Adherence to Respiratory Supports in OSA and COPD

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Abstract: Chronic respiratory diseases constitute a serious public health problem in all countries, and Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are two of the most prevalent. Positive airway pressure (PAP) is recommended for ongoing treatment of OSA in adults while Long-term oxygen therapy (LTOT) is indicated for stable COPD patients with Chronic Respiratory Insufficiency. In real contexts, the clinical efficacy of these therapies is limited by an often-low adherence with consequent rising back of symptoms and adverse consequences on the quality of life. Until now, several driving factors have been identified for a low adherence to CPAP and LTOT and several solutions are proposed in many papers. In this review we identify and discuss the driving factors reported for a low adherence (addressing personal conditions, social context and specificities of the device) and the strategies adopted to mitigate them (behavioral, educational and supportive interventions) and to monitor actual compliance (self-reporting, eHealth solutions and consumptions of device accessories). An overall picture of these aspects allows planning the healthcare service and adequate support for OSA and COPD patients with an attention to the individual, social and cultural level. Further investigation is still needed to explore the value of combinations of the reported approaches on different patient phenotypes and at what cost.

Keywords: Adherence, Obstructive Sleep Apnea, Chronic Obstructive Pulmonary Disease, Continuous Positive Airway Pressure, Long-Term Oxygen Therapy.

INTRODUCTION

Chronic respiratory diseases (CRDs) constitute a serious public health problem in all countries. In fact, these diseases exert considerable global health burden and are associated with high mortality and morbidity: in 2017, it is estimated that more than 500 million people worldwide suffer from a CRD, a 40% increase compared to 1990 and with the highest prevalence in high-income regions. Approximately 4 millions deaths are attributed to CRDs globally with an 18% increase since 1990 [1].

Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) represent two of the most prevalent CRDs in clinical practice [2]. A possible association between these disorders was described in the mid-1980s by Flenley, who named it "overlap syndrome" [3].

OSA is characterized by recurrent episodes of upper airway obstruction during sleep that result in recurrent oxyhemoglobin desaturation and sleep fragmentation [4]. The overall prevalence of any OSA (with an Apnoea Hypopnoea Index ≥ 15) in general adult population ranged from 6% to 17%, although much higher in the elderly groups [5]. Positive airway pressure (PAP) is recommended for ongoing treatment of OSA in adults either in the continuous (CPAP) or in the auto-adjustable (APAP) form [6]. The use of PAP allows to reduce daytime sleepiness and consequently increase the quality of life and safety of patients with OSA [6].

COPD, a common, preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation, [7] is the third leading cause of death worldwide, causing 3.23 million deaths in 2019 [8].

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Long-term oxygen therapy (LTOT) is indicated for stable patients who have with $PaO_2 \leq 7,3$ kPa or $SaO_2 \leq$ 88%, or PaO_2 between 7,3 and 8.0 kPa, or SaO_2 of 88%, if other specific comorbidities are present [7]. Oxygen therapy significantly improves survival and quality of life, and reduces exacerbations or hospitalizations [9].

In real contexts, the clinical efficacy of CPAP and LTOT is limited by an often-low adherence with consequent reappearance of symptoms and negative consequences on the quality of life [10].

In the case of CPAP, Rotenberg et al. [11] reported stubbornly persistent overall rates with high non-adherence of 30-40%. In their review they found that the mean duration of night use was 4.7 hours, thus below the optimal therapeutic threshold which falls between 5 and 6 hours at night [11].

Regarding LTOT, Lacasse et al. [12] described an adherence rate between 45 and 70%.

Up until now, several driving factors have been identified for a low adherence to CPAP and LTOT and several kinds of solution are proposed in many papers. Starting from the available body of evidence, the aim of this review is to identify these factors and report strategies adopted to mitigate them.

DRIVING FACTORS OF REDUCED ADHERENCE TO CPAP AND LTOT

Understanding the driving factors for adherence to CPAP and LTOT is a necessary step in defining and selecting targeted interventions. These have been reported in Table **1** with a distinction among personal conditions, social conditions and device factors.

Personal Conditions

Psychological factors such as depression and anxiety are reported to reduce compliance with the

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respiratory supports [13,14]. Patients using CPAP and LTOT may have apprehension about how the tool will make them look and feel (for example, ridiculous when wearing the CPAP mask), fear of oxygen addiction, or may be embarrassed to use oxygen in public with the recognizable stigma of smoking-related lung disease [15,16]. In a previous study, Earnest MA concluded that stigma and isolation associated with oxygen use led to reduced compliance and non-use outside the home [17]. Individuals who have high negative affectivity and social inhibition, classified as Type D personality [18], are likely associated with self-neglect with possible implications of poor adherence to treatment [19].

The importance of providing specific information to allow patients to self-manage a chronic condition is well documented [22,23]. Literature reports that the patient's low level of understanding of the therapy and low education could be another reason for the shortened duration of treatments, as well [20,21]. For instance, patients with a low level of education may not understand the scientific terms of the instructions and get confused about the use of oxygen [21]. For both CPAP and LTOT, the lack of confidence in one's own ability to organize and carry out the actions necessary to manage the therapy and the perceived benefit of the treatment [16,24] led to a negative attitude towards respiratory supports. The absence of perceived benefit could result from an inappropriate prescription, therefore, the provision of specific information on oxygen therapy could reduce the development of unrealistic expectations. Another risk factor of low adherence to CPAP and LTOT is cigarette smoking. Recently, Baratta and colleagues [25] reported that this factor is an independent predictor of non-compliance to CPAP. Even hypoxaemic COPD patients, who are active smokers, prefer keeping on smoking rather than using the recommended oxygen therapy with harmful consequences for health [26].

Social Context and Status

Insufficient emotional and practical support from the family or partner leads to worse treatment experiences with CPAP and LTOT [24,27,28]. It has been shown that social support, partner involvement in the treatment and partner sleep quality positively influence CPAP adherence [29]. For LTOT, social support is essential to overcome feelings of embarrassment and to enable participants to overcome physical barriers to use of the oxygen therapy outside the home [30].

Finally, patients receiving CPAP therapy who have a low socioeconomic status, defined as a monthly income below the national average, have both low initial acceptance of prescribed therapy and poor continued adherence to treatment [31]. Simon-Tuval and colleagues found that, when the CPAP is an out-of-pocket cost, its purchase is determined by the level of income [32]: 21.8%, 51.4% and 75.6% of individuals with low, average and high income accepted and purchased CPAP. In another paper, significantly lower compliance was found in subjects who were long-term unemployed compared to those who were at work, with an odds ratio of 4.6 for sub-optimal compliance at 6 months [33].

There are several tools to investigate the above dimensions with very different levels of detail. For example, the assessment of depression can range from the very simple 2-item version of the depression module of the Patient Health Questionnaire (PHQ-2) [34] to a comprehensive clinical investigation by a psychiatrist. The choice of the measurement methods obviously depends on the availability of resources (time and personnel) and tools validated for the specific patient population, language and culture. Future researches could apply to the development of multivariate predictive models that combine the above dimensions and identify the most significant drivers for predicting adherence.

Devices Factors

Side effects and factors linked to the functioning of CPAP and LTOT devices greatly affect adherence.

CPAP therapy is known to be highly invasive and require a drastic lifestyle change, which is difficult for many to tolerate. In this regard, besides the noise of the machine, the mask air leak and being a cumbersome therapy [35], the most reported factor is nasal complaints. About 50% of all patients treated with the device can develop nasal obstruction, congestion, rhinorrhea, sinusitis, nosebleeds and mucosal dryness [36]. Other factors include rhinitis or skin sores, sore eyes due to mask leaks, dry throat and/or mouth, airway drying, claustrophobic reactions to the mask [37] and frequent awakenings [38].

Even in the case of LTOT, many adverse side effects are known to be associated with decreased adherence due to their interference with normal life. Dryness and nasal bleeding, loss of taste and smell, lack of breath and dizziness are reported by Melani and colleagues [39]. The amount of time a patients may be away from the stationary source is limited and this leads them to fear because they should also contact the home-care provider to schedule home deliveries to provide the required refills [16]. Other device issues, such as weight and size, can influence the adherence as well. Many ambulatory sources are bulky and heavy so they discourage, if not prevent, the ambulation of elderly patients and subjects with reduced strength and endurance [16]. Literature also reports that the cylinder weight is a barrier to the ability to walk anywhere and the patients complain of feeling ridiculous [30]. When this issue become very critical, lightweight portable oxygen concentrators (POCs) can be evaluated as a viable alternative. This solution is appreciated by patients for its ease of transport and lower weight [40].

PREVENTIVE STRATEGIES TO MITIGATE THE DRIVING FACTORS REDUCING ADHERENCE

Based on the above reported considerations, in the presence of elements that could suggest a high risk of

Table 1: Driving factors reducing CPAP and LTOT adherence.

Dimension	Driving factors	Reference
Personal Conditions	Anxiety and depression	[13,14]
	Type D personality	[19]
	Lack of understanding and low level of education	[20,21]
	Lack of confidence in one's own ability and perceived benefit from treatment (self-efficacy)	[16,24]
	Smoking habits	[25,26]
Social Context and Status	Insufficient emotional and practical support from the family	[24,27]
	Low socio-economic status	[31–33]
Device Factors	*For CPAP and LTOT*	
	Being bulky and cumbersome	[16][35]
	Being noisy	[35][16]
	Only for CPAP	
	Being heavy	[16]
	Nasal problems	[36]
	Skin irritation	[37]
	Eye irritation	[37]
	Dry throat and/or mouth	[37]
	Airway drying	[37]
	Claustrophobic reactions to the mask	[37]
	Nocturnal awakenings	[38]
	Pressure intolerance and difficulty exhaling	[41]
	Mask Air leaks	[37]
	Only for LTOT	
	Lack of breath	[39]
	Loss of taste and smell	[39]
	Dizziness	[39]

non-compliance, the clinician may consider taking action to mitigate them.

In accordance with the review of Wozniak and colleagues [38], we split the strategies into behavioral, educational and supportive.

Behavioral Interventions

Behavioral interventions are mainly focused on promoting self-efficacy, assessing outcome expectations and influencing decision-making in favor of treatment and include [38,42]: a) motivational interviews to assess and stimulate the subject's readiness to change, the perceived importance of the change, and the confidence in his ability to change; b) cognitive behavioral therapy to modify irrational and incorrect beliefs that can lead to unhealthy behaviors.

Educational Interventions

Educational interventions could be primarily useful for providing information about treatment (in particular, accurate and simplified instructions on appropriate oxygen use with a special attention to illiterate patients [16]) and more generally on the disease in order to improve the patient's understanding of the condition and the benefits of the intervention. Educational interventions should ideally be provided continuously (during the physician's consultation, the diagnostic testing procedure, the initiation of the therapy which is the most critical period for adherence [43], and follow-up) [44]. The literature on these interventions is difficult to interpret as many studies have used a combination of interventions making it difficult to assess the effects of individual measures [45]. Bakker and colleagues point out that only a few studies have assessed whether the reported measures were effective in leading to a thorough understanding of OSA and CPAP and of the benefits of the intervention, with the consequent impossibility of knowing the real reasons for the improvements in adherence. Nevertheless, a strategy that showed promising results is the patient involvement in viewing the results of their diagnostic charts and data [46]. In fact, it has been reported that showing the results of sleep tests, after having highlighted the cardiovascular, metabolic and neurocognitive effects of an untreated disorder, and explaining the benefits of therapy to patients, has a positive impact on adherence

[47,48]. For LTOT, to ensure adherence, it is essential to follow up patients at home, at a time when feelings of discomfort are likely to have diminished and attention to information may be improved: the physician should provide patients with the opportunities to talk about their perceptions of benefits and problems and repeatedly explain the importance of compliance also through regular domiciliary visits by reinforcing health messages [16,49]. Furthermore, in the case of OSAS, it is important to sensitize the patient to some practical consequences of a non-treated syndrome, due to excessive daily sleepiness. In Europe, for example, the Commission Directive 2014/85/EU states that "driving licenses may be issued to applicants or drivers with moderate or severe obstructive sleep apnoea syndrome who show adequate control of their condition and compliance with appropriate treatment and improvement of sleepiness" [50].

Supportive Interventions

Among the supportive strategies, telecommunication tools are really important to facilitate communication between the patient at home and healthcare providers [42,51]. A study by Hwang and colleagues shows that tele-messaging on the use of CPAP improves adherence at 3-month follow-up [52]. A randomized clinical trial by Kuna and colleagues demonstrated that subjects with daily web-based access to CPAP data improved their adherence compared to the usual treatment group (6 vs. 4.7 hours) at 3-month follow-up [53]. Telemonitoring of CPAP use and daily feedback to patients to provide encouragement together with support for solving problems have been shown to increase adherence [52,54]. A recent meta-analysis found that telemedicine interventions were able to increase the CPAP usage compared to no intervention in a follow-up period up to 6 months [55].

Typically, family members have a great responsibility for the care and coordination of a person with a long-term condition (LTC) [56] and have a key role in shaping perceptions of the disease [57] and improving adherence to treatment regimens [58]. As a consequence, family-focused care (FFC) is believed to be more effective in improving health and functioning of subjects with LTC than patient-centred care [59]. FFC has been defined as "an approach to care delivery whereby health and social care professionals respect and respond to the needs of the individual and their family as a complete unit, recognizing the family role in supporting the individual with an LTC" [60]. FFC interventions should aim at improving skills for LTC self-management through independence in symptoms monitoring, optimized adherence to therapy and problem-solving [58]. Multicomponent interventions are then necessary [61] and should consider the specific needs of the disease (specifically to maintain treatment and care regimens), social and financial constraints, and the importance of preserving family relationships [62]. Furthermore, the definition of family should take into account broader, more comprehensive and accurate human relationships that encompass a wide range of family members and close friends in which such persons are concerned about and care for each other [63,64]. As found by J Smith and colleagues [60], there is great heterogeneity in the definition of FFC and a lack of explicit theoretical foundations for FFC: its role has not been understood and it is being identified as relevant research topic. Finally, great attention needs to be paid to social and cultural context, and interventions are expected to vary widely across countries to reflect different care priorities and service delivery systems [65].

TREATMENT ADHERENCE MONITORING

In addition to preventive strategies, it is important to periodically monitor the use of respiratory supports in order to measure effective adherence and activate possible corrective measures.

Several monitoring solutions are possible which can be mainly classified into three approaches: self-reports, eHealth, and devices accessories.

Self Report

Patient self-report is the most common approach [66]; this method has advantages and disadvantages. It is typically applied by using low-cost noninvasive instruments, with minimal patient burden. As reported in the same study, it allows the collection of useful information such as the level of understanding of the medication regimen, the reasons for possible non-adherence, attitudes and beliefs toward medicines, and other psychosocial factors. On the other hand, social desirability and memory biases may lead patients to overestimate the time of use of respiratory supports [67]. In fact, several studies have showed that patients wish to avoid confrontation, are embarrassed by their difficulty to follow medical advice, or desire to be "good" patients [68].

eHealth

A way to overcome the above reported problems could be through the adoption of information and communication technologies. In a recent Meta-Analytic Review [69] aimed to investigate the effectiveness of eHealth interventions in improving CPAP adherence in adult populations with OSA, the authors conclude that eHealth technologies can promote and reinforce adherence to CPAP treatment for adults with OSA, being able to help in delivering standardized education to patients and monitoring their daily-life CPAP data. eHealth allows the early detection of problems and non-adherence, and consequent timely and adequate remote response. Their results are very encouraging: many eHealth interventions, when compared with usual care alone, have shown to increase average CPAP adherence by about half an hour per night. On the contrary, the efficacy of telemonitoring remains unclear for the LTOT therapy. A recent Meta-Analysis of telemonitoring interventions on severe COPD exacerbations [70] suggests that its adoption in the routine of care, while reducing unnecessary emergency

room visits, is unlikely to prevent hospitalizations from COPD exacerbations: patients receiving LTOT are generally those with severe disease, so it may be important to focus on selecting suitable patients who can adapt and function with eHealth to increment its effectiveness.

Devices Accessories

Measuring refill rates of accessories (mask, tubes, filters, humidifier, oxygen concentrator, liquid oxygen, etc.) may be a powerful tool for indirectly measuring adherence that can be easily and cost-effectively integrated into monitoring systems [71]. Scharf and colleagues showed in their retrospective cohort of veterans with OSA that low mask refills in the first month were significantly associated with less 90-day PAP use [72].

CONCLUSION

CPAP and LTOT are clearly recommended as key strategies in patients with OSAS and COPD (with chronic respiratory insufficiency) to improve quality of life, reduce exacerbations and hospitalizations and also increase survival rates. However, adherence is currently a major concern due to personal conditions, social background and device-related factors. Knowing the main factors responsible for poor compliance allows to identify measures to prevent or reduce it. Our review identifies solutions on an individual, social and cultural level: patient counseling at the time of prescription and at follow-up, behavioral interventions, patient empowerment, and telemonitoring appear to be the most effective interventions to promote adherence. Further investigation is still needed to explore the value of combinations of these approaches on different patient phenotypes and at what cost.

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