Compliance of Various Forms of Obstructive Sleep Apnea Treatment

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Introduction

The therapeutic armamentarium for obstructive sleep apnea (OSA) comprises several treatment options. To provide effective treatment for OSA, careful consideration of the individual patient, available medical and surgical therapies, and inherent risks and complications of those interventions must be taken into account. Continuous positive airway pressure (CPAP) has the firmest evidence base in the treatment of OSA. A growing body of evidence is becoming available supporting the practice of other treatment modalities, especially mandibular advancement devices (MADs), weight loss, positional therapy (PT) and sleep surgery.

Treatment is generally approached in a stepwise manner and begins with behaviour modification, indicated for all patients with a modifiable risk factor [1]. This includes weight loss, alcohol and sedative abstinence and avoidance of worst sleeping position.

Continuous Positive Airway Pressure

Continuous positive airway pressure (CPAP) first introduced by Sullivan in 1981, is regarded as the gold standard in the treatment of moderate and severe cases and is the most efficacious treatment modality of OSA [2]. CPAP functions as a pneumatic splint to maintaining upper airway patency. CPAP is considered successful when the apnea-hypopnea index (AHI) is reduced to below 5 when CPAP is used. In a

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meta-analysis of the Cochrane Collaboration, compared with control, CPAP was shown to be significantly effective in reducing the AHI as well as improving measurements of quality of life, cognitive function and objective and subjective measures of sleepiness [3]. Possible side effects can be related to the interface (skin abrasion from contact with the mask, claustrophobia, mask leak, irritated eyes), pressure (nasal congestion and rhinorrhea with dryness or irritation of the nasal and pharyngeal membranes, sneezing, gastric and bowel distension, recurrent ear and sinus infections) and negative social factors [4, 5].

Mandibular Advancement Devices

Mandibular advancement devices (MADs), also known as mandibular reposition appliances (MRA) or oral appliances (OA), have become increasingly popular as a treatment alternative [6]. By advancing the mandible and its attached soft tissue structures forward, they aim to increase upper airway size [7]. MADs have been found to be effective in reducing the AHI, especially in patients with mild to moderate OSA. Studies have shown that MADs are more effective when compared to "control devices" (which do not protrude the mandible), in reducing the AHI [6, 8–12]. When compared to CPAP, there was a significant effect in favor of CPAP compared with MADs [13–16].

Side effects have been reported with the use of MADs: excessive salivation or dryness of the mouth; gum irritation; discomfort of the temporomandibular joint, teeth or facial musculature; bite change; and temporomandibular disorders [6–8, 17–25]. Long-term treatment with a MAD can result in changes in dental morphology [24].

Sleep Surgery

Sleep surgery aims to increase the surface area of the upper airway, to bypass the pharyngeal airway or to remove a specific pathology [26, 27]. Surgical procedures developed to treat OSA can predominantly be classified according to site of intervention, mechanism of action and invasiveness [4].

Uvulopalatopharyngoplasty (UPPP) is the most commonly performed surgical procedure for OSA [28–31]. The procedure aims to increase the retropalatal lumen and reduce the collapsibility of the pharynx, by resection of the free edge of the uvula and soft palate, often in combination with a tonsillectomy [26, 27]. Unfortunately, UPPP is often misused as the first line of surgical therapy for OSA, without adequate assessment of obstruction site(s) and regardless of predictive factors such as obesity [32]. As a result, an isolated UPPP is often unsuccessful in treating OSA, especially in badly selected patients. Palatal surgery is indicated in patients who have airway collapse at the level of the velum. There are no widely accepted standardized methods or algorithms to identify suitable candidates.

In a literature review by Sher et al., published in 1996, an overall response rate of 40.7 % was reported (with response defined as a 50 % decrease in the respiratory disturbance index [RDI] and a postoperative RDI of 20, or as a 50 % decrease in the AI and a postoperative AI of 10) in patients with OSA treated with UPPP alone, regardless of site of obstruction. In patients with suspected hypopharyngeal obstruction, the response rate was a mere 5.3 %, whilst in patients with suspected palatal narrowing alone, the response rate increased to 52.3 % [33]. As in all surgery, meticulous patient selection is crucial. The type and extent of surgical intervention mainly depends on the severity of the disease and the site(s) of obstruction as well as patient's characteristics, sleep position dependence, comorbidity and the patient's preference [34]. Over the years, the scope of surgical treatment modalities has broadened significantly.

No surgery is without risks. Possible late complications, in order of descending frequency, of UPPP are pharyngeal dryness and hardening, postnasal secretion, dysphagia, incapability of initiating swallowing, prolonged angina, taste disorders, speech disorders, numbness of tongue, permanent velopharyngeal incompetence and nasopharyngeal stenosis. Furthermore, although more clarification is needed, studies suggest that the response to UPPP for OSA decreases progressively over the years after surgery [35–40].

Treatment modalities designed to prevent obstruction at the level of the hypopharynx vary from minimally invasive, such as radiofrequency ablation of the base of the tongue, to invasive genioglossal advancement (GA) or maxillomandibular advancement (MMA), for example. An evidence-based medicine review reported a success rate ranging from 20 % to 83 % achieved in patients undergoing tongue radiofrequency, 25–83 % in reports on midline glossectomy and 39–78 % on GA. Surgical success is defined as a reduction in AHI of 50 % or more and an AHI of less than 20 [41].

Compliance

CPAP and MAD treatment are regarded as successful if the AHI drops below 5 whilst the devices are used; an AHI below 5 is the bar for CPAP adjustment. It is however common knowledge that a majority of patients are not adherent to the treatment during 100 % of the total sleep time under everyday non-laboratory conditions [42]. Current arbitrary trends define compliance as 4 h per night as an average over all nights observed [43].

Treatment outcome based on individual compliance in conservative treatment can currently most reliably be reported in patients with CPAP. Built-in counters have become a standard feature in CPAP devices, and hours of use can easily be assessed by every physician. Until recently accurate assessment of compliance for other conservative interventions was limited to subjective self-report.

Despite the efficacy of CPAP, it is, however, a clinical reality that the use of CPAP is often cumbersome. Patients seem to either tolerate the device well or not

at all—a bimodal distribution [44]. Studies have shown that 29–83 % of patients are non-adherent, when adherence is defined as at least 4 h of CPAP use per night. [45] More support and care is needed to improve compliance, especially on a long-term basis, such as addressing CPAP side effects.

Objective usage data for MAD are harder to collect than for CPAP, but self-reported treatment compliance is high [8, 11, 15, 17, 18]. Compliance rates vary greatly between studies varying between 4 and 82 % after 1 year of treatment [46]. Long-term compliance has been reported to decrease over time. Over a 2- to 5-year follow-up period, studies have reported a subjective therapeutic adherence ranging from 48 % to 90 % [47–50]. Discontinuation of treatment is due to side effects or lack of perceived benefit [51]. Self-reported adherence tends to overestimate actual use [4].

Reporting on the efficacy of OA in a 3-month prospective clinical trial, Vanderveken et al. took objective OA compliance into consideration through an embedded microsensor thermometer with on-chip integrated readout electronics [52]. The mean AHI was calculated based on the objective OA use and treatment period.

Compliance Positional Therapy

Ineffectiveness, backache, discomfort and no improvement in sleep quality or daytime alertness have been responsible for poor compliance and subsequent disappointing long-term results of PT of various tennis ball techniques.

Skinner et al. included 20 patients in a randomized cross-over comparing the efficacy of the thoracic anti-supine band (TASB) with nCPAP [51]. Subjects were randomly assigned to receive the TASB or nCPAP for the first month followed by a 1-week washout before commencing the alternative treatment. The self-reported compliance was significantly better with TASB than with nCPAP. Nineteen of 20 patients reported a 7-h nightly use with the TASB. In contrast only 9 of 20 subjects met the 4 h per night CPAP compliance criteria.

Next to the efficacy study of PT (vest with semi-rigid foam on dorsal part) by Wenzel et al., the group contacted the patients approximately 13.7 months later by telephone to assess PT compliance [53]. Only 4 of the 14 patients were still using PT (on average for 7.3 h and 6.4 nights); their ESS was reduced from 8.5–6.5. The remaining 10 patients had stopped using PT due to the following reasons: discomfort and tightness of the vest, frequent awakenings, restless sleep, increased sweating during the night and prevention of preferred sleeping position.

Oksenberg et al. assessed the use of PT (TBT) during a 6-month period in 78 consecutive POSA patients [54]. Of the 50 patients who returned the questionnaire, 38 % were still using PT; 24 % no longer used PT, as they claimed to have learned to avoid the supine position; and 38 % no longer used PT but had not learned to avoid the supine position.

Bignold et al. studied the compliance of 67 patients, who had been prescribed PT (TBT) 2.5 ± 1 year earlier, using a follow-up questionnaire [55]. 6 % were still using

PT; 13.4 % no longer used PT, as they claimed to have learned to avoid the supine position; and a staggering 80.6 % no longer used PT, but had not learned to avoid the supine position. Reasons to abort the PT included ineffectiveness, backache, discomfort and no improvement in sleep quality or daytime alertness.

Of the 9 patients randomized to PT (triangular pillow), in a study performed by Svatikova et al., 3 months post-stroke, the self-reported adherence was 3 (33 %) all nights, 1 (11 %) most nights, 2 (22 %) some nights and 3 (33 %) no nights [56].

In a second study performed by Bignold et al., patients were assigned with PT for 3 weeks (a position monitoring device and supine alarm device) [57]. The device was active for 1 of the 3 weeks. Patients used the device 85 % of nights over the full 3 weeks with an average of 6.8 h of use per night.

Recent developments have seen the introduction of a new generation of PT, which successfully prevents patients from adopting the supine position without negatively influencing sleep efficiency. In a recent study by van Maanen et al., studying the effect of the sleep position trainer (SPT) in patients with POSA, the median percentage of supine sleeping time decreased from 49.9 % [20.4–77.3 %] to 0.0 % [range: 0.0–48.7 %] ($p<0.001$) [58]. The median AHI decreased from 16.4 per hour [6.6–29.9] to 5.2 per hour [0.5–46.5] ($p<0.001$). 15 patients developed an overall AHI below 5 per hour. Sleep efficiency did not change significantly, the Epworth Sleepiness Scale decreased significantly, and Functional Outcomes of Sleep Questionnaire increased significantly. Compliance after 1 month was found to be 92.7 % [62.0–100.0 %].

At present, evidence of PT effectiveness is based on small-scale case series and a few randomized trials. Little is known about the long-term compliance of PT. It has been suggested that patients may learn to avoid the supine position following PT and therefore do not need to use PT on a regular basis [59]. Others may need PT either periodically to reinforce training or consistently.

Reporting on Compliance

The effectiveness of conservative treatment regarding the reduction of AHI depends both on its impact on airway obstruction and compliance. Current evidence demonstrates that clinical outcome is dependent on compliance to treatment in a dose-dependent manner.

In a double-blind, placebo-controlled cross-over trial by Sharma et al., 86 patients with OSA were randomly assigned to therapeutic CPAP or sham CPAP for a period of 3 months with a washout period of 1 month in between [60]. A statistically significant greater mean reduction in systolic and diastolic blood pressure (BP), glycated haemoglobin, triglycerides, LDL cholesterol and total cholesterol was observed in a subgroup of patients who used CPAP ≥ 5 h ($n=51$). Similar results were found in a prospective long-term follow-up study and a randomized controlled trial: a significant decrease in the 24-h mean arterial pressure (MAP) was achieved in patients who used CPAP >5.3 h per day ($n=27$), and a statistically significant

decrease in systolic BP was observed in patients who use CPAP ≥ 5.6 h per night [61, 62]. Hours of CPAP use was an independent predictor of reduction in BP [61].

Campos-Rodriguez et al. reported in a retrospective cohort study that the 5-year cumulative survival rate was significantly higher in patients with sleep apnea and hypertension who used CPAP ≥ 6 h per night [63].

Weaver et al. reported a linear-dose relationship between hours of CPAP use and improvement in daytime sleepiness after 3 months of therapy in a recent follow-up cohort study of patients with severe OSA [64].

This current evidence demonstrates that clinical outcome is dependent on compliance to treatment in a dose-dependent manner.

As cardiovascular effects and long-term survival are relatively hard to assess, the AHI is mostly used as a surrogate outcome measure. The current evidence however demonstrates that compliance also needs to be taken into account when reporting treatment outcome in terms of AHI reduction.

Currently, when reporting on treatment effectiveness of conservative treatment, the reduction in AHI whilst using CPAP in laboratory situations is documented. An artificial compliance of 100 % is assumed.

Two current publications have suggested methods to include compliance into the calculation of the AHI under conservative treatment. Ravesloot and de Vries proposed mathematical formulas to assess mean AHI with regard to treatment compliance based on the hours of CPAP use as documented by the built-in counters of the CPAP devices [65]. They suggest that a mean AHI in CPAP therapy is more realistic than using arbitrary compliance rates which in fact hide insufficient reductions in AHI. Almost simultaneously, Stuck et al. published data on treatment effects of CPAP on the AHI in a cohort of patients with OSA. The mean AHI could also be calculated based on the treatment period and the hours of use of the device [66].

The following formula was described in both papers using the estimated total sleep time (TST), the hours of CPAP use in the treatment period as assessed with the devices' built-in counters (HOURSonCPAP), the AHI as assessed in the sleep lab before treatment (AHIoffCPAP) and whilst using CPAP (AHIonCPAP):

$$\text{Mean AHI for CPAP} = \frac{\left(\text{AHIonCPAP} \times \text{HOURSonCPAP}\right) + \left[\text{AHIoffCPAP} \times \left(\text{TST} - \text{HOURSonCPAP}\right)\right]}{\text{TST}}$$

For example, if we take a patient with an AHI of 38 (*AHIoffCPAP*). Using the compliance criteria cut-off discussed, our patient sleeps using CPAP 7 nights per week (*NIGHTSonCPAP*). The AHI (*AHIoffCPAP*) is reduced to 2 (*AHIonCPAP*) during 4 h, again using the compliance cut-off criteria discussed (*HOURSonCPAP*). During the residual 4 h (*HOURSoffCPAP*), the AHI remains 38. Using the generalized formula above and the parameters for this patient, we can calculate the mean AHI during compliant use of CPAP:

$$\text{Mean AHI for CPAP} = \left(\frac{\left(4 \times 2\right) + \left(4 \times 38\right)}{8}\right) = 20.$$

The mean AHI is 20, so the AHI is reduced by 47.37 %.

This formula can be generalized to other PSG outcomes such as the apnea index or desaturation index. This mathematical formula is based on the assumption that the AHI will revert to baseline once the CPAP appliance is no longer used. CPAP is thought to play a role in reducing edema resulting from snoring-associated vibration and apnea-induced mechanical stress of the upper airway. It can be argued that the baseline AHI may be reduced by a fraction in chronic CPAP use and that after termination of CPAP during the night the AHI may not completely revert to baseline. The precise effect however remains to be elucidated. If future research allows quantification of the magnitude of this effect, the formula could easily be extended by a factor addressing this aspect.

Future Perspectives

Treatment outcome based on individual compliance in conservative treatment can currently most reliably be reported in patients with CPAP. Built-in counters have become a standard feature in CPAP devices, and hours of use can easily be assessed by every physician. Until recently accurate assessment of compliance for other conservative interventions was limited to subjective self-report.

Reporting on the efficacy of OA in a 3-month prospective clinical trial, Vanderveken et al. took objective OA compliance into consideration through an embedded microsensor thermometer with on-chip integrated readout electronics [52]. The mean AHI was calculated based on the objective OA use and treatment period. Their results support the hypothesis that higher compliance with OA therapy translates into a similar adjusted effectiveness as compared with CPAP [52, 67]. Despite not being a common practice as yet, compliance to OA devices can be measured objectively with the introduction of this new device [52].

In future studies comparing the effects of different devices (e.g. CPAP or OA) on the AHI with alternative treatment methods, especially those with 100 % adherence (e.g. surgery), adherence should to be taken into account with the formula mentioned above. In doing so, one could compare the effectiveness of OA, CPAP and surgery.

The following example may illustrate this approach: in a recent systematic review and meta-analysis reporting on the efficacy of maxillomandibular advancement (MMA) on the AHI in OSA patients, the mean AHI decreased from 63.9 to 9.5 per hour ($p<0.001$) following surgery [12].

In the previously mentioned study by Stuck et al. addressing the effects of CPAP, the mean AHI decreased from 35.6 to 11.9 per hour when individual adherence was taken into account [12]. The mean AHI under CPAP was 2.4 per hour. Juxtaposed, these treatment modalities seem to be equally effective in reducing the AHI when adherence is taken into account, although the population in the MMA study was more severely affected. This approach may also be used to compare the effects of other current treatment strategies.

Following this train of thought, recent studies suggest that higher compliance with OA therapy translates into a similar adjusted effectiveness as compared with CPAP [11, 13].

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