

LETTER TO THE EDITOR

Salmeterol in smokers with COPD

Having recently read the study by Ulrik (July 1995;50:750-4) regarding the use of salmeterol in chronic obstructive pulmonary disease (COPD), I wish to make comment on the methodology used and conclusions drawn. The choice of a forced expiratory test and, particularly, the peak expiratory flow rate as the main end point for efficacy is inappropriate, given its known insensitivity at picking up bronchodilator response due to effects of dynamic expiratory airway compression. Effort independent tests such as relaxed vital capacity or trapped gas volume are much more sensitive in this respect.¹⁻³ Are we therefore to believe, on the basis of peak flow recordings, that a mean treatment effect of 12 l/min is really a worthwhile return for an investment of £1.07/day?⁴

In this study no conclusions regarding efficacy in terms of spirometric parameters can be deduced because these were only measured 24 hours after washout of salmeterol, before nebulised salbutamol. Thus, to make a statement that bronchodilator efficacy in COPD should be assessed from daily peak flow recordings is not based on sound methodology, at least from this study. It was also hardly surprising that it was not possible to detect any diminution in response to nebulised salbutamol, given that the response signal was of such small magnitude. In this respect we have shown that chronic dosing with salmeterol in COPD had a mean effect on FEV₁ of 0.11 litres compared with placebo, and was not associated with any improvement in walking distance or exercise parameters.⁵ Properly designed studies with carefully chosen end points are required if we are to make any serious conclusions regarding the use of salmeterol in COPD.

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- 1 Bellamy D, Hutchison DCS. The effects of salbutamol aerosol on lung function in patients with pulmonary emphysema. *Br J Dis Chest* 1981;75:190-8.
- 2 Chrystyn H, Mulley BA, Peake MD. Dose response relationships to oral theophylline in severe chronic obstructive airways disease. *BMJ* 1988;297:1506-10.
- 3 Newnham DM, Dhillon DP, Winter JH, Jackson CM, Clark RA, Lipworth BJ. Bronchodilator reversibility to low and high doses of terbutaline and ipratropium bromide in patients with

chronic obstructive pulmonary disease. *Thorax* 1993;48:1151-5.

- 4 British National Formulary No. 29, March 1995.
- 5 Grove A, Lipworth BJ, Ramage L, Smith R, Ingram CG, Reid P, et al. Effects of regular salmeterol on lung function and exercise capacity in patients with partially reversible COPD. *Eur Respir J* 1995;8(Suppl 19):94S.

AUTHOR'S REPLY In his letter Dr Lipworth discusses two main points, namely the methodology used and conclusions drawn. I agree that repeated measurements of trapped gas volume might have been more sensitive to pick up changes after administration of bronchodilator in this group of patients. However, it seems reasonable to use only the more simple measurements of pulmonary function like spirometric tests for evaluation of treatment effect in these patients as most of them, at least in Denmark, are diagnosed and treated by their general practitioner. Furthermore, measurable improvements in not only PEF, but also FEV₁, in response to salmeterol have previously been reported in patients with COPD.^{1,2} As there is so little to offer the group of patients included in the present study, I don't believe that we should decide whether the observed mean treatment effect is a worthwhile return for a cost of DKr 11.85/day or not.

Detecting an acute (single dose) effect of salmeterol compared with placebo on spirometric testing would, of course, not be possible 24 hours after the last dose. However, given that long term treatment with salmeterol could induce a stable increase in baseline pulmonary function, it would probably have been revealed by the present study. Due to the fact that previously published studies have been unable to demonstrate a significant improvement in FEV₁ following a single dose of β agonist in patients with COPD,^{3,4} it was decided beforehand to use PEF and not FEV₁ as the primary outcome variable. Evaluation of the degree of bronchodilator reversibility is not an easy task,⁵ particularly in patients with moderate to severe COPD, and using this as the main end point therefore appears to be inappropriate.

The use of PEF as the primary outcome variable in this setting seems reasonable and, furthermore, I am still confident that the data presented in the paper support the view that treatment with long acting β agonists may result in an improvement in functional status in patients suffering from moderate to severe COPD.

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- 1 Boyd G, Crawford C. Salmeterol for treatment of patients with chronic obstructive pulmonary disease. To be presented at the ERS meeting in Barcelona, September 1995.
- 2 Grove A, Lipworth BJ, Ramage L, Smith R, Ingram CG, Reid P, et al. Effects of regular

salmeterol on lung function and exercise capacity in patients with partially reversible COPD. To be presented at the ERS meeting in Barcelona, September 1995.

- 3 Teale C, Morrison JFJ, Jones PC, Muers MF. Reversibility tests in chronic obstructive airways disease: their predictive value with reference to benefit from domiciliary nebuliser therapy. *Respir Med* 1991;85:281-4.
- 4 Evald T, Keitelmann S, Sindrup JH, Lange P. The effect of inhaled terbutaline on FEV₁, FVC, dyspnoea, and walking distance in patients with chronic obstructive lung disease. *Respir Med* 1992;86:93-6.
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NOTICES

Basic Clinical Allergy

A course entitled "Basic Clinical Allergy" will take place at the National Heart & Lung Institute, London, UK on 25-29 March 1996. This five-day course consists of lectures, demonstrations, "hot spots", and special lectures by international experts, and is aimed at both clinicians and scientists interested in basic aspects and recent advances in allergy, asthma, and inflammation. The course has been approved for CME purposes. Topics will include: mechanisms in allergy; viruses, asthma and allergy; allergic rhinitis; genetics of atopy and asthma; immunotherapy; practical aspects of the allergy clinic; "hot spots" in asthma research; treatment of asthma; major allergic problems.

For information please contact: Conference Centre, National Heart & Lung Institute, Dovehouse Street, London SW3 6LY, UK. Telephone +44 (0)171 351 8172; fax +44 (0)171 376 3442.

IXth International Pulmonary Fibrosis Colloquium

The International Pulmonary Fibrosis Colloquium has taken place every two years since the first meeting in London in 1980. This is an informal meeting involving about 70 participants presenting and discussing the latest research in this area, and is attended by scientists and physicians with presentations predominantly of a scientific nature. The next meeting will be held in Mexico in October 1996 and will be organised by Drs Moises Selman and Anne Pardo. If interested, please contact them at: Instituto Nacional de Enfermedades Respiratorias, Calz. de Tlalpan 4502, Col. Seccion XVI, C.P. 14080, Mexico DF, Mexico. Tel 525 665 4623. Fax 525 665 4748.