Symptomatic use of beclomethasone plus albuterol and regular use of beclomethasone did not differ for control of mild asthma

Papi A, Canonica GW, Maestrelli P, et al. **Rescue use of beclomethasone and albuterol in a single inhaler for mild asthma.** N Engl J Med. 2007;356:2040-52.

Clinical impact ratings: Allerg & Immunol ★★★★★★☆ Pulmonology ★★★★★★★

QUESTION

In patients with mild, persistent asthma, is symptomatic use of beclomethasone and albuterol in combination as effective as regular use of the same dose of beclomethasone and superior to symptomatic use of albuterol for controlling asthma?

METHODS

Design: Randomized controlled trial (Beclomethasone plus Salbutamol Treatment [BEST] study).

Allocation: Unclear allocation concealment.*

Blinding: Blinded (unclear).*

Follow-up period: 6 months.

Setting: 25 centers in Italy, Austria, Poland, and Spain.

Patients: 466 patients, 18 to 65 years of age, with mild, persistent asthma for ≥ 6 months, prebronchodilator FEV_1 ≥ 75% of predicted value, and controlled asthma during 4-week run-in (beclomethasone, 250 µg, twice daily plus albuterol, 100 µg, as needed). Exclusion criteria included current or past smoker (> 10 packs/y), chronic obstructive pulmonary disease, history of serious asthma (near-fatal or hospitalization in past 1 y), ≥ 3 courses of oral corticosteroids, and > 6 months of regular treatment with beclomethasone, ≥ 500 µg/d, or equivalent.

Intervention: 4 groups: 2 groups with placebo twice daily plus either as-needed combination therapy (n = 124) or as-needed control therapy (albuterol, 100 µg, n = 119); and 2 groups with regular twice-daily treatment using either beclomethasone, 250 µg, (n = 110) or combination therapy (n = 113), plus as-needed albuterol, 100 µg. Combination therapy consisted of beclomethasone, 250 µg, and albuterol, 100 µg, in a single inhaler.

Outcomes: Mean morning peak expiratory flow (PEF) during weeks 23 and 24. Secondary outcomes included asthma exacerbations, lung function measures, asthma scores, and percentage of days without asthma symptoms or use of albuterol. Equivalence between groups was defined as < 10% (40 L/min) difference on the primary PEF outcome.

Patient follow-up: 84% (modified intention-to-treat analysis included 455 patients [mean age 39 y, 59% women]).

MAIN RESULTS

At 6 months, as-needed beclomethasone plus albuterol was more effective than as-needed albuterol for controlling morning PEF (Table). The as-needed combination and regular beclomethasone treatments were not significantly different on any measures, and both treatments resulted in fewer asthma exacerbations than as-needed albuterol (Table).

CONCLUSIONS

In patients with mild, persistent asthma, as-needed use of combined beclomethasone and albuterol did not differ from daily use of beclomethasone with as-needed albuterol for control of asthma. Both were superior to as-needed use of albuterol.

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*See Glossary.

As-needed beclomethasone + albuterol (bec + alb) vs regular beclomethasone (bec) or as-needed albuterol (alb)†

Outcomes at 6 mo	Comparisons	Difference in least squares means‡ (95% CI)	*P* value for superiority
Morning PEF (L/min)	Bec + alb vs bec	–4.44 (–12.39 to 3.52)	–
	Bec + alb vs alb	8.31 (0.58 to 16.04)	0.04

	Bec + alb	Alb	Bec	RRR (CI)	NNT (CI)
Exacerbations (% patients)	4.9%	18%	–	72% (36 to 88)	8 (5 to 20)
	4.9%	–	5.7%	13% (–149 to 70)	Not significant

†PEF = peak expiratory flow; other abbreviations defined in Glossary. RRR, NNT, and CI calculated from data in supplement.
‡Maximum likelihood method; CI for equivalence comparison.

COMMENTARY

The importance of regular suppressive treatment in asthma is now being challenged. Boushey and colleagues (1) showed that mild asthma could be controlled by intermittent courses of corticosteroids, and studies have shown that combinations of inhaled corticosteroids (ICSs) and a long-acting bronchodilator with a fast onset of action can be effective when used both regularly and on an as-needed basis (2, 3).

All these studies show that, within clinical trials, a lower dose of ICSs, with flexibility of use, can maintain asthma control. In the study by Papi and colleagues, patients on as-needed ICSs combined with a β_2-agonist used ≤ 125 µg/d of beclomethasone dipropionate on average. An advantage claimed for this approach is that it legitimizes what many patients do already.

There are a number of caveats for these results. Patients in the study had very mild asthma at baseline, with FEV_1 at 88% of the predicted value, 32% on ICS, 51% symptom-free days, and rescue β_2-agonist use of 0.5 puffs/d. In addition, the study was not powered to assess severe exacerbations and had a duration of only 6 months. Larger, longer studies are needed to establish the safety of as-needed use.

Patients with asthma require an individualized treatment approach, with discussion of their expectations and management aims. In guidelines, asthma control has been defined as minimal or no use of rescue medication. Management plans around this new approach, which only uses as-needed medication, must establish clear criteria for switching to regular medication.

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References

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