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Follow-up and outcomes of nasal CPAP therapy in patients with sleep apnea syndrome

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ABSTRACT: ***Follow-up and outcomes of nasal CPAP therapy in patients with sleep apnea syndrome. W.T. McNicholas.***

The large and growing numbers of patients with obstructive sleep apnea syndrome (OSAS) attending sleep disorders clinics create major logistical difficulties for the follow-up of these patients, particularly those on nasal continuous positive airway pressure therapy (CPAP). Follow-up of patients on CPAP should focus on treatment efficacy, side effects, and compliance with therapy. The adequacy and comfort of mask fit and the appropriate selection of pressure level at the time of initial titration have a major influence on treatment efficacy. Outcome measures of treatment efficacy include improvements in daytime performance and quality of life measures in addition to impact on cardiovascular morbidity, particularly hypertension. Side effects and compliance with CPAP are also influenced greatly by the adequacy of mask fit and pressure selection, which underlines the great importance of adequate technical expertise and patient education at the time of initiation of therapy. The recent development of automatically adjusting CPAP devices should greatly simplify the initiation of CPAP therapy and also the subsequent follow-up of OSAS patients on CPAP therapy. However, the much higher cost of auto-CPAP devices compared to standard CPAP does not justify the routine use of these more expensive devices at this time.
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Sleep apnea syndrome is now recognised to be a very common clinical condition with prevalence figures ranging between one and at least four percent, depending on the diagnostic criteria used [1]. This establishes obstructive sleep apnea syndrome (OSAS) as second only to asthma in the prevalence league table of chronic respiratory disorders. The current management of moderate to severe sleep apnea is largely dependent on nasal continuous positive airway pressure (nCPAP), which acts to splint the upper airway open during sleep, and thus counteracts the negative suction pressure during inspiration, which promotes upper airway collapse in these patients. Nasal CPAP completely controls the condition, and has a dramatic effect on the patient's awake performance [2–4], because of the normalised sleep pattern. However, while nCPAP is highly effective in controlling sleep apnea, the device is cumbersome, and compliance data demonstrate only moderately satisfactory compliance [5–7]. Nonetheless, nCPAP has become the most widely prescribed treatment for moderate to severe forms of OSAS and has transformed the lives of many patients.

The high prevalence of OSAS and the need for ongoing therapy in most cases raises the important clinical issue of the requirements for adequate follow-up of these patients, which can pose major logistical problems for sleep units because of the high numbers of patients involved. This review will focus on CPAP therapy and the important issues that need to be addressed in follow-up of patients with OSAS, namely treatment efficacy, side effects and compliance. The review will also examine a newer form of CPAP therapy, auto-CPAP, since this form of CPAP greatly simplifies the follow-up of patients with OSAS.

Treatment efficacy

This issue is fundamental to the success and patient tolerance of CPAP. There are several aspects to be considered.

1. Mask Fit and comfort

The selection of a comfortable mask, which provides an effective seal against the face to minimise air leaks, is a critically important aspect of CPAP therapy in OSAS. This aspect should be addressed at the initiation of CPAP, and has a major impact on the ongoing success of therapy. Mask fitting is a highly skilled process, and is best performed by a trained and experienced technologist or nurse practitioner. The technology of nasal masks has evolved greatly over the years, and there are now a large variety of masks available. Adequate time is essential for proper fitting and

patient education and careful attention to this aspect of therapy will have a significant knock-on benefit in terms of treatment efficacy, side effects, and compliance.

Leakage of air through the mouth can occur, which reduces the effective pressure delivered to the oropharyngeal airway. Mouth leak also increases the likelihood of nasal side effects in addition to the noise of the device since the pressure generator automatically increases the flow rate in an effort to correct the loss of pressure at the level of the pharynx. Mouth leak can usually be overcome by using either a chinstrap or a full-face mask that covers both nose and mouth. The pressure required to maintain upper airway patency using a full-face mask appears to be similar to that with a nasal mask. Potential problems with the full-face mask include coughing and vomiting, and the risks associated with failure of the device may be greater.

2. Pressure delivery

It is essential for treatment success that adequate pressures be delivered throughout the night to prevent sleep apneas/hypopneas, and also to eliminate snoring. On the other hand there is evidence that too high pressures are detrimental, not only by increasing the incidence of side effects, but also by predisposing to the development of central apnea. There are a number of commercial devices that help to determine the optimum pressure, and these devices are also helpful in ongoing monitoring of pressure requirements during patient follow-up. Many of these devices are suitable for use in the patient's home. The need for careful pressure titration becomes less important when auto-setting pressure devices are used, since these continuously adjust the pressure during sleep. These devices also make follow-up easier, and are likely to be associated with better patient tolerance and lower incidence of side effects. While quite expensive when first introduced, auto-setting CPAP devices have come down in price and are likely to be used with increasing frequency in the future.

3. Follow-up assessment of efficacy

Effects of CPAP on daytime function and quality of life

Patients with OSAS principally complain of excessive daytime sleepiness (EDS), whereas the bed partner is usually more affected by the snoring and restless sleep. Many reports have documented improvements in daytime sleepiness with CPAP, including several recent studies that have been randomised, prospective, and controlled in design [3, 8–10]. Studies have documented reductions in subjective sleepiness of greater than 50% as measured by the Epworth sleepiness scale in addition to improvements in measures of attention and concentration. Most of these reports have focused on patients with severe disease, but several recent reports have also documented significant improvements in these variables among patients with relatively mild OSAS [9, 10].

Several reports have also demonstrated significant improvements in objective measures of sleepiness such as multiple sleep latency testing (MSLT) and maintenance of wakefulness testing (MWT) with CPAP therapy, both at the severe end of the disease spectrum, and also among patients with relatively mild OSAS. The degree of improvement in MSLT appears to correlate with the hourly use of CPAP at night. OSAS has also been reported to have adverse effects on sleep quality and daytime alertness of the bed partner. A recent report from this department has also demonstrated improved subjective sleep quality and daytime well being in the bed partners of OSAS patients treated with CPAP [11].

Other reports have focused on neuropsychological effects of CPAP therapy, and have demonstrated improvements in indices of depression and mood [12], although some neuropsychological deficits appear to persist, perhaps reflecting hypoxic brain damage. Improvements in vigilance, driving simulator performance, memory and cognitive function have all been reported with CPAP. Several measures of quality of life, including the short form 36 (SF-36) and functional limitations profile (FLP), have been shown to be impaired in patients with OSAS and CPAP therapy produces a significant improvement in these measures, particularly at the severe end of the disease spectrum.

As a consequence of EDS, OSAS patients have more road traffic accidents than the general population [13–15] and this increased risk has been estimated at about 7 times that of the general population. However, the increased accident risk is largely removed after successful therapy with CPAP. This aspect assumes particular significance in countries where significant OSAS is regarded as a medical condition that requires the withdrawal of a patient's driving licence. Follow-up of these patients may require the formal assessment of the extent to which CPAP therapy has been associated with a reduction in driving accident risk.

OSAS can also be associated with a large variety of somatic symptoms including headache, heartburn, nocturia, impaired libido, and sweating, all of which may benefit from CPAP therapy [4]. Previous reports indicate that gastro-esophageal reflux (GOR) may induce respiratory abnormalities during sleep, seems to be common in OSAS patients [18, 19], and appears to benefit from CPAP therapy [16].

Effects of CPAP on cardiovascular morbidity

While the evidence is now reasonably strong that OSAS predisposes to hypertension, the impact of CPAP therapy on blood pressure levels is less clear-cut, and there is a great need for controlled studies to evaluate the impact of CPAP on cardiovascular morbidity. In most of the studies of the effects of CPAP on blood pressure, the subjects acted as their own controls, which is far from ideal. However, a recent randomised, placebo-controlled study has demonstrated small but significant re-

ductions in 24-hour blood pressure with CPAP [17]. Other reports have also demonstrated beneficial effects of CPAP on hypertension. One report demonstrated a fall in blood pressure levels with CPAP, independent of weight change, and an associated fall in elevated catecholamine levels [18], suggesting that OSAS is an important co-factor in the pathogenesis and possibly the maintenance of hypertension in these patients. Nocturnal cardiac rhythm disturbances have been reported to be common in patients with OSAS but also in control subjects. A recent report from this department has shown that CPAP therapy is associated with resolution of nocturnal cardiac rhythm disturbances within 24-48 hours of instituting therapy [19], which provides supportive evidence of a real association between OSAS and cardiac dysrhythmias.

Effects of CPAP on daytime gas exchange

The majority of patients with OSAS have normal awake blood gases, but particular categories may be associated with awake hypoxemia and hypercapnia, particularly those with associated severe obesity and/or co-existing chronic lung disease such as chronic obstructive pulmonary disease (COPD). Long-term CPAP treatment has been reported to be associated with improved awake arterial partial pressure of oxygen (PaO_2) levels in a subgroup of OSAS patients with daytime hypoxemia [20]. Patients with both COPD and OSAS may be better managed with bi-level PAP (BIPAP), since this modality provides a degree of assisted ventilation over and above that achieved with regular CPAP. A minority of OSAS patients display hypercapnia during wakefulness, which usually normalises with CPAP therapy.

Side effects of CPAP therapy

Side effects are common with CPAP therapy, but are rarely serious. Most side effects are minor and their main consequence is poor compliance. Optimizing the comfort and fit of the nasal mask have a major impact on the likelihood of side effects, which emphasizes the importance of adequate expertise of the personnel responsible for initiation of therapy. Furthermore, side effects usually occur early on after institution of therapy and close patient follow-up in the initial weeks of therapy is very important. This goal is usually best achieved by providing telephone contact numbers to each patient together with an early appointment for outpatient follow-up review.

The most common adverse effects related to the nasal mask are local pressure effects that can cause irritation or ulceration of the bridge of the nose, and air leaks, which can cause eye irritation. Refitting of the nasal mask, or switching to a different type of mask that covers only the nasal orifice can often correct these problems. Nose and throat problems occur in about 40% of patients using CPAP and include dry mouth, rhinorrhea, sneezing, nasal congestion and pain [21]. Air leak through the mouth is an important mechanism contributing to dry mouth and nasal side effects. Such mouth leaks lead to a higher airflow through the nose and can result in a large increase in nasal mucosal blood flow and resistance [22]. In most cases, heated humidification is successful in controlling these problems, but if nasal congestion and blockage are the principal concerns, an intranasal steroid spray may be more appropriate. There is evidence that uvulopalatopharyngoplasty (UPPP) may compromise subsequent nasal CPAP therapy [23] and it has been reported that, after UPPP, patients have mouth air leak at lower levels of pressure and also tolerate higher pressures badly. Furthermore, long-term compliance with CPAP appears to be lower in patients after UPPP. These considerations underline the importance of avoiding UPPP in patients whose OSAS severity may justify CPAP therapy.

Major side effects are very rare and have been described as single case reports. These include pneumocephalus, massive epistaxis, atrial arrhythmia, bacterial meningitis, subcutaneous emphysema after facial trauma, and pneumopericardium after cardiac surgery. One patient developed suffocation during application of CPAP where a large and floppy epiglottis was blown downward by the positive pressure and occluded the hypopharynx.

Compliance

After the initial CPAP titration, about 80% of patients accept CPAP as ongoing therapy [6]. Problems and side effects are generally encountered during the first few weeks of therapy, which may adversely affect compliance. This experience further emphasises the importance of close patient follow-up and support in the early weeks of therapy. About 10% of patients abandon CPAP after initial acceptance, usually during the first few months of home therapy. The major reasons for refusal or discontinuation of CPAP therapy are lack of perceived benefit and the obvious drawbacks of the system such as discomfort, claustrophobia, and the noise of the system. Patients' subjective reports are unreliable in determining compliance with therapy and self-reports usually overestimate the actual use by about one hour per night on average. Objective compliance data can be obtained from the built-in time-counter, which records the cumulative machine run time, or from an additional microprocessor, which records both machine run time and the time spent at effective pressure. These data indicate that the patient is wearing the mask and that the prescribed pressure is being delivered. Compliance can be improved by follow-up support where education, symptom treatment and equipment monitoring is provided.

Several cross-sectional studies of long-term compliance in large groups of patients followed up for at least one year have reported an average of 5 to 6.5 hours of nightly use [24, 25], although some reports have described fewer hours of nightly use. Long-term compliers apply CPAP on more than 90% of nights and their rate of use does not appear to decrease over time [26]. Such compliance levels compare favourably with levels reported for the

treatment of other chronic diseases such as asthma and hypertension. Compliance with CPAP is only weakly correlated with indices of OSAS severity at diagnosis [25] and cannot reliably be predicted before prescription. Thus, objective evaluations of use should be regularly obtained in all patients where possible.

Auto-CPAP

Automatically adjusting CPAP devices (auto-CPAP) have been developed over the past 5 years or so and probably represent the greatest advance in CPAP technology since the original description in 1981. Auto-CPAP machines can be used to help determine the optimum pressure for use with a standard CPAP machine or alternatively can be used for long-term home therapy. These machines are designed to continuously adjust the applied pressure to the "optimal" level throughout the night. This design makes intuitive sense since the concept of a single ideal level of positive pressure for any individual is over-simplistic. Upper airway resistance is dependent on multiple factors such as body position, sleep stages, sleep deprivation, body weight, and fluctuations of nasal congestion [27, 28], any or all of which may change within a single night and/or between nights. For example, it has been demonstrated that sleeping upright or in the lateral position can reduce the therapeutic level of CPAP by nearly 50% in non-rapid eye movement (REM) sleep [29]. Alcohol intake can also depress the tone and contractility of the upper airway muscles and thus result in higher pressure requirements to maintain upper airway patency. Therefore, a single level of pressure throughout the night will likely result in a situation where the pressure is excessive for parts of the night, but may be insufficient at other times and under particular circumstances such as after alcohol consumption.

Several studies have confirmed that auto-adjusting CPAP devices are at least as effective as manually determined pressure in correcting the respiratory events [30, 31] and the immediate effects on sleep are similar to manual titration, including the reduction of micro-arousals and improvement of EDS. Depending on the particular device, auto CPAP devices use pressure and/or flow signals to detect apneas, hypopneas or flow limitation. Snoring is detected as high frequency changes in pressure, which are considered as reflecting the acoustic vibrations of snoring. Most machines are regulated by an algorithm based on detection of apneas and hypopneas alone or in combination with snoring. Other algorithms include inspiratory flow limitation derived from the shape of the inspiratory flow/time relation. Obstructive can be distinguished from central apnea from the calculated airway conductance.

While more expensive, auto-CPAP devices greatly simplify CPAP initiation, since a single optimum pressure no longer needs to be calculated. Furthermore, patient follow-up is also simplified since repeat titration over subsequent years of therapy is no longer required. Auto-CPAP may be particularly useful in patients intolerant of higher pressures or in patients in whom the ideal pressure is highly variable. At present, there is insufficient evidence that auto-CPAP has sufficient advantages over traditional fixed CPAP in unselected OSAS patients to justify the additional cost. The hourly rate of use has been shown to be higher with auto-CPAP in one study compared with standard CPAP (7.1 vs. 5.7 h), despite the fact that the mean mask pressure was not lower than the fixed CPAP [32]. The long-term benefits of auto-CPAP have not been determined and less expensive constant CPAP should still be considered as the standard home therapy for the majority of patients. However, it is likely that auto-setting CPAP machines will become increasingly popular over the coming years, and may replace the standard fixed pressure machines in the future, particularly if the price is reduced towards that of the standard CPAP machines.

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