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Article

Obstructive Sleep Apnea Syndrome and Type II Diabetes Mellitus in the Elderly

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Abstract: Older people with sleep disturbances also have other chronic pathologies that may interfere with these disturbances. One of the comorbidities that is frequently present is type II diabetes. **Objetives:** This research aims to find out whether type 2 diabetes mellitus present in elderly people affects the level of severity of obstructive sleep apnoea syndrome (OSAS). **Methods:** Cross-sectional descriptive study, with a sample of 75 elderly people who attended the Sleep Unit of Doctor Sagaz Hospital in Jaen to be diagnosed with OSAS, and classified according to severity. **Results:** Significant differences were obtained in the severity of OSAHS between the participants who had type II diabetes mellitus and those who did not, with the former showing higher scores ($U=326$, $p=0.02$). **Conclusions:** Therefore, the presence of type 2 diabetes in the elderly in our study was associated with more severe OSA. The main discrepancies when comparing this research with other studies result from the lack of research addressing these variables in this population group, as well as from the great heterogeneity of methods and techniques used in the different studies (different sample sizes, age range of the population, and diagnostic methods used), causing great variability in the results found. Given the findings obtained in this research, we hope to contribute to future translational research and improve the quality of life of this population.

Keywords: OSA; type II diabetes; elderly; sleep

1. Introduction

Obstructive Sleep Apnoea Syndrome (OSAS) is characterised by recurrent episodes of upper airway collapse during sleep, resulting in apnoea (airflow blocked for at least 10 seconds) and hypopnoea (decreased airflow by 50% associated with oxygen desaturation) associated with daytime symptoms, particularly excessive sleepiness. OSAS is a highly prevalent and often unrecognised disease in the elderly with important cardiovascular and metabolic consequences. Severely affected patients experience more than 30 apnoeas per hour, with repeated hypoxia, and altered sleep architecture characterised by frequent awakenings and increased respiratory effort. The main treatment used to manage OSAS is continuous positive airway pressure or CPAP, which is a non-invasive device that helps regulate upper airway pressures during sleep. The gold standard for diagnosing OSAS is a polysomnography (PSG) study performed in a sleep laboratory [1].

Another highly prevalent disease is diabetes, which is a chronic disease caused by impaired glucose metabolism. Due to high morbidity and mortality, diabetes is considered a public health problem that severely affects the quality of life of patients. The latest estimates show that the global prevalence of type 2 diabetes is 382 million (8.3 %), and it is expected to increase to 592 million (10.1 %) by 2035 [2]. The reasons for this growth include the ageing of the population and improved diagnostic standards [3].

OSA and type 2 diabetes are comorbidities with important clinical, epidemiological and public health implications. Studies over the past 20 years suggest that OSAS, through the effects of intermittent hypoxaemia, elevated sympathetic nervous activity, sleep fragmentation, and low

amounts of slow wave sleep, may contribute to the development of insulin resistance, glucose intolerance and type 2 diabetes [1,4–7].

Regarding the severity of OSAS, a recent prospective population-based study with a 4-year follow-up period found that the presence of moderate to severe OSAS is an important risk factor for developing incident diabetes. Furthermore, dysregulation of the hypothalamic-pituitary-adrenal axis in patients with severe OSAS has also been described as an additional factor in metabolic disturbances [8]. Moreover, type 2 diabetes may increase susceptibility or accelerate the progression of OSAS severity, possibly through the development of peripheral neuropathy and abnormal neural control of ventilation and upper airways [3,9].

The prevalence of OSAS in patients with type 2 diabetes is in the range of 50-80% [9]. As known and highly prevalent pathologies, OSAS and type 2 diabetes share similar risk factors, such as advanced age, visceral adiposity and obesity, thus some patients present both pathologies simultaneously [2,3]. The prevalence of OSA in people over 65 years of age with diabetes mellitus is 60% [10].

In older people, there is a lack of scientific evidence to corroborate the relationship between these two variables. Older people, compared to younger adults, have more recurrent and intermittent hypoxia, a higher frequency of spontaneous arousal (lower threshold for stimulation) and decreased upper airway muscle reflexes to negative pressure [9,11]. The occurrence of OSAS with age may be due to the four physiological factors considered important in the pathogenesis of OSAS, such as: poor upper airway anatomy (highly collapsible airways), ineffective upper airway dilator muscle activity, a low respiratory activation threshold or an unstable ventilatory control system. These factors, which can occur in the normal ageing process in healthy individuals, suggest that OSAS may be caused by different mechanisms in older and younger individuals [11].

Although further research is needed to elucidate the mechanisms underlying the bidirectional association between these two disorders, their frequent coexistence should prompt the adoption, in the clinical practice, of screening for a patient presenting with one disorder or the other. Early detection of OSA in patients with type 2 diabetes and screening for metabolic abnormalities in patients with OSA may reduce the risk of cardiovascular disease, and improve the quality of life of people with these chronic diseases [4].

Therefore, the present research aims to determine whether type 2 diabetes mellitus present in elderly people affects the level of severity of obstructive sleep apnoea syndrome, expecting to find that elderly people with type 2 diabetes mellitus will have a higher degree of OSAS.

2. Materials and Methods

2.1. Design

The study was designed as a cross-sectional study.

2.2. Sample and Setting

The inclusion criteria used for people to take part in this research were: People over 65 years of age, diagnosed with OSA through conventional polysomnography (PSG) and with their own AHI, which indicates the severity of the disease, treated at the Sleep Unit of Doctor Sagaz University Hospital, in the province of Jaen. The participants included in this study signed the informed consent form before the beginning of the study.

2.3. Data Collection

The diagnosis of type 2 diabetes mellitus was made by obtaining data from the Andalusian Health Service, by means of the standardised test of glycosylated haemoglobin fraction (HbA1c) $\geq 6.5\%$. This parameter was determined from blood samples collected from the participants after a fasting period of no less than 8 hours, or through plasma glucose, two hours after performing the oral tolerance test, where a figure equal to or higher than 200 mg/dL was considered hyperglycaemia [12].

OSAS was defined through the PSG test, which considers neurophysiological and cardiorespiratory variables, and provides the AHI that determined the severity of the disease. When the person suffers 5-15 apnoeas and hypopnoeas/hour, it is considered mild apnoea; when 16-29 apnoeas and hypopnoeas/hour are obtained, it is considered moderate apnoea; and if more than 30 apnoeas and hypopnoeas/hour are obtained, it is considered severe apnoea [13,14].

The variables that could affect the results, based on biological plausibility and previous literature, were age and sex, which were obtained from the medical history. Another variable taken into account was the Body Mass Index (BMI), which was obtained using a scale and a measuring tape, and calculated through the mathematical formula kg/m^2 . BMI was classified as: $<18.4 \text{ kg/m}^2$ underweight; $18.5\text{-}24.9 \text{ kg/m}^2$, normal weight; $25\text{-}29.9 \text{ kg/m}^2$, overweight; and $>30 \text{ kg/m}^2$ obesity [15].

The patients' data were collected when they attended the Sleep Unit of Doctor Sagaz Hospital, in the period between January 1st 2019 and December 31st 2019. These patients attended the unit to review their CPAP treatment or to be diagnosed with OSA, and the level of severity of the disease was established through the Apnoea and Hypopnoea Index (AHI) obtained by PSG.

The results were classified according to the degree of severity of OSA presented by the participant: mild OSA, moderate OSA, severe OSA, or no OSA (when AHI was under 5 apnoeas-hypopnoeas/hour), and the presence or absence of a diagnosis of type 2 diabetes mellitus.

2.4. Statistical Analysis

Firstly, a descriptive analysis of the different variables considered in the study was carried out. In the case of qualitative variables, frequencies were used, and for quantitative variables, measures of central tendency (mean or median, depending on whether or not the distribution of the variables was normal) and dispersion (standard deviation or range) were calculated.

The normality of the distribution of the variables was assessed using the Kolmogorov-Smirnov test (with Lilliefors correction). Since the assumption of normality was not met, non-parametric tests were used.

Analyses were performed with SPSS statistical package version 23. A significance level of 5% was used for all tests.

All data generated or analysed during this study are included in the published article.

2.5. Ethical Considerations

Older people were informed about the purpose of the study, and the data we would extract from their medical history. Those who agreed to participate would become part of the research after reading and signing the informed consent form (LOD2018).

3. Results

The total sample consisted of 75 people, of whom 33 (44%) were women and 42 (56%) were men. The mean age was 71.27 years and the median age was 72 years, with a minimum of 65 years and a maximum of 89 years (range = 24 years).

Twenty-four percent of the participants had type 2 diabetes mellitus. Regarding anthropometric measurements, the sample had a mean BMI value of 31.99 kg/m^2 ($\text{SD} = 5.53 \text{ kg/m}^2$) and a median of 31, with a minimum value of 21 and a maximum value of 53 (range = 32). The results relating to the severity of OSAS and type II diabetes mellitus were adjusted by BMI.

Severity of OSAS

OSAHS severity data showed that 45.33% of the participants had no OSAHS (AHI less than 5 apnoeas and hypopnoeas/hour); 22.67% had mild OSAHS (AHI between 5 and 14.9 apnoeas-hypopnoeas/hour); 13.33% had moderate OSAHS (AHI between 15 and 29.9 apnoeas-hypopnoeas/hour); and 18.67% had severe OSAHS (AHI greater than or equal to 30 apnoea-hypopnoea/hour).

With regard to the sociodemographic variables collected in this study, we found more men without OSAHS (65.7%) than women (34.3%), and more women with severe OSAHS (57.1%) than men (42.9%), although there were no significant relationships or differences.

Below is a Table 1 with the results of the number of patients with type II diabetes mellitus distributed by severity of OSAHS.

Table 1. Number of patients with type II diabetes mellitus by severity of OSAHS.

	Mild OSAHS	Moderate OSAHS	Severe OSAHS
DMII	5	3	7
Not DMII	12	7	7
Total	17	10	14

Note: DMII: Diabetes mellitus type II.

With regard to weight, significant differences were found for the severity of OSAHS ($H=10.120$, $p=0.02$). Differences were established between the group of people without apnoea and that with mild apnoea, as well as between the group with mild apnoea and that with severe apnoea.

Moreover, the possible existence of differences according to the use/non-use of CPAP in these variables was analysed. In this case, significant differences were found in BMI ($F(1, 73) = 6.77$, $p=0.01$), as people who used CPAP had a higher BMI than those who did not use it.

Effect of Type 2 Diabetes on the Severity of OSAHS

We analysed the possible differences between the AHI according to the presence or absence of type 2 diabetes mellitus in the sample. Significant differences were found in the AHI between the participants who had type II diabetes mellitus and those who did not ($U=326$, $p=0.02$), since the scores were higher in the case of diabetes.

On the other hand, in terms of CPAP use, no significant differences were found in people with type 2 diabetes ($U=414$, $p=0.16$).

4. Discussion

The aim of this study was to determine whether type 2 diabetes mellitus in elderly people affected the level of severity of OSAHS, obtaining significant differences in these variables; for instance, elderly people with diabetes mellitus had a higher degree of OSAHS.

This is justified on the basis of the inherent changes of the ageing process. Thus, research such as that carried out by Edwards et al. [11] and Fallahi et al. [2] shows that ageing increases the risk of comorbid diseases for patients with type 2 diabetes mellitus, also worsening existing diseases, thereby causing adverse effects in the person's sleep condition.

Authors such as Redline et al. [17], Reutrakul et al. [16], Subramanian et al., [6] and Sulit et al. [18], have shown a bidirectional association between type 2 diabetes mellitus and OSAHS, meaning that the neuropathy caused by diabetes can affect the central control of breathing and the neural reflexes of the upper airways, resulting in OSAHS (6,16-18). On the other hand, changes in the ageing process, such as the lengthening of the soft palate, the change in structure and increased fat deposition in the pharyngeal area, or the intermittent hypoxia and frequent awakening during sleep that occurs in OSAHS, may increase the body's sympathetic activity and oxidative stress, leading to systemic inflammation, activation of the hypothalamo-adrenal axis and hormonal imbalances, leading to insulin resistance and beta-cell dysfunction [1,5-7,17,18]

Subramanian et al. [6] found that patients with type 2 diabetes mellitus are 50% more likely to develop OSAHS compared to people without diabetes mellitus, regardless of traditional risk factors or confounders of OSAHS. In the mentioned study, the authors found incident predictors of OSAHS in patients with type 2 diabetes mellitus, including male sex, obesity, cardiovascular disease, and depression [6]; this does not coincide with the results found in our study, except for the relationship found with obesity, where we did find a relationship between the variables in people with mild apnoea compared to those with severe apnoea.

With regard to sex, it is worth noting the existence of studies in which an association was found between excessive daytime sleepiness and glycaemic control in men with obesity; no such relationship was found in the worsening of OSAHS in non-obese diabetic men or women with any BMI category. In contrast, other studies that included mostly women with type II diabetes reported higher scores on the daytime sleepiness scale with higher HbA1c levels [19,20].

On the other hand, with regard to the age variable, authors such as Alshehri et al. [20], Edwards et al. [11] and Fallahi et al. [2] have shown that the prevalence of OSAHS tends to increase with age in people with type 2 diabetes, although no significant relationship has been found [2,11,20]. The lack of a relationship between age and the incidence of OSAHS in patients with type 2 diabetes is explained by the fact that the main studies reviewed did not take into account the age variable, as they included an adult population aged 18 years and older. There is only one epidemiological study that examines a large cohort of healthy elderly people, which found OSAHS as a risk factor for developing type 2 diabetes, although without taking into account the severity of the condition [21]; for this reason, our research is the main contribution of this knowledge to the scientific world.

Aronsohn et al. [10] found a clear and graded inverse relationship between OSAHS severity and glucose control in patients with type 2 diabetes mellitus, after controlling for confounding factors, such as degree of adiposity [10]; however, this and subsequent studies have been carried out in young and middle-aged adults, leaving out the elderly, or including them along with the middle-aged adults [5,8–10,19,22]. In the case of the research by Aurora et al. [19], the association between severe OSAHS and type 2 diabetes mellitus was found only in people with excessive daytime sleepiness [19], while in the study by Byun et al. [5] this association was established with sleep fragmentation, oxygen desaturation and anatomical dysfunction [5]. On the other hand, studies have found no association between OSAHS severity and microvascular endothelial dysfunction in patients with type 2 diabetes. The lack of association in the aforementioned studies may be due to the short PSG recording (4 hours) in some of these investigations, which is insufficient to detect an association between OSAS severity and type 2 diabetes [9,23].

In line with this, authors such as Aronsohn et al. [10] and Duc et al. [24] support the hypothesis that a reduction in OSAHS severity may improve glycaemic control, thereby reducing the number of drugs taken, contributing to the improvement of millions of patients with type 2 diabetes [10,24]. Previous work has demonstrated the efficacy of CPAP in people with and without type 2 diabetes mellitus depending on the obesity of the individual [19]. After sustained use of CPAP for a period of 6 months, improvements in nocturnal glucose levels and increased insulin sensitivity were found after 3 months with CPAP [19,25–30]. In the present investigation, no relationship was found between these variables and CPAP use.

There are studies that advocate proper weight control, since avoiding obesity improves insulin resistance caused by increased plasma adiponectin levels in OSAHS [22]. Pharmacotherapy in type 2 diabetes, such as sulphonylureas, glitazones and insulin, contributes to undesirable consequences like weight gain, or exacerbation of the severity of existing OSA, thus increasing the cardiovascular risk [6,10]. In this regard, and considering that elderly patients are generally polymedicated as a result of associated comorbidities, they may also present sleep pattern disturbance as an adverse effect [3].

Given the high prevalence of OSA in people with type 2 diabetes mellitus, the International Diabetes Federation (IDF) considered screening people with diabetes for OSA. However, due to the large number of patients with type 2 diabetes mellitus and the high cost of diagnostic methods for OSAHS, this recommendation has proved difficult to implement [6].

Therefore, and as a result of the discrepancies observed in the published studies, given the sample selection bias due to the heterogeneity of the sample, the variability of severity due to the use of different diagnostic methods, the duration of the disease, the wide age range, and the non-consideration of the elderly, it was difficult to make comparisons with other studies based on the results obtained in the present investigation.

This study has strengths and limitations that must be pointed out. On the one hand, elderly people aged 65 years and over were considered as the only population group, in order to be able to

treat this population without discrimination, and the diagnosis of OSAHS was obtained through the gold standard PSG; on the other hand, the main limitation of the study is its cross-sectional design.

Thus, it is essential to conduct future research with a large cohort of elderly subjects, followed longitudinally, in order to assess how the ageing process alters the factors that cause these diseases, as well as their sequelae.

5. Conclusions

Therefore, and by way of conclusion, it is crucial to recognise elderly diabetic patients at risk of developing OSAHS exacerbation, in order to programme nursing interventions that prioritise prevention, assessment and control strategies for these conditions.

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