA, King TS, et al. **Daily versus as-needed corticosteroids for mild persistent asthma.** N Engl J Med. 2005;352:1519-28.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Pulmonology ★★★★★★☆

QUESTION

In patients with mild persistent asthma, how does intermittent, short-course corticosteroid treatment (ISCT) guided by a symptom-based action plan alone compare with ISCT plus daily treatment with either budesonide or zafirlukast for improving morning peak expiratory flow (PEF)?

METHODS

Design: Randomized controlled trial (Improving Asthma Control Trial [IMPACT]).
Allocation: {Concealed}†.*
Blinding: Blinded (clinicians, patients, outcome assessors, {data collectors, data analysts, data safety and monitoring committee, and manuscript writers}†).*
Follow-up period: 1 year.
Setting: 6 centers in the United States.
Patients: 225 patients 18 to 65 years of age (mean age 33 y, 61% women) with mild persistent asthma and $FEV_1 \geq 70\%$ of predicted value. Exclusion criteria included cigarette smoking, respiratory tract infection, and corticosteroid use in the previous 6 weeks. All patients participated in a run-in phase.
Intervention: ISCT guided by a symptom-based action plan alone ($n = 76$); ISCT plus inhalation of budesonide, 200 µg twice daily ($n = 73$); or ISCT plus oral zafirlukast, 20 mg twice daily ($n = 76$). ISCT consisted of open-label budesonide, 800 µg twice daily for 10 days, or prednisolone, 0.5 mg/kg of body weight/d for 5 days, if asthma symptoms worsened. The run-in and treatment phases ended with 10 to 14 days of intense combined therapy with oral and inhaled steroids, zafirlukast, and albuterol.
Outcomes: Change in morning PEF from the final 2 weeks of the run-in period to the final 2 weeks of the year of treatment. Secondary outcomes included changes in pre- and postbronchodilator FEV_1, frequency of asthma exacerbations, percentage of eosinophils in sputum, and exhaled nitric oxide levels; asthma control; and number of symptom-free days.
Patient follow-up: 88%.

MAIN RESULTS

The groups did not differ for change in morning PEF (Table), change in postbronchodilator FEV_1, or frequency of asthma exacerbations. However, statistically significant improvements in prebronchodilator FEV_1, percentage of eosinophils in sputum, exhaled nitric oxide levels, and number of symptom-free days were greater in patients who received daily budesonide than in those who received ISCT only. Daily zafirlukast and ISCT did not differ for any outcome.

CONCLUSION

In patients with mild persistent asthma, intermittent, short-course corticosteroid treatment guided by a symptom-based action plan alone did not differ from daily treatment with budesonide or zafirlukast for improving morning peak expiratory flow.

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*See Glossary.

†Information provided by author.

Intermittent corticosteroid treatment guided by a symptom-based action plan alone (intermittent treatment) vs intermittent treatment plus budesonide vs intermittent treatment plus zafirlukast‡

Outcome at 1 y	Intermittent treatment		Daily budesonide		Daily zafirlukast		Overall *P* value
	n	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)	
Change from baseline in morning PEF (%)	70	7.1 (2.0)	66	8.3 (1.9)	62	7.9 (2.1)	0.90§

‡SD = standard deviation; PEF = peak expiratory flow.
§Differences between groups are not significant (analysis of covariance).

COMMENTARY

The use of as-needed inhaled corticosteroids (ICSs) eventually may be shown to be an alternative in the treatment of mild persistent asthma, but because of limited data, such use is not ready for standard practice. In the trial by Boushey and colleagues, the 14-day "intense combined" initial therapy, consisting of oral prednisone, inhaled budesonide, and zafirlukast, is not required or usual in the management of patients with mild persistent asthma and thus may limit the generalizability of the study.

PEF, the primary outcome, correlates with FEV_1 and is a reasonable outcome measure for monitoring chronic asthma. Quality-of-life measurements and symptom scores show limited correlations with laboratory measurements, such as FEV_1 or morning PEF, but the former are more important to patients. The daily ICS group showed improvement in symptom-free days and a trend toward improvement in quality-of life scores compared with as-needed therapy. The daily ICS group also showed improvement in all inflammatory measurements. Patients with asthma may have minimal symptoms even with significant lung inflammation and variability in obstruction. Studies have shown that inflammatory markers, such as nitric oxide levels, bronchial hyperresponsiveness, and sputum eosinophilia, may help to titrate ICS doses (1-3). Ideally, symptom severity and objective measurements of both airway obstruction and airway inflammation should be used to adjust corticosteroid therapy.

The study by Boushey and colleagues suggests that daily ICS should be the first treatment offered to patients with mild persistent asthma because secondary endpoints slightly favored this intervention. However, undertreatment with ICS is also a concern in those patients who do not perceive airflow obstruction when it is present. This possibility will necessitate airflow monitoring in minimally symptomatic patients if the as-needed approach is confirmed in other studies.

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References

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