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Sleep apnea in patients with primary chronic headache

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ABSTRACT

Introduction. Sleep apnea syndrome (SAS) can accompany patients with chronic primary headache (CPH), being a frequent cause of persistence of symptoms in these patients, however, the data studying this disorder in patients with CPH are still limited.

Objective. To determine the frequency of SAS in patients with CPH.

Methods. A retrospective cohort was analyzed in patients with a diagnosis of CPH in a third level hospital. CPH was diagnosed according to the criteria of the International Headache Society and SAS with a polysomnographic record with an apnea-hypopnea index (AHI) >5/h, the frequency of SAS was determined among the total number of patients with AHI >5/h over the total number of patients undergoing polysomnography.

Results. A total of 114 subjects were included, where the SAS in CPH was 83.3%, of which 56.8% were men and 60% older than 50 years; 89% of the population had a body mass index (BMI) greater than 27 kg/m^2. Fatigue and sleepiness during the day were the most frequent symptoms, reported in 89.5% of the population with SAS compared to 47.4% of the population without a diagnosis of SAS.

Conclusion. Sleep apnea is a frequent condition in patients with CPH undergoing polysomnography, mainly overweight men over 50 years of age. The main associated symptoms are fatigue and sleepiness.

Keywords: headache, sleep apnea, signs and symptoms, polysomnography, prevalence

INTRODUCTION

Chronic primary headache (CPH) is a public health problem and one of the main reasons for outpatient consultation, it is highly frequent, with its prevalence between 3% and 5% of the population worldwide [1,2]. Only a third of the patients respond to standard analgesic measures, requiring a multidisciplinary approach and the study of multiple etiologies for its management, including sleep apnea syndrome (SAS). SAS is one of the most frequent conditions that can accompany the symptoms of a CPH [2]. An important relationship has been seen between sleep disorders and headache, since multiple pathophysiological alterations that can occur in SAS can trigger headache. Hypercapnia, impaired autoregulation of cerebral blood flow, transitory increases in intracranial pressure, hypoxemia during sleep, and microarousals that patients with SAS present independently lead to headache, which if not diagnosed and treated adequately can evolve into a chronic disorder [3–5].

KoÇ et al. described, in a cohort of 648 patients diagnosed with SAS, headache episodes associated with a higher apnea-hypopnea index (AHI) [6]. Kristiansen et al reported a prevalence of headache of 11.6% in patients with an AHI ≥ 15 and 13.3% with an AHI ≥ 30 [7]. In addition, the relationship between the severity of the SAS and the presence of headache, this symptom may also be the only manifestation of the SAS. Between 18 and 41% of patients

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with SAS can present CPH [2], usually in the morning, bilateral, duration less than 4 hours, which tends to be chronic (greater than 15 days a month) and is refractory to medical management [3,8–10]. Positive pressure treatment of SAS significantly improves the CPH associated with this syndrome, and complete pain relief is even reported in two-thirds of patients with this condition [9].

CPH and SAS are highly prevalent diseases [3,11,12] but data describing the presence of SAS in patients with CPH remain limited. Knowing the prevalence in a population of patients with chronic headache could be aimed at how relevant the polysomnographic study is for the diagnosis of SAS. The objective of this study is to determine the frequency of SAS in a population of patients with CPH undergoing polysomnography.

METHODS

Retrospective cohort study in patients who attended the neurology outpatient clinic of a third level hospital in Bogotá, Colombia with a diagnosis of CPH between 2014 and 2017. The patients who entered the study answered questions about symptoms of SAS and chronic headache, and were later taken to basal polysomnography.

Eligibility criteria

Patients older than 18 years who fulfilled the clinical diagnostic criteria of the *International Headache Society* of CPH were included [4]. That is headache that occurs on more than 15 days a month for more than 3 months, and without structural alteration of the skull studied by diagnostic images. Pregnant women, patients with a diagnosis of psychiatric disease, patients with disorders of cognitive compromise, comprehensive or expressive language that prevent obtaining information, and patients with secondary headache or with alarm criteria were excluded.

Variables

Demographic characteristics such as age, gender, weight, height, neck circumference, place of origin, education, and area of performance in the armed forces were evaluated. Additionally, the characteristics of headache, AHI, and maximum and minimum saturation during polysomnography were evaluated. Data was collected by trained personnel verifying clinical records, and data review was performed by two investigators to avoid possible transcription errors. All subjects with CPH undergoing polysomnography during the study period were entered sequentially.

Statistical analysis

The data was collected in an Excel spreadsheet to later be analyzed in a licensed program SPSS V.25. For the description of the qualitative variables, absolute frequencies and percentages were used; for the quantitative ones, means, standard deviations, medians and interquartile ranges according to the normality of the data distribution determined with the Shapiro-Wilks test. The prevalence of sleep apnea was determined with the total number of subjects with AHI greater than 5 over the total population with CPH undergoing polysomnography. Additionally, a comparison was made between qualitative variables with the chi-square test and quantitative variables with Student's t or Mann-Whitney U according to their distribution between subjects with and without sleep apnea. A significance level of $p < 0.05$ was considered.

Ethical aspects

The development of this study was adjusted to the principles indicated in the Declaration of Helsinki, of the World Medical Association, the Belmont Report and the Colombian regulations established by Resolution 8430 of 1993. The study protocol was reviewed and approved by the ethics and research committee of the Central Military Hospital. All the participants included in the study signed the informed consent.

RESULTS

During the study period, a total of 114 subjects were admitted. The prevalence of SAS observed among patients with CPH was 83.3% (95/114) and it was observed that more than half of the population studied was older than 50 years. The proportion of men was 56.8% in the group with SAS versus 63.2% in patients without a diagnosis of SAS. Table 1 shows the characteristics of the population of subjects who entered the study.

89% of the population presented a body mass index (BMI) outside normal limits, with 47% being obese. The distribution of mean BMI is similar between the groups with and without apnea. The mean BMI of all patients was 29.8 Kg/m^2 (SD ± 5.1), and the average neck circumference of all patients was 39.2 cm (SD ± 2.64), for the SAS group the average was 39.3cm (SD ± 2.7) and in the group without SAS it was 38.7cm (SD ± 2.3).

Fatigue and sleepiness during the day were the most frequent symptoms, reported in 82.5% of the total population; these symptoms were found in 89.5% of the population with SAS compared to 47.4% of the population without a diagnosis of SAS. Fatigue and sleepiness were more frequent than snoring,

TABLE 1. Demographic characteristics of the total population

	Total population n=114	Sleep apnea n=95	Without sleep apnea n=19	P-Value
Age in years x (sd)	54,7 (15,15)	55,7 (15,57)	49,6 (11,94)	0,609
Over 50 years of age n (%)	64 (56,1)	57 (60,0)	7 (36,8)	0,063
Male sex n (%)	66 (57,8)	54 (56,8)	12 (63,1)	0,611
Weight in Kg x (sd)	81,5 (14,22)	81,6 (14,02)	80,8 (15,55)	0,941
Size in m x (sd)	1,66 (0,1)	1,7 (0,1)	1,7 (0,11)	0,965
BMI Kg/m^2 x (sd)	29,8 (5,1)	29,9 (4,92)	29,5 (6,08)	0,934
Neck circumference cm x (sd)	39,2 (2,64)	39,3 (2,69)	38,7 (2,33)	0,934
Neck circumference > 40 cm n (%)	53 (46,4)	49 (51,5)	4 (21,0)	0,015
Place of origin n(%)				
Urban	109 (95,6)	93 (97,8)	16 (84,2)	<0,001
Rural	10 (4,3)	4 (2,1)	6 (15,7)	
User quality n(%)				
Military	21 (18,4)	14 (14,7)	7 (36,8)	0,063
Retired	28 (24,5)	24 (25,2)	4 (21,0)	
Beneficiary	38 (33,3)	36 (37,8)	2 (10,5)	
Pensioner	25 (21,9)	19 (20,0)	6 (31,5)	
Other	2 (1,7)	2 (2,1)	0 (0)	
Schooling n(%)				
Primary	11 (9,6)	10 (10,5)	1 (5,2)	0,192
Secondary	37 (32,4)	34 (35,7)	3 (15,7)	
Technical	27 (23,6)	22 (23,1)	5 (26,3)	
University	39 (34,2)	29 (30,5)	10 (52,6)	
Force n(%)				
Army	81 (71,0)	67 (70,5)	14 (73,6)	0,851
Navy	18 (15,7)	14 (14,7)	4 (21,0)	
Air Force	10 (8,7)	10 (10,5)	0 (0)	
Other	5 (4,3)	4 (4,2)	1 (5,2)	

Notes: sd, standard deviation; kg, kilogram; m^2, square meter; BMI, body mass index; cm, centimeters

which was reported in only 57% of the total population.

Regarding the clinical characteristics of headache, it is observed that less than half of the patients studied (49,1%) reported having presented between 5-10 episodes of pain randomly; additionally, it was evidenced that 66.7% of the patients reported the intensity of the headache as moderate. Table 2 shows

TABLE 2. Characteristics and treatment of headache

Variables	Total population n=114	Sleep apnea n=95	Without sleep apnea n=19	P-Value
Pain frequency n(%)				
Least 5 episodes	36 (31,58)	28 (29,47)	8 (42,11)	0,203
5 to 10 episodes	56 (49,12)	46 (48,42)	10 (52,63)	
More than 10 episodes	22 (19,3)	21 (22,11)	1 (5,26)	
Intensity n(%)				
Mild	23 (20,18)	18 (18,95)	5 (26,32)	0,336
Moderate	76 (66,67)	66 (69,47)	10 (52,63)	
Severe	15 (13,16)	11 (11,58)	4 (21,05)	
Duration in hours n(%)				
Less than 1	28 (24,56)	20 (21,05)	8 (42,11)	0,080
Between 1-4	61 (53,51)	53 (55,79)	8 (42,11)	
Between 5-12	23 (20,18)	20 (21,05)	3 (15,79)	
More than 12	2 (1,75)	2 (2,11)	0 (0)	
Time of day n(%)				
Tomorrow	42 (36,84)	38 (40)	4 (21,05)	0,001
Afternoon	11 (9,65)	5 (5,26)	6 (31,58)	
Evening	8 (7,02)	7 (7,37)	1 (5,26)	
Any time	53 (46,49)	45 (47,37)	8 (42,11)	

TABLE 3. Tests to confirm the diagnosis of sleep apnea-hypopnea syndrome

Variables	Total population n=114	Sleep apnea n=95	Without sleep apnea n=19	P-Value
AHI x(sd)	23,5 (17,91)	27,8 (16,56)	2,1 (1,39)	<0,001
Minimum oxygen saturation x(sd)	75 (9,85)	72,8 (9,31)	85,8 (2,59)	0,001
Maximum oxygen saturation x(sd)	89,5 (3,83)	88,6 (3,37)	93,9 (2,7)	0,005
Polysomnogram result n(%)				
Mild 5-15 events/hour	26 (22,8)	26 (27,3)	0 (0)	<0,001
Moderate 15-30 events/hour	35 (30,7)	35 (36,8)	0 (0)	
Severe more than 30 events/hour	34 (29,8)	34 (35,7)	0 (0)	
No SAS	19 (16,6)	0 (0)	19 (100)	

Notes: AHI, apnea-hypopnea index; sd, standard deviation; SAS, Sleep apnea syndrome

the clinical characteristics of the patients with headache who underwent polysomnography.

Among the different states of severity of sleep apnea, moderate SAS (15-30 events/hour) was the most frequent, Table 3 shows the results of the polysomnography of the patients with CPH.

DISCUSSION

In this study, a high prevalence of SAS diagnosed by polysomnography was obtained in subjects with a previous diagnosis of CPH, Male patients older than 50 years is the population group with the highest frequency of SAS; being overweight is the most common physical finding in patients with SAS and CPH; fatigue and sleepiness as the most common clinical symptoms among the patients studied.

In the present study, the prevalence of SAS was higher than the reported in the literature by Graff-Radford et al, in whose study of 31 patients found that 80.6% of subjects with cluster headache had an index of respiratory disturbances more than 5/hour [13]; and Nobre, 31.3% of patients with this type of headache had SAS (AHI more than 5/hour) [14]; in patients with chronic headache (more than 2 years of evolution) of any etiology, the prevalence of SAS has been reported between 1.5 and 11.8% [3,7] and in patients with headache refractory to analgesic management 29.2% [15]; which suggests that SAS is a common finding in patients with CPH [3,7,13,14]. Additionally, a possible relationship has been found between cluster headache attacks and nighttime desaturation episodes that patients with SAS may present [16], which may lead one to think that the use of positive pressure may be a management alternative in this population [9,15,17].

SAS has been found to be related to age and male sex [18–20], Hoch et al found a gradual increase in the prevalence of sleep-disordered breathing with each decade of life. In the 60s, SAS was found in 2.9%, in the 70s the 33.3% and in people older than 80 years, in 39.5% [21], being from the age of 65 the age where there is the greatest increase in the frequency of sleep apnea and associated respiratory disorders [22]. SAS is also common in men, in a court of 602 subjects older than 30 years, sleep apnea occurred in 24% of men versus 9% of women [20], in our study we found that men over 50 years of age with CPH had a higher frequency of SAS, possibly due to the epidemiological behavior of this disease. The female sex, on the contrary, has a decrease in the frequency of SAS but a higher frequency of chronic headache [23].

Overweight was a frequent finding in the patients evaluated in our study. There is information that overweight can be associated with CPH and SAS [18,19,23,24]; Jahromi et al. describe that overweight and obesity can be related to CPH, among the pathophysiological mechanisms described for this possible association is the persistent inflammatory state and the alteration in hypothalamic regulation that is generated with weight gain and that can influence the persistence of headache symptoms; elevated levels of C-reactive protein have been found in obese and migraine patients [24]. Scher et al. in a case-control study who followed up for 1 year, found that 3% of subjects with episodic headache progressed to CPH, and determined that one of the risk factors for progression was obesity and predominantly overweight [25,26]. Additionally, SAS and obesity are related to multiple comorbidities, this being a situation to take into account for the management of these patients [18,19,27].

The most common symptom of patients with SAS is daytime sleepiness, which is generally reported to be above 50% [28,29], however, this symptom is often accompanied by fatigue, lack of energy, and tiredness. Chervin reports that these symptoms occur in 18%, 40% and 20% respectively [30]. In our study, sleepiness and fatigue continued to be the most frequent symptoms in patients undergoing polysomnography, which may further complicate the symptoms of patients with CPH; these patients tend to be polysymptomatic and most likely polymedicated [28,30]. The above symptoms must be taken into account when studying a patient with

CPH, since they may be the first clinical manifestation of SAS.

Among the limitations of this study is its retrospective nature, which increases the risk of information slant, however, the team that obtained the data from the clinical records has training and medical knowledge to obtain the information. The number of subjects obtained provides information for a good description of the population, however, it is limited for bivariate or multivariate analyses. CPH of multiple etiologies was studied without specifying the frequency of SAS for each type of CPH. It would be important in future studies to delve into the possible associations between SAS and CPH and the impact of positive pressure treatment on the control of CPH.

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Studies like this one opens the door to new questions such as the screening of SAS in all patients with chronic headaches that are difficult to manage. High-quality, low-cost studies should assess the ability of health personnel to interpret these results and effectively refer patients to higher levels of complexity or specialized centers for these disorders.

CONCLUSION

Sleep apnea is a frequent condition in patients with CPH undergoing polysomnography, mainly overweight men over 50 years of age, with fatigue and sleepiness being the main associated symptoms.

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