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Adherence to CPAP Therapy - a necessity in the Pulmonary Rehabilitation of patients with Obstructive Sleep Apnea

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Abstract

Obstructive sleep apnea (OSA) has become a major worldwide health concern and affects 2-4% of males and 1-2% females. In subjects diagnosed with mild or severe OSA, CPAP (Continuous Positive Airway Pressure) is highly efficacious in improving the specific quality of life and the cardiovascular outcome but adherence to treatment limits its overall effectiveness. Factors that influence the adherence to CPAP therapy include patients' individual characteristics, disease severity, titration procedures, the presents of side effects and the psychosocial factors. The management of this pathology is multidimensional and is based on some interventions such as lifestyle modifications, physical training, oral appliance and educational, pharmacological, technological strategies. These measures are implemented to limit the adverse effects of CPAP therapy in order to maximize the CPAP usage and to obtain a decrease of symptomatology and an optimum quality of life in OSA patients.

Key words: *CPAP adherence, obstructive sleep apnea, pulmonary rehabilitation,*

Introduction

Obstructive sleep apnoea (OSA) is a prevalent disorder that has become a major worldwide health concern. It is characterized by episodes of periodic collapse of the upper airway during sleep caused by anatomical modifications and a decrease of pharyngeal dilator muscle tone (1).

In more than 60% of patients OSA is associated with obesity, being responsible for daytime sleepiness, reduced quality of life, increased risk of motor vehicle accidents, cardiovascular and metabolic disease, impacting the healthcare use and mortality (2,3,4).

OSA affects 2-4% of males and 1-2% females but the last category seems to be underdiagnosed due to atypical symptoms such as fatigue, morning headaches, insomnia with less witnessed sleep apneas. Recent studies showed that 6% of women and 13% of men had moderate to severe sleep apnea that correlates with a large increased risk of all-cause mortality through cardiac arrhythmias, pulmonary and systemic hypertension, stroke, insulin resistance, myocardial infarction and road accidents (5,6,7).

Continuous Positive Pressure (CPAP) Therapy

In accordance to international guidelines CPAP is recognized as the gold standard treatment in cases of moderate to severe OSA (5).

CPAP was first discovered in the 1980s and its role is to provide a continuous mild air pressure in order to maintain the airway open and to prevent the collapse or the obstruction. The system include a CPAP machine capable to create the pressure gradient, tubing and CPAP mask. In the case of OSA, the preferred CPAP mask it only covers the nose but also, in selected cases, can cover the nose and the mouth (5).

In patients with moderate or severe OSA (AHI≥15 events/hour of sleep), CPAP therapy is indicated, independently from the severity of symptoms or diagnosis of comorbidities. In cases of mild OSA, (AHI is above 5 and below 15) CPAP is indicated if the subjects associate other comorbidities, such as hypertension, coronary artery disease, or previous cerebrovascular accidents, or in the presence of other symptoms (i.e., sleepiness, impaired cognition, mood disorders). Alternative options include weight control, oral appliance, oropharyngeal exercises, mandibular advancement devices, upper airway stimulation and a number of upper airway surgical approaches (8).

CPAP is capable of improving the symptomatology such as snoring, choking, nocturia, daytime somnolence and the lack of memory or concentration. Beside this, CPAP is considered to improve specific quality of life and minimize the cardiovascular risk by reducing the blood pressure and the systemic inflammation. A very important factor in CPAP therapy is the patient compliance,

mostly because poor adherence limits treatment efficacy (5, 9).
Compliance has been defined as usage of CPAP machine more than 4 hours per night for more than 70% of nights. In the literature, adherence rates range from 40-85% but there is no specific threshold that guarantee that efficacy is absolute (10,11). So, recent studies has stipulated that the greater the use of CPAP machines the better the results of the outcomes (5).
However CPAP therapy is associated with some side effects including dermatitis, epistaxis, rhinitis, nasal congestion, mask leak, barotrauma, aerophagia and claustrophobia, that must be controlled in order to obtain optimum compliance (5).

Exploring the Concept of a "Dose-Response" Relationship between Adherence and Outcomes

Taking into account the relationship between CPAP usage and outcomes, the term "dose" it refers to hours of usage per night more than pressure setting. This parameter should be established according to habitual sleep duration of each subject, level of impairment and the sensitivity of each outcome measure. The clinicians must remember that the CPAP usage time is not the same thing as total sleep time. For clinicians identifying ways to increase CPAP compliance is a major challenge mostly because OSA has an impact on cognition, work place performance, sleepiness, mood, functional status and driving ability, aspects that can be improved by CPAP treatment (12).

Optimal Adherence for Controlling Daytime Symptoms

The recent literature in this domain claims that the clinician should establish an individualized usage level, taking into account the outcome of CPAP treatment. Weaver et al. suggested in an uncontrolled study including 149 subjects diagnosed with severe OSA that the amelioration of symptoms occurred at different usage level: objective sleepiness at 6 h CPAP therapy per night, self reported sleepiness at 4 h therapy per night and functional status at 7,5 h per night (13). In another study Antic et al. observed an improvement in subjective sleepiness in those wearing CPAP more than 5 h per night and the normalization of objective sleepiness in those wearing CPAP more than 7 h per night (14). Beside this, in patients which associate cognitive and memory impairment it was seen an amelioration of symptoms in patients with a usage of 5,2 h of CPAP therapy per night (15).

Optimal Adherence for Controlling Cardiovascular Symptoms

In the last decades there are more evidences that suggest that greather CPAP use is responsible for improvements of cardiovascular outcomes. Barbe et al. developed a study including 359 subjects diagnosed with OSA and hypertension which do not associate excessive daytime sleepiness and concluded that the reduction of blood pressure (BP) was more evident in patients with an adherence more than 5,6 h per night (16). Even if the normalization of BP can be cofounded by other factors (greater adherence to antihypertensive medication, lifestyle modifications), a meta-analyses conducted by Haentjens et al. stipulated that there is a reduction in mean BP of 1.4mmHg with each 1h improvement in CPAP compliance with direct effects on cardiovascular morbidity and mortality compared with subjects with nonadherence (17).
These improvements were better observed in patients with OSA, excessive daytime sleepiness and arterial hypertension. Montesi et al. noticed a reduction of 1.9mmHg of the systolic values of BP and of 1.4mmHg of the diastolic BP in patients with a higher CPAP compliance which have a 5 point reduction of the baseline Epworth sleepiness scale (18). Since the peaks of higher BP occurs at the termination of obstructive respiratory events, the main role of CPAP is to reduce the arousals and the baseline sleepiness and to improve the sleep quality, that is why the adherence to therapy is very important (12).

Factors That Influence or Predict CPAP Use

In literature there are a lot of studies that summarize the factors that can influence or predict CPAP use, which can clarify the patients' decision to adhere to CPAP treatment.

Disease and patients characteristics

First of all, disease severity measured by apnea-hypopneea index, oxygen desaturations and symptomatologies (excessive daytime sleepiness-EDS) are the influential factors that contribute to the CPAP adherence. In these conditions the delivery of CPAP must take into account the patency of upper airway structures moreover because a decrease in nasal volume is responsible for nasal resistance which influence the CPAP use (19).

Lee et al. proved that patients with a smaller nasal cross sectional area and a decreased nasal cavity volume had a lower CPAP adherence. In another study conducted by Morris et al. , OSA patients with various degrees of obstruction at the inferior turbinate were observed for 18 months (20). From those, 48% had a lower compliance to CPAP therapy and the majority of subjects were not using at all CPAP after 18 months. So, it was stipulated that acoustic rhinometry has a high sensitivity and specificity and is capable to exclude the patients with CPAP intolerance. It was recommended that all OSA patients perform an acoustic rhinometry measure at baseline and after 3 months of CPAP therapy (19).

The nasal resistance may influence the initial acceptance of CPAP, so Sugiura et al. concluded that the odds of rejecting CPAP were almost 50% greater for every increase of 0,1 $Pa/cm^3/s$. So, nasal anatomy may have an influence on CPAP adherence, but not necessarily subjective nasal complains (21).

Other factors that influence CPAP compliance are depression and low mood at the diagnosis moment, by altering the perception of symptoms and the experience of side effects. Wells et al. concluded that by controlling depressive symptoms of patients which require CPAP treatment, the clinicians can achieve a better improvement in daytime symptoms associated with OSA (22). Brostom et al. showed that OSA subjects which associate a personality type of social inhibition and negative affectivity had low adherence to CPAP treatment (23).

Another well known factor implicated in the development of OSA and another respiratory disease is smoking, but its role is controversial in literature. At first sight nicotine decrease the upper airway resistance with a consequent reduction in the risk of OSA. In case of withdrawal, this resistance would become more important and would cause a greater risk of OSA. It was demonstrated that tobacco smoke contains a thousand compounds potentially harmful to human health such as heavy metals, nicotine and volatile organic compounds that increase oxidative stress and systemic inflammation, which play roles in the occurrence of cardiovascular, metabolic and cognitive disorders (24,25).

In another hand race and social environmental factors influence the CPAP adherence. Scharf et al. suggested that in African-American, CPAP usage rates are lower than in Caucasian, probably because of socioeconomic status. From a clinical perspective, a plan which takes into consideration the individuals characteristics should be developed for diverse patients groups (26).

Another factors that influence the compliance to CPAP therapy are patients comorbidities, moreover, pulmonary diseases.

Chronic obstructive pulmonary disease (COPD) is a comorbidity often related with OSA, and their association is known as “overlap syndrome” (27). This syndrome has a prevalence of 1.0 to 3.6% in the general population, 366% in COPD patients and 8-56% in OSA patients (28). In 45% of the cases who have poor sleep quality and hypoventilation episodes during sleep, a severe form of OSA has been diagnosed. Higher rates of mortality were found in patients with overlap syndrome compared to OSA ones, confirming that a right and complex management of both pathologies is required (29, 30).

Asthma is frequently associated OSA, both having many nocturnal and diurnal symptoms in common like poor sleep quality, excessive daytime sleepiness and poor quality of life. The prevalence of OSA is about 49% in patients with poor asthma control (31).

Treatment titration procedures

With the increasing prevalence of OSA, there are more demands for sleep diagnosis and titration services. There are two ways to deliver continuous positive airway pressure: a standard mode airway pressure (CPAP) and an auto titrating mode (APAP). Ayas et al compared APAP and CPAP devices and concluded that age was associated with adherence differences, younger participants favoring APAP to CPAP (32). However, Hukins et al reported that there were differences between the two titration modes in side effects, with fewer adverse reactions reported by the ones using APAP (33). Massie et al conducted a study including subjects which required CPAP pressures >10 cmH2O randomly treated with CPAP or APAP for 6 weeks and observed that even if there were no differences between the groups concerning the number of nights CPAP was used, the duration of use was higher in APAP group (34). So, the clinicians must take into account the initiation of APAP therapy mode for certain subjects, including younger persons, those with persistent side effects on CPAP or those needing higher CPAP pressures (19).

In addition, in patients with low tolerance with standard CPAP, APAP mode may become an add-on option to enhance overall compliance (19).

Technological device factors and side effects

Two third of CPAP users complains about side effects including claustrophobia, pressure intolerance, interface leak, nasal dryness, dermatitis, rhinitis, epistaxis, congestion, barotrauma, aerophagia and bloating. There are other patophysiological conditions that can interact with CPAP adherence including allergic or vasomotor rhinitis for which patients require counselling allergen avoidance advice, appropriate education and treatment with intranasal steorids or antihistamines. The development of these adverse events contributed to the innovation of comfort-related technological advances.

When speaking about side effects, the main concern refers to mask comfort but there are few studies that examined the effects of leaks, mask selections, mask changes or fit on CPAP compliance (35). Still the studies approaching this subject haven't found a significant influence of the mask interface on CPAP adherence. In order to combater the nasal/ pharyngeal dryness it has been developed a system of heated humidification, important in OSA treatment, moreover because CPAP is capable to produce airway inflammation, to modify mucus transport and ciliary motility responsible for discomfort. But heated humidification is not recommended for the first CPAP initiation. By contrast, Sommer et al. observed a decreased mucus transport and an increased ciliary beat frequency in patients using CPAP with heated humidification compared to standard CPAP (36). In addition, Nilius et al. found that patients which used heated humidification had a better improvement in nasal symptoms but this did not significantly improve compliance except for the patients with nasal pharyngeal complains (37). Massie et al. found that CPAP adherence in OSA subjects is improved by adding heated humidification, so patients experienced greater satisfaction with an refreshed attitude in the morning based on the fact that they used CPAP more in the night (38). Rakotonanahary et al. developed a system of markers that can appreciate the need of humidification: presence of chronic mucosa disease, age more than 60 years, drying medications or uvulophalatopharyngoplasty (39).

The initial acceptance of CPAP is influenced by the presence of claustrophobia, so as Weaver et al. identified, about half of newly-diagnosed patients stated that they do not want to use CPAP if they feel claustrophobic (40). In contrast, even if at the beginning of treatment the claustrophobia influence the CPAP compliance, the persistent use of the machine may improve the claustrophobia feeling and not necessarily lead to non-adherence (19).

d. Psychosocial and social factors

There is a multifactorial nature of CPAP adherence influenced by psychological and social factors which include self efficacy, risk perception of disease, coping mechanisms used in challenging moments, knowledge, treatment outcome expectancies and common treatment related expectancies. Many subjects does not associate their OSA diagnosis with depression, car accident, sexual performance, impaired concentration or memory and falling asleep while driving. In contrast, 66% of patients treated with CPAP realized that after treatment they were more alert and 53% had an improvement in sexual performance and desire. Through the system of self-efficacy measure in sleep apnea (SEMSA), Sawyer et al. found that outcome expectancies and self efficacy were important factors in CPAP adherence, so cognitive perceptions are important contributors to daily perceived responses of effective sleepiness (19).

Another factor that influences the OSA patients CPAP tolerance is the bad partner's opinion. McArdle et al. evaluated the bad partener's quality of life and sleep quality in OSA patients treated with CPAP and after one month of therapy. In subjects which received active CPAP, the bad partener's reported less sleep disturbances and a better sleep quality (41). These effects influence the subject decision to follow CPAP therapy (19).

What Interventions Promote CPAP Adherence or Compliance?

OSA treatment must include a multidisciplinary approach targeting symptoms control in order to provide a greater quality of life. Beside CPAP therapy, alternative options include weight control, oral appliance, mandibular advancement devices, upper airway stimulation, oropharyngeal exercises, and a number of upper airway surgical approaches (8).

In patients with severe OSA it is important to recognize and implement the strategies capable of improve the adherence to CPAP in order to accomplish a good health and an adequate functional outcomes. These interventions must be examined in terms of cost benefit ratio, clinical utility, resource utilization and patient acceptance (19).

Lifestyle intervention

Obesity is the main risk factor for OSA, and over 60% of patients with OSA are affected. It is a well-known fact that obesity is the most significant risk factor, with other factors such as smoking, alcohol abuse, male gender, the use of sedative mediation, age, increasing the risk of developing OSA (42,43). Recently, it has been found a correlation between the body mass index (BMI) and AHI, so weight loss has become an important strategy in the management of OSA and all patients should be encouraged to control their weight. In addition, it is a well known fact that physical activity (PA) is a key determinant for good health. A PA plan is structured, scheduled, repetitive and purposive in order to improve one or more objectives [44]. Moreover, several studies have demonstrated that low levels of PA are associated with higher incidence of OSA, obesity, and metabolic syndrome (45, 46,47). Due to fatigue or excessive daytime sleepiness, many patients with OSA are unable to do physical exercises (45,48). The physical activity has multiple beneficial effects on OSA, such as improving the fatigue, decreasing the severity of central sleep apnea in patients with chronic heart failure, reducing the occurrence of cardiovascular diseases and improving the severity of OSA (49). The curent guidelines recommends training programs as a treatment option for patients with OSA, taking into account that that regular exercises reduces the prevalence of OSA (50,51). Several recent studies have investigated the role of oropharyngeal myotherapy (OMT) on OSA, considering the role of the dilator muscles of the upper airway. Oropharyngeal exercises are a treatment modality capable of increasing sensitivity, coordination, strenght of orofacial structures, proprioception and mobility. At the same time, OMT favors a good performance of respiration, speech, deglutiton and mastication (8). In adition, lifestyle interventions refers to measures that encourage the patients to quit smoking, reduce the alcohol intake and minimize the use of sedative medications (52).

Educational strategies

Educational strategies are recognized as a standard of care in the management of OSA patients and have become an important factor for the acceptance of CPAP treatment. In the healthcare plan, the clinician must include reinforced education interventions with increased frequency that must provide expanded explanations. Golay et al. developed a study including OSA patients which received a variety of educational strategies (demonstrations, discussions, videos) and obtained a raise in the CPAP adherence at 3 months (53). Another study focused on behavioral therapy providing two 45 min one-on-one therapy sessions and concluded that at 12 weeks the adherence was substantial increased (54). It was developed a motivational enhancement therapy (MET) consisting in interventional viewing in order to highlight the patient's own motivating statements around therapy. It was proved that MET along education was efficient in patients with moderate adherence, but with no effect in patients with poor adherence (55). Another measure introduced to enhance the CPAP compliance is testing cognitive-behavioral therapy (CBT), which included a video of recent CPAP users and which describes their experiences, providing specific information's about goal development, symptoms, treatment relevance and expectations, cognitive testing performance and changes in symptoms with CPAP. This intervention was developed by Richards et al. and it was associated with higher scores for outcome expectancy and self-efficacy due to increased time spent discussing OSA as well as hearing about real experiences of CPAP users via the video. Its role it's to correct distorted beliefs, promote treatment initiation and positive perspective toward CPAP and enhance CPAP knowledge (56,57).

Since social support is associated with CPAP greater compliance, an alternative approach to CBT/MET requires group therapy with experienced CPAP users offering support and encouragement (58). In contrast Parthasarathy et al. observed that peer support had no influence on CPAP tolerance even if is more efficient than individual education, however one pilot trial offering peer support one on one demonstrated a significantly higher adherence during the first week of CPAP therapy which persisted over the first 90 days of therapy (59).

Behavioral therapy customized to increased CPAP compliance is low risk intervention that can be incremented in the standardized management. Still approaches such as CBT/MET require highly trained stuff, which has limited their applicability in clinical evaluation (12).

Technological strategies

The ability to monitor CPAP compliance and other important therapy parameters such as pressure profiles must click and estimated residual disease provide potential to use remote monitoring or telemedicine in order to implement a web-based

adherence intervention. The role of these strategies include: targeted troubleshooting, personalized feedback for patients through web-or-app based education via a couching website or smartphone app. The telephone-linked communication device (TLC) additional to usual care functioned as a monitor of CPAP use, educated and counselor with automated responses offered subjects included weekly calls, had a significant effect on CPAP compliance. Another intervention called tele-health provided a higher CPAP use at 12 weeks in OSA patients compared to placebo (60). In contrast, telemonitoring had no effect on adherence, neither the computer-based "health-buddy" introduced by Taylor et al. which included internet information, feedback and support with no statistical differences between intervention and control group (61). In contrast Kuna et al. obtained a raise of CPAP compliance by giving acces to web-based feedback (62). By providing automated feedback, Hwang et al. concluded that it is a helpful instrument to obtain and sustain a long term beneficial effect on adherence (63). In 2018, Pepin et al. developed a multimodal approach including data from connected physical activity and sleep trackers, oximetry, home BP monitors in addition to CPAP telemonitoring data. It was observed that patients improved their daytime excessive sleepiness, physical activity, quality of life and CPAP compliance (64).

In the last years, manufacturers of CPAP machines had developed a theory driven coaching and support services including dashboard summarizing therapy data, educational materials, goal focused emails or text messages and troubleshooting materials, which had an impact on CPAP adherence in patients who used it (12).

So, the telemedicine is a method for rapid clinical implementation and its advantages include the ability to scale to large patient populations and to decrease the burden on clinical systems by reducing the need for office clinical visits.

Pharmacological strategies

In OSA patients using CPAP therapy which associate insomnia or anxiety, as Haniffa et al. recomens, the clinicians should introduce adjuvant hypnotic therapy additional to education, motivational interviewing and cognitive behaviour, to obtain a greater adherence (65).

Lettieri et al. examined the effects of a short time administration of Eszopiclone on 160 adults using CPAP therapy and observed an increase CPAP use, without significant adverse effects (66).

In addition, in order to maintain an adequate adherence to CPAP therapy is important to control the adverse effects. In patients with nasal obstruction, the standard first line treatment is medical therapy which include both steroids and antihistamines intranasal and systemic, alone or in combination. Sicolli et al. observed in subjects with allergic rhinitis which was treated with topical nasal steroids significant improvements in daytime sleepiness and sleep quality (67). There are evidence that suggests an improvement in sleep quality and a reduction of AHI in patients using nasal steroids (68,69). In contrast, intranasal decongestants are not so effective, with modest improvement in AHI scores (70). In patients with persistent nasal obstruction, there are two nasal dilators available, consisting in nasal valves which showed improvement in OSA with a decrease of AHI. So, the patients who have benefits of these systems may become candidates for definitive nasal valve repair (5).

Still, there are other otolaryngological factors that can contribute to failure of CPAP in relation to the nasal cavity and paranasal sinuses that can be corrected with surgical intervention.

Application modifications and patients interventions

In the last years, many non surgical and surgical options were developed for subjects who do not tolerate CPAP. Taking into account that higher CPAP pressures are associated with discomfort and side effects, the new CPAP technologies, allowed clinicians to deliver to patient's airway lower pressures, observation that need to be studied in extensive randomized trials. The auto titrating devices had demonstrated better tolerability but in clinical practice, many parameters have been suggested to predict CPAP pressure requirements: mean respiratory disturbance index, body mass index, gender, oxygen saturation, depression and mask leak (71, 72). The challenge is to establish the optimum CPAP pressures moreover because higher pressures are associated with CPAP induced rhinitis due to inflammatory changes in the nasal mucosa. Other pathological processes include sinusitis and nasal polyposis that can be missed during routine respiratory review but can be effectively treated medically or surgically (73,74).

Moreover, OSA patients following CPAP therapy need lifestyle interventions including a reduce alcohol intake, weight loss (bariatric surgery if indicated) and sleep positional therapy (5). The last

one can be highly efficient when used with other devices such a chin strap (69). However, these interventions have no significant long term effect on cardiovascular outcomes (5).

Another additional device useful in selective patients is oral appliance which involves the application of dental splits to prevent upper airway obstruction during sleep. The therapy efficacy is determined by the level of advancement but this device is indicated in patients with mild OSA (75). Mandibular advancement splints (MAS) action by protruding the hyoid bone anteriorly along with the mandible in order to increase the retroglossal distance, but this device can cause discomfort. However, it is contraindicated in patients with poor dentition or uncontrolled epilepsy. Their clinical use is indicated in subjects with retrognathism or bulky tongue, in combination with CPAP, even if there is no greater effect on cardiovascular outcome (76, 77).

Conclusions

In conclusion, obstructive sleep apnea is a high prevalent disorder responsable for a significant health and socio-economic burden. In cases of moderate or severe OSA, CPAP therapy is recognized as a gold standard treatment. Its role is to maintain the airway open and to prevent the nocturnal collapse of the airway. CPAP is considered to improve the symptomatology, the specific quality of life and the cardiovascular outcome. In order to obtain these effects, the patients should achieve an adequate compliance despite the side effects, such as dermatitis, epistaxis, rhinitis, nasal congestion, mask leak, barotrauma, aerophagia and claustrophobia.

The clinicians should implement measures taking into account the disease and patients' characteristics, the titration procedures, the evolution of the technological device and the psychosocial and social factors. The interventions that can promote CPAP adherence are based on lifestyle changes, physical training, educational strategies, social support, technological and pharmacological strategies and the usage of devices that can minimize the CPAP side effects.

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