Sleep apnoea: clinical importance and facilities for investigation and treatment in the UK

ADDENDUM TO THE 1993 ROYAL COLLEGE OF PHYSICIANS SLEEP APNOEA REPORT

ABSTRACT — The potential importance of the obstructive sleep apnoea syndrome (OSA) has been recognised only in the last few years. Epidemiological studies suggest that symptomatic OSA occurs in 1–2% of middle-aged men and in approximately half that number of women. The relation of OSA to vascular disease is uncertain and the main indication for treatment is the relief of disabling sleepiness. Two recent evidence based analyses have produced diametrically opposed conclusions on the efficacy of treatment with nasal continuous positive airway pressure (CPAP). However, recent controlled studies confirm the overwhelming clinical experience of benefit. Facilities for the investigation and treatment of patients with OSA in the UK are subject to severe financial constraints and the availability of CPAP treatment lags markedly behind that in other countries for which data are available.

Obstructive sleep apnoea (OSA) was described formally only 30 years ago and its potential importance has been acknowledged only in the last 10–15 years. Advances in the understanding of the pathophysiological mechanisms of OSA and its important clinical and socio-economic consequences have been rapid.

The Royal College of Physicians (RCP) published a detailed report on sleep apnoea and related conditions in 1993¹. This reviewed several areas including epidemiology, clinical features, socio-economic consequences, investigation and management. In addition, the report outlined the facilities recommended for the provision of a clinical service. Since the publication of this report, there have been considerable advances in several areas, including:

- More information on epidemiology with large studies increasing the previous estimates of prevalence.
- Greater recognition of the importance of sleep disruption and consequent impaired daytime function, especially in relation to driving.
- Increasing acceptance of the efficacy of nasal continuous positive airway pressure (CPAP), together with controlled studies confirming the overwhelming clinical experience.

Facilities for the investigation and treatment of sleep apnoea in the UK have expanded but still lag considerably behind those in several other countries. Despite increasing awareness, dissenting voices have been raised questioning the efficacy of treatment with CPAP and even the reality of the condition².

In light of these changes, this paper reviews the most important recent developments in the areas of epidemiology and treatment. We also survey the extent to which the recommendations of the 1993 RCP report are matched by current practice in the UK.

Background and definitions

Apnoeas are classified as either ‘obstructive’, when the upper airway narrows or closes recurrently during sleep, or ‘central’, when the drive to breathe is reduced periodically. This review is confined to the obstructive sleep apnoea/hypopnoea syndrome (OSA) which is far more common than central apnoea. An apnoea is defined arbitrarily as ‘cessation of breathing for 10 seconds or more’, while the term ‘hypopnoea’ refers to a reduction in ventilation of similar duration. Many authorities describe this sleep abnormality in terms of the apnoea/hypopnoea index (AHI), ie the average number of periods of apnoea ± hypopnoea per hour of sleep. However, opinion has recently moved away from such rigid definitions and, for practical purposes, OSA requires the presence of demonstrable apnoeas, hypopnoeas or flow limitation (the so-called ‘upper airway resistance syndrome’) during sleep in the context of an appropriate clinical picture. In effect, the latter usually implies troublesome (and often disabling) daytime sleepiness. The sleepiness results from nocturnal sleep disruption, as each apnoea or hypopnoea is terminated by a transient arousal which restores the tone in the muscles surrounding the pharynx, allowing the airway to re-open. This may occur hundreds of times each night and as a result patients with OSA essentially suffer from sleep deprivation.

Treatment of OSA with nasal CPAP was introduced by Sullivan in 1981³ and is now widely accepted as the treatment of choice for most symptomatic patients. The principle is simply that of a ‘pneumatic splint’ with a flow of air delivered to the pharynx at a low pressure, usually via the

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nose (occasionally via nose and mouth) during sleep. The pressure of air supports the collapsible pharyngeal wall, thus preventing it narrowing or closing during inspiration. The treatment is usually introduced under supervision in hospital with the pressure adjusted to a value sufficient to overcome all, or virtually all, the apnoeas and hypopnoeas. The flow of air is generated by a small electrically-driven compressor. The equipment is regularly being improved and modern machines are much smaller and quieter than earlier devices.

Epidemiology of sleep apnoea

The latest work on the epidemiology of sleep apnoea referred to in the 1993 RCP report was by Young et al. of Wisconsin, USA. The results of this important study are now cited widely because of both the quality of the data and the high prevalence of sleep apnoea found. For example, of the male subjects studied in their sleep laboratory, as many as 9% showed an AHI >15 events per hour. Of more direct clinical relevance, the prevalence of subjects with an AHI >15 and significant symptoms was 1.4%. These figures are higher than those reported in an Oxford study, perhaps in part because the Wisconsin population was more obese and also because the American group used polysomnography, which is likely to identify more patients than oximetry alone.

The results of three large epidemiological studies have become available since 1993:

1 Bearpark et al. in Bussleton, Australia, using a limited monitoring system at home, found that 3.1% of men aged 40–65 years had a 'respiratory disturbance index' exceeding five events per hour, together with frequent daytime sleepiness.

2 Olson et al. in Newcastle NSW, Australia, using limited domiciliary monitoring, also found a high prevalence of sleep apnoea, with approximately 11% of men having an AHI >15 events per hour, a value similar to that found in the Wisconsin study.

3 Kripke et al. in San Diego, USA, using domiciliary oximetry, found that 9% of men had dips in oxygen saturation >4% more than 20 times per hour.

In both the Wisconsin and Newcastle NSW studies there was no significant association between sleep apnoea frequency and daytime symptoms as assessed by questionnaire. There was, however, a highly significant association between a history of snoring and daytime symptoms in both studies, suggesting that, as discussed in the 1993 RCP report, apnoeas and hypopnoeas considered alone are not necessarily the key physiological variables that determine the presence of daytime symptoms. It is likely that sleep fragmentation, which results not only from apnoeas and hypopnoeas but also, in some subjects, from airway narrowing associated with heavy snoring, may prove to be a better predictor of daytime symptoms. Nevertheless, in patients presenting with symptoms due to sleep apnoea, the frequency of apnoeas and hypopnoeas shows the best correlation with daytime function. Furthermore, a recent community study has shown that AHI correlates well with quality of life.

The high prevalence of sleep apnoea in recent epidemiological studies has led to some scepticism about the importance of the condition in clinical practice. However, this view fails to understand that these studies have looked predominantly at the prevalence of measurable physiological phenomena in the community rather than at the syndrome as it appears in symptomatic patients in sleep clinics. Thus, as the 1993 RCP report emphasises, the diagnosis and management of OSA should be based on a combination of the findings from a sleep study and attributable symptoms, and not on a sleep study alone. Overall, the recent studies described above suggest a prevalence of symptomatic OSA in middle-aged men of 1–2%.

Consequences and treatment of sleep apnoea

Since the 1993 RCP report was published, evidence that treatment of OSA is beneficial has increased significantly. One randomised placebo-controlled crossover study showed that CPAP improved symptoms, quality of life, cognitive function, IQ, driving simulator performance, objective sleepiness and mood in 32 patients with AHI ranging from 7 to 129 (median 28) per hour of sleep. A second placebo-controlled crossover study in 16 patients with milder OSA, and AHI of 5–15 (median 11) events per hour, also showed improvements in symptoms, cognitive function and mood with CPAP therapy. Furthermore, longer-term prospective studies have shown that subjective sleepiness improves significantly after both six months and one year of CPAP treatment and that the quality of life improves markedly after treatment. A small study in 19 patients showed that the gain of quality adjusted life years (QALYs) was significant, with an average gain of 5.5 QALYs indicating a 'very favourable cost-utility ratio'. A further study from Wessex also indicated a gain in QALYs at a cost of approximately £2,000 per QALY gained. In a retrospective study, 204 patients questioned between 2 weeks and 8 years (mean 21 months) after starting CPAP reported highly significant improvements in sleepiness, work efficiency, time off work, and ability to drive long distances. There was also a significant decrease in the number of road accidents and 'near misses'.

Most patients on treatment with nasal CPAP do not use the machine all night, every night. The average use is approximately four hours per night and many patients appear to 'titrate' the inconvenience of the device against the benefits of therapy. Such usage represents approximately 50% of the prescribed time, a level of compliance similar to that found in other chronic diseases such as asthma or hypertension. The optimal duration of CPAP treatment is not known but it is clear that patients derive marked benefit from treatment at this level.
Evidence based analyses of OSA and CPAP treatment

Recently, two evidence based analyses of OSA and CPAP treatment have been published with conclusions that are diametrically opposed: one by Wright et al\(^2\) and the other by the Australian National Health Medical Research Council\(^30\). In the former, Wright and colleagues conclude that the relevance of sleep apnoea to public health has been exaggerated. They acknowledge that it causes daytime sleepiness in some individuals and that this possibly leads to an increase in vehicle accidents. However, we believe that this review underestimates the importance of vehicle accidents because the authors focus on poorly-designed negative studies and consequently underestimate the impact of well-designed positive studies\(^31-36\). Furthermore, they ignore one well-designed study published as a letter\(^37\), and omit a recent article showing that sleep apnoea patients perform worse on driving simulators than well matched controls\(^18\). It is noteworthy that in the simulator study, patients with sleep apnoea performed worse when sober than did normal subjects with a mean blood alcohol level of 95mg/dl. A later study by the same group has confirmed that the impaired simulated driving performance of patients with OSA is reversed by treatment with nasal CPAP\(^39\).

Wright et al\(^2\) conclude that there is insufficient evidence to indicate whether sleep apnoea is associated with increased morbidity or mortality due to vascular disease. We agree that the data in this area are inconclusive and that long-term prospective studies are required. However, the conjunction in their article of two reviews – one dealing with possible long-term vascular complications and a second reviewing evidence on the effectiveness of treatment with CPAP – could easily mislead the reader into assuming incorrectly that the prime aim of such treatment is to prevent long-term complications rather than to provide rapid and sustained relief of disabling symptoms.

Moreover, whilst Wright et al\(^2\) conclude that their results ‘...do not therefore provide sufficiently robust evidence for the effectiveness of continuous positive airways pressure’, the authors of the second study, the Australian National Health Medical Research Council\(^30\), conclude that there is good evidence that CPAP improves cognitive function, mood and other symptoms related to quality of life. The Australian report further concludes that CPAP is cost effective and should be used in symptomatic patients with sleep apnoea. It is noteworthy that the steering committee responsible for the Australian report included clinicians with experience in sleep apnoea, whereas the report by Wright et al did not. Both reviews identify one randomised placebo-controlled trial of CPAP in sleep apnoea\(^15\) but, while Wright et al conclude that this study had ‘important weaknesses’, the Australian report concludes that there were ‘no major methodological threats to its validity’.

The Australian review\(^30\) also compiled evidence from meta-analysis of non-experimental studies showing that CPAP reduced sleep disturbance and daytime sleepiness. No such analysis was performed by Wright et al\(^2\). Overall the Australian authors conclude that there is evidence of benefit from CPAP from a randomised controlled trial, from meta-analysis of non-experimental studies and from individual non-experimental studies. Two further randomised controlled trials of CPAP treatment have been reported since these analyses were carried out\(^16,40\). Both confirm improvements with treatment in symptoms, cognitive function and mood, even in patients with only mild sleep apnoea.

Sackett highlights ‘the fear that evidence based medicine may be hijacked by purchasers and managers to cut the costs of healthcare\(^41\). We are concerned that the article by Wright et al might be seen as an attempt to do precisely this, a fear not allayed by the fact that their original report\(^42\) was initiated by a request from a purchasing authority.

In summary, there is now good evidence that CPAP therapy offers benefit to patients with sleep apnoea. This is based on the three randomised controlled trials reported to date\(^15,16,40\), as well as the other levels of evidence identified in the Australian review\(^30\). We recommend that CPAP treatment should be used to help patients with daytime sleepiness or impaired daytime functioning resulting from sleep apnoea. More research is required to identify which patients are most likely to benefit from treatment, especially among those with milder symptoms. In individuals, however, the benefits and tolerability of CPAP are likely to remain a matter of trial and error. In light of current knowledge, there is no indication for CPAP to be used solely to diminish vascular risk.

Other forms of treatment

Obesity is an important contributory factor to OSA in many patients and the recommendation to lose weight is a logical approach in such individuals. Unfortunately such dietary advice is rarely successful, either in obesity in general\(^43\) or in obese patients with OSA in particular\(^30\). Palatopharyngeal surgery (uvulopalatopharyngoplasty) has been the subject of several studies but since its results in OSA are markedly inferior to those of CPAP\(^30\), it is not generally recommended.

Evidence is increasing that intraoral devices, most of which advance the mandible during sleep, can be useful in treatment of some patients. Most of the available data have come from uncontrolled studies\(^44\) but two recent controlled investigations show significant improvement in overnight breathing pattern\(^45,46\) and symptoms\(^46\). The precise role of these devices in relation to CPAP treatment should become clearer when current randomised studies are completed, but on current evidence it appears likely that their role will be mainly in patients with mild to moderate disease.

Facilities for investigation and treatment in the UK

We surveyed the facilities for investigation and treatment of OSA and related conditions in the UK by sending a questionnaire to all physicians known to be offering this
service. Questions covered: the equipment or systems available for respiratory sleep studies; the number of diagnostic studies performed during the 12 months from 1 April 1995 to 31 March 1996; and the number of non-medical personnel (to nearest 0.1 whole time equivalent) available to support the sleep service. Physicians were also asked about the number of CPAP systems issued for long-term treatment during that period, together with the total number of patients currently receiving CPAP for whom they had prime responsibility. They were asked to identify the sources of funding for both investigation and treatment of OSA, and to indicate if any problems had arisen in securing adequate funding for the sleep service under the National Health Service during the financial year 1995-6. Questionnaires were sent to 45 physicians and hospitals; responses were received from 43.

During the year surveyed, the responses indicated a total of 11,636 diagnostic studies. The great majority were performed using 'limited' study systems, ie without electro-physiological signals; we estimate that the proportion performed using traditional polysomnography, ie with EEG monitoring, was 19%.

The total number of CPAP devices issued during the year was 2,310 and the overall total in use in 1996 for long-term treatment was estimated at 7,071. Financial problems in providing the sleep service had been encountered by 34 of the 43 respondents, related variously to diagnostic studies (23 centres), problems with supply of CPAP systems (26) and provision of adequate support staff (25). When asked to specify the particular problems encountered, six physicians indicated that NHS purchasers had completely rejected applications for funding and 14 other physicians responded that purchasers had imposed inadequate limits on the number of CPAP machines that could be provided. The service was dependent on charitable funds in part or in whole in 13 centres and seven physicians indicated that CPAP machines sometimes had to be bought by patients themselves. A CPAP machine with a face mask costs approximately £350-400.

Information from the manufacturers of the equipment suggests that the rate of CPAP prescription in the UK is considerably less than in other countries for which data are available. Industry estimates in 1996 (M Winter, personal communication) for the number of CPAP units supplied per annum in four countries are shown in Table 1. (Note that the estimate of 2,000 pa for the UK is close to the value of 2,310 obtained in our survey.)

### Table 1. Industry estimates of number of CPAP units supplied per annum, 1996.

| Country | Estimated CPAP sales pa | Estimated CPAP sales pa per 10^4 population |
|---------|-------------------------|------------------------------------------|
| USA     | 50,000-100,000          | 190–380                                  |
| Germany | 14,000                  | 171                                      |
| France  | 6,000                   | 103                                      |
| UK      | 2,000                   | 34                                       |

### Conclusions

Obstructive sleep apnoea frequently causes disabling symptoms for which effective and inexpensive treatment is available. It is clear that although the importance of the condition is increasingly recognised, adequate facilities for investigation and treatment in the UK continue to lag appreciably behind the perceived need. In many centres the service has had to be developed and maintained without the support of NHS purchasers and the majority of physicians and centres involved in investigation and treatment of these patients are experiencing major financial problems.

Based on the considerable epidemiological data now available, we have revised our previous estimates of the prevalence of sleep apnoea. We estimate that symptomatic sleep-disordered breathing occurs in about 1.5% of middle-aged men with a prevalence of about half that rate in middle-aged women. We would, therefore, anticipate that in an average health district with a population of 0.25 million, approximately 900 individuals might benefit from treatment with nasal CPAP. This estimate would imply a total of around 180,000 such individuals in the UK compared with 7,071 identified users. Thus, even with a conservative estimate of prevalence, less than 1 in 20 individuals likely to benefit are currently receiving treatment.

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