Chapter 4

Hypertension and Sleep Apnea

Attila Frigy and Ildikó Kocsis

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.76029

Abstract

Diagnosis and treatment of comorbid conditions in hypertension are essential for efficient blood pressure control and for decreasing adverse clinical events and mortality. Sleep apnea, mainly its obstructive form, has a high prevalence both in the general population and in hypertensive patients, the main reason being the worldwide epidemic of obesity. This chapter summarizes the principal issues related to hypertension-sleep apnea relationship: definition of terms, epidemiological data and evidences, clinical manifestations of sleep apnea, pathophysiological background of the adverse effects of sleep apnea on the cardiovascular system, screening and definitive diagnosis, and the effects of specific and nonspecific sleep apnea interventions on hypertension.

Keywords: hypertension, sleep apnea, pathophysiology, diagnosis, treatment

1. Introduction

Cardiovascular and non-cardiovascular comorbidities are frequently present in the setting of hypertension. Usually, they influence adversely the clinical course and treatment; thus, their identification (diagnosis) and management is mandatory. In this regard, sleep apnea, due to its high prevalence and the multiple ways it could affect the patients, is considered one of the most important non-cardiovascular comorbidities in hypertension [1, 2].

2. Definitions, quantification of sleep apnea

Sleep apnea (SA) is a sleep-related breathing phenomenon and consists of the involuntary cessation (or near cessation, >90%) of airflow to the lungs for at least 10 seconds. SA takes part

from the large family of sleep disorders, being the most important manifestation of sleep-related breathing disorders ("sleep disordered breathing"). The latter entity also comprises the sleep-related hypoventilation syndromes, their most frequently occurring form, the obesity hypoventilation syndrome, being also present (with or without SA) in some patients with hypertension and/or metabolic syndrome [3, 4].

While apnea is the most characteristic and important phenomenon, there also exist other respiratory events related to sleep, which have to be considered. Hypopnea represents an at least 30% reduction of airflow for 10 seconds from the pre-event baseline, associated with 3% oxygen desaturation and/or an arousal signal on the EEG, or, alternatively, a 4% oxygen desaturation (the arousal being not mandatory in this case) [3, 4].

Respiratory effort-related arousals (RERAs), lasting at least 10 seconds, are induced by airflow limitation (increased upper airways resistance), which do not fulfill the criteria for apnea or hypopnea. In fact, increased upper airways resistance, hypopnea, and apnea represent a continuum and denote progression of the of the sleep-related upper airways obstruction [3, 4].

The most used parameter for the quantification of SA is the so-called apnea-hypopnea index (AHI), which represents the number of (apneas + hypopneas)/hour of sleep and is determined more exactly by polysomnography (PSG). The AHI is <5 normally, and the SA is considered significant if the AHI is ≥15. An AHI ≥ 30 heralds a severe SA. Another approach of quantification uses the respiratory disturbance index (RDI), which represents the number of (apneas + hypopneas + RERAs)/hour of sleep. In the case of home sleep apnea testing (HSAT), the devices used are not capable of EEG recording (which identifies the sleep phases and arousals); thus, the American Academy of Sleep Medicine (AASM) recommends the term "respiratory event index" (REI) instead of AHI or RDI. In this case, the number of sleep hours is replaced by the number of recording hours. On the other hand, different indices of the degree of hypoxemia occurring during sleep could also be calculated—hypoxemic burden, oxygen desaturation index, average oxygen saturation, etc. [3–6].

Obstructive sleep apnea (OSA) is a form of SA, when the lack of airflow is caused by the collapse of the upper airways (mainly at the level of oropharynx) and the—inefficient—respiratory movements are maintained during apnea/hypopnea (similarly to forced inspiration against a closed glottis = Müller's maneuver). An arousal reaction with or without awakening re-establishes the normal breathing. OSA is the typical form of SA encountered in the setting of hypertension.

In the case of central sleep apnea (CSA), the malfunction of the respiratory center and the lack of efferent impulses to respiratory muscles cause the airflow cessation. A specific form of CSA is the so-called periodic or Cheyne-Stokes respiration (CSR), with breathing "spindles" (gradually increasing and decreasing breathing amplitudes) between apneas. CSA and CSR are characteristic in hypertension only if congestive heart failure or cerebral lesions (e.g., post-stroke status), the main determinants of the appearance of CSA, are present as associated conditions. Mixed (obstructive + central) SA could also occur in patients with hypertension [2, 3].

Because of its high prevalence and clinical importance in hypertension, in the following, mainly data related to OSA will be presented.

http://dx.doi.org/10.5772/intechopen.76029

3. Epidemiological data and evidences regarding the close relationship between OSA and hypertension

The prevalence of OSA (AHI ≥ 5 and the presence of at least one symptom induced by altered sleep) in the general population is high, especially because of the increasing occurrence of obesity. Roughly, 20–30% of men and 10–15% of women suffers from OSA. Significant OSA (moderate or severe, with AHI ≥ 15) is present in about 15% of males and 5% of females. However, there is a concern regarding underestimation of the real prevalence of OSA especially in women, who frequently have atypical symptoms. The prevalence increases with advancing age, race, ethnicity (African Americans and Hispanics) and body mass index [7, 8].

There exists a large amount of epidemiological data and evidences regarding the bidirectional, complex relationship between OSA and hypertension. The prevalence of OSA in hypertensive patients is about 30–50%, while hypertension is present in OSA patients in about 50%. The relationship between the prevalence/severity of OSA and the grade of hypertension is almost linear. The best example for this fact serves the case of resistant hypertension, when the prevalence of any OSA is about 80%, while the presence of moderate or severe OSA reaches 56% [2, 9–11]. Relative to other hypertensive patients, the risk of OSA is 2.5-fold increased in patients with resistant hypertension, and, in the same time, OSA is more severe in patients with resistant hypertension than in those without [12].

Despite of the existence of potential confounders, like obesity, age, sex, metabolic syndrome, and diabetes mellitus, epidemiological data clearly demonstrate the independent association between OSA and incident and prevalent hypertension [13–15].

4. Risk factors of OSA, clinical manifestations, and nocturnal clinical events

Epidemiological data consistently support the existence of risk factors of developing and progression of OSA. These risk factors contribute to the anatomical and/or functional narrowing of the upper airways (e.g., fat deposition in the surrounding tissues in obesity), enhancing their susceptibility to collapse [16].

The principal risk factors of OSA are age, male gender, obesity, and abnormalities of the upper airways and craniofacial structures (especially in Asian subjects) [17]. Obesity and overweight could be considered the most important risk factors due to their high prevalence both in patient with OSA and hypertension. Also, the increasing tendency of obesity in the general population could be considered as the main responsible for the continuously increasing prevalence of both OSA and hypertension. A 10% increase in body mass is associated with a sixfold increase in risk of incident OSA, and, in a population-based study, moderate to severe OSA (AHI ≥15) was present in 63%/22% (male/female) of patients with BMI ≥30 kg/m^2 [17–21].

Other important risk factors of OSA include smoking, alcohol use, sedative or narcotic intake before sleep, nasal obstruction, menopause, and family history (for snoring or OSA).

Nocturnal symptoms	Diurnal symptoms
Heavy, loud snoring	Feeling of an inadequate, unrestful sleep
Restless, interrupted sleep	Excessive sleepiness with/without episodes of involuntary
Awakenings with choking, gasping	Tiredness, falling asleep (e.g., causing car accidents)
Insomnia	Attention, memory, and cognition deficits
Observed apneas by sleep partner	Decreased performance at school, workplace, etc.
Nocturia	Mood disorders: depression, anxiety
Sweating	Sexual dysfunction: loss of libido, impotence
Dry mouth	
Acid reflux	
Morning headache and dizziness	
Nocturnal clinical events	
Myocardial ischemia—silent, angina, myocardial infarction	
Arrhythmias—bradycardias, supraventricular arrhythmias, atrial fibrillation, ventricular arrhythmias, sudden cardiac death	
Blood pressure ascensions	
Acute cardiac decompensation (left and/or right heart failure)	
Stroke (ischemic, hemorrhagic)	

Table 1. Nocturnal and diurnal symptoms and nocturnal clinical events related to OSA [2, 22, 23].

The prevalence of OSA was found to be increased in association with some medical conditions, such as pregnancy, congestive heart failure, chronic pulmonary disease (asthma, chronic obstructive pulmonary disease, pulmonary fibrosis), end-stage kidney disease, stroke, and endocrine disorders (hypothyroidism, acromegaly, polycystic ovary syndrome) [16, 17, 22].

The main clinical manifestations of OSA are presented in **Table 1**. Diurnal symptoms are the consequences of the insufficient, fragmented, low-quality sleep caused by multiple arousals induced by apnea. The complex pathophysiology of the nocturnal clinical events will be presented in detail later.

5. Pathophysiological basis of sleep apnea-hypertension relationship

The complex pathophysiological mechanisms behind acute clinical events and chronic medical conditions, including hypertension, induced and/or aggravated by OSA, are presented in **Table 2**.

The most important mechanisms related to OSA that play a role in the genesis and progression of hypertension are the long-term activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system. Also, during arousals, the acute sympathetic

Pathophysiological mechanism	Consequences
Hypoxemia Hypercapnia Repetitive hypoxia-normoxia cycles (also present in CSA)	**1.** Ischemia (myocardial, cerebral, etc.) **2.** Bradycardia (during apnea)—tachycardia (caused by arousal) **3.** Oxidative stress and systemic inflammatory reaction • Endothelial dysfunction—accelerated atherosclerosis **4.** Hypoxic pulmonary vasoconstriction • Acute and chronic increase of pulmonary arterial pressure with right ventricular overload **5.** Decreased baroreflex activity—contributing to hypertension **6.** Activation of the sympathetic nervous system due to increased chemoreflex sensitivity • Hypertension (acute and chronic) • Sinus tachycardia • Arrhythmias • Ischemia (increased oxygen demand) • Cardiac toxicity and remodeling (e.g., hypertrophy) • Endothelial dysfunction—accelerated atherosclerosis • Insulin resistance, metabolic syndrome **7.** Activation of the renin-angiotensin-aldosterone system
Arousals (with or without awakenings) (also present in CSA)	**1.** Acute activation of the sympathetic nervous system and withdrawal of the parasympathetic cardiac control
Negative intrathoracic pressure during inspiratory effort (only in OSA)	**1.** Increased transmural pressure of cardiac cavities, great vessels, and pulmonary arterial bed • Increased left and right ventricular afterload ○ Acute and chronic cardiac decompensation ○ Ischemia (increased oxygen demand) ○ Arrhythmias • Atrial dilation—favoring atrial fibrillation • Aortic dilation • Pulmonary fluid retention, contributing to acute cardiac decompensations

Table 2. Pathophysiological mechanisms and their consequences in the setting of OSA [2, 23, 24].

hyperactivation causes blood pressure increases, which could precipitate acute cardiac decompensation, myocardial ischemia, arrhythmias, or stroke.

The characteristics of hypertension in the case of significant OSA as comorbidity are the high blood pressure values during nighttime (nocturnal blood pressure surge) and the concomitant non-dipping behavior of 24-hour values. Also, blood pressure variability is increased and heart rate variability is blunted, as markers of cardiac autonomic dysfunction. The control of blood pressure values could be difficult in many cases, development of resistant hypertension with target organ damage (e.g., left ventricular hypertrophy) being the rule [25, 26].

Masked hypertension was also found to be more prevalent in patients with OSA; in one study 30% of newly diagnosed OSA patients had masked hypertension [27].

In patients with hyperaldosteronism, there is a higher prevalence of OSA (1.8 times). Fluid retention induced by aldosterone and its redistribution to the neck tissues is a major contributor to this finding. This mechanism (a vicious circle) contributes significantly to the higher prevalence of coexisting resistant hypertension and severe OSA in these patients [28].

Experimental and human studies data support that the relationship between hypertension and OSA is bilateral. Blood pressure increases, by baroreceptor activation, could inhibit the upper airways muscle tone, enhancing their tendency to collapse [29].

6. Diagnosis of SA in clinical practice

The diagnosis of SA in hypertensive patients does not differ from those without hypertension. The diagnostic approach has two main elements: screening and confirmation (definitive diagnosis).

First, screening is mandatory when significant nocturnal and/or diurnal symptoms are present in a patient. These could be observed or find out by the patient itself, by his/her bed partner, or by different surrounding persons (including the medical personnel). The most important symptoms in this regard are heavy snoring, restless sleep, awakenings associated with choking, witnessed apnea, and excessive daytime sleepiness. Also, screening is recommended if pronounced risk factors or certain clinical conditions are present: severe obesity, hardly controllable, resistant hypertension (usually with target organ damage and non-dipping 24-hour pattern), frequent nocturnal palpitations or proven nighttime arrhythmias, atrial fibrillation recurrence(s) after cardioversion(s), therapy refractory heart failure or frequent decompensations, "unexplained" pulmonary hypertension and right ventricular overload, and nocturnal stroke without an overt etiology [2, 5].

The most used screening tools are the comprehensive sleep evaluation, the sleep apnea questionnaires, and the overnight pulse oximetry. The latter method consists of a demonstration of oxygen desaturations (an indirect measure of SA) during the night. It cannot differentiate the obstructive and central apneas.

There are multiple validated (against PSG and HSAT) sleep questionnaires, morphometric and clinical prediction models which are based on the testing of the presence of the most

important symptoms and features related to SA/OSA. The most used are the Epworth's, Berlin, and STOP-BANG questionnaires. The Epworth Sleepiness Scale (moderate sensitivity, good specificity) involves eight questions to assess excessive daytime sleepiness [5, 30, 31]. The Berlin questionnaire (good sensitivity, moderate specificity) uses eleven questions (from three categories) to determine the risk of patient for OSA [5, 31, 32]. The STOP-BANG questionnaire (high sensitivity and good specificity) is a more and more popular tool for OSA screening and is based on four yes/no questions and on four clinical features (**Table 3**) [5, 31, 33, 34]. Current guidelines recommend against using any screening tool to diagnose OSA in adults, in the absence of PSG or HSAT [5].

The definitive diagnosis of SA is always device-based. Every patient with high clinical suspicion of SA, based on a comprehensive sleep evaluation, screening tools, and/or the presence of the cardinal symptoms of OSA (excessive daytime sleepiness and at least two of the following: loud snoring, witnessed apnea or gasping or choking, diagnosed hypertension), has to undergo overnight sleep monitoring [5].

1. Snoring?	**Yes/No**
Do you snore loudly (loud enough to be heard through closed doors or your bed partner elbows you for snoring at night)?	
2. Tired?	
Do you often feel tired, fatigued, or sleepy during the daytime (such as falling asleep during driving or talking to someone)?	
3. Observed?	
Has anyone observed you stop breathing or choking/gasping during your sleep	
4. Pressure?	
Do you have or are being treated for high blood pressure?	
5. Body mass index more than 35 kg/m^2?	**Yes/No**
6. Age older than 50?	
7. Neck size large? (measured around Adam's apple)	
For male, is your shirt collar 17 inches/43 cm or larger?	
For female, is your shirt collar 16 inches/41 cm or larger?	
8. Gender = Male?	
OSA—Low risk: Yes to 0–2 questions	
OSA—Intermediate risk: Yes to 3–4 questions	
OSA—High risk: Yes to 5–8 questions	
or Yes to 2 or more of 4 STOP questions + male gender	
or Yes to 2 or more of 4 STOP questions + BMI > 35 kg/m^2	
or Yes to 2 or more of 4 STOP questions + neck circumference 17 inches/43 cm in male or 16 inches/41 cm in female	

Table 3. The STOP-BANG questionnaire and its evaluation.

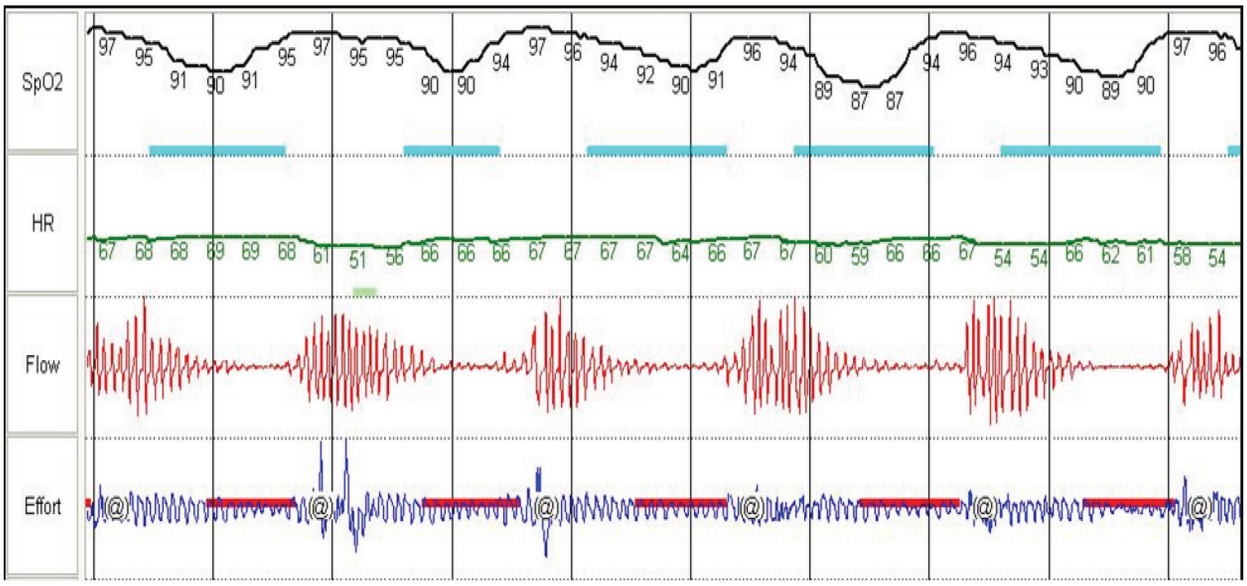

Figure 1. A typical registration with a Type III sleep monitor from a patient with OSA. SpO2—oxygen saturation, HR—heart rate, flow—nasal airflow, effort—chest movements (maintained during apneas).

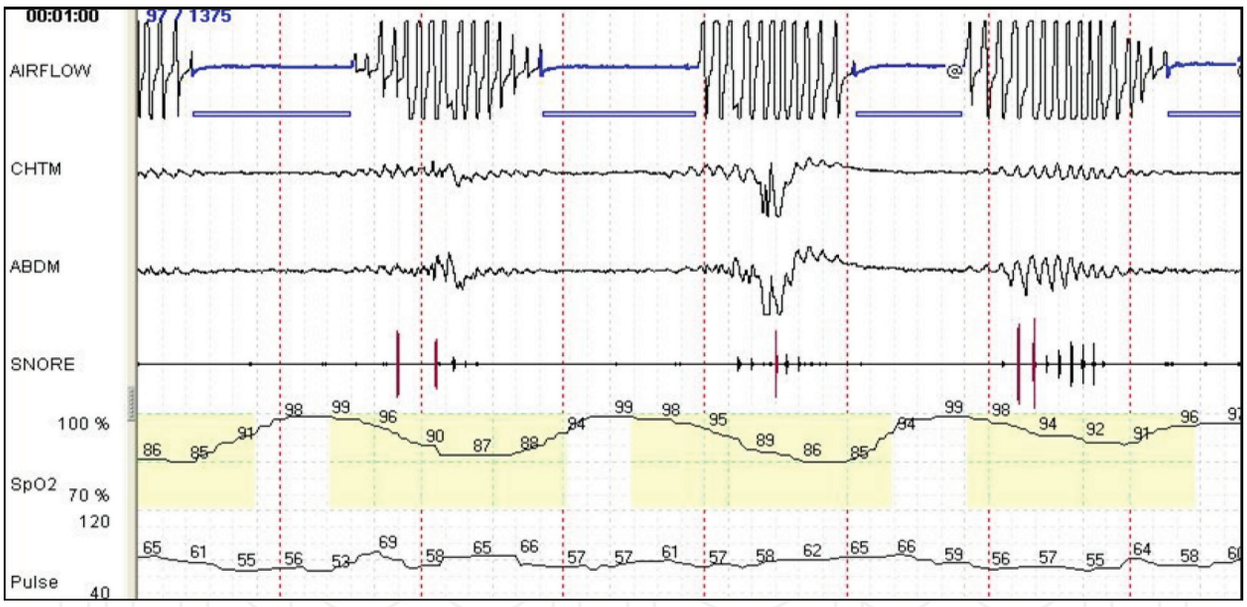

Figure 2. A typical registration with a Type III sleep monitor from a patient with CSA. Airflow—nasal airflow; CHTM, ABDM—chest and abdominal movements (absents during apneas); SNORE—snoring; SpO2—oxygen saturation; pulse—heart rate.

The diagnostic devices are categorized as Type I to IV depending on the number of biological signals (channels) monitored. PSG represents the gold standard of sleep monitoring, having the capability to register the following channels: EEG, EOG, ECG/heart rate, chin EMG, limb EMG, respiratory effort at thorax and abdomen, airflow from a nasal cannula, pulse oximetry, etc. (a minimum of 7 channels). PSG could be used for Type 1 (attended, in the sleep laboratory) and Type 2 (unattended, at home) sleep studies. In the case of HSAT, as a rule, Type III

	Recommendation statement	Strength of recommendation
1.	We recommend that clinical tools, questionnaires, or prediction algorithms not be used to diagnose OSA in adults, in the absence of PSG or HSAT	Strong
2.	We recommend that PSG, or HSAT with a technically adequate device, be used for the diagnosis of OSA in uncomplicated adult patients presenting with signs and symptoms that indicate an increased risk of moderate to severe OSA	Strong
3	We recommend that if a single HSAT is negative, inconclusive or technically inadequate, PSG be performed for the diagnosis of OSA	Strong
4.	We recommend that PSG, rather than HSAT, be used for the diagnosis of OSA in patients with significant cardiorespiratory disease, potential respiratory muscle weakness due to neuromuscular condition, awake hypoventilation or suspicion of sleep-related hypoventilation, chronic opioid medication use, history of stroke, or severe insomnia	Strong
5.	We suggest that, if clinically appropriate, a split-night diagnostic protocol, rather than a full-night diagnostic protocol for PSG, be used for the diagnosis of OSA	Weak
6.	We suggest that when the initial PSG is negative, and there is still clinical suspicion for OSA, a second PSG be considered for the diagnosis of OSA	Weak

Table 4. Current recommendations of the AASM regarding the use of PSG and HSAT for diagnosing OSA [5].

devices with minimum 4 channels (airflow, respiratory movements, pulse oximetry—heart rate; optionally: ECG, body position, snoring, etc.) are used. In **Figures 1** and **2** typical recordings, using a Type III device, are presented from a patient with severe OSA and from another with severe CSA. The portable, Type III devices used for HSAT have the disadvantage vs. PSG, that they do not monitor the sleep itself (lack of EEG, EOG, EMG) and do not provide real-time data with the possibility of on-line corrections of monitoring. Due to these facts, and to the relatively frequent measurement artifacts, patients with equivocal sleep monitoring results have to undergo a standard, attended PSG in the sleep laboratory [5, 6, 35].

Current recommendations of the AASM regarding the diagnostic use of PSG and HSAT are presented in **Table 4**.

7. The effect of OSA interventions on comorbid hypertension

Complex treatment of moderate/severe OSA is mandatory in the setting of hypertension, the expected results being a better quality of life of the patients and a more efficient blood pressure control.

The control of modifiable factors which contribute to both conditions—reducing obesity, smoking, and alcohol consumption—is considered a very effective, first step treatment modality of comorbid OSA and hypertension [23, 24, 36].

The standard and efficient device-based therapy of OSA consists of the utilization of continuous positive airway pressure (CPAP). In the literature, there are a plenty of studies, usually

sham-CPAP controlled, concerning the impact of CPAP treatment on comorbid hypertension with diverse grades. The results of these studies, sometimes contradictory, are presented and commented in detail in recent meta-analyses and critical reviews [37, 38, 39]. The effects of CPAP treatment on blood pressure (hypertension) in OSA patients could be summarized as follows: (1) prehypertension and masked hypertension are reduced [40], (2) there is a clear tendency of decreasing both the nighttime and daytime blood pressure values (but only modest reductions, generally 2–5 mmHg), (3) there is a slight reversal of the non-dipping behavior, and (4) the effect of CPAP treatment seems to be more pronounced if there is a good treatment adherence (use of the device at least 5 hours/night), the patient is more symptomatic, and the OSA and/or hypertension are more severe [37, 38, 39]. As a conclusion, CPAP treatment in comorbid OSA and hypertension is a relatively modest, but efficient, additive modality of controlling blood pressure values. The beneficial effects of CPAP treatment are the results of reducing sympathetic overactivity by controlling hypoxemia, arousals, and negative intrathoracic pressure.

Oral appliance therapy, a treatment option in mild and moderate forms of OSA, also could improve blood pressure control in the case of concomitant hypertension [41, 42].

Regarding the effect of antihypertensive drugs on OSA in hypertensive patients, the (sometimes conflicting) data do not support clearly a specific beneficial effect of the usually prescribed drugs (angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, calcium-channel blockers, diuretics, beta-blockers) [23, 24]. However, hypertensive patients with hyperaldosteronism and those with resistant hypertension could benefit from spironolactone as first choice therapy, with proven beneficial effects on OSA. Generally, diuretics by reducing fluid retention, including that at the level of parapharyngeal tissues, could ameliorate upper airway obstruction and OSA [43, 44].

8. Conclusion

Hypertension and SA, especially OSA, are frequently associated, and there is a well-documented pathophysiological link between OSA and development and aggravation of hypertension. Screening and diagnosis of OSA is mandatory whenever increased nocturnal and daytime symptoms and/or difficult to control hypertension (resistant, as a rule, with high nocturnal blood pressure values and target organ damages) is present. The treatment of OSA by specific (e.g., CPAP) or nonspecific means could contribute significantly to a better quality of life of the patients, to a better control of blood pressure values, and to the decrease of OSA-related adverse clinical events.

Acknowledgements

The chapter was ellaborated as part of the Grant nr. 15276/03.11.2015 of the UMF Tirgu Mures, Romania.

Conflicts of interest

The authors declare that there are no conflicts of interest regarding the writing of this chapter.

Author details

Attila Frigy* and Ildikó Kocsis

*Address all correspondence to: afrigy68@gmail.com

Department of Internal Medicine IV, University of Medicine and Pharmacy of Tirgu Mures, Tirgu Mures, Romania

References

[1] Mancia G, Fagard R, Narkiewicz K, et al. ESH/ESC guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). European Heart Journal. 2013;**34**:2159-2219

[2] Parati G, Lombardi C, Hedner J, et al. Position paper on the management of patients with obstructive sleep apnea and hypertension: Joint recommendations by the European Society of Hypertension, by the European Respiratory Society and by the members of European COST (COoperation in scientific and technological research) ACTION B26 on obstructive sleep apnea. Journal of Hypertension. 2012;**30**:633-646

[3] American Academy of Sleep Medicine. International Classification of Sleep Disorders. 3rd ed. Darien: American Academy of Sleep Medicine; 2014

[4] Berry RB, Brooks R, Gamaldo CE, et al. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 2.4. Darien: American Academy of Sleep Medicine; 2017

[5] Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: An American Academy of sleep medicine clinical practice guideline. Journal of Clinical Sleep Medicine. 2017;**13**:479-504

[6] Rosen IM, Kirsch DB, Chervin RD, et al. American Academy of Sleep Medicine Board Of Directors. Clinical use of a home sleep apnea test: An American Academy of Sleep Medicine position statement. Journal of Clinical Sleep Medicine. 2017;**13**:1205-1207

[7] Young T, Palta M, Dempsey J, et al. Burden of sleep apnea: Rationale, design, and major findings of the Wisconsin sleep cohort study. WMJ. 2009;**108**:246

[8] Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults. American Journal of Epidemiology. 2013;**177**:1006-1014

[9] Young T, Peppard P, Palta M, et al. Population-based study of sleep-disordered breathing as a risk factor for hypertension. Archives of Internal Medicine. 1997;**157**:1746-1752

[10] Sjöström C, Lindberg E, Elmasry A, et al. Prevalence of sleep apnoea and snoring in hypertensive men: A population based study. Thorax. 2002;**57**:602-607

[11] Muxfeldt ES, Margallo VS, Guimarães GM, et al. Prevalence and associated factors of obstructive sleep apnea in patients with resistant hypertension. American Journal of Hypertension. 2014;**27**:1069-1078

[12] Demede M, Pandey A, Zizi F, et al. Resistant hypertension and obstructive sleep apnea in the primary-care setting. International Journal of Hypertension. 2011. Article ID 340929

[13] Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep-disordered breathing and hypertension. The New England Journal of Medicine. 2000;**342**:1378-1384

[14] O'Connor GT, Caffo B, Newman AB, et al. Prospective study of sleep-disordered breathing and hypertension. American Journal of Respiratory and Critical Care Medicine. 2009;**179**:1159-1164

[15] Pedrosa RP, Drager LF, Gonzaga CC, et al. Obstructive sleep apnea: The most common secondary cause of hypertension associated with resistant hypertension. Hypertension. 2011;**58**:811-817

[16] Drager LF, Genta PR, Pedrosa RP, et al. Characteristics and predictors of obstructive sleep apnea in patients with systemic hypertension. The American Journal of Cardiology. 2010;**105**:1135-1139

[17] Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. Journal of the American Medical Association. 2004;**291**:2013-2016

[18] Romero-Corral A, Caples SM, Lopez-Jimenez F, et al. Interactions between obesity and obstructive sleep apnea. Implications for treatment. Chest. 2010;**137**:711-719

[19] Landsberg L, Aronne LJ, Beilin LJ, et al. Obesity-related hypertension: Pathogenesis, cardiovascular risk, and treatment. A position paper of the Obesity Society and the American Society of Hypertension. Journal of Clinical Hypertension (Greenwich, Conn.). 2013;**15**:14-33

[20] Tufik S, Santos-Silva R, Taddei JA, et al. Obstructive sleep apnea syndrome in the Sao Paulo epidemiologic sleep study. Sleep Medicine. 2010;**11**(5):441-446

[21] Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. Journal of the American Medical Association. 2000;**284**:3015-3021

[22] Strohl KP. Overview of obstructive sleep apnea in adults. In: UpToDate, Collop N, editor. UpToDate, Waltham, MA. http://www.uptodate.com [Accessed on 30 December 2017]

[23] Ahmad M, Makati D, Akbar S. Review of and updates on hypertension in obstructive sleep apnea. International Journal of Hypertension. 2017; Article ID: 1848375. DOI: 10.1155/2017/1848375

[24] Cai Y, Zhou J, Chen L, et al. Hypertension and obstructive sleep apnea. Hypertension Research. 2016;**3**:391-395

[25] Loredo JS, Ancoli-Israel S, Dimsdale JE. Sleep quality and blood pressure dipping in obstructive sleep apnea. American Journal of Hypertension. 2001;**14**:887-892

[26] Hla KM, Young T, Finn L, et al. Longitudinal association of sleep-disordered breathing and nondipping of nocturnal blood pressure in the Wisconsin sleep cohort study. Sleep. 2008;**31**:795-800

[27] Baguet JP, Levy P, Barone-Rochette G, et al. Masked hypertension in obstructive sleep apnea syndrome. Journal of Hypertension. 2008;**26**:885-892

[28] Gonzaga CC, Gaddam KK, Ahmed MI, et al. Severity of obstructive sleep apnea is related to aldosterone status in subjects with resistant hypertension. Journal of Clinical Sleep Medicine. 2010;**6**:363-368

[29] Schwartz AR, Rowley JA, O'Donnell C, et al. Effect of hypertension on upper airway function and sleep apnoea. Journal of Sleep Research, Supplement. 1995;**4**:83-88

[30] Johns MWA. New method for measuring daytime sleepiness: The Epworth sleepiness scale. Sleep. 1991;**14**:540-545

[31] Chiu HY, Chen PY, Chuang LP, et al. Diagnostic accuracy of the berlin questionnaire, STOP-BANG, STOP, and Epworth sleepiness scale in detecting obstructive sleep apnea: A bivariate meta-analysis. Sleep Medicine Reviews. 2017;**36**:57-70

[32] Netzer NC, Stoohs RA, Netzer CM, et al. Using the berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Annals of Internal Medicine. 1999;**131**:485-491

[33] Chung F, Subramanyam R, Liao P, et al. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. British Journal of Anaesthesia. 2012;**108**:768-775

[34] Prasad KT, Sehgal IS, Agarwal R, et al. Assessing the likelihood of obstructive sleep apnea: A comparison of nine screening questionnaires. Sleep & Breathing. 2017;**21**(4):909-917

[35] Ferber R, Millman R, Coppola M, et al. Portable recording in the assessment of obstructive sleep apnea. ASDA standards of practice. Sleep. 1994;**17**:378-392

[36] Rubinstein I, Colapinto N, Rotstein LE, et al. Improvement in upper airway function after weight loss in patients with obstructive sleep apnea. The American Review of Respiratory Disease. 1988;**138**:1192-1195

[37] Hu X, Fan J, Chen S, et al. The role of continuous positive airway pressure in blood pressure control for patients with obstructive sleep apnea and hypertension: A meta-analysis of randomized controlled trials. Journal of Clinical Hypertension (Greenwich, Conn.). 2015;**17**:215-222

[38] Fatureto-Borges F, Lorenzi-Filho G, Drager LF. Effectiveness of continuous positive airway pressure in lowering blood pressure in patients with obstructive sleep apnea: A critical review of the literature. Integr Blood Press Control. 2016;**9**:43-47

[39] Feldstein AC. Blood pressure effects of CPAP in nonresistant and resistant hypertension associated with OSA: A systematic review of randomized clinical trials. Clinical and Experimental Hypertension. 2016;**38**:337-346

[40] Drager LF, Pedrosa RP, Diniz PM, et al. The effects of continuous positive airway pressure on prehypertension and masked hypertension in men with severe obstructive sleep apnea. Hypertension. 2011;**57**:549-555

[41] Iftikhar IH, Hays ER, Iverson MA, et al. Effect of oral appliances on blood pressure in obstructive sleep apnea: A systematic review and meta-analysis. Journal of Clinical Sleep Medicine. 2013;**9**:165-174

[42] Andren A, Hedberg P, Walker-Engstrom ML, et al. Effects of treatment with oral appliance on 24-h blood pressure in patients with obstructive sleep apnea and hypertension: A randomized clinical trial. Sleep & Breathing. 2013;**17**:705-712

[43] Gaddam K, Pimienta E, Thomas J, et al. Spironolactone reduces severity of obstructive sleep apnea in patients with resistant hypertension: A preliminary report. Journal of Human Hypertension. 2010;**24**:532-537

[44] Bucca CB, Brussino L, Battisti A, et al. Diuretics in obstructive sleep apnea with diastolic heart failure. Chest. 2007;**132**:440-446