CHEST

# Relationship Between OSA and Hypertension

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There is a bidirectional association between OSA and systemic hypertension. The strengths of this relationship appear to be modulated by factors such as age, sex, and somnolence. The 24-h BP circadian pattern also appears to be influenced by OSA. Patients with this syndrome exhibit a high prevalence of nondipping or riser circadian patterns, which are related to clinical and subclinical organ damage in the heart and brain. However, the influence of OSA on nocturnal hypertension development has not yet been clarified. A special area of interest is the recognized relationship between OSA and resistant hypertension. The majority of patients with resistant hypertension suffer OSA. CPAP treatment significantly reduces BP in such patients and could play a clinical role in the management of BP in these patients. Several meta-analyses have demonstrated a concordant mild effect of CPAP on systemic hypertension. This effect is related to CPAP compliance, somnolence status, and baseline BP. The effects of oral appliances on BP in patients with OSA must be evaluated in randomized controlled trials. In the absence of additional data reported by clinical studies on other antihypertensive drug treatments, diuretics, particularly antialdosteronic diuretic agents, should be considered the first-line antihypertensive drug treatment in patients with OSA. By reducing parapharyngeal edema and secondary upper airway obstruction, these drugs appear to improve OSA severity and also to reduce BP.

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**ABBREVIATIONS:** ABPM = ambulatory BP monitoring; ACE = angiotensin-converting enzyme; AHI = apnea-hypopnea index; DBP = diastolic BP; RCT = randomized controlled trial; SBP = systolic BP; VSC = Vitoria Sleep Cohort; WSCS = Wisconsin Sleep Cohort Study

OSA is a common disease that is caused by a collapse of the upper airway during sleep, which leads to transient asphyxia. Because of these events, patients experience intermittent hypoxemia, brain arousals, sleep disturbances, daytime somnolence, and poor quality of life. However, these events also lead to important metabolic and neurohormonal disturbances that may have adverse cardiovascular consequences.[1] The prevalence of OSA is increasing in developed countries in parallel with the increasing prevalence of obesity. Among middle-aged adults aged 30 to 70 years, the prevalence of OSA is approximately 24% to 26% in men and 17% to 28% in women.[2,3]

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Epidemiologic data suggest that there is a strong association between OSA and systemic hypertension, with important implications for cardiovascular outcomes. There is a high prevalence of OSA in hypertensive individuals (30%-50%).[4] If we consider only patients with resistant hypertension, then a dramatic increase in prevalence, reaching 83%, is observed.[5] The epidemiologic relationship between hypertension and OSA is bidirectional. Not only do patients with hypertension appear to be more likely to suffer OSA, data from community and population studies indicate that patients with OSA present a high prevalence of hypertension.[6-8] The prevalence of hypertension in patients with moderate or severe OSA was reported to be 46% or 53%, respectively.[8] The results of experimental studies describe pathophysiologic features that support a causal, bidirectional relationship between OSA and hypertension. On the one hand, mechanisms based on sympathetic and renin-angiotensin-aldosterone activation, as well as oxidative stress and endothelial dysfunction, implicate OSA as an independent cause of hypertension.[1] On the other hand, acute increases in BP may cause an inhibition of the upper airway muscles. This phenomenon, together with volume overload and its displacement to the upper body during sleep, which can be experienced by subjects with hypertension and can lead to pharyngeal edema, may explain the link between hypertension and OSA.[9-11] In addition to these observations, the purpose of this review of OSA and hypertension is to present an overview of state-of-the-art strategies that address issues that may be relevant to daily clinical practice.

## OSA and the Incident Risk of Hypertension

Epidemiologic studies show that patients with OSA have a high prevalence of obesity.[2,11] Therefore, obesity may be the nexus that explains the high prevalence of hypertension in these patients. However, the results of a large, prospective, longitudinal study, the Wisconsin Sleep Cohort Study (WSCS), suggest that moderate to severe OSA (apnea-hypopnea index [AHI] $\geq$ 15/h) is an independent cause of hypertension. Subjects with this degree of OSA severity showed a 3.2-fold increase in the odds of developing hypertension, compared with subjects without OSA.[12] The WSCS results impacted the American guidelines for the management of hypertension (The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [JNC VII]), and OSA was recognized as the first secondary cause of hypertension.[13] Similarly, Marin et al[14] conducted an observational study that included 1,889 subjects without hypertension who were admitted to a sleep clinic and were followed up for a mean of 10.1 years. The authors found an increased incidence of hypertension in subjects with untreated OSA, compared with treated patients. Other studies have shown that age, somnolence, and sex could influence and modulate this independent relation. Bixler et al[15] examined 741 men and 1,000 women aged 20 to 100 years and found that the strength of the association between OSA and hypertension may become attenuated with age. Haas et al[16] confirmed these results and established a cutoff age of 60 years. Above this age, the strength of the association declines. Conversely, the results of a 5-year follow-up of participants in the Sleep Heart Health Study (SHHS),[17] after adjusting for BMI, did not confirm the independent relationship between OSA and hypertension found in the Wisconsin cohort.

One of the most accepted explanations for these differences is the divergence between the characteristics of the two cohorts, particularly in terms of age. Subjects from the SHHS were significantly older than those from the WSCS (60 years vs 47 years old). Data reported by Kapur et al[18] showed that an increase in daytime somnolence, measured with the Epworth Sleepiness Scale, correlated positively with a stronger association between OSA and the risk of hypertension. In addition, the effect of CPAP treatment on the incidence of hypertension has been evaluated in nonsleepy patients. In a randomized controlled trial (RCT) that included 725 subjects with a median follow-up of 4 years, the Spanish Sleep and Breathing Network found that CPAP did not reduce the incidences of hypertension or cardiovascular events in nonsleepy subjects.[19] These data again suggest that the presence or absence of sleepiness may influence the risk of incident hypertension. Finally, in a population-based case-control study, Hedner et al[20] found that the association may be more evident in men than in women.

Despite all these considerations, the association between OSA and the incident risk of hypertension remains unresolved. The Vitoria Sleep Cohort (VSC)[21] followed, for 7.5 years, 1,180 subjects aged 30 to 70 years who were not hypertensive. The results did not suggest an association between OSA and the incidence of hypertension after adjusting for age, sex, and BMI. These discordant results, in comparison with those of the WSCS, may be explained by two critical features: differences in population characteristics, especially in terms of BMI and sex, and differences in the diagnostic procedure used. The subject samples in the WSCS were more obese (BMI of 29 kg/m$^2$ compared with 26 kg/m$^2$ in the VSC) and included more men (56% compared with 48% in the

VSC). However, variation in the sleep study procedures, with polysomnography applied in the WSCS and home polygraphy in the VCS, may be the most relevant difference. Polygraphy shows good concordance with polysomnography in moderate to severe OSA,[22] but this effect has not been observed in normal and mild OSA. The majority of the subjects in the VSC had no or mild OSA. Among the 1,180 patients included in the study, 377 patients had OSA at baseline, and proportionately few, 149 subjects, had a respiratory disturbance index that was ≥ 14/h.

It is important to consider several potential methodologic differences in the studies that have examined BP and OSA. These differences should be considered when comparing the results from different studies. For example, the following components of the studies can vary: definition of hypertension, BP measurement methodology (patient position, time of day, technique), controlling for medications, definition of sleepiness based on multiple sleep latency tests or the Epworth Sleepiness Scale, and definition of OSA based on an AHI assessed by polysomnography or polygraphy. Moreover, several studies have suggested that the degree of hypoxemia could play an important role beyond AHI. Accounting for all of these considerations, we conclude that OSA is an independent cause of hypertension but with less significance than initially suspected.

## Circadian Pattern of BP in Patients With OSA

Studies involving 24-h ambulatory BP monitoring (ABPM) have shown that subjects with hypertension with a decrease in BP of < 10% during the night (nondippers) and those who present an increase in BP at night (risers)[23] exhibit greater organ damage and worse cardiovascular outcomes than do subjects with hypertension who present a decrease of > 10% during the night (dippers).[24,25] Initial case-control studies using 24-h ABPM showed that patients with OSA had a high prevalence of an unfavorable circadian pattern, compared with subjects without OSA.[26] One study found that 84% of patients with mild to severe OSA had a nondipper circadian pattern.[27] Similarly, Ancoli-Israel et al[28] studied 140 patients with hypertension and found that patients with OSA had a higher dipping ratio, defined as the ratio between the mean nighttime BP and the mean daytime BP, compared with subjects without OSA. Data from a 328-subject subsample of the WSCS, with an average of 7.2 years of follow-up, showed that there was a dose-response relationship between increased odds of developing a nondipping systolic BP (SBP) and the severity of OSA at baseline.[29] These results suggest that there is a causal link between OSA and an altered circadian pattern.

The presence of a high nocturnal BP, defined as a nighttime BP ≥ 120 mm Hg (SBP) and/or 70 mm Hg (diastolic BP [DBP]), is the most important BP prognostic variable for cardiovascular outcomes,[30-32] and it has shown strong correlations with subclinical brain[33,34] and heart damage.[35] Thus, the presence or absence of nighttime hypertension on ABPM analysis may be more important than the circadian pattern. In an initial study of 2,877 subjects, Cuspidi et al[36] found a positive relationship between the nondipper pattern and left ventricular hypertrophy. However, a second study[37] examined heart damage in patients with nocturnal hypertension, compared with dippers and nondippers, and no differences were detected. These results suggest that, rather than the circadian pattern, the critical factor in determining organ damage is the presence or absence of nocturnal hypertension. To date, data are lacking regarding the prevalence of a high nocturnal BP in patients with OSA.

Beat-to-beat BP monitoring studies have provided a deeper analysis of nocturnal BP in patients with OSA.[38,39] These small studies (examining beat-to-beat BP and OSA) found that during apnea events in patients with severe OSA, a dramatic increase in SPB from baseline could develop. Unfortunately, the conditions in which ABPM must be performed make this tool unable to capture these BP fluctuations. Organ damage consequences related to this increase in SBP could be expected, but the magnitude of this effect in patients with hypertension has still not been elucidated. Additionally, CPAP treatment, and its protective effect against these BP increases, may be beneficial in this context.

## OSA and Resistant Hypertension

Resistant hypertension is defined as the clinical situation in which lifestyle changes plus pharmacologic treatment with three drugs (including a diuretic) fail to lower the BP to below 140/90 mm Hg.[23,40] Depending on the population studied, the prevalence of this condition ranges from 5% to 30% of subjects with hypertension.[40]

The reported data have shown a high prevalence of OSA in patients with resistant hypertension (71%-83%).[5,41] In a study that included 125 subjects with resistant hypertension, Pedrosa et al[42] found that OSA was the most frequent condition related to resistant hypertension (64%). In fact, OSA showed a much greater association with resistant hypertension than with primary hyperaldosteronism (5.6%). Demede et al[43] found that patients with resistant hypertension had a 2.5-times increased risk of

OSA compared with other subjects with hypertension. The high level of aldosterone in resistant hypertension and its consequences in terms of volume overload and rostral fluid shift during sleep, which lead to secondary pharyngeal edema that increases upper airway obstruction, have been hypothesized to be the mechanisms that underlie the link between hypertension and OSA.[10,44]

The causal relationship between OSA and resistant hypertension was recognized as relevant in the 2013 European Society of Hypertension/European Society of Cardiology guidelines[23] and in the resistant hypertension consensus by the Professional Education Committee of Council for High Blood Pressure Research of the American Heart Association.[40] Organ damage in resistant hypertension has been well established, but the impact of the coexistence of OSA on this damage and on the cardiovascular outcomes of patients with resistant hypertension must be clarified.

## Effect of OSA Treatment on Hypertension

### *CPAP Treatment*

Many studies have evaluated the effect of CPAP treatment on BP in patients with OSA (Fig 1). However, most of these studies evaluated short-term effects and had important limitations and design differences.[45] These differences and limitations can be divided into two categories. One set of factors depends on the study population, such as age, sex, BMI, hypertension degree, and adequate antihypertensive treatment, as well as OSA severity. Another set of factors depends on the methodology, such as the number of subjects included, whether the study had a multicenter or a single-center design, the treatment used in the control group (sham-CPAP use or not), the hypertension definition used, how the evaluation of the effect on BP was conducted (office BP or ABPM), and the variability in follow-up time or CPAP compliance. Despite these handicaps, several meta-analyses[45-52] have demonstrated a concordant mild effect of CPAP on BP, with a drop of approximately 2 mm Hg (Table 1[46-54]). This effect is significantly inferior to those achieved by most of the commonly used antihypertensive drugs. Despite this modest decrease, this effect is not negligible and could have beneficial effects on cardiovascular outcomes.[55] Moreover, similar to the effects of certain antihypertensive drugs, an increase in protective organ damage beyond that associated with the observed BP reduction cannot be excluded.

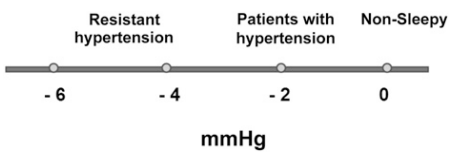


Figure 1 – *Effect of CPAP on BP.*

Certain variables, such as CPAP compliance,[50,51,53,56] somnolence status,[51,53] and baseline BP,[50,52] may modulate the strength of the effect of CPAP treatment on BP. The decrease in BP achieved by CPAP treatment is clearly related to the hours of CPAP use and likely to its use during rapid eye movement sleep.[57] In relation to symptoms, a recent meta-analysis found no effect of CPAP on BP in patients without somnolence.[53] Another characteristic is the influence of OSA severity on BP drop magnitude during CPAP treatment. Two meta-analyses found a relationship between OSA severity and the magnitude of the drop in BP during CPAP treatment.[49,51] Conversely, Montesi et al[50] showed an independent relation between OSA severity and BP reduction. A later patient-level meta-analysis, using individual patient data from the trials, confirmed these results.[52]

Lifestyle modifications, including weight loss, should be recommended in patients receiving hypertension treatment.[23] Chirinos et al[58] randomized 181 patients with obesity and moderate to severe OSA to three possible interventions for 24 weeks: CPAP treatment alone, weight-loss intervention alone, and CPAP plus weight-loss intervention. Among 136 patients who completed the study, in the per-protocol population, the reduction in SBP at 24 weeks was greater in the combined intervention group (14.1 mm Hg) than in the weight-loss group (6.8 mm Hg) or in the CPAP group (3.0 mm Hg). The reduction in mean arterial pressure was also significantly greater in the combined treatment group. Thus, the combined treatment reduced BP more than either intervention alone. These results suggest the possibility of an interaction effect between lifestyle modifications, weight-loss measures, and CPAP in the control of BP.

In patients with resistant hypertension, CPAP treatment showed a clearer drop in BP compared with other subjects with hypertension.[56,59-63] A recent meta-analysis[54] showed that the effects of CPAP in patients with resistant hypertension on the drop in ambulatory BP were −7.21 (95% CI, −9.04 to −5.35; $P < .001$; $I^2$, 58%) and −4.99 (95% CI, −6.01 to −3.96; $P > .001$; $I^2$, 31%) for SBP and DBP, respectively. Considering only the results from RCTs, the mean net changes in ambulatory BP were −6.74 mm Hg (95% CI, −9.98 to −3.49; $P < .001$; $I^2$, 61%) and −5.94 mm Hg (95% CI, −9.40 to −2.47; $P = .001$; $I^2$, 76%) for SBP and DBP, respectively, favoring the CPAP groups (Table 2). The study that provided the

**TABLE 1** ] Published Meta-analyses of the Effect of CPAP on BP in Patients With OSA

| Study/Year | No. Studies | No. Subjects | BP Measurement | Follow-up Duration, wk | BP Effect, mm Hg |
|---|---|---|---|---|---|
| Bazzano et al[46]/2007 | 16 | 818 | Office | 2 | SBP −2.46 |
| | | | Ambulatory | | DBP −1.83 |
| Alajmi et al[47]/2007 | 10 | 587 | Office | 4 | SBP −1.38[a] |
| | | | Ambulatory | | DBP −1.52[a] |
| Mo and He[48]/2007 | 7 | 471 | Ambulatory | 4 | 24-h SBP −0.95[a] |
| | | | | | 24-h DBP −1.78 |
| Haentjens et al[49]/2007 | 12 | 572 | Ambulatory | 1 | 24-h SBP −1.64 |
| | | | | | 24-h DBP −1.48 |
| Montesi et al[50]/2012 | 28 | 1,948 | Office | 1-24 | Daytime SBP −2.58 |
| | | | Ambulatory | | Daytime DBP −2.01 |
| | | | | | Nighttime SBP −4.09 |
| | | | | | Nighttime DBP −1.85 |
| Fava et al[51]/2014 | 31 | 1,820 | Office | 4-208 | SBP −2.6 |
| | | | Ambulatory | | DBP −2.0 |
| | | | | | Daytime SBP −2.2 |
| | | | | | Daytime DBP −1.9 |
| | | | | | Nighttime SBP −3.8 |
| | | | | | Nighttime DBP −1.8 |
| Bakker et al[52]/2014 | 8 | 968 | Office | 6-52 | SBP −2.27 |
| | | | Ambulatory | | DBP −1.78 |
| | | | | | Subjects with uncontrolled hypertension: |
| | | | | | SBP −7.1 |
| | | | | | DBP −4.3 |
| | | | | | (after controlling for OSA severity) |
| Nonsleepy subjects | | | | | |
| Bratton et al[53]/2014 | 4 | 1,206 | Office | 4-208 | SBP +1.1[a] |
| | | | Ambulatory | | DBP −0.8[a] |
| Subjects with resistant hypertension | | | | | |
| Iftikhar et al[54]/2014 | 4 | 329 | Ambulatory | 3-24 | 24-h SBP −6.74 |
| | | | | | 24-h DBP −5.94 |

24-h DBP = 24-h ambulatory diastolic BP; 24-h SBP = 24-h ambulatory systolic BP; DBP = diastolic BP; SBP = systolic BP.
[a] Not significant.

most patients for this meta-analysis was the HIPARCO (Effect of Continuous Positive Airway Pressure [CPAP] Treatment in the Control of Refractory Hypertension) RCT,[56] which included 194 patients. In that study, a significant reduction in 24-h BP of 4.4 mm Hg (95% CI, 1.8-7; $P = .001$) was observed, and this reduction was more evident at night. This reduction was assessed according to CPAP tolerance and compliance (per-protocol analysis). The linear regression analysis showed that BP improved by 1.3 mm Hg for each additional hour of CPAP use. The HIPARCO study also showed that CPAP use led to the recovery of the normal circadian pattern, with a secondary potential cardiovascular benefit. However, there was significant variability in the BP drop among subjects, and the factors that influence the BP response to CPAP in patients with resistant hypertension have not been identified. Thus, there is a need for long-term RCTs to provide relevant information regarding

**TABLE 2** ] Randomized Controlled Trials Evaluating the Effect of CPAP on BP in Patients With OSA and Resistant Hypertension

| Study/Year | No. Subjects | Age, y (SD) | BMI (SD) | AHI (SD) | BP Measure | Follow-up Duration, wk | CPAP Compliance (SD) | BP Effect, mm Hg | BP Effect Referring to Compliance, mm Hg |
|---|---|---|---|---|---|---|---|---|---|
| Lozano et al[61]/2010 | 75 | 59.2 (8.7) | 30 (4.3) | 52.67 (21.5) | ABPM | 12 | 5.6 (1.5) | SBP −6.8 | SBP −6.9[a] |
| | | | | | | | | DBP −6.9 | DBP −9.7[a] |
| Pedrosa et al[63]/2013 | 40 | 57 (2) | 36 | 36 | ABPM | 24 | 6.1 (0.2) | SBP −6.6 | … |
| | | | | | | | | DBP −4.5 | |
| Litvin et al[62]/2013 | 44 | 55.5 (9.6) | 37.7 (7.8) | 63.4 (26.3) | Office | 3 | 5.1 (1.6) | SBP −8.0 | … |
| | | | | | | | | DBP −7.6 | |
| Martínez-García et al[56]/2013 | 210 | 56.0 (9.5) | 34.1 (5.4) | 41.3 (18.7) | ABPM | 12 | 5 (1.9) | SBP −4.7 | SBP −5.4[b] |
| | | | | | | | | DBP −3.9 | DBP −4.2[b] |

ABPM = ambulatory BP monitoring; AHI = apnea-hypopnea index. See Table 1 for expansion of other abbreviations.
[a] > 5.8 h.
[b] > 4 h.

the cost effectiveness of CPAP treatment in the management of resistant hypertension in these patients.

### *Oral Appliances*

Oral appliances are a recommended treatment of patients with mild to moderate OSA. Currently, the studies that have evaluated the effects of this treatment on BP have included small patient sample sizes. In a meta-analysis of seven studies that included a total of 399 patients, Iftikhar et al[64] found that oral appliance treatment in subjects with hypertension and OSA provided a BP reduction that was similar to that achieved with CPAP. The mean changes were −2.7 mm Hg (95% CI, −8.5 to −4.6; $P = .04$) for SBP, −2.7 mm Hg (95% CI, −0.9 to −4.6; $P = .004$) for DBP, and −2.40 mm Hg (95% CI, −4.01 to −0.80; $P = .003$) for BP. An important limitation of this meta-analysis is that most of the included studies were observational. Therefore, the authors recommended that these results be confirmed by performing RCTs with large patient samples.

## Effects of Hypertension Treatment on OSA

According to the available physiopathologic knowledge of the relationship between OSA and hypertension, antihypertensive drugs that modulate sympathetic activity and the renin-angiotensin-aldosterone axis may be the best treatment options for hypertension in patients with OSA. To date, the studies that have evaluated the effects of antihypertensive drug treatment on OSA severity have included small subject samples and no comparable populations, and they have had important methodologic differences. Therefore, it is not possible to establish definitive recommendations based on the results of the available clinical studies. Previous work has evaluated β-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers and spironolactone. ACE inhibitors, such as enalapril and cilazapril,[65,66] and β-blockers, such as atenolol,[67] have been shown to control nighttime BP in patients with OSA. The classic study was conducted by Kraiczi et al,[67] who evaluated the five most commonly used antihypertensive drugs (atenolol, amlodipine, enalapril, losartan, and hydrochlorothiazide) and their effects on AHI (OSA severity). They did not detect any variations in OSA severity according to the drug used, but the study was underpowered to allow for a comparison of the drugs, and it lacked a placebo control.

Data from other studies have provided controversial results. On the one hand, some studies with very limited samples executed at single centers with short-term

follow-ups have shown an improvement in OSA severity in response to treatment with ACE inhibitors (cilazapril),[68,69] β-blockers (metoprolol, nebivolol),[69,70] and angiotensin receptor blockers (valsartan).[70] On the other hand, other studies have questioned the use of ACE inhibitors in patients with hypertension and OSA because of the side effects of these antihypertensive drugs, which may cause rhinopharyngeal inflammation and increase upper airway obstruction.[71] Additionally, β-blockers can favor weight gain, which may negatively impact the severity of OSA. Most of these negative side effects require a long period of time to become evident; thus, the short duration of follow-up in these studies could not rule out their impact on the severity of OSA. Additionally, Nerbass et al[72] reported negative effects of calcium channel blockers that shortened sleep duration.

The most promising class of antihypertensive drug treatment, based on their effects on OSA severity and BP, are diuretics,[73,74] especially spironolactone.[74] By reducing parapharyngeal edema and secondary upper airway obstruction, these drugs appear to improve OSA severity[74] and to greatly reduce BP. In conclusion, there is a need for well-designed, multicenter, large-sample studies with long follow-up periods to improve our knowledge and allow solid recommendations to be established.

## Conclusions and Future Directions

There is an epidemiologic relationship between OSA and hypertension that is especially important in subjects with resistant hypertension. Despite this, the causal relationship between OSA and hypertension is probably not as important as initially thought. Certain population characteristics, such as age, sleepiness associated with OSA, and sex, may be important in determining the role of OSA as a cause of hypertension. OSA may also lead to the development of an unfavorable circadian pattern of BP, with worse cardiovascular outcomes. In addition, some characteristics that are specifically linked to the nocturnal BP effect of sleep apnea remain to be clarified.

Meta-analyses and RCTs have reported a modest effect of CPAP on the decrease in BP of approximately 2 mm Hg in patients with OSA. The effect of CPAP is more evident in patients with resistant hypertension (a decrease of approximately 6 mm Hg). Long-term RCTs are needed to clarify the role of CPAP treatment in the clinical management of resistant hypertension. Compliance with CPAP is the key issue for the achievement of BP reduction. However, other features, such as somnolence status and BP level prior to treatment, could be relevant. The interaction between CPAP treatment, lifestyle modifications, and antihypertensive drugs and their effects on decreases in BP must be explored.

The effects on BP of oral appliances used for OSA may be similar to those of CPAP, but only a limited number of studies have investigated this topic. Finally, diuretics, particularly antialdosteronic diuretic agents, in the absence of additional data reported by clinical studies on other antihypertensive drug treatments, should be considered the first-line antihypertensive drug treatment in patients with OSA.

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