LETTERS TO THE EDITOR

Revision of BTS guidelines for treatment of asthma

The paper by Ward et al confirms the findings of Laitinen et al showing that airways inflammation are never controlled and optimal lung function is never attained. Over time, structural changes (remodelling) occur leading to a progressive decline in lung function and the risk of fixed obstruction (chronic obstructive pulmonary disease). The present widespread dependence on bronchodilators in the UK may contribute to the fact that we have one of the highest respiratory death rates in Europe. The use of bronchodilators alone as in step 1 of the BTS guidelines should be discouraged, and treatment started at step 2 with regular inhaled corticosteroids to control symptoms and maximise peak flow rate. Bronchodilators should be used only as necessary for breakthrough wheezing. These principles have been used in Finland since 1994 with remarkable success in treating asthma. The new BTS guidelines would do well to follow their example.

George Strube
33 Goffs Park Road, Crawley, West Sussex RH11 8AX, UK
Gstrube@blinternet.com

References

Authors’ reply

We would like to thank Dr Strube for his interest in our recent paper and his stimulating letter which is topical given that the new BTS guidelines on asthma management are currently in preparation. Our study was an attempt to investigate the interrelationships between airway inflammation, airway structural change (remodelling), lung function, and bronchial hyperreactivity to methacholine in patients with mild to moderate symptomatic asthma.

Our paper is supportive of a further point, adding to work from others, which we feel is potentially substantive, of possible importance to future guideline considerations, and perhaps relates to some of Dr Strube’s concerns. The potential paradigm shift is that determining appropriate treatment only by reference to symptoms and lung function, as in current international and draft BTS guidelines, or even against indices of inflammation, may be oversimplified, with prolonged treatment necessary to benefit airway remodelling reflected by improvement in BHR. It should be recognised that this remains a hypothesis and, pragmatically, it is of interest that the inclusion of BHR as an asthma management tool in the UK is not resourced and is not currently practicable.

We also realise that the demanding and detailed preparation of the BTS asthma guidelines has followed a due process that relies on the available evidence base with “levels of evidence” leading to “grades of recommendation” and, in turn, to “recommended best practice”. If appropriate pathophysiological research relevant to the clinical questions does not exist, it cannot be included. We feel that longitudinal data that seek to integrate information on airway inflammation, airway remodelling, lung function, and bronchial hyperreactivity and the effects of treatment are required. Such work, though demanding, is possible and would require multidisciplinary cooperation, dialogue, and appropriate support.

Chris Ward is a European Respiratory Society long term research fellow. The work was also supported by Australian NHMRC and a grant in aid from Glaxo Smith Kline.

C Ward
Lung Biology and Transplant Group, University of Newcastle upon Tyne and The Freeman Hospital, Newcastle upon Tyne, UK
chris.ward@ncl.ac.uk

D Reid, E H Walters
Clinical Sciences, University of Tasmania, Australia

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PostScript
Chronic respiratory failure

The recent case report by Smyth and Riley describes an extremely uncommon chronic respiratory failure due to hypoventilation secondary to brainstem stroke, and documents a new treatment option with medroxyprogesterone acetate.

We recently saw two patients also with central hypoventilation resulting in chronic type II respiratory failure and treated both with, among other things, medroxyprogesterone acetate (30 mg twice daily) with good results.

The first patient, a 69 year old man with a medical history of glomus caroticum resection in 1979, presented to our outpatient clinic with polycythaemia. Arterial blood gas analysis revealed marked hypoxaemia (Pao, 4.8 kPa) and hypercapnia (Paco, 6.9 kPa). An intensive search for the cause showed no abnormality of the lungs that could have fitted with medroxyprogesterone acetate and his blood gas tensions improved within days to normal values (Pao, 10.3 kPa, Paco, 5.1 kPa).

The second patient, a 38 year old woman, was known from birth to have a hypothyroid pituitary gland deficiency with (stable) adipsitas (quetet index 53). She had complained of weakness, general malaise, and dyspnoea on several occasions before being sent to our department. Arterial blood gas analysis revealed hypoxaemia and marked hypercapnia (Pao, 8.0 kPa, Paco, 7.2 kPa). She probably suffered from Pickwick syndrome and at the time of examination was 170 cm tall with a body mass index (BMI) of 36.7 kg/m². She lost 7.5 kg in weight over 4 weeks after treatment.

When ascertaining the normal ranges for offline exhaled NO measurements we observed that some individuals had raised differences between baseline levels and the levels 0.5 hour after caffeine consumption (4.7 (2.6–6) ppb, p=0.007). This was also found in hypercapnic COPD patients, indicating that medroxyprogesterone acetate acts centrally on the respiratory centres. This supports the hypothesis of medroxyprogesterone acetate in central hyperventilation. Further- more, the combined treatment of acetazolamide and medroxyprogesterone acetate increases ventilation and improves arterial blood gas values—that is, it decreases Pco₂ to normocapnic values and increases Paco₂ to almost normocapnic values in hypercapnic and hypoxic patients with COPD.

In conclusion, we agree with Smyth and Riley that medroxyprogesterone acetate can be used in patients with central hypventilation disorders.

G P Bootma, Y Heijdra, M Wagenaar
P O Box 9101, Nijmegen 6500 HB, The Netherlands;
G.Bootma@long.umn.nl

References


Caffeine and exhaled nitric oxide

We read with interest the paper by Bruce et al which reported a significant decrease in exhaled nitric oxide (NO) levels 1 hour after caffeine consumption. However, we do not believe that this study has fully clarified the role of caffeine in asthma.

To further clarify this effect, exhaled NO levels after caffeine consumption were measured and compared with those of Warke et al. We conclude that levels of exhaled NO are higher after caffeine consumption than those of Warke et al.

P S Thomas, D H Yates, C Bruce
Faculty of Medicine, University of New South Wales, NSW 2052, Australia;
Paul.thomas@unsw.edu.au

References


Morbid obesity and hypersomnolence in several members of an ancient royal family

Recent studies have described an inherited basis for the sleep apnoea syndrome, as suggested by reports of families with multiple affected members.

We present evidence indicating that several members of the Ptolemy family, the royal family that ruled Egypt from 305 to 30 BC, suffered from obesity and sleep disordered breathing. Most of the information was reported by the Greek philosopher and historian Athenaeus (170–230 BC). The family’s pedigree with all affected members (shaded) is shown in fig. 1. Magas I (case 1) was morbidly obese. Athenaeus reported that Magas “was weighted down with monstrous masses of flesh in his last days; in fact he choked himself to death.”

Ptolemy II (case 2) and his sister Arsinoe III were extremely obese. Ptolemy II was not an energetic man and he disliked physical exertion. Although he lived to the age of 62, he was troubled by ill health throughout most of his life. Ptolemy IV, the Philopator (case 3),...
Ptolemy VIII Evergetes II (case 6) was described as licentious even by the standards of his contemporaries. Calvin Wells reported that he was obese and he languished in habitual lethargy, perhaps because of reported that he was obese and he languished in daytime somnolence. This dynasty was probably the first reported family with sleep disordered breathing that had a familial predisposition.

Ptolemy VIII Evergetes II or Kakergetes (benefactor), Alexandrians labelled him Kakergetes (malefactor) and—because of his obesity and large belly—"Physkon" (large bubble). Ptolemy VIII's belly was so large that he had a man on either side to help him walk. He was idle, drunken, and extravagant in his lifestyle.

From these descriptions it is clear that obesity was present in all of them and, at least four of the seven kings, there were reports of daytime somnolence. This dynasty was probably the first reported family with sleep disordered breathing that had a familial predisposition.

**Figure 1** The pedigree of the Ptolemaic dynasty (shading indicates affected members).
Caffeine and exhaled nitric oxide

T J Warke, M D Shields, J Finnegan and M D Shields

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