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Prevalence of Obstructive Sleep Apnea-Hypopnea in Severe Asthma

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Abstract

Background: Obstructive sleep apnea syndrome (OSA) and asthma are two common respiratory diseases. An overlap between the two diseases has been widely reported. It is established that OSA may affect control of asthma. This study aims to highlight OSA prevalence in patient with difficult to control asthma and to point out the feature of this overlap syndrome.

Methods: We conducted a prospective study including sixty patients with difficult control asthma who had symptoms suggestive of OSA (Epworth scale>10). Based on the findings of the respiratory polygraphy, a comparative analysis of clinical, biologic, lung function testing and therapeutic features was performed.

Results: OSA was confirmed in 63.3% of cases, and was severe, moderate and mild in 26%, 61% and 13% of them respectively. Comparison between the OSA and non-OSA arms showed no significant differences in the asthmatic disease features: date of onset, atopy, history of near fatal asthma and medication use. However, OSA patients were older than non OSA patients (54 *vs.* 45 years old; p=0.05). Furthermore there was a difference in the proportion of males between both arms (50% in OSA *vs* 23% in non OSA; p=0.05). Gastro-oesophageal reflux disease (GERD) was more common in the OSA group (57.9% *vs*. 21.7%; p=0.034). There was no significant difference between the two arms regarding obesity, allergic rhinitis and smoking.

Conclusion: This study shows that OSA is more prevalent in difficult to control asthma patients. The presence of overlap syndrome was correlated with age, male gender and GERD.

Keywords: Severe asthma; Obstructive sleep apnea; Control asthma

Introduction

Asthma and obstructive sleep apnea syndrome (OSAS) are both common respiratory illnesses in the general population. In adults, obstructive sleep apnea (OSA) is highly and increasingly prevalent [1]. OSAS is associated with cardiovascular morbidities, insulin resistance, neural injury, and accelerated mortality [2]. Accumulating evidence suggests a bidirectional relationship between asthma and OSA, whereby each disorder deleteriously influences the other [3]. However, to our knowledge, no major epidemiologic study was conducted to this date.

Subjects and Methods

The study was conducted on 60 patients diagnosed with difficult asthma between March 2014 and September 2014 including patients with Asthma confirmed by clinical examination or in need by lung function testing or Metacholin bronchial provocation test. Their asthma was considered Moderate-to-severe with difficult control according to the GINA based on the Asthma control Test (ACT) despite a good therapeutic observation and a good use of inhaled drugs for asthma. Patients had symptoms suggestive of OSAS (Epworth scale>10) Pregnant women and patients with acute exacerbation or chronic obstructive pulmonary disease, or patients with long term oxygen therapy are excluded in this study. All patients benefited from a polygraph.

Statistical analysis

Statistical analysis was performed using SPSS Statistical Software version 19. In addition to the descriptive statistics(mean, standard deviation, median, frequency and ratio), Student's t test was used to compare normally distributed variables and the Mann-Whitney U test was used to compare variables that did not show normal distribution. Spearman's correlation analysis was used to evaluate the association between the parameters. The results were expressed at a 95 % confidence interval, and the level of statistical significance was established at p<0.05.

Results

The sample consisted of 60 patients with difficult control asthma and symptoms suggestive of OSA, with light female predominance (57%). Table 1 shows some demographic and clinical characteristics of the patients divided into two groups: patients with OSA (Group 1) and without OSA (Group 2). It was observed that patients with OSA were older than those without OSA (54 years *vs.* 45 years), in fact that was statistically significant (p=0.05 with 95% confidence interval). Fifty percent of patients were males in the group 1 *vs.* 22% in group2 (p=0.05) It is also important to refer that comparison was statistically significant regarding Gastro-oesophageal reflux disease (GERD). It was more common in the OSA group (57.9% *vs.* 21.7%; p=0.034). However, in both groups, similar values of BMI were observed. There was no significant difference between the two arms regarding comorbidities, allergic rhinitis and smoking. All the evaluated patients reported night symptoms. The mean value of the Epworth Sleepiness Scale was 12.61 (G1) *vs.* 12.05 (G2). At the time of the study the age of the asthmatic disease was comparable in the 2 groups. All patients had difficult control asthma. The mean of ACT score was 13.92 (G1) *vs.* 14.4 (G2) p=0.82. Regarding the lung function tests, spirometry revealed values within the normal range in 40% of the patients. In the remaining patients, an obstructive pattern was detected 6%, according to the values of the FEV1/CVF ratio. The values varied between 46% and 104%. The mean value of FEV1 was 83.5% (± 19%). A restrictive pattern in 3.2% cases and a mixed ventilator disorder in 13% cases. There was no

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Characteristics	Asthma$^+$ OSA$^+$	Asthma$^+$ OSA$^-$	P
	G1	G2	
N (%)	38 (63.3)	22 (36.7)	
Age, years (mean ± SD)	54 ± 12	45 ± 11	0.05
Female, n (%)	19 (50)	17 (77)	0.3
Male, n (%)	19 (50)	5 (23)	0.05
BMI	34	35	0.67
Active Smoking n (%)	9 (23)	2 (9)	0.39
Passive smoking n (%)	6 (18)	5 (22)	0.51
Nonsmoking n (%)	18 (56)	15 (68)	0.28
Comorbidities			
Hypertension n (%)	18 (47)	5 (22)	0.097
Diabetes n (%)	7 (18)	3 (13)	0.73
Heart rhythm disorder n (%)	3 (16)	0 (0)	0.29
Left heart failure n (%)	3 (5)	2 (9)	0.61
Cerbrovascular event n (%)	2 (5)	1 (4,5)	1
Psychiatric disease n (%)	4 (10)	0 (0)	0.28
Dysthyroidism n (%)	3 (7)	2 (9)	1
Dyslipidemia n (%)	4 (10)	3 (13)	0.7
GERD n (%)	22 (57,9)	6 (27,27)	0.032
Allergic rhinitis n (%)	18 (47)	6 (27)	0.17
Non allergic rhinitis n (%)	4 (10)	4 (18)	
Chronic sinusitis n (%)	7 (18)	3 (13)	0.73

Table 1: Demographic and physiologic characteristics, smoking history and comorbidities of the enrolled patients.

Characteristics	Patients with OSA	Patients without OSA	P
	G1	G2	
Apnea/hypopnea index	21	2.47	0
Oxygen desaturation index (*n*/h)	13.8	2.6	0.001
Apnea index	6	0.68	0.217
Mean oxygen saturation during sleep	94.78	96.05	0.13

Table 2: Diagnostic sleep study results of the enrolled patients.

significant difference between the two arms. All of patients underwent a respiratory polygraphy. In 38 (63%) patients it was diagnosed OSA. The results of the Sleep studies are shown in Table 2. As expected, the Apnea Hypopnea Index (AHI) was higher in the group of patients With OSA. The percentage of patients with mild or moderate OSA was similar in the 2 groups and 10 (26%) patients presented an AHI>30. The therapeutic approach in most patients consisted on general sleep hygiene measures, such as weight loss, positional therapies, and regular hours of sleep. In addition to these measures, 11 patients initiated positive airway pressure therapy (CPAP). Clinical follow-up was performed 3 months after the beginning of the therapeutic measures. Interestingly, the majority of patients of group 1 reported an improvement of the symptoms, especially in the nighttime complaints. They also referred improvement in quality of sleep, fewer exacerbation episodes, and improvement in neuro-cognitive complaints.

Discussion

In our study, sleep studies showed that the prevalence of OSA in the group of investigated patients was 63.3%, which is consistent with already known fact that symptoms of sleep disordered breathing, especially OSA, are common in asthmatic patients. Overnight polysomnography is the gold standard for the diagnosis of OSA, often replaced by the ventilatory polygraphy lack of resources. Indeed, the cost of these tests is high and their interpretation is not simple, which explains the poor use of studies that are based on polysomnography and ventilatory polygraphy to determine the prevalence of OSAS in asthmatics. Some studies were based on questionnaires. Auckley et al. [4] used the Berlin Questionnaire. They noted a higher prevalence of OSAS symptoms in an asthmatic population compared with a primary care population (39.5% *vs.* 27.2%, p=0.004). This study suggested the increased likelihood of OSAS in asthmatic patients compared with non-asthmatic patients [4]. Study Teodorescu made in 2009 was based on "Sleep Apnea Scale of the Sleep Disorders Questionnaire (SDQ-SA)" and revealed a high risk of OSA in 40% of asthmatic among 244 included in the study [5]. Another study in South Korea by Mi-Yeong Kim et al. in order to estimate the risk of OSAS in 217 patients followed for severe asthma based on the Berlin questionnaire and to determine the clinical characteristics of the association Asthma-OSAS and its impact on the quality of life of patients by the QLQAKA (Quality of Life Questionnaire of Asthmatic Korean Adults) questionnaire which is an adapted form of ACT including 32 items: 11 to evaluate activity limitation, 12 for symptoms, 5 for psychological status and 4 for environmental stimuli. The results of this study showed that the risk of OSAS in this population was 41%. Patients with a high risk of OSAS were older, more obese, had a longer duration of asthma treatment and had no atopic predisposition, and their quality of life more impaired with a QLQAKA below 64 ± 10 *vs.* 68 ± 11 (p=0.026) and the difference in control level of asthma was not significant [6]. The most recent studies have been based on polysomnography as a baseline test to determine the prevalence of OSAS in asthmatics, like the Canadian study by Julien et al. comparing the prevalence of OSAS in 3 groups of patients: Severe asthma, 2nd moderate asthma and 3rd non-asthmatic subjects. This prevalence was 50%, 23% and 12% (0.007), respectively, and there was no correlation between the severity of asthma and the severity of OSAS [7] A recent study by Shaarawy et al. found an OSAS prevalence of 25% in 60 patients followed for uncontrolled asthma [8] Min Kwang Byun et al. published a study concluding a prevalence of OSAS of 66.5% in moderate to severe asthmatics [9] The majority of studies have considered OSAS as a factor in the poor control of asthma through various mechanisms, including sleep disorders, upper respiratory tract edema and systemic inflammation associated with OSAS. [10] On the other hand Some authors have tried to analyze the influence of asthma on the occurrence and severity of OSAS and have concluded that asthma may contribute to the onset and aggravation of OSAS by altering anatomy and physiology Of the upper airways [11] In our study, all patients had moderate to severe persistent asthma that was difficult to control and there was no correlation between the clinical characteristics of the asthmatic disease and the prevalence or severity of OSAS These results are similar to those of Auckley et al. who did not find a correlation between the risk of OSAS occurrence and the severity of asthma [4] Guven et al. made the same findings On the other hand, Teodorescu, et al. demonstrated that a high risk of OSAS did not depend on other known factors of poor asthma control or control level (ACT) [5]. By comparing the polysomnographic results of three groups of patients with moderate asthma, severe asthma, and non-asthmatic patients, Julien et al. found no correlation between the occurrence of OSAS and the severity of asthma, atopy, rhinitis, Nasal polyposis, use of prednisolone, use of high dose inhaled corticosteroids, long acting β2 agonist or antileukotrienes [8]. Teodorescu et al. found a prevalence of OSAS of 21% in asthmatics in general and this risk multiplies 2.87 times in uncontrolled asthmatics [5]. Symptoms of OSAS seems to be frequent in asthmatics because, according to the authors, these people can wake up periodically due to the presence of cough, dyspnea or choking, leading in many cases to insomnia and/or excessive diurnal drowsiness, Snoring would be explained by the presence of apneas and not by the perturbation of the brooch tree. Although snoring seems to be a factor responsible for this association, this was demonstrated by

Larsson et al. who found a prevalence of nocturnal snoring of 17% and sleep apnea of 14.3% in asthmatic patients [12]. Klara et al. found a high prevalence of snoring in women with atopy and a significant association between snoring and asthma [13]. So it is clear, in addition to the risk factors that bronchial asthma and OSAS share, age, post menopause, obesity, GERD, nasal congestion and nasal polyposis, others physio-pathological phenomena explain the frequency of this association and the impact of OSAS on the evolution and control of asthma as well as the role of asthma in the occurrence and severity of OSAS.

Conclusion

Given the high prevalence of OSAS in patients who have difficulties in controlling asthma and despite the lack of correlation between the clinical features of asthma and the presence of OSA, it is interesting to systematically search this association before moving to the next step of GINA. This strategy is even more justified in the presence of an advanced age, a male gender and a history of GERD. However, faced with a current database limited by the small sample size, heterogeneity of the study populations and the poor of studies on the effects of CPAP on asthma, it is difficult to establish an optimal management strategy of an overlap syndrome Asthma OSAS. Given the high prevalence of OSA in the asthma population, it is important to reinforce that sleep studies should be used to document OSA and are helpful in prescribing proper treatment to achieve a better control of the disease.

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