Thorax 1993;48:776

LETTERS TO THE EDITOR

Sex differences in hypokalaemic and electrocardiographic effects of inhaled terbutaline

We were interested to read the paper by Dr ARA Rahman and coworkers (December 1992;47:1056–9) in which the authors reported gender related differences in the pharmacologically predictable side effects of the β agonist drug terbutaline. Greater degrees of hypokalaemia, ST segment depression, and QTc interval prolongation were observed in women than in men following single doses of inhaled terbutaline. The authors concluded that women were more sensitive to β agonist effects, and speculated on the relevance of this finding to the wider issue of the adverse effects of β agonists.

In the light of this report we have carried out three further analyses of data from our own study which compared the effects of regular administration of β agonist with "as needed" β agonist in the management of asthma.[1 2] Overall control of asthma, baseline lung function, and changes in plasma potassium levels were reanalysed to identify any effect of gender on the results. Of the 64 evaluable patients 57 were better controlled during one or other of the two treatment periods; 17 when taking regular fenoterol and 40 when taking "as needed" bronchodilator ($p < 0{\cdot}005$). In table 1 this result has been stratified for gender, and χ^2 testing shows that there were no significant differences between the sexes as far as overall asthma control was concerned. For the entire group (n = 64) the mean (SE) change in baseline FEV_1 during regular fenoterol treatment was $-0{\cdot}15$ (0·06) litres compared with "as needed" treatment (MANOVA: SPSSX). The changes in lung function were more marked in men than in women but the difference was not significant (table 2).

The only variable which correlated with the decline in FEV_1 during the period of regular β agonist administration was that subjects experiencing more than six exacerbations of asthma during the treatment period had a significantly greater fall in FEV_1 than those patients who experienced six exacerbations or fewer (table 2).

Table 1 Numbers of subjects with better overall control of asthma stratified for treatment and gender

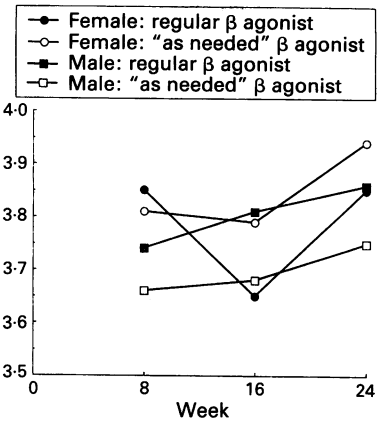
	Regular fenoterol	*"As needed" β agonist*	*Total*
Men	7	17	24
Women	10	23	33
Total	17	40	57

$\chi^2 = 0{\cdot}04$; $p = 0{\cdot}84$.

Table 2 Mean (SE) changes in FEV_1 (litres) which occurred during first two months of treatment with regular β agonist (fenoterol)

Group	*n*	*ΔFEV_1*
All subjects	64	−0·15 (0·06)
Men	28	−0·20 (0·07)*
Women	36	−0·12 (0·09)*
>6 exacerbations	13	−0·40 (0·17)**
⩽6 exacerbations	51	−0·09 (0·07)**

*NS; **$p \leqslant 0{\cdot}05$.



Serum potassium levels by gender, week and treatment.

We measured serum potassium levels every eight weeks throughout each of the two treatment periods and found no gender differences in these measurements (fig) nor, in fact, was there any significant difference in serum potassium levels between the regular and "as needed" treatment arms of the study. However, it requires to be noted that these measurements were made at least six hours after the most recent administered dose of inhaled β agonist.

From our long term clinical study we therefore found no important gender related differences in the outcomes following regular use of an inhaled β agonist.

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1 Sears MR, Taylor DR, Print CG, Lake DC, Li Q, Flannery EM, *et al.* Regular inhaled beta-agonist treatment in bronchial asthma. *Lancet* 1990;**336**:1391–6.
2 Taylor DR, Sears MR, Herbison GP, Flannery EM, Print CG, Lake DC, *et al.* Regular inhaled β agonist in asthma: effects on exacerbations and lung function. *Thorax* 1993;**48**:134–8.

AUTHOR'S REPLY Dr Taylor and colleagues have reported on a subgroup analysis from their study comparing regular versus on-demand β_2 agonist use and showed no gender differences in serum potassium levels during the study. There are two possible explanations for this result. Firstly, as the authors have pointed out, they did not measure the peak hypokalaemic response which occurs at 30–60 minutes, returning to baseline by three hours, but performed their measurements at least six hours after dosing. Secondly, the dose of β_2 agonist used in their study was low (400 μg for fenoterol) and is not on the steep part of the dose-response curve for systemic effects. Indeed, in a study reported by Windom *et al* in asthmatics[1] it was shown that even a dose as high as 1600 μg only produced a group mean fall in potassium of 0·4 mmol/l. In order to assess systemic β_2 receptor responsiveness it is therefore important to choose a dose on the steep part of the dose-response curve which is why we chose a dose of 5 mg inhaled terbutaline in our study. It is also worth mentioning that after eight weeks of treatment systemic tachyphylaxis would have occurred due to downregulation of extrapulmonary β_2 receptors[2] which might conceivably have masked a small gender difference in response.

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1 Windom H, Burgess D, Siebens RWL, *et al.* The pulmonary and expulmonary effects of inhaled β-agonists in patients with asthma. *Clin Pharmacol Ther* 1990;**48**:296–301.
2 Lipworth BJ, Struthers AD, McDevitt DG. Tachyphylaxis to systemic but not in airways responses during prolonged therapy with high-dose inhaled salbutamol in asthmatics. *Am Rev Respir Dis* 1989;**140**:586–92.

Inhalation trauma due to overheating in a microwave oven

I enjoyed the report by Drs AL Zanen and AP Rietveld (March 1993;**48**:300–2) on inhalation trauma due to overheating in a microwave oven. I disagree with the conclusion that pet birds should not be kept in the kitchen because of their high sensitivity to toxic gases. The selfless parakeets gave their owner a half hour warning of the danger to her lungs. As long as the risks of ornithosis and extrinsic allergic alveolitis are considered, the authors should encourage the placement of birds in the kitchen.

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NOTICES

XII International Symposium of Respiratory Psychophysiology
The XIIth International Symposium on Respiratory Psychophysiology will take place on 20–22 September 1993 at the Wellcome Centre, London. For further details contact: Miss Janette Shiel, Department of Medicine, Charing Cross & Westminster Medical School, Fulham Palace Road, London W6 8RF. Tel: 081 846 7176, Fax: 081 846 7170.

Dr HM (Bill) Foreman Memorial Fund
The Trustees of the above Fund invite applications for grants relating to study in respiratory disease. Limited funds are available for registered medical practitioners to assist in travelling to countries other than their own to study respiratory disease, and also for support of clinical research abroad. For further details contact Dr Brian H Davies, Llandough Hospital, Penarth, South Glamorgan CF6 1XX, UK.

Tuberculosis in the 90s
This conference will be held on 26 October 1993 at the Royal College of Nursing, London. Topics will include: The state of TB today; Immunotherapy; Immunology of TB; Tuberculosis: the global challenge. RCN members: £30.00, non-members: £45.00. Further details and an application form from Sandra Treadwell (071 409 3333 ext. 315).