Letters to the Editor

Mechanisms proposed whereby \( \beta \)-blockers might worsen obstructive sleep apnoea (OSA)

Obstructive sleep apnoea (OSA) is a serious breathing disorder characterized by repeated collapse of the upper airway during sleep leading to asphyxia and arousal. This cycle of throat closure, wakening, a few breaths, snoring and throat reblockage can occur hundreds of times in the night greatly disturbing the sleep of the sufferer and cause excessive daytime sleepiness.

In a recent paper Fletcher (1) reported that hypertension is diagnosed in 90% of OSA patients and OSA can be found in 30–35% of patients with diagnosed systemic hypertension. \( \beta \)-blockers are often the drug of choice to treat hypertension in the general population.

Longstaff (2) reported the sudden nocturnal death of an OSA sufferer after 5 weeks on \( \beta \)-blocker medication, during which time the deceased had complained of more sleep disruptions and constant fatigue. Increased daytime sleepiness, memory lapses, morning confusion and apnoea were witnessed. Two possible mechanisms (C. W. Zwillich, pers. comm., 1997) whereby \( \beta \)-blockade might have worsened apnoea were invoked: (a) bradycardia associated with apnoea may be worse during \( \beta \)-blockade and could lead to cardiac arrest and (b) autonomic excitation which occurs during hypercapnia and hypoxaemia may be blunted by \( \beta \)-blockade, resulting in altered arousal responses or extreme levels of vasodilation, which is usually counter-balanced by some adrenergic stimulation during hypercapnia.

Vanuxem et al. (3) reported impairment of muscle energy metabolism in OSA patients which was linked to repeated bouts of nocturnal hypoxaemia. These findings may be pertinent to this issue, since any further reduction in energy to key muscles, as a result of medication, might possibly lead to unwelcome consequences in individuals with certain heart problems. D. Vanuxem (pers. comm., 1998) has acknowledged that \( \beta \)-blockers might interfere with energy metabolism to the striated muscles of the upper airways and has proposed the following mechanism: in muscle metabolism, the activation of phosphorylase kinase by cyclic AMP is triggered by epinephrine and therefore can at least be partly impaired by \( \beta \)-blockade.

According to Peter et al. (4) cardiac arrest is to be expected with severe OSA and \( \beta \)-blockers are not used in their sleep laboratory.

The hypothesis that \( \beta \)-blockers might prolong throat closure in OSA sufferers would seem to call for an investigation, using animal models, into the effect of these drugs on upper airway muscle metabolism.

References

2. Longstaff M. Do \( \beta \)-blockers pose an unacceptable risk to patients with obstructive sleep apnea (OSA)? Sleep 1997; 20: 920.

Dear Sir


The report by Hill et al. (Respir Med 1998; 92: 156–161) makes for depressing reading and will reinforce the prejudice in the U.K. against intubation and ventilation in acute exacerbations of COPD. In a retrospective study, lack of medical documentation should not be taken, necessarily, to indicate that treatment options were not discussed with patients or relatives. Furthermore, what is the evidence that this discussion would limit the demand for ICU admission? We advocate discussion about the use of mechanical ventilation with patients between exacerbations but recognize the difficulty of neutrality in this, especially in the acute situation.

How many of the patients in Dr Hill’s series were admitted from the ward having deteriorated with medical therapy? Was admission delayed too long leading to an increase in mortality (1)? The value of non-invasive ventilation (NIV) is to avoid the morbidity and mortality of intubation (2), yet this was only attempted in two of the 46 cases. More pertinently, NIV may enable early extubation (3). The finding that ICU stay was longer in the
survivors than non-survivors is not surprising. For instance, in seven cases death followed withdrawal of mechanical ventilation. Was early tracheostomy practised? This increasingly is recognized to enable earlier discharge from the ICU.

It is difficult to evaluate quality of life in chronic illness. Dependency does not equate with reduced quality (4). A better evaluation would have been to interview survivors and ascertain whether they would opt for mechanical ventilation again. Other series (5), involving a much larger number of patients, suggest a better outcome than is reported here.

As with previous studies, analysis of prognostic indicators demonstrates that there are no sensitive measures and that an ‘on the spot’ decision, leaning towards provision of mechanical ventilation, is justified. NIV should be employed unless contra indications exist. If it fails to reverse the spiral towards intubation, it may be employed to speed weaning following a short period of MV. Surely this is a more appropriate way to care for our patients than the nihilistic one suggested by Dr Hill and colleagues.

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References


Reply to Drs Davidson and Treacher

The letter by Davidson and Treacher suggests that the paper by Hill et al. (Respir Med 1998; 92: 156–161) makes for depressing reading and suggests that other series show better outcomes. Our series revealed a 49% hospital mortality and 59% 1 year mortality. Similar outcomes were found in U.S. and more recent U.K. studies. In the SUPPORT study (1) the 180 day mortality for 348 ventilated patients was 43% (1 year mortality not reported) but in another large U.S. study (2), 1 year follow-up was available on 167 ventilated COPD patients and in this series hospital mortality was 30%, 180 day mortality 48%, and 1 year mortality identical to our series at 59%.

The largest U.K. series by Wildman et al. (3) of 242 ventilated COPD patients reports a hospital mortality of 34-2% and 180 day mortality of 35-5% (1 year mortality data not yet reported). We would not agree with the suggestion that the article will ‘reinforce the prejudice in the U.K. against intubation and ventilation in acute exacerbations of COPD’. Davidson and Treacher seem to have missed the point of the study which was to stratify a complex case mix and identify factors that could prejudice poor outcome in 1993 when there was little discussion of this important topic in the U.K.

The low use of NIPPV in our series reflects evidence-based practice appropriate to the study period between 1993 and 1995. At that time the Bott paper (4) had been published suggesting the potential for NIPPV within clinical trials, but did not provide a secure evidence base for its wholesale adoption. The subsequent randomized controlled trials suggesting a role for NIPPV were not published until 1995 (5,6) and we agree with the two authors that the ICU management of COPD patients will not involve NIPPV, with data likely to emerge soon to help decide its role outside the ITU.

Davidson and Treacher question whether admission was delayed leading to an increase in mortality and whether early tracheostomy was practised in the series by Hill et al. The paper did look at whether being admitted to ITU on the day of hospital admission influenced outcome. In this study there was no difference in outcome whether being admitted directly to ITU or following deterioration with medical therapy from a medical ward. Tracheostomy was and is practised in our intensive care unit if there are no signs of ability to wean early and earlier still if tracheo-bronchial toilet is a problem.

Davidson and Treacher comment that lack of medical documentation should not be taken to indicate that treatment options were not discussed with patients or relatives, and question whether this would influence ICU admission. The courts would not necessarily agree with this; what is not recorded possibly has not been done — present views are not to give professionals the benefit of the doubt where medical records are concerned. Discussion can certainly influence decision making, for example, one would be more likely to ventilate someone with a good pre-morbid history without co-morbidities.

We would restate our contention that the high absolute and opportunity costs along with the significant morbidity and mortality in this group emphasizes the need for further prospective studies to better identify the patients who will benefit. We are presently initiating such a study at Birmingham Heartlands Hospital and preliminary results are expected later in 1999.