Beneficial Effects of Continuous Positive Airway Pressure Therapy

9

Deepak Shrivastava

Abbreviations

AHI	Apnea-hypopnea index
APAP	Auto-adjusting positive airway pressure
BiPAP	Bilevel positive airway pressure
CPAP	Continuous positive airway pressure
CRP	C-reactive protein
DSAT	Dental sleep appliance therapy
ESS	Epworth sleepiness scale
GERD	Gastroesophageal reflux disorder
IL-6	Interleukin-6
NIV	Noninvasive ventilation
OSA	Obstructive sleep apnea
RDI	Respiratory disturbance index

9.1 Introduction

Continuous positive airway pressure (CPAP) treatment has become the standard treatment for obstructive sleep apnea (OSA) introduced in the 1980s [1]. During CPAP therapy, air is applied via a nasal/facial mask at a constant increased pressure. This pressure is produced by forcing air through the nose into the pharynx causing a "pneumatic splint," which prevents the airway from collapsing [2, 3]. It has been demonstrated to resolve sleep disorder breathing and improve several clinical outcomes. The CPAP results in elimination of obstructive apneas, hypopneas, and

D. Shrivastava (✉)
UC Davis School of Medicine and SJGH, Sacramento, CA, USA
e-mail: drshrivastava@sjgh.org

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respiratory effort-related arousals as quantitatively measured by apnea-hypopnea index (AHI) and respiratory disturbance index (RDI).

9.2 CPAP Therapy

Optimal CPAP pressure is established in a sleep laboratory setting. The pressure finally chosen by the sleep laboratory technician for long-term treatment is a compromise between the need to keep the pressure high enough to prevent most apneas, hypopneas, and snoring and keep the pressure low to avoid compromising patient acceptance and the side effects of too high a pressure [4]. Side effects of CPAP therapy are leakage of air from the mask causing irritation of the conjunctiva of the eyes, disturbance of the patient by machine, mask noise which increases at higher pressure [5, 6], and by the increased resistance on expiration associated with high CPAP pressure [7–10].

The optimal CPAP pressure required for patients may change over time due to changes in weight, nasal obstruction, sleep deprivation, and use of hypnotic or sedative medications [11]. The pressure needed varies during the night based on changes in sleep posture and sleep stage such as higher pressure is required in supine position and in REM sleep than in the lateral (side) position or during slow-wave sleep [12–14]. The constant pressure CPAP chosen should be high enough to abolish all obstructive events throughout the night and dictates the maximum pressure needed at any time during the night. This pressure might be too high if the patient is mostly sleeping on their side throughout the night. Self-adjusting CPAP machines [auto-adjusting positive airway pressure (APAP) and bilevel positive airway pressure (BiPAP)] were developed to treat the pressure to the patient's needs. Ideally, such an APAP machine should lead to a reduction in the mean CPAP pressure and pressure-associated side effects. This, in turn, would presumably improve patient acceptance [15].

CPAP therapy is associated with improvement in OSA consequences such as oxygen desaturation and high AHI. Randomized control trials have demonstrated CPAP therapy to be superior to placebo at improving stage N3 and REM sleep. With the improvement in OSA, the large negative swings in juxta-cardiac pressure during the upper airway occlusion improves. CPAP decreases the transmural pressure and improves the wall tension across the right and left ventricle.

Hemodynamic change results in a decrease in the afterload as well as the resultant decrease in myocardial oxygen consumption and increased stroke volume. CPAP improves oxygenation and hypercapnia with a resultant decrease in sympathetic activity, neurohormonal activation, oxidative stress, and inflammation. According to some studies, CPAP may reduce morbidity and mortality.

Treatment with CPAP reduces sympathetic activity, diminishes platelet activation and aggregation, and improves oxidation of low-density lipoprotein particles. It also decreases the production of reactive oxygen species in neutrophils and monocytes. Circulating levels of C-reactive protein (CRP) fibrinogen and interleukin-6 (IL-6) are elevated in OSA patients and decreased significantly after treatment with

CPAP. Clinical data suggests that IL-6 levels are elevated in patients with OSA but not in patients with OSA and obesity. The baseline level of CRP is an independent predictor of future myocardial infarction, stroke, cardiovascular death, and incidence of peripheral arterial disease. CRP level is a risk factor for atherosclerosis and it is considered an active pathogenic agent. A decrease in CRP level in OSA becomes evident when CPAP is used for more than 4 h per night.

CPAP may reduce daytime sleepiness in adults with OSA. A systematic review of over 70 studies evaluating dental sleep appliance therapy (DSAT) or CPAP for 1 week or more in adults with obstructive sleep apnea-hypopnea showed that CPAP is associated with nonsignificantly reduced sleepiness based on Epworth sleepiness scale (ESS) and improved AHI better than oral appliances. ESS measures the likelihood of falling asleep during daily activities on a scale of 0–24 points, with higher scores indicating more severe daytime sleepiness, while AHI measures the average number of apneas or hypopneas per hour [1].

CPAP is associated with improvement in sleepiness and reduction in AHI compared with no treatment. At the same time, CPAP had inconsistent effects for quality of life outcomes, cognitive measures, and blood pressure. There were no adverse events with potentially long-term consequences noted with CPAP therapy [2].

According to the literature, CPAP is associated with reduction in sleepiness and improved quality of life in patients with moderate-to-severe obstructive sleep apnea [3]. CPAP may improve quality of life and daytime sleepiness compared to conservative treatment in women with moderate-to-severe OSA [4]. CPAP may reduce fatigue, increase energy, and improve AHI score in adults with moderate-to-severe OSA [5]. CPAP might improve some aspects of cognitive performance in middle-aged patients with obesity and severe OSA [6].

In mild-to-moderate OSA, CPAP therapy reduces excessive daytime sleepiness although with small effects of limited clinical significance [7]. When compared with subtherapeutic CPAP, nasal CPAP reduces excessive daytime sleepiness and improves self-reported health status.

However, in asymptomatic patients with OSA, CPAP does not appear to improve quality of life or objective sleepiness [8]. Studies that reviewed the effect of CPAP on traffic accidents and effect on spouse sleep show that CPAP is associated with reduced risk of motor vehicle crashes and improved daytime sleepiness and quality of life in bed partners [9, 10].

The effect of CPAP therapy on the risk for cardiovascular events in patients with OSA is limited and inconsistent. CPAP may improve neurologic recovery after stroke and may be associated with reduced risk of mortality and recurrent stroke. CPAP therapy is associated with small reduction in blood pressure and may not improve glycemic control or insulin resistance in patients with OSA.

In patients with heart failure and OSA, CPAP improves left ventricular systolic function. CPAP therapy may improve left ventricular diastolic function and is associated with reduction in frequency of ventricular premature beats during sleep [11]. CPAP does not appear to reduce frequency of arrhythmia in patients with OSA but may be associated with reduced rate of recurrent atrial fibrillation in patients with OSA reported to reverse heart block in patients with apnea-associated heart block.

According to the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines—Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults, the effectiveness of CPAP to reduce blood pressure is not well established in adults with hypertension and obstructive sleep apnea [12].

Based on a systematic review without clinical outcomes, there is established consensus that CPAP and DSA therapy may each reduce blood pressure slightly in patients with obstructive sleep apnea. CPAP is associated with decreased systolic blood pressure (weighted mean difference 2.6 mmHg, 95% CI 1.6–3.6 mmHg) and diastolic blood pressure (2.1 mmHg, 95% CI 1.4–2.8 mmHg). These results are considered limited by significant heterogeneity. DSAT is associated with decreased systolic blood pressure (1.9 mmHg, 95% CI 0.6–3.2 mmHg) and diastolic blood pressure (1.9 mmHg, 95% CI 0.5–3.2 mmHg). One series of four trials showed no significant difference in systolic or diastolic blood pressure comparing CPAP vs. DSAT in an analysis of 370 patients. These results are consistent with other meta-analyses and indirect comparisons [13].

A controversial recent randomized trial concluded that CPAP might not reduce the risk of major cardiovascular or cerebrovascular events in patients with moderate-to-severe OSA and coronary or cerebrovascular disease [14]. A number of studies have demonstrated that CPAP ventilation within 28 days of stroke may improve neurologic function in patients with stroke or transient ischemic attack and sleep disordered breathing [15]. CPAP during stroke rehabilitation or 2 months after stroke may have benefits in patients with obstructive sleep apnea with reduced mortality. CPAP during rehabilitation following stroke might reduce sleepiness and stroke-related impairment in patients with obstructive sleep apnea [16, 17]. Confirming the dose–response relationship, one study showed that CPAP compliance is associated with reduced risk of recurrent stroke in older patients with sleep apnea [18].

In patients with heart failure, CPAP may improve left ventricular systolic function in heart failure and reduce systolic blood pressure in patients with heart failure and OSA patients with OSA who do not have Cheyne-Stokes events [19, 20]. Inhospital OSA treatment with APAP may improve left ventricular ejection fraction in patients with acutely decompensated heart failure and OSA [21]. At least one study has documented that a BiPAP may increase left ventricular ejection fraction more than CPAP in heart failure patients with newly diagnosed OSA [22]. A number of studies have evaluated the effect of positive airway pressure therapy. Addition of CPAP therapy for 6 months does not appear to improve glycemic control in patients with newly diagnosed OSA and type 2 diabetes [23].

On the other hand, CPAP therapy for 6 months may improve glycemic control and insulin resistance in patients with OSA and suboptimally controlled type 2 diabetes, based on a randomized control trail [24]. CPAP therapy for 3 months does not appear to improve glycemic control or insulin resistance in men with type 2 diabetes and OSA [25].

Long-term use of CPAP is found to be associated with improved nocturnal gastroesophageal reflux disorder (GERD) symptoms in patients with OSA. Based on

two cohort studies, eighty-five patients with OSA were followed for 6 months. Six patients treated with medication for GERD symptoms were excluded. Sixty-two of 79% of patients (78%) had GERD symptoms at baseline. CPAP was associated with significantly improved GERD symptoms and Epworth sleepiness score in all patients and more significantly in CPAP compliant patients [26].

In another study 331 patients with OSA were prescribed CPAP. CPAP is associated with significantly improved nocturnal GERD symptoms (from mean 3.38 to 1.75, $p < 0.001$) while no significant differences were noted in nocturnal GERD symptoms in 16 patients not using CPAP [27].

Obesity is a risk factor for OSA. Noninvasive ventilation (NIV) and CPAP are associated with similar hospitalization rates in patients with obesity hypoventilation syndrome and severe obstructive sleep apnea [28]. Lifestyle modification is an emerging process to change the course of many chronic diseases. NIV or CPAP may improve daytime sleepiness compared to lifestyle modifications in patients with obesity hypoventilation syndrome and severe obstructive sleep apnea [29]. CPAP appears as effective as bilevel ventilatory support for daytime sleepiness for obesity hypoventilation syndrome without severe nocturnal hypoxemia [30].

9.2.1 Metabolic Syndrome

CPAP may improve markers of metabolic syndrome in patients with moderate-to-severe OSA according to a peer-reviewed journal [31].

9.2.2 Alzheimer Disease

CPAP is reported to improve nighttime sleep quality in patients with Alzheimer disease and OSA [32]. CPAP is associated with reduced daytime sleepiness in patients with Alzheimer disease and OSA [33].

9.2.3 Seizures

Most seizures occur at night. CPAP may decrease seizure frequency in compliant patients with epilepsy and OSA [34]. CPAP is reported to decrease seizure frequency in patients with epilepsy and OSA [35].

CPAP may reduce mortality and hospitalization in patients with chronic obstructive pulmonary disease and OSA. A combination of these two entities occurring in the same patient is known as “overlap syndrome.” This has worsened morbidity and mortality [36]. CPAP may improve depressive symptoms in adults with OSA and depression [37].

A comprehensive understanding of the underlying pathophysiology of obstructive sleep apnea forms the foundation of how treatment improves the adverse effects and abnormalities of organ systems. The treatment modality may be different, but

the desired outcomes are the same. This chapter reviews the evidence-based benefits of CPAP therapy. This serves as a guide map for the dental sleep scientists and clinical dental sleep specialists to design future research and current patient treatment plans.

References

1. Strollo PJ Jr, Rogers RM. Obstructive sleep apnea. N Engl J Med. 1996;334:99–104.
2. Ficker JF, Wiest GH, Lehnert G, Wiest B, Hahn EG. Evaluation of an auto-CPAP device for treatment of obstructive sleep apnea. Thorax. 1998;53:643–8.
3. Strohl KP, Redline S. Nasal CPAP therapy, upper airway muscle activation, and obstructive sleep apnea. Am Rev Respir Dis. 1986;134:555–8.
4. American Thoracic Society. Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. Am J Respir Crit Care Med. 1994;150:1738–45.
5. Waldhorn RE, Herrick TW, Nguyen MC, et al. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. Chest. 1990;97:33–8.
6. Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. Am Rev Respir Dis. 1992;145:841–5.
7. Ficker JH, Müller D, Wiest G, Lehnert G, Dertinger SH, Katalinic A, Hahn EG. Nasal CPAP therapy of obstructive sleep apnea syndrome with expiratory pressure reduction: a prospective randomized study of acceptance of treatment during therapy initiation. Pneumologie. 1997;51:586–91.
8. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis. 1993;147:887–95.
9. Reeves-Hoche MK, Hudgel DW, Meck R, Witteman R, Ross A, Zwillich CW. Continuous versus bilevel positive airway pressure for obstructive sleep apnea. Am J Respir Crit Care Med. 1995;151:443–9.
10. Sanders MH, Gruendl CA, Rogers RM. Patient compliance with nasal CPAP therapy for sleep apnea. Chest. 1986;90:330–3.
11. Polo O, Berthon-Jones M, Douglas NJ, Sullivan CE. Management of obstructive sleep apnea/hypopnea syndrome. Lancet. 1994;344:656–60.
12. Issa FG, Sullivan CE. Upper airway closing pressures in obstructive sleep apnea. J Appl Physiol. 1984;57:520–7.
13. Meurice JC, Marc I, Series F. Efficacy of auto-CPAP in the treatment of obstructive sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med. 1996;153:794–8.
14. Series F, Marc I, Cormier Y, La Forge J. Required levels of nasal continuous positive airway pressure during treatment of obstructive sleep apnea. Eur Respir J. 1994;7:1776–81.
15. Grunstein RR. Sleep-related breathing disorders. 5. Nasal continuous positive airway pressure treatment for obstructive sleep apnea. Thorax. 1995;50:1106–13.
16. Sharples L, Glover M, Clutterbuck-James A, Bennett M, Jordan J, Chadwick R, Pittman M, East C, Cameron M, Davies M, Oscroft N, Smith I, Morrell M, Fox-Rushby J, Quinnell T. Clinical effectiveness and cost-effectiveness results from the randomised controlled trial of oral mandibular advancement devices for obstructive sleep apnea-hypopnea (TOMADO) and long-term economic analysis of oral devices and continuous positive airway pressure. Health Technol Assess. 2014;18(67):1–296.
17. AHRQ. AHRQ comparative effectiveness review, vol. 32. Rockville: AHRQ; 2011.
18. Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnea in adults. Cochrane Database Syst Rev. 2006;3:CD001106.

19. Campos-Rodriguez F, Queipo-Corona C, Carmona-Bernal C, et al. Continuous positive airway pressure improves quality of life in women with obstructive sleep apnea. A randomized controlled trial. Am J Respir Crit Care Med. 2016;194(10):1286.
20. Tomfohr LM, Ancoli-Israel S, Loredo JS, Dimsdale JE. Effects of continuous positive airway pressure on fatigue and sleepiness in patients with obstructive sleep apnea: data from a randomized controlled trial. Sleep. 2011;34(1):121.
21. Pan YY, Deng Y, Xu X, Liu YP, Liu HG. Effects of continuous positive airway pressure on cognitive deficits in middle-aged patients with obstructive sleep apnea syndrome: a meta-analysis of randomized controlled trials. Chin Med J (Engl). 2015;128(17):2365.
22. Marshall NS, Barnes M, Travier N, Campbell AJ, Pierce RJ, RD ME, Neill AM, Gander PH. Continuous positive airway pressure reduces daytime sleepiness in mild to moderate obstructive sleep apnea: a meta-analysis. Thorax. 2006;61(5):430.
23. Barbé F, Mayoralas D, Masa JF, et al. Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. A randomized, controlled trial. Ann Intern Med. 2001;134(11):1015–23.
24. Tregear S, Reston J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. Sleep. 2010;33(10):1373–80.
25. Parish JM, Lyng PJ. Quality of life in bed partners of patients with obstructive sleep apnea or hypopnea after treatment with continuous positive airway pressure. Chest. 2003;124(3):942–7.
26. Egea CJ, Aizpuru F, Pinto JA, Ayuela JM, et al. Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: a multicenter study. Sleep Med. 2008;9(6):660–6.
27. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol. 2018;71(19):e127–248.
28. Bratton DJ, Gaisl T, Wons AM, Kohler M. CPAP vs mandibular advancement devices and blood pressure in patients with obstructive sleep apnea: a systematic review and meta-analysis JAMA 2015;314(21):2280–2293.
29. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. N Engl J Med. 2016;375(10):919–31.
30. Brill AK, Horvath T, Seiler A, Camilo M, Haynes AG, Ott SR, Egger M, Bassetti CL. CPAP as treatment of sleep apnea after stroke: a meta-analysis of randomized trials. Neurology. 2018;90(14):e1222–30.
31. Ryan CM, Bayley M, Green R, Murray BJ, Bradley TD. Influence of continuous positive airway pressure on outcomes of rehabilitation in stroke patients with obstructive sleep apnea. Stroke 2011;42(4):1062–1067.
32. Martínez-García MA, Soler-Cataluña JJ, Ejarque-Martínez L, Soriano Y, et al. Continuous positive airway pressure treatment reduces mortality in patients with ischemic stroke and obstructive sleep apnea: a 5-year follow-up study. Am J Respir Crit Care Med. 2009;180(1):36–41.
33. Martínez-García MA, Galiano-Blancart R, Román-Sánchez P, Soler-Cataluña JJ, Cabero-Salt L, Salcedo-Maiques E. Continuous positive airway pressure treatment in sleep apnea prevents new vascular events after ischemic stroke. Chest. 2005;128(4):2123–9.
34. Egea CJ, Aizpuru F, Pinto JA, Ayuela JM, Ballester E, et al. Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: a multicenter study. Sleep Med. 2008;9(6):660–6.
35. Kaneko Y, Floras JS, Usui K, Plante J, Tkacova R, Kubo T, Ando SI, Bradley TD. Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med. 2003;348(13):1233–41.
36. Khayat RN, Abraham WT, Patt B, Pu M, Jarjoura D. In-hospital treatment of obstructive sleep apnea during decompensation of heart failure. Chest. 2009;136(4):991–7.
37. Khayat RN, Abraham WT, Patt B, Roy M, Hua K, Jarjoura D. Cardiac effects of continuous and bilevel positive airway pressure for patients with heart failure and obstructive sleep apnea: a pilot study. Chest. 2008;134(6):1162–8.