Comparison of blood pressure levels between continuous positive airway pressure-adherent and non-adherent patients with obstructive sleep apnea syndrome.

Comparación de la presión arterial entre pacientes con síndrome de apnea obstructiva del sueño con y sin apego al tratamiento con presión positiva continua en la vía aérea

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Abstract

OBJECTIVE: To compare blood pressure levels in patients with obstructive sleep apnea syndrome and hypertension, treated with continuous positive airway pressure (CPAP) devices with adequate *vs* inadequate adherence.

MATERIALS AND METHODS: An observational, analytical, retrospective, and cross-sectional study including patients 18 years of age and older with obstructive

sleep apnea syndrome by means of polysomnography and systemic arterial hypertension under pharmacological therapy and treatment with CPAP devices for at least three months.

RESULTS: There were included 513 patients with obstructive sleep apnea syndrome; systemic arterial hypertension prevalence was 61.8% (n = 317). Overall CPAP adherence was 57.1% (n = 293), and 59.3% (n = 188) within the hypertensive subgroup. Global blood pressure control (systolic ≤ 139 and diastolic ≤ 89 mmHg, optimal, normal, and normal-high categories) was observed in 71% of the population. When comparing the groups according to adherence, the group with adequate use (n = 188) showed a higher rate of blood pressure control compared to the non-adherent group (n = 129; 74% *vs* 65%); however, this difference did not reach statistical significance (p = 0.064).

CONCLUSIONS: A clinical trend towards better blood pressure control was observed in patients adherent to CPAP (74% *vs* 65%). Although this difference did not reach statistical significance, these findings suggest a potential cardiovascular benefit. However, inherent biases and unmeasured confounders limit these findings, requiring further prospective research.

KEYWORDS: Obstructive sleep apnea syndrome; Continuous positive airway pressure; Antihypertensive; Hypertension.

Resumen

OBJETIVO: Comparar los niveles de presión arterial en pacientes con síndrome de apnea obstructiva del sueño e hipertensión tratados con dispositivos de presión positiva continua en la vía aérea (CPAP) con apego adecuado e inadecuado.

MATERIALES Y MÉTODOS: Estudio observacional, analítico, retrospectivo y transversal que incluyó pacientes de 18 años de edad y mayores con síndrome de apnea obstructiva del sueño mediante polisomnografía e hipertensión arterial sistémica en tratamiento farmacológico y con dispositivos de CPAP durante al menos tres meses.

RESULTADOS: Se incluyeron 513 pacientes con síndrome de apnea obstructiva del sueño; la prevalencia de hipertensión arterial fue del 61.8% (n = 317). El apego general al tratamiento con CPAP fue del 57.1% (n = 293) y del 59.3% (n = 188) en el subgrupo de hipertensos. El control global de la presión arterial (sistólica ≤ 139 y diastólica ≤ 89 mmHg, categorías óptima, normal y normal-alta) se observó en el 71% de la población. Al comparar los grupos según el apego, el grupo con uso adecuado (n = 188) mostró mayor tasa de control de la presión arterial en comparación con el grupo sin apego (n = 129; 74 *vs* 65%); sin embargo, esta diferencia no alcanzó la significación estadística (p = 0.064).

CONCLUSIONES: Se observó una tendencia clínica hacia un mejor control de la presión arterial en los pacientes que seguían la CPAP (74 *vs* 65%). Si bien esta diferencia no alcanzó significación estadística, estos hallazgos sugieren un posible beneficio cardiovascular. Sin embargo, sesgos inherentes y factores de confusión no medidos limitan estos hallazgos, por lo que se requiere mayor investigación prospectiva.

PALABRAS CLAVE: Síndrome de apnea obstructiva del sueño; presión positiva continua en la vía aérea; antihipertensivo; hipertensión.

INTRODUCTION

Obstructive sleep apnea syndrome is characterized by repeated episodes of partial or complete blockage of the upper airway during sleep resulting in a recurring desaturation of oxyhemoglobin and sleep fragmentation.[1] Several authors consider this a significant public health problem due to its high global prevalence; studies have reported prevalences with levels ranging between 13% and 33% in males and 6% and 19% in females, it is estimated that more than a billion people worldwide between 30 and 69 years of age suffer from this condition;[1,2,3] it is an underdiagnosed disorder, secondary to the limited access to the diagnostic gold standard, polysomnography; and lastly, for the multiple health damages it provokes, among which the most notable, due to their high prevalence, are cardiovascular comorbidities, especially systemic arterial hypertension.[4,5,6]

Systemic arterial hypertension constitutes a controllable, chronic disease of a multifactorial etiology, characterized by sustained systolic arterial pressure numbers above 140 mmHg and/or diastolic arterial pressure equal to or above 90 mmHg.[7] As with obstructive sleep apnea syndrome, systemic arterial hypertension represents a major health problem (prevalence at 32.3% worldwide, 39.1% in Mexico) whose long-term negative outcomes result in high costs for the healthcare system.[4,7] Systemic arterial hypertension is the most common modifiable risk factor of cardiovascular disease and death. In our country, it has been estimated that

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close to 25.5 million people older than 19 years of age suffer from systemic arterial hypertension, of which 40% are not aware that they suffer from it, and of the 60% who know they dohe, as in other reports, only 50% adhere to the treatment and approximately half of these are under control <140/90 mmHg.[7-11]

The coexistence of both diseases is highly prevalent, in fact, the independent causal role of obstructive sleep apnea syndrome in the development of systemic arterial hypertension has been described. It is estimated that around 50% of patients with obstructive sleep apnea syndrome have systemic arterial hypertension, between 30% and 40% of hypertensive patients suffer from obstructive sleep apnea syndrome, and more than 80% of patients with resistant hypertension (high arterial pressure with the use of three antihypertensive drugs or the need to take at least four drugs to control arterial pressure) suffer from obstructive sleep apnea syndrome. Other authors have described the correlation between the severity of obstructive sleep apnea syndrome and the prevalence of systemic arterial hypertension, with reports of 59%, 62% and 67% in mild, moderate and severe obstructive sleep apnea syndrome, respectively.[2,4,12,13]

The repeated ventilatory pauses characteristic of obstructive sleep apnea syndrome cause intermittent periods of hypoxia-reoxygenation, with the subsequent release of reactive species of oxygen and the decrease in the antioxidative response mechanisms, leading to oxidative stress, which affects cellular components and functions due to the damage at the molecular level to proteins, lipids, carbohydrates and deoxyribonucleic acid, resulting in cell death. The reactive oxygen species cause the activation of multiple cellular signaling pathways which activate nuclear transcription factors, such as the nuclear transcription factor kappa B (NF-κB), which is activated and enters the inflammatory cell nucleus, increasing the production of proinflammatory cytokines, such as C-reactive protein, anti-tumor necrosis factor-α and interleukins 6 and 8 , in addition to increasing the production of cell adhesion molecules and adipokines, causing a state of low grade chronic systemic inflammation, and promoting the sympathetic and vagal activation.[2,12] The increased sympathetic activation (noradrenergic activity), also promoted by the arousals and sleep fragmentation present in obstructive sleep apnea syndrome, stimulates the renin-angiotensin-aldosterone system, thus increasing the blood levels of endothelin 1, angiotensin II and aldosterone.

Angiotensin II is a potent vasoconstrictor which plays a part in arterial pressure regulation, a function that also takes place through the stimulation of aldosterone adrenal secretion. Patients with obstructive sleep apnea syndrome show elevated angiotensin II and aldosterone levels, which cause a loss of the normal heart rate in the arterial blood regulation and a lack of response to antihypertensives, hence these patients require the 24-hour monitoring of pressure values in order to identify nocturnal hypertension and non-dipper patterns. The elevation of reactive oxygen species and the increased expression of adhesion molecules and inflammatory cytokines mitigate nitric oxide release and activity, provoking endothelial dysfunction (an essential organ in vascular tone control) with muscular relaxation disruption, hypercoagulability, platelet aggregation and formation of atherosclerosis plaques. In addition, obstructive sleep apnea syndrome also causes changes in intrathoracic pressure, which decreases to -30 cmH_2O when inhaling through an obstructed or collapsed pharynx, thus resulting in an increase in left ventricular afterload, which leads to left ventricular disfunction, a decrease in systolic ejection fraction and cardiac output.[2,12,14]

Obstructive sleep apnea syndrome treatment is multidisciplinary, and the existing therapeutic alternatives are not mutually exclusive. They include lifestyle modifications, weight

control, drugs for the improvement of the upper respiratory airways, oral devices and surgical procedures. However, treatment with continuous positive airway pressure devices is the first-line therapy representing the gold standard and any alternative treatments proposed as useful in obstructive sleep apnea syndrome management should be compared to it, due to its efficacy and disease reversibility.[15,16,17]

The treatment with the above mentioned devices reduces mortality and improves quality of life as it contributes to controlling the comorbidities related to the syndrome. Evidence in developed countries suggests that their use decreases the risk of developing systemic arterial hypertension, and it has been shown that they exert a hypotensive effect, especially in controlling resistant hypertension with a significant impact, since the average reduction in the abovementioned population is 5 mmHg in systolic and diastolic pressure. Said hypotensive effect shows a dose-response relationship, related to the time (> 3 months) and hours of use, that is, it is closely related to adherence (use equal to or longer than 4 hours every night for at least 70% of nights);[4,18-21] 8% to 15% of patients reject continuous positive airway pressure (CPAP) treatment on the first night and 50% abandon treatment after the first year of use (range, 28 to 83%). The reported adherence rate is low, around 34% to 56%, hence treatment discontinuation constitutes a global problem. Non-adherence to CPAP devices has been attributed to disease severity, side effects of their use (leakage, skin irritation, conjunctivitis, nasal congestion, pharyngeal dryness and claustrophobia), psychological factors, and the sociodemographic and economic characteristics of treated patients.[17,19-22]

Available evidence stems from trials conducted in populations with distinct characteristics from our own; thus, the current state of the art warrants studies in local contexts to evaluate long-term health outcomes.[23] Therefore, this research aims to determine the prevalence of hypertension in patients with obstructive sleep apnea syndrome and assess objective continuous positive airway pressure adherence via microprocessor readings, analyzing the relationship between adherence levels and blood pressure control in patients under conventional clinical follow-up.

MATERIALS AND METHODS

An observational, retrospective, and cross-sectional study including patients from the Sleep Clinic database of a third-level hospital in México City. Inclusion criteria were: diagnosis of obstructive sleep apnea syndrome of any severity (confirmed by polysomnography), comorbid systemic arterial hypertension, under pharmacological treatment, and continuous positive airway pressure (CPAP) use for at least three months. Study variables were identified, and the obtained information was analyzed by means of the Statistical Package for the Social Sciences version 29 statistical software. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The prevalence of systemic arterial hypertension was determined and CPAP adherence rates based on objective microprocessor reports, sociodemographic characteristics (gender, age, marital status, education and socioeconomic level) and obstructive sleep apnea syndrome severity distribution were described, the relationship between clinical/sociodemographic characteristics and CPAP adherence was analyzed. Finally, we compared blood pressure control between adherent and non-adherent groups. Blood pressure was categorized based on the average of the last three clinical measurements, these measurements were taken under a standardized protocol, by medical and nursing staff, with the patient seated and resting for 5 minutes, using a classification scale of systemic arterial hypertension, which establishes

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seven categories: Optimal, systolic < 120 and diastolic < 80 mmHg. Normal, systolic 120-129 and diastolic 80-84 mmHg; normal high, systolic 130-139 and diastolic 85-89 mmHg; hypertension grade 1 or mild, systolic 140-159 and diastolic 90-99 mmHg; hypertension grade 2 or moderate, systolic 160-179 and diastolic 100-109 mmHg; hypertension grade 3 or severe, systolic 180 and diastolic 110 mmHg; and isolated systolic hypertension, systolic 140 and diastolic < 90 mmHg;[3] for analysis purposes, controlled blood pressure was defined as falling within the optimal, normal, or normal-high categories (≤ 139/89 mmHg), while the remaining categories were considered uncontrolled.

RESULTS

A total of 513 patients with obstructive sleep apnea syndrome were included, the prevalence of systemic arterial hypertension was 61.8% (n = 317). Overall continuous positive airway pressure (CPAP) adherence, based on microprocessor readings, was 57.1% (n = 293) for the total sample and 59.3% (n = 188) within the hypertensive subgroup.

The sample was predominantly female (59.9%, n = 190) and showed a non-normal distribution, with a median age of 67 years interquartile range (IQR): 62-74. Age group distribution by gender revealed that 1.3% were in the group of patients younger than 50 years of age; 38.5% in the group of 51 to 65 years of age; and 60.3% were older than 65 years of age. For the first group, frequency by gender was 0% in females and 3.1% in males; for the second group, 32.6% in females and 47.2% in males; and for the third group of patients older than 65 years of age the frequency by gender was 67.4% in females and 49.6% in males, reaching statistical significance (p = 0.001).

Two hundred sixty-five participants (83.6%) had a sentimental partner, while 52 (16.4%) were single at the time of the study. Education levels were as follows: primary school, 36.6% (n = 116); 18.6% (n = 59), secondary school; 23% (n = 73), high school; 13.2% (n = 42) had a graduate degree; 6.6% (n = 21) had a postgraduate degree; and 1.9% (n = 6) of participants were illiterate. As regards socioeconomic level, 70.7% (n = 224) pertain to the middle class; 1.3% (n = 4) to the lower middle class; 22.4% (n = 71) to the upper middle class; and 5.7% (n = 18) to the upper class.

In terms of obstructive sleep apnea syndrome severity, 72.9% (n = 231) presented severe disease (apnea-hypopnea index > 30/h), followed by moderate (14.5%) and mild (12.6%) grades.

Statistical analysis showed significant associations between CPAP adherence and several factors: male gender (p = 0.024), age group older than 65 years (p = 0.050), severe obstructive sleep apnea syndrome (p = 0.005), and higher educational level (p = 0.045). Socioeconomic level showed a borderline association (p = 0.053).

As shown in **Table 1**, overall blood pressure control (optimal, normal, and normal-high categories) was achieved by 71% of the hypertensive population (n = 225). When comparing groups by adherence (**Table 2**), the adherent group showed a higher percentage of blood pressure control than the non-adherent group (74% *vs* 65%, respectively); however, this difference was not statistically significant (p = 0.064).

DISCUSSION

The prevalence of systemic arterial hypertension in patients with obstructive sleep apnea syndrome was estimated at 61.8%, which is higher than the 50% reported in international

Table 1. Blood pressure classification according to its level of control

Categories		Frequency	Percentage	Valid percentage	Cumulative percentage
Controlled arterial hypertension	Optimal	59	18.6	18.6	18.6
	Normal	82	25.9	25.9	44.5
	Normal-high	84	26.5	26.5	71.0
Uncontrolled arterial hypertension	AHT 1	27	8.5	8.5	79.5
	AHT 2	6	1.9	1.9	81.4
	AHT 3	1	.3	.3	81.7
	Isolated systolic	58	18.3	18.3	100
	Total	317	100	100	

In the hypertensive subgroup (n = 317), optimal 18.6%, normal 25.9%, normal high 26.5%, AHT 1 (hypertension grade 1), 8.5%, AHT 2 (hypertension grade 2), 1.9%, AHT 3 (hypertension grade 3) 0.3%, isolated systolic 18.3%.

Table 2. Comparison of blood pressure in patients adherent and non-adherent to continuous positive airway pressure

Categories	Adherence		Total
	No	Yes	
Optimal, n (%)	19 (32.2)	40 (67.8)	59 (100)
Normal, n (%)	38 (46.3)	44 (53.7)	82 (100)
Normal high, n (%)	28 (33.3)	56 (66.7)	84 (100)
AHT 1, n (%)	11 (40.7)	16 (59.3)	27 (100)
AHT 2, n (%)	5 (83.3)	1 (16.7)	6 (100)
AHT 3, n (%)	1	0	1 (100)
Isolated systolic, n (%)	27 (46.6)	31 (53.4)	58 (100)
Total, n (%)	129 (40.7)	188 (59.3)	317 (100)

The adherent group showed a higher percentage of blood pressure control than the non-adherent group (74% *vs* 65%): p = 0.064.
AHT: hypertension grade.

literature. This figure doubles the global prevalence of systemic arterial hypertension (32.3%) and significantly exceeds the 39.1% reported for the general population in our country.[2,4,7,12,13] Regarding treatment, the objective CPAP adherence rate was 57.1% (n = 293) for the total sample and 59.3% (n = 188) within the hypertensive subgroup, slightly above the 34%-56% range reported by other authors.[17,19-22]

In contrast with other reports, our sample was predominantly female (59.9%); median age was 67 years old, with an IQR 62-74 years old, 1.3% were patients younger than 50 years of age, 38.5% were between 51 and 65 years old and 60.3% were older than 65 years of age, which confirms the data described in other publications that sustain that this condition is more frequent at age 65 years and older.[2,12,19] In the first and second age groups, the proportion by

gender was greater for males, while in patients older than 65 years of age the proportion was inverted, the syndrome being more prevalent in females, which confirms what other series have reported, that the incidence increases in females after menopause.[2,12]

Furthermore, severe obstructive sleep apnea syndrome was the most frequent grade (72.9%), consistent with findings by Serrano et al., who reported a 70% prevalence of severe obstructive sleep apnea syndrome in a similar national population.[6]

Male gender, age > 65 years, higher educational and socioeconomic levels, and severe obstructive sleep apnea syndrome were clinical and sociodemographic factors significantly associated with higher CPAP adherence ($p < 0.05$), which supports the findings published in other reports and the need for targeted education and support strategies to improve adherence in less-compliant subgroups.[17,19-22]

Finally, 71% of our population achieved blood pressure control (< 140/90 mmHg), substantially surpassing the control rates reported for the general hypertensive population in our country (approximately 50%).[7,10,11] Although the difference between adherent and non-adherent groups reached a p value of 0.064, the high overall control rate and the 9% gap suggest that adequate CPAP adherence plays a clinically relevant role in blood pressure management within a conventional clinical follow-up setting. However, the authors acknowledge that this study has limitations inherent to its retrospective design, such as the inability to evaluate key confounding variables that could influence blood pressure control. Factors including BMI, specific antihypertensive medication types, and pharmacological treatment adherence, among others, were not measured. This limits the interpretation of the isolated impact of CPAP and suggests the need for future prospective studies.

CONCLUSIONS

This research represents one of the first studies in our country to objectively analyze the prevalence of hypertension and continuous positive airway pressure (CPAP) adherence rates through microprocessor readings in patients with obstructive sleep apnea syndrome, as well as their relationship with blood pressure control. Seventy-one percent of the patients showed blood pressure control, a figure superior to the 50% reported for the general hypertensive population in Mexico. A clinical trend toward better blood pressure control was observed in CPAP-adherent obstructive sleep apnea syndrome patients. Although the difference was not statistically significant ($p = 0.064$), the 9% margin suggests a benefit of treatment that could be confirmed through prospective studies with greater variable control to verify the isolated impact of CPAP on hypertension control within our population.

STATEMENTS

Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee (Research Committee of the Naval Medical Center, Mexico City, COFEPRIS registration number 20 CI 09 003 026), and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

For this retrospective study formal consent is not required.

Data availability

The authors confirm to have included a data availability statement in the main manuscript file.

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