

On demand use of β_2 -agonists led to better asthma control than regular use in moderate to severe asthma

Richter B, Bender R, Berger M. *Effects of on-demand β_2 -agonist inhalation in moderate-to-severe asthma. A randomized controlled trial.* *J Intern Med* 2000 Jun;247:657–66.

QUESTION: In patients with moderate to severe asthma, is on demand β_2 -agonist inhalation as effective and safe as regular use?

Design

Randomised [allocation concealed]*, blinded (outcome assessors and statistician), crossover trial with 24 weeks of follow up for each treatment condition.

Setting

Outpatient clinic at Düsseldorf University Medical Centre, Germany.

Patients

80 patients (mean age 48 y, 74% women) with moderate to severe asthma on regularly scheduled β_2 -agonist (minimum daily intake of 6 puffs) and corticosteroid inhalation for ≥ 2 years. Exclusion criteria were non-respiratory illnesses or pregnancy. 73 patients (91%) completed the study.

Intervention

Two 24 week periods in which patients were allocated to on demand inhalation (salbutamol or fenoterol) or regular use β_2 -agonists (2 inhalations 4 times daily plus salbutamol or fenoterol on demand) and crossed over to the other regimen after completion of the first period. All patients used constant doses of inhaled corticosteroids.

Main outcome measures

The primary outcome measure was asthmatic episodes, defined as asthma attacks that could be treated by β_2 -agonist inhalation only. Secondary endpoints were safety and consequences of reduction in β_2 -agonists.

Main results

No difference existed between the treatment groups for asthmatic episodes and exacerbations (66% of days symptom free in on demand treated patients v 62% in regularly treated patients). However, daytime use of β_2 -agonists was lower in on demand patients than in those in the regular use group (3.3 v 7.9 puffs/d, $p < 0.001$). Also, patients in the on demand group needed fewer prednisolone days for asthma exacerbations than those in the regular use group (mean 44 v 52 prednisolone d, $p = 0.001$). Forced expiratory volume at 1 second (FEV₁), forced vital capacity, and midexpiratory flow at 25% to 75% of forced vital capacity were all higher in patients in the on demand group than in those in the regular use group (2.53 v 2.42 l, $p = 0.008$; 3.66 v 3.54 l, $p = 0.003$; 1.85 v 1.74 l s⁻¹, $p = 0.02$, respectively). No differences existed between the groups for immunoglobulin E, peripheral blood eosinophils, or other blood chemistry values; or for unwanted effects. Reductions in β_2 -agonist use did not produce changes in concomitant medications.

Conclusion

In patients with moderate to severe asthma, on demand β_2 -agonist inhalation led to better asthma control than regular β_2 -agonist inhalation treatment.

*Information provided by author.

COMMENTARY

Regular use of β -agonists as maintenance treatment for asthma is under increasing scrutiny in the face of evidence of an association between regular use and increased risk of death.^{1,2} This study by Richter *et al* contributes to the debate by looking at the issue in a group of patients with more severe asthma who were well established on multiple baseline treatments including inhaled corticosteroids.

The participants all attended one university medical centre in Germany; it is important to bear in mind that standard asthma treatment protocols vary between countries. For example in the UK, patients similar to those in this study are highly likely to be receiving long acting β -agonists such as salmeterol alongside inhaled corticosteroids, with short acting drugs such as salbutamol reserved for rescue treatment on demand.³ Studies have shown that long acting β -agonists are more effective for reducing asthma symptoms than the short acting type used in this study.^{4,5} This new study is therefore difficult to interpret in the light of these more modern treatment regimens. The patients in this study had previously participated in an intensive asthma education programme and were highly motivated; this may not be typical of patients seen elsewhere.

The results will be of interest to general and asthma/respiratory specialist nurses in acute and primary care settings. The study suggests that many people with moderate to severe asthma may be overtreated with short acting β -agonists, and in this study most patients were able to reduce their intake by at least 50%. The study also reminds us of the importance of regular critical review of the often complex treatment regimens in this group of patients, particularly in the light of new, effective treatments.

Janice Quarton, RN
Respiratory Specialist Nurse
York Health Services NHS Trust
York, UK

- Mullen M, Mullen B, Carey M. The association between beta-agonist use and death from asthma. A meta-analytic integration of case-control studies. *JAMA* 1993;270:1842–5.
- Spitzer WO, Suissa S, Ernst P, *et al*. The use of beta-agonists and the risk of death and near death from asthma. *N Engl J Med* 1992;326:501–6.
- British Asthma Guidelines Coordinating Committee. British guidelines on asthma management: 1995 review and position statement. Suspected acute pulmonary embolism: a practical approach. British Thoracic Society, Standards of Care Committee. *Thorax* 1997;52:S1–24.
- Pearlman DS, Chervinsky P, LaForce C, *et al*. A comparison of salmeterol with albuterol in the treatment of mild-to-moderate asthma. *N Engl J Med* 1992;327:1420–5.
- D'Alonzo GE, Nathan RA, Henschowicz S, *et al*. Salmeterol xinafoate as maintenance therapy compared with albuterol in patients with asthma. *JAMA* 1994;271:1412–6.

Source of funding: no external funding.

For correspondence:
Dr B Richter,
Heinrich-Heine-Universität
Düsseldorf, Klinik für
Stoffwechselerkrankungen
u. Ernährung,
Moorenstr 5, Postfach
101007, D-40001
Düsseldorf, Germany.
richterb@uni-duesseldorf.de.

A modified version of this abstract appears in *ACP Journal Club*.