REVIEW ARTICLE

Optimizing CPAP

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Introduction

Sleep apnea is a sleep disorder characterized by pauses in breathing during sleep. These episodes, called apneas, occur repeatedly throughout the sleep. Sleep apnea-hypopnea syndrome (SAHS) is highly prevalent in the middle-aged active and productive population.[1] It significantly interferes with quality of life[2] and is associated with an increase in morbidity and mortality.[3] The pathophysiology of SAHS is characterized by repetitive occlusions of the posterior pharynx during sleep that obstructs the airway, followed by oxyhemoglobin desaturation, persistent inspiratory efforts against the occluded airway, and termination by arousal from sleep.

It is currently admitted that nasal continuous positive airway pressure (nCPAP) represents one of the most effective treatment for SAHS, because it is effective at both correcting respiratory events and related arousals, and also improving morbidity.[4]

CPAP Titration

The following methods are generally used to titrate the CPAP pressure –

1. Attended full-night laboratory polysomnography during which a technician adjusts the pressure until all or most of the obstructive respiratory events are eliminated.
2. Attended split-night laboratory polysomnography during which the initial two, or more, hours are used to diagnose obstructive sleep apnea and the remainder of the night is used to adjust pressures for prescribing CPAP.
3. Formulas to derive pressures from clinical, polysomnographic, and/or anthropometric variables. The calculated pressure can also be used as a starting CPAP pressure for laboratory titration.
4. Unattended home or laboratory recordings using autotitrating positive pressure devices (APAP).[5, 6]

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Indications for CPAP

CPAP is a safe and effective mode of treatment in patients with clinically important SAHS. Treatment is indicated when there is documented sleep-related apnea hypoapnea and evidence of clinical impairment. It is also effective in the treatment of patients with clinically significant Cheyne Stokes respiration or central sleep apnea syndromes where treatment may be indicated if there is documented central apnea and clinical impairment. On the other hand, CPAP is not routinely indicated in individuals with simple snoring that is not associated with pauses in respiration or with clinical impairment.[4] There are no absolute contraindications for CPAP use. Relative contraindications include bullous lung disease and recurrent sinus or ear infections.[4]

Mechanism of Action

The upper airway in patients with SAHS is not only smaller but is also more collapsible.[7] Despite these abnormalities, during wakefulness the upper airway is patent. Subjects with OSA protect themselves while awake by increased activation of their airway dilator

muscles, at least the genioglossus.[8] During sleep, there is reduction of activity of upper airway dilator muscles, thereby shifting the balance of forces toward collapse.

Airway collapse occurs when the intraluminal pressure is less than the critical opening pressure or the pressure required to keep it open (Pcrit). As nasal pressure is raised above Pcrit by applying a positive airway pressure through CPAP, inspiratory airflow increases in proportion to the level of positive pressure applied until airway occlusions are abolished.[9] This restores adequate airflow and oxygen saturation.

Efficacy of CPAP Obstructive Sleep Apnea (OSA)

The goal of treatment in a patient with obstructive sleep apnea (OSA) is complete elimination of all apneas, hypopneas, desaturations, arousals, snoring and other related symptoms in all body positions and at all sleep stages.

CPAP is extremely safe and very effective in patients with moderate and severe OSA. However, the extent to which patients with mild OSA benefit from CPAP is less certain. Also, the minimal diagnostic threshold at which application of CPAP will be beneficiary is not well documented.[10, 11] Application of CPAP has been shown to have an immediate and dramatic effect in patients with neurocognitive dysfunction and daytime sleepiness[12,13] but, improvements in cardiopulmonary function are more long-term.[14, 15]

Sleep Quality

CPAP is effective in lowering the number of arousals and the respiratory disturbance index (RDI), and in raising SaO_2.[16] As compared to nocturnal oxygen, CPAP is associated with an improvement in sleep quality by improving slow wave and REM sleep. On the other hand, the effectiveness of supplemental oxygen is limited to prevention of nocturnal desaturation.[17]

Daytime Sleepiness

CPAP is effective in reducing symptoms of daytime sleepiness and improving quality of life in people with moderate and severe obstructive sleep apnoea.[18] Subjective sleepiness rated by the Epworth sleepiness scale and road traffic incident rate are significantly reduced by CPAP.[19]

Patient Satisfaction

A questionnaire to assess patient satisfaction with CPAP therapy mailed to 148 patients and phone calls to 42 patients with SAHS indicated continued CPAP use 17 $\pm$ 11 (mean $\pm$ SD) months after initiation of therapy by 105 patients. Out of these, the majority (81%) perceived CPAP as effective, 5% were unsure, and only 14% believed that CPAP was ineffective for treating SAHS. Improvement was also noted by the family members in 83% of the patients.[20]

Morbidity and Mortality

Patients with SAHS have systemic arterial hypertension, ischemic heart disease, transient ischemic attacks, or stroke more often than control populations and have a shorter life expectancy.[3] Apneas also may give rise to cardiac arrhythmias, including potentially life-threatening bradyarrhythmias.[21] A cause-and-effect relationship has been suggested between OSA and systemic hypertension.[22] CPAP affects the circadian profiles of blood pressure and heart rate in patients with OSA. Average blood pressure and heart rate decreases significantly in patients with hypertension in response to CPAP therapy.[23]

Exacerbations of ischemic events during sleep have been reported in patients with SAHS which may be explained by the combination of increased myocardial oxygen consumption and decreased oxygen supply due to oxygen desaturation. Treatment with CPAP has been shown to ameliorate nocturnal ischemia by improving nocturnal saturation.[24]

SAHS is associated with greater mortality especially in those with 20 or more apneas per hour of sleep. This difference in apnea-associated mortality was more evident in younger patients, aged less than 50 years, in whom all-cause mortality is less frequent. Treatment with CPAP can reverse the increase in apnea-associated mortality.[3]

Compliance of CPAP

CPAP therapy is only as beneficial as its utilization. Compliance in published studies is defined as continuous nightly use reported by patients during a specific period of observation of 1 to 6 months.[4] Patients with SAHS

treated by CPAP need to use CPAP on a long-term basis to prevent recurrence of symptoms and hence long-term compliance is needed to have any beneficial effects.

A large European multicenter study reported good therapeutic adherence with 80% of the patients using the machine 4 or more hours per night on more than 70% of nights. 77%, 82%, and 79% of patients adhered to therapy at 1, 2, and 3 months, respectively.[25] Rosenthal et. al.[26] found that patients who regularly used CPAP during the first week of treatment continued using CPAP for the entire first year. By contrast, patients with mild OSA had a high rate of CPAP discontinuation.

Although use of CPAP is associated with minimal side effects (Table 1),[27-31] on a long-term basis only two thirds of patients continue with CPAP after 5 years, with a median nightly use of 5.7 hours.[32] Early CPAP use data are strongly predictive of continuing use and may help decisions about perseverance with CPAP treatment and allow early identification of patients who might benefit from more intensive education and support. It is not always easy to predict who will be non-compliant. Factors that can lead to non-compliance are included in table 2.[32, 33]

Table 1: Side effects of CPAP

Mask related	• Claustrophobia • Allergy to the face • Air leaks • Abrasions of the ridge of the nose • Discomfort • Eye irritation
Pressure effects	Bloating Difficulty breathing out Chest discomfort
Upper airway problems	Dry nose Nasal congestion Sore throat Sneezing Rhinorrhea Nasal drip Epistaxis
Machine effects	Noise
Rare complications	Pneumocephalus Bacterial meningitis Conjunctivitis Massive epistaxis Atrial arrhythmia

Improving CPAP Compliance

Among the various studies, the most consistent factor associated with improved compliance is the patient and family recognition of symptomatic improvement in the sensation of sleepiness which is associated with perceived increases in the level of alertness.[20, 34, 35] Adherence to CPAP therapy can be improved by addressing the various factors listed in Table 3.[33]

Table 2: Factors associated with CPAP non-compliance

- Female sex
- Current smokers
- Adverse events to treatment
- Patients with only mild OSA
- Patients with no excessive sleepiness
- Previous uvulopalatopharyngoplasty (UPPP)
- Level of CPAP education given

Table 3: Factors that can improve CPAP compliance

- Treatment of nasal obstruction
- Appropriate titration
- Attention to mask-fit issues
- De-sensitisation for claustrophobia
- Use of heated humidification
- Patient education
- Regular follow-up
- Use of compliance software
- Referral to support groups

CPAP Education

Education regarding proper use of CPAP, its benefits, side effects and the need for prolonged and regular use can increase patient compliance. This should be started early in the course of treatment and may include – personal interview with the patient, patient support groups, and use of literature and videos. Family members should also be involved in all discussions so that they can help the patient to be more tolerant with CPAP.

CPAP Interfaces

There are many different CPAP interfaces now available for the treatment of OSA. The type of CPAP delivery interface is likely to influence a patient's acceptance of CPAP therapy and long term compliance. The masks generally used are nasal masks, face masks and nasal pillows. Compliance is greater with nose mask than with face mask because the overall comfort is better but mouth leaks represent a fairly common situation leading to discomfort and dissatisfaction with CPAP.[36] Chinstraps can sometimes correct this problem; however, at other times a full-face mask is needed. Additionally, full-face masks may help in patients who are obligate mouth breathers or who are unable to tolerate nasal masks. But overall, nasal masks appear to be preferred by most patients. Full face masks have also been shown to be less effective in abolishing sleep apneas as they simultaneously increase the intraluminal airway pressure as well as the pressures of the oropharynx; and hence the transmural pressure of the upper airway is not increased.[37] Therefore, the face mask can not be recommended as a first line interface, but may be considered if nasal obstruction or dryness limits the use of a nasal mask. Also, nasal pillows may be useful alternatives when a patient is unable to tolerate conventional nasal masks, but are effective only when the pressure required is not too high.

Humidifiers

Upper airway symptoms are caused by mouth leaks that produce high unidirectional airflow over nasal and oral mucosa. Humidity is employed to alleviate dryness and congestion in OSA patients. Specific side effects such as dry mouth or throat and dry nose are reported less frequently when CPAP is used with heated humidity with improved compliance.[38]

Pressure Ramp

"Pressure ramp" is a feature that allows pressure to be reset to a low level and then gradually increased over time. The amount of time and rate of increase are usually adjustable. It is supposed to improve patient comfort by theoretically allowing a patient sufficient time to fall asleep before higher pressures are reached but only some patients find the ramp feature useful. The main disadvantage of having lower pressures at sleep onset is that it may permit obstructive events during subtherapeutic CPAP levels and allow sleep-onset central apnea episodes to occur and repeated activation of the ramp can decrease effective CPAP therapy.[39]

Using Sedative-Hypnotics

Sedative-hypnotics are sometimes used by clinicians in patients who have difficulty sleeping with CPAP. Sometimes they are used to assist patients during the acclimatization phase of initial CPAP use. Other times they are used when CPAP therapy successfully unmasks insomnia once the longstanding accumulated apnea-related sleepiness resolves. However, great caution should be taken whenever sedative-hypnotics are used for this purpose as they may increase arousal threshold, thereby prolonging apnea duration and increasing oxyhemoglobin desaturations.

Other Modes of Positive Airway Pressure

Auto CPAP (APAP)

It is a type of CPAP machine that monitors changes in breathing of the patient and compensates automatically by making appropriate adjustments in pressure by monitoring the patient's airflow. APAP may be used for initial pressure titration or in long term treatment of patients with OSA. Recent data from the literature demonstrate that auto-CPAP therapy is as effective as conventional CPAP in treatment of OSA.[40-42]

Traditionally, the effective pressure is titrated in the sleep laboratory by means of polysomnography, and is defined as a pressure level able to eliminate most apneas, hypopneas, and snoring. However, this effective pressure can vary in a given subject from night to night and even during a given night, depending on body and neck or mandibular position, fatigue level, sleep stage, nasal patency, upper airway edema, ingestion of alcohol, or sedative agents.[43] Using a fixed single pressure based on a sample usually obtained when the patient was sleeping supine during REM sleep, when pressure requirement is often maximal, may amount to using more pressure than needed for large portions of the night. In one study, 49.3% of home treatment time on APAP was spent at a pressure equal to or less than the effective pressure level determined during a polysomnographic recording.[41] The

disadvantage of using more pressure than needed is that higher pressures increase the propensity of mask leaks, mouth leaks, and pressure intolerance. Any of these factors can reduce CPAP acceptance and therapeutic adherence. Furthermore, regular maintenance CPAP therapy itself and weight loss may alter the effective pressure in the long term.[43] Also this method of titrating CPAP pressure by polysomnography is expensive, time intensive, uses sleep lab resources and requires trained technicians. There could be wide variation between technicians and a scope for human error when using this method.

One way to bypass the changes in effective pressure needed to abolish sleep apneas is to use automatic CPAP machines which can compensate for these changes. The variable pressure response of Auto-CPAP allows for treatment under different situations such as upper airway infections, different sleeping positions, and changes in weight. The average Auto-CPAP pressures tend to be lower than conventional CPAP because it is a proactive form of treatment.[41] It increases pressure in response to subtle airflow limitation episodes, which precede conventional apneas and hypopneas. The application of variable pressure according to a patient's airflow during sleep may improve comfort and possibly increase treatment compliance. Current Auto-CPAP devices retain in memory information regarding the pressure and airflow events during several nights. This information can be downloaded and analyzed to further adjust the treatment and monitor compliance. It can be used safely and easily at home, with minimal monitoring, for setting of CPAP pressures.

APAP improves long term comfort in most patients with OSA and improves compliance in patients with side effects from CPAP therapy.[44] It is particularly useful in patients requiring higher pressures.[45] Another potential advantage of Auto-CPAP includes permitting the initiation of treatment while awaiting a standard CPAP titration.

However, the accuracy and efficacy of Auto-CPAP in titrating pressure depend on the machine that is used[46] and also high leak may interfere with these auto-adjusting devices.[5] Although APAP may abolish apneas, residual hypoxia may persist in patients with underlying lung disease.[45] Up to now the identification of patients who will benefit from APAP remains unknown because of inadequate data, regarding comparison of medium- or long-term efficacy of fixed and auto-CPAP on sleep and respiratory variables, treatment compliance, improvement in objective daytime sleepiness, and risk factors, is available, making constant CPAP the standard treatment mode in the majority of patients with SAHS.

The Standards of Practice Committee of the American Academy of Sleep Medicine[47] has developed evidence based practice parameters as a guide to the appropriate use of APAP. Recommendations of the committee for the use of auto-CPAP are as followed:

(1) The presence of obstructive sleep apnea (OSA) must be established by an acceptable diagnostic method.

(2) APAP titration and treatment are not currently recommended for patients with congestive heart failure, significant lung disease such as chronic obstructive pulmonary disease, daytime hypoxemia and respiratory failure from any cause, or prominent nocturnal arterial oxygen desaturation due to conditions other than OSA (e.g., obesity hypoventilation syndrome). Also, patients who do not snore, either due to palate surgery or naturally, should not be titrated with an APAP device that relies on vibration or sound in the device's algorithm.

(3) APAP devices are not currently recommended for split-night studies.

(4) Certain APAP devices may be used during attended titration to identify by polysomnography a single pressure for use with standard CPAP for treatment of OSA.

(5) Once an initial successful attended CPAP or APAP titration has been determined by polysomnography, certain APAP devices may be used in the self-adjusting mode for unattended treatment of patients with OSA.

(6) Use of unattended APAP to either initially determine pressures for fixed CPAP or for self-adjusting APAP treatment in CPAP-naive patients is not currently established.

(7) Patients being treated with fixed CPAP on the basis of APAP titration or being treated with APAP must be followed to determine treatment effectiveness and safety.

(8) A re-evaluation and, if necessary, a standard attended CPAP titration should be performed if symptoms do not resolve or the CPAP or APAP treatment otherwise appears to lack efficacy.

Bilevel Positive Airway Pressure BiPAP)

BiPAP devices provide two pressure levels, one during inspiration and a lower one during expiration. Complaints of dyspnea or discomfort during CPAP use, especially during expiration against the continuous pressure, may represent a barrier to CPAP adherence in some patients. Gay and associates[48] showed that although BiPAP appeared to be as effective as CPAP for the treatment of OSA but offered no advantages, in terms of side effects or compliance, in patients receiving first-time therapy for OSAS. However, in spite of CPAP therapy, oxygen desaturation due to hypoventilation persists in some patients. These patients with OSA resistant to CPAP therapy are often morbidly obese and

also have abnormal awake blood gas values, significantly lower PaO2 and higher PaCO2. BiPAP may be indicated in such patients as it may improve nocturnal ventilation and awake blood gas values in such patients.[49]

Conclusion

Positive airway pressure is the preferred treatment for most of the individuals with moderate or severe OSA. It improves airway patency during sleep, which in turn improves sleep quality, sleep continuity, daytime alertness, and overall quality of life in symptomatic patients. The effectiveness of CPAP is compromised because a large proportion of patients cannot tolerate or are non-adherent to regular use of the mask and machine. Adherence reportedly can be improved by ensuring increased mask comfort, patient education, heated humidification, and prompt correction of mask and machine related adverse events. APAP devices show great promise in both diagnosis and treatment of OSA, however, at present they are not recommended as a replacement for CPAP.

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