Nasal continuous positive airway pressure treatment for obstructive sleep apnoea

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In 1984 Bradley and Phillipson wrote an editorial reviewing the early data from surgical and non-surgical treatments for sleep apnoea entitled “Therapy for sleep apnoea, separating the wheat from the chaff”. At that time one anonymous humorist (well versed with 1960s American vernacular) photocopied the editorial and placed it on a department notice board in a Sydney hospital with an added comment to the title, “Which treatment will make the most ‘bread’?”. The answer to this “revised” editorial title is that it was estimated that, in 1993, over 100 000 nasal continuous positive airway pressure (CPAP) units were sold worldwide – a health care expenditure of approximately US$100 million for equipment alone. After a decade of controversy over the relative benefits of upper airway surgery and CPAP, there is now reasonable consensus that CPAP is the first choice therapy for obstructive sleep apnoea. Nevertheless, it is also recognised that CPAP is an imperfect therapy and recent studies describing the objective measurement of CPAP use in patients have revealed much lower compliance figures than those previously reported by early advocates of this form of treatment. The purpose of this brief review is to summarise recent data on the use of CPAP in obstructive sleep apnoea, practical aspects of this therapy, and future developments in “intelligent” CPAP devices and how they will impact on treatment of sleep-related breathing disorders. This review will concentrate on obstructive sleep apnoea rather than other forms of sleep-disordered breathing such as central apnoea and hypventilation in sleep. Issues such as CPAP initiation, compliance, side effects, and the approach to the patient intolerant of CPAP will be discussed.

Historical aspects and mechanism of action

The original experiments with CPAP in obstructive sleep apnoea followed from the concept that closure of the oropharynx was the result of an imbalance in the forces that normally keep the upper airway open. This concept was delineated in the model presented by Remmers et al in 1978. In the first description of CPAP use for treatment of obstructive sleep apnoea by Sullivan et al in 1981 it was suggested that nasal CPAP acts as a pneumatic splint to prevent collapse of the pharyngeal airway – that is, increasing the pressure in the oropharyngeal airway, reversing the transmural pressure gradient across the pharyngeal airway. This notion has subsequently been confirmed by a number of studies which either demonstrate the “pneumatic splint” by endoscopic or other imaging or show that CPAP does not reflexly increase upper airway muscle activity.

Following the first description of CPAP use in obstructive sleep apnoea there was a period of several years before it was widely believed that this therapy was truly effective. One problem was the need to use silastic glue to fix the mask on the patient’s nose each night. Several groups developed different mask prototypes but the involvement of new technology companies led to more user friendly CPAP systems by 1986.

Comparison with other treatments

One of the great advantages of nasal CPAP is that it is immediately and demonstrably effective in relieving obstructive sleep apnoea. The other advantage is that it can be given on a “trial” basis and withdrawn if not tolerated, in contrast to surgical options. This is particularly important in milder cases of obstructive sleep apnoea or where the contribution of obstructive sleep apnoea to the patient’s symptomatology is unclear. Few studies have attempted to compare CPAP with other treatments for obstructive sleep apnoea using formal protocols. Virtually all of these studies have failed to randomise treatments. The effectiveness of nasal CPAP has been confirmed by a recent study from the UK that compared CPAP with an oral placebo in patients with a range of sleep apnoea and demonstrated improvements in MSLT scores and cognitive function, despite a mean CPAP use of less than four hours per night.

The first night of treatment

Sleeping with a nose mask and feeling the pressure sensation of CPAP, although not necessarily uncomfortable, are certainly novel
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Airflow

Nasal airflow in a patient receiving continuous positive airway pressure (CPAP) treatment. The underlined breaths are “chopped off” – that is, they lack the normal rounded contour seen in the normal breath at the extreme right and are caused when subcritical levels of CPAP are used, resulting in residual partial upper airway obstruction.

experiences for the patient. Physician explanation, video programmes, and mask “acclimatisation” sessions prior to commencing CPAP are routine in our centre. Although the benefits of these techniques have not been scientifically evaluated, it is obvious that patient education about CPAP will be beneficial in reducing anxiety and improving acceptance of treatment.

On the first night of treatment it is important to ensure that the CPAP level finally determined is sufficient to prevent apnoea in all sleep stages and in all postures of sleep. It is important to ensure that the airflow/CPAP pressure trace is normal and not “chopped off” to avoid residual partial airway obstruction (figure).10

When the correct CPAP level is reached and the airway is open, sleep should no longer be fragmented by repetitive arousals. In fact there is often “rebound” slow wave and REM sleep.11 This rebound phase of recovery from severe sleep fragmentation lasts about a week; the duration and intensity of these rebound sleep episodes decrease quickly after the first night of treatment.211 However, the improvement in sleep architecture is usually immediate and can be used as a sign of an effective CPAP level.

The supine posture will require a higher CPAP pressure than a lateral posture, and a higher pressure is usually required in rapid eye movement (REM) sleep than in non-rapid eye movement (non-REM) sleep.2 Moreover, it is important to provide enough pressure to prevent snoring as well as apnoea. If the patient is still snoring on CPAP (even though apnoea is prevented) there is a high probability that the patient will have runs of apnoea at some stage of the night. This pattern is due to an insufficient safety margin, because the pressure being used is too close to the critical opening pressure. Another approach would be to start treatment with a high pressure and lower it during the night. However, the problem with this procedure is that the patient, when awake, may not be able to tolerate the mask and high pressure sensation. In general, the higher the pressure, the more likely it is that the patient will find it uncomfortable. Pressures of 10-12 cm H₂O are usually tolerated without any problem, but at the other end of the range (15-18 cm H₂O) patients often find the pressure uncomfortable. However, some studies have found that the level of CPAP does not influence compliance (see below).

One unresolved issue which impacts on compliance and effectiveness of CPAP is whether a CPAP level accurately set on one night is effective on subsequent nights. Early work and clinical experience suggest this is the case in some patients but detailed studies are lacking. When confronted by patients who may respond immediately to CPAP but report continued daytime sleepiness on home treatment some physicians empirically increase CPAP pressure. Several factors may affect CPAP pressure. Weight gain may lead to a need for a higher CPAP setting.12 Heavy alcohol consumers pose other problems in CPAP usage. We frequently find that the critical CPAP pressure required is higher after large quantities of alcohol have been ingested, presumably because of the effect of alcohol in depressing the neuromuscular tone of the upper airways.13 However, this may not be a problem in moderate drinkers.19 One practical approach is to ask patients to drink their usual amounts of alcohol in the evening before a CPAP pressure determination is performed. Variable nasal obstruction may also lead to variable “correct” CPAP levels. This issue of varying CPAP requirements has led to interest in developing “intelligent” CPAP systems that vary the pressure according to the presence of upper airways limitation (see later).

Incorrect CPAP pressure setting may lead to compliance problems. In addition, in patients with severe sleep apnoea and marked depression of the arousal response to a variety of stimuli there may be a vulnerability to life threatening hypoxaemia in REM sleep.5 This phenomenon can occur in patients with carbon dioxide retention when a subcritical level of CPAP is selected, which results in partial upper airways obstruction during abnormally long “rebound” episodes of REM sleep. For this reason, such patients should always be treated for the first night under close supervision.

Can CPAP be commenced on the same night as sleep apnoea is diagnosed?

It has been suggested that CPAP can be initiated on the same night as the diagnosis is established.15 This would imply set laboratory policies on CPAP initiation and CPAP prescription in all patients. The success of this procedure with abbreviated diagnostic and subsequent CPAP titration in all patients by the same night has been questioned by Sanders et al.16 These workers observed that, after such a “split night” study, most patients still required a subsequent change in CPAP pressure, mask, or switch to a BiPAP system. Although such split night studies may appear attractive from a short term economic point of view, incorrect treatment prescription may result in CPAP failure, more frequent outpatient visits with CPAP problems, and the need for further sleep studies negating short term financial advantages. The long term utility of “split night” studies is unproven as yet.

Can CPAP be commenced at home?

The economic advantages of starting CPAP at home and avoiding a formal polysomnographic CPAP pressure determination has been suggested by several groups.17 18 However, this has not been studied in any formal randomised protocol. In one case series from the USA19 patients without health insurance were given progressively increasing nightly CPAP settings at home with CPAP pressure and oxygen sat-
Adherence
Acceptance
Usage
Compliance

The proportion of patients using CPAP machines and delivering a pre-set level, i.e. the mask is likely to be on the patient's face.

Compliance and CPAP

How do these general issues in compliance impact on CPAP? In assessing the long term results of CPAP different words have been used including “acceptance”, “tolerance”, “adherence”, “usage”, “compliance”, “efficacy” in descriptions of patient-CPAP interaction. To a large extent these terms describe different manifestations of the same construct but are subjective terms used in early studies whereas more recent studies measure CPAP “usage” or “compliance” utilising time meters or more sophisticated devices that measure both run time and pressure delivery. True “efficacy” studies have yet to be performed as they would need to measure total sleep time over a set period and compare this with CPAP usage and the actual number of respiratory events not prevented by CPAP. For the purposes of this review, the terms used in relation to CPAP usage are listed in table 1. The criteria set for the terms may vary - for example, compliance for one group may be six hours of CPAP, six nights per week, while for others such criteria may be too strict.

Several specific factors affect CPAP compliance studies including machine cost, type of machine, the technical advances in masks, and prescriber motivation. In some countries machines are provided free of cost while in others cost may vary from US$1 to US$3000. Clearly this may lead to variable acceptance and prescription of the therapy. In addition, there have been rapid changes in CPAP technology. Current machines are quieter, with better masks and a smaller profile.
and with a “ramp” facility to slowly increase the pressure over the first period of sleep. Most CPAP usage studies have employed superseded equipment and compliance data need to be continually updated to verify whether these technical changes do actually influence CPAP use or are purely cosmetic marketing ploys. This situation is analogous to clinical trials of new medications within the same drug class – for example, comparative studies of beta blockers.

Unlike the study of Rand and colleagues it appears that CPAP “dumping” is not a major factor. If a CPAP mask is taken off the face, then there is a detectable drop in pressure. If patients were simply switching on their machine and leaving the mask on the floor then there would be a major discrepancy between “machine on time” and “mask on face” time. This is not the case as simultaneous studies of CPAP use and pressure delivery at the mask reveal a high correlation between usage and compliance.4,25 “Dosage” studies are not available for CPAP. Do patients have to use CPAP every night to receive beneficial therapeutic effects? Mean CPAP use of less than four hours per night produces demonstrable reduction in sleepiness.6 Another study showed that one night of CPAP in compliant CPAP users led to a recurrence in daytime sleepiness.28 A number of “biological” markers of CPAP usage may exist in all or certain patient subgroups.27,28 However, these studies have not simultaneously measured the biological end point and objectively measured CPAP usage. At this stage all criteria for CPAP usage or non-usage, or compliance or non-compliance,2425 are essentially arbitrary.

**Studies of CPAP usage**

Early data from Sydney suggested that there was a high level of long term acceptance of CPAP.2930 However, these patients had more severe forms of apnoea, were highly motivated by staff, and their subjective reports could not be corroborated by objective data. These early patients had to use a silastic sealant to glue a fibreglass mask onto their face. Interestingly, as the glue was provided by the sleep laboratory, glue usage provided a primitive form of objective measurement and it was clear at this early stage of CPAP development that “usage” was very variable.

In the section below, using the terminology (suggested) in table 1, available data on how patients interact with CPAP are discussed under separate headings.

**HOW MANY PATIENTS WILL ACCEPT CPAP?**

Few accurate data are available on this point as most studies only discuss patient data from the night of CPAP pressure determination or later. In one study 70% of patients offered a CPAP trial night accepted.31

**HOW MANY PATIENTS WILL AGREE TO PRESCRIPTION OF HOME CPAP?**

The percentage of patients who refuse CPAP after an inhospital trial is variable. Two studies have reported prescription rates in excess of 80%,3233 while other authors observed only a 58% prescription rate after an inhospital trial.34 There are many potential sources of prescription rate variability including machine cost which has a major impact in Australia, whether more than one night of an inhospital CPAP trial is possible, and the original selection criteria for CPAP. For example, we often first try certain patients with severe forms of sleep apnoea on CPAP simply on economic grounds, knowing that it is likely to be less effective and poorly tolerated compared with more expensive forms of therapy such as nasal ventilation.

**HOW MANY PATIENTS WILL CONTINUE TO USE CPAP LONG TERM?**

The data answering this question come from a range of subjective and objective studies, some of which are summarised in table 2. CPAP use at one month follow up can predict CPAP usage at three months follow up.34

**WHAT BASELINE INDICATORS INFLUENCE CPAP USAGE?**

Data from the general compliance literature suggest that it is hard for physicians to predict good compliers at the time of initiation of therapy. This may be the case for medications but it may be a different situation for a mechanical treatment such as CPAP. In addition, CPAP provides immediate reinforcement of its efficacy in may patients with relief of daytime sleepiness. It is therefore possible that severity of symptoms has some role in maintaining
usage of CPAP. Several studies have confirmed the hypothesis that patients with good objective usage or reported adherence are sleepier at baseline, although other studies have not found this relationship. Although MSLT measured daytime sleepiness improves following CPAP, baseline MSLT scores do not appear to predict CPAP compliance. It is controversial whether the amount of improvement in MSLT scores will predict compliance in contrast to MSLT results at baseline. It is possible that in sleep apnoea the MWT (Multiple Wakefulness Test) may be a better predictor of CPAP use but this is untested. Other factors which may be related to a reduced usage include previous palatal surgery, absence of hypoxaemia, and fewer years of education. Surprisingly, in two larger series the CPAP pressure level was no higher in those having difficulties using CPAP.

**Does physician and/or technologist motivation/support improve usage?**

This is a subject of some controversy. It would seem obvious that the more positive reinforcement given to patients the more likely the patient is to use CPAP as prescribed. However, this has been questioned by one study.

Moreover, two recent objective studies employing different intensities of patient follow up did not seem to differ greatly in compliance rates. However, in a subsequent paper on CPAP by Kribs et al usage was higher than in their previous work. The authors explain “these self-report and objective monitor figures suggest that subjects used CPAP more often and for a somewhat longer duration than was found in our study of patterns of use. This result is not surprising, since the current protocol intervened to urge subjects to be as compliant as possible to daily use of CPAP; the other study was structured to avoid affecting patient use of CPAP.” Clearly these authors recognise that patient support and motivation will impact on compliance.

**Impact on bi-level positive airway pressure on management of obstructive sleep apnoea**

Sanders and coworkers first reported the potential benefits and efficacy of reducing the expiratory positive airway pressure (EPAP) level relative to inspiratory pressure (IPAP) in the management of obstructive sleep apnoea. They confirmed previous work by Lopata and coworkers showing that there are differences in the magnitudes of the forces destabilising the upper airway during inspiration and expiration. A device that permitted independent adjustment of EPAP and IPAP and demonstrated that obstructive sleep-disordered breathing can be eliminated at lower levels of EPAP compared with conventional nasal CPAP therapy may have advantages. They speculated that such a device may reduce the adverse effects associated with nasal CPAP therapy and improve long term therapeutic compliance. The first such commercial device, the BiPAP system (Respironics, Monroeville, USA), has been used extensively but there are no convincing data that bi-level positive airway pressure is more effective than CPAP in patients with obstructive sleep apnoea and normal awake respiratory function. One report observed no difference in hours of device use in patients with obstructive sleep apnoea randomised to receive either BiPAP or CPAP. However, in the same study a higher proportion of patients “adhered” (see table 1) to bi-level positive airway pressure than to CPAP. More data are needed before widespread use of the more costly bi-level positive airway pressure devices can be advocated in patients with obstructive sleep apnoea.

**Table 3: Potential uses of “intelligent” CPAP devices**

| (1) CPAP compliance diagnostics | Able to produce an accurate record of pressure delivered and residual untreated sleep apnoea i.e. “dose” of uncorrected obstructed sleep apnoea over a period of time (if any). Can “autoset” CPAP level and may reduce technologist time during CPAP titration, reducing labour costs in sleep laboratory | **Minor**

Most side effects related to CPAP use are minor and their major long term effect is discontinuation or reduced usage of CPAP. Common (approximately 30-50% of patients) side effects include inconvenience, poor mask fit, claustrophobia, and nasal problems. Inconvenience is a common complaint but is largely
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insurmountable, given the need for some form of mask and a pressure generating device. Mask fitting problems also require expert help and the wide variety of masks available will assist in reducing this as a problem. Claustrophobia can be reduced in some patients by use of a pressure “ramp”, slowing increasing pressure at onset of sleep or by gradual desensitisation or even with the use of a bi-level positive airway pressure device. However, some patients will remain completely intolerant.

Nasal side effects occur in 15–45% of patients. Most patients experience initial self-limiting congestion. In the long term, nasal mucosal drying which can be painful or chronic congestion are the main side effects. There appear to be several reasons for nasal symptoms. CPAP may provoke pressure sensitive mucosal receptors, leading to vasodilation and mucus production. In some patients it may unmask allergic rhinitis by restoring the nasal route of breathing after years of “mouth breathing”. In others, fixed nasal obstruction with polyps or a deviated septum may produce symptoms. Recently, studies of patients with mouth leak have revealed that the loss of nasally humidified air through the mouth will in turn lead to a disruption of the ability of the nasal mucosa to maintain humidification. Prevention of mouth leaks reduces rhinitis (G Richards, personal communication). There are few published data on the pathophysiology of nasal side effects of CPAP.

A multimodality treatment approach is required for nasal symptoms. Although an initial trial of an intranasal vasoconstrictor or intranasal steroids at bedtime may be helpful, in other patients with constant daytime nasal streaming an intranasal anticholinergic can be used on a short term basis. Patients with persistent symptoms of nasal congestion or those with obvious nasal obstruction should have nasopharyngoscopy performed and may require corrective surgery for an obstructive lesion such as polyps, or thick nasal thickening, or deviated septum. However, in our experience such nasal obstruction needs to be quite marked to be significant. Most patients in whom the ability to tolerate CPAP is affected by chronic nasal congestion benefit from attempts to reduce mouth leakage with chin straps or by adding a humidification system to their CPAP circuit. There are no objective data available on the effect of nasal decongestants or humidification on compliance rates.

Management of CPAP failure
What constitutes CPAP failure? This is a very subjective issue and practice will vary from centre to centre in the absence of hard data. Kribbs et al defined CPAP failure as “the use of CPAP for less than four hours per night on 70% of the nights and/or lack of symptomatic improvement”. The specific figure of four hours was based on minimal criteria for adequate sleep from the general sleep literature on average sleep duration and the figure of 70% of nights was an arbitrary figure based on their group's expert clinical opinion. Based on the objective part of this definition, 54% of 35 patients were CPAP failures.

Clearly it is important to identify the cause of CPAP failure. Some of the commonest side effects and potential solutions are listed above. Claustrophobia is frequently a major cause of complete CPAP failure. Our practice is to run through a check list including looking for the possibility of secondary gain. Because of the nature of their illness, some patients with obstructive sleep apnoea are receiving or are potential recipients of some form of social welfare. A subgroup of these patients may not have the incentive to improve their fitness for work by use of the CPAP device to increase alertness. It is important also to consider if an incorrect diagnosis has been made. It is rare in the setting of comprehensive nocturnal respiratory monitoring or full polysomnography to make a false positive diagnosis of sleep-disordered breathing. However, it is more common to attribute patient symptoms to the degree of sleep-disordered breathing when there may be other co-existing disorders (recognised or unrecognised). An example of this may include patients with mild sleep apnoea and narcolepsy or idiopathic hypersomnolence where CPAP may be totally ineffective at abolishing sleepiness to any extent. Provided the physician recognises the potential causes of symptoms, a CPAP trial may be warranted and then CPAP failure may be entirely due to the patient for example patients with sleep-disordered breathing CPAP may be inadequate to manage the respiratory disorder. For example, patients with obesity-hypventilation syndrome may require nasal ventilation initially or, in some cases, long term. In other patients low flow oxygen needs to be administered in conjunction with CPAP. Cases of CPAP failure are frequently admitted to hospital for a period of intensive inpatient training. The success of such treatment has not been investigated objectively. However, after exhausting all the relevant cases of CPAP failure in a patient with sleep apnoea who is completely intolerant of all varieties of nasal mask therapy (including bi-level positive airway pressure or nasal ventilation) despite intensive inpatient training, then the following issues need to be considered:

(1) What is the potential risk of leaving the patient untreated?
(2) How much does the patient want to be treated knowing the medical answer to question 1?
(3) If the patient and physician agree on trying a different treatment, what should it be? This

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Despite the many thousands of patients currently using CPAP, major complications have rarely been reported. One case of massive epistaxis due to a drying effect of nasal CPAP has been observed. Nasal CPAP should not be used in patients with a history of either recent surgery or trauma that has caused a cerebrospinal leak. One report described the development of pneumocephalus after use of nasal CPAP in such a situation. Leakage of cerebrospinal fluid must be adequately corrected before nasal CPAP is recommenced.

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would usually occur in patients where (i) coexisting sleepiness is seriously impairing daytime function; (ii) coexisting disease may be exacerbated by sleep apnoea with risk to the patient (this risk may at times be a potential risk due to a lack of hard data in the medical literature); (iii) there is evidence of severe hypoxaemia or awake cardiorespiratory failure even without sleepiness.

Treatment options for patients with CPAP failure

SURGERY

Although strong claims are made for maxillomandibular surgery, published experience is predominantly from one group with particular expertise.11 Therefore, at this stage such surgery must be considered experimental, particularly until long term follow up is available from a number of groups. Uvulopalatopharyngoplasty (UPPP) has no place or only a very limited role in CPAP failure, particularly in categories (i), (ii) and (iii) above. This view is based on the increasing literature demonstrating the limited efficacy and risks of UPPP for patients in these categories.52-53 “Minimalist” tracheostomy54 is an effective option for CPAP failure despite the potential complications and effects on lifestyle. This is not a simple decision to make and detailed patient evaluation and re-study should be performed before tracheostomy.

OTHER ALTERNATIVES

Oral appliances which repositional the mandible and maxilla or tongue have been suggested treatments for obstructive sleep apnoea.55 These may be potentially useful in patients with CPAP failure but documentation is limited at this stage. One problem is that the long term effects of such devices on temporo-mandibular joint dysfunction is not known. Oxygen therapy has been used in obstructive sleep apnoea with mixed results, but its role may be limited to CPAP failures with marked hypoxaemia who have a demonstrated reduction in hypoxaemic events on oxygen therapy. Transtracheal oxygen has recently been used in obstructive sleep apnoea but experience is limited.56

Summary

CPAP should be considered the first line of treatment in patients with moderate to severe obstructive sleep apnoea. In our centre in Sydney this generally means patients with more than 20 apnoea/hypopnoeas per hour with repeated dips in oxyhaemoglobin saturation and usually some symptomatology. Despite this first line role of nasal CPAP, recent objective studies question whether earlier enthusiastic reports on adherence to CPAP are correct. The role of technical innovations in new CPAP machines in improving usage remains to be tested. The “drop out” rate from physician selection for a CPAP trial to highly compliant user is certainly more than 50% of patients. What happens to these patients? Data from some studies suggest that surgical treatments are used, at least in the USA, but in all probability many of these patients remain untreated. The challenge in the next decade is either to improve CPAP devices to increase usage in this group or to develop other treatment options. The role of intensive inhosupal “acclimatisation” to CPAP also has yet to be objectively tested.

It is unclear whether “intelligent” CPAP will make huge inroads in increasing the number of patients who accept CPAP trials, prescriptions, or compliance. It will have minimal impact on patients with mask problems or claustrophobia or those who feel that CPAP is inconvenient. There is a high likelihood that it will reduce technologist workload during CPAP titration studies. “Intelligent” CPAP may help to reduce total overnight mouth leakage and therefore reduce nasal side effects. The current expense of developing such devices will mean that they are unlikely to supersede much cheaper standard “one pressure” CPAP machines in the next few years.

8 Abbey NC, Cooper KR, Kwetus JR. Benefit of nasal CPAP in obstructive sleep apnoea is due to positive pharyngeal pressure. Sleep 1989;12:420-2.
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