Depressive symptoms, quality of sleep, and disease control in women with asthma

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Abstract

Purpose A large number of asthmatic patients, particularly females, present inadequate disease control. Depressive symptoms are reportedly common in asthma and have been related to poor disease control, but the mechanism of this association is still unclear. Poor quality sleep, frequently observed in asthmatics, is also a manifestation of depression and has been related to uncontrolled asthma. This study aimed to investigate the relationship between depressive symptoms, sleep quality, and asthma control.

Methods This was a cross-sectional study of 123 women with previous diagnosis of asthma from a reference center in Fortaleza, Brazil. Depressive symptoms were assessed by the Beck Depression Inventory (BDI); quality of sleep was evaluated by the Pittsburgh Sleep Quality Index (PSQI), daytime sleepiness by the Epworth Sleepiness Scale (ESS), and asthma control by the Asthma Control Test (ACT).

Results Inadequate asthma control (ACT <20) was found in 94 (76.4 %) subjects, depressive symptoms in 92 (74.8 %), poor quality sleep (PSQI >5) in 99 (80.49 %), and excessive daytime sleepiness (ESS ≥10) in 34 (27.64 %). Depressive symptoms were associated with both poor quality sleep ($R = 0.326$) and inadequate asthma control ($R = -0.299$). Regression analysis showed that depressive symptoms and

sleep quality were independent predictors of the level of asthma control.

Conclusion Asthma control in women is independently associated with depressive symptoms and quality of sleep, suggesting that these patients might benefit from simple measures to promote healthy sleep behavior and sleep hygiene and also that routine screening for depression can be relevant, particularly, in poorly controlled cases.

Keywords Asthma · Depression · Sleep · Disorders of excessive somnolence

Introduction

Asthma is a common disease affecting all age groups, with prevalence rates ranging from 1 to 18 % in different regions of the world [1]. Although in childhood, asthma is more common in boys, after puberty, it becomes more frequent and more severe in the female gender [2]. Patients with asthma characteristically present variable airflow limitation and respiratory symptoms, including dyspnea, wheezing, chest tightness, and cough, which tend to be more pronounced at night [3].

The level of asthma control, i.e., the extent to which disease manifestations can be observed or reduced as a result of treatment, is an important parameter in clinical evaluation, and its monitoring over time has been recommended to guide adjustments to treatment. Asthma control is known to be influenced by genetic factors; gender; underlying disease process; comorbidities, including obstructive sleep apnea; treatment; and psychosocial factors [1]. Depressive symptoms and asthma control have been reported to be negatively correlated, although the exact nature and implications of this association have not been satisfactorily clarified [4, 5].

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Nocturnal worsening of asthma may represent an accentuation of the normal circadian variation in airway caliber. It has been demonstrated that inflammation and airway hyperresponsiveness, key components of the disease, also exhibit a circadian pattern, being more pronounced at night [6]. Poor quality sleep and excessive daytime sleepiness have both been reported in individuals with asthma and may have a negative effect on lung function, daytime performance, and quality of life of these patients [7–10]. It is well recognized that nocturnal exacerbations, which are more common in cases of unsatisfactory control of asthma, lead to sleep fragmentation and poor subjective and objective quality of sleep [11]. However, even in patients who are clinically stable, disrupted sleep is often present [12]. Prospective studies have shown that insomnia and poor quality sleep are risk factors for the initial development of depression as well as for episodes of recurrence [13]. While poor sleep quality could be a vulnerability factor for the later development of depression, it has also been suggested that it could be a marker of subclinical depression [14]. Thus, sleep problems, common in patients with depression and/or asthma, may contribute to a potential vicious circle. Adequate clarification of the relationship between these conditions can be of major importance for the adequate treatment and control of asthma [10].

The main purpose of this study was to investigate the relationship between depressive symptoms, sleep quality, and degree of asthma control.

Methods

Patients and study design

This is a cross-sectional, descriptive study of female patients from the asthma outpatient clinic at a reference center in Fortaleza, Brazil. The study sample comprised 123 consecutive women with asthma who attended scheduled appointments, from August 2012 to January 2013. Shift workers, patients presenting significant respiratory discomfort during the interview, and those with severe cognitive impairment were not included. Research protocol was approved by the local research ethics committee (number 889/12), and all the participants signed an informed consent form prior to their inclusion in the study.

Instruments and measures

Demographic, anthropometric, and clinical data were obtained by interview and chart review. Diagnosis of asthma was based on previous identification of a characteristic pattern of respiratory symptoms, such as wheezing, dyspnea, chest tightness, or cough, and objective demonstration of variable airflow limitation, according to current recommendations [1]. Asthma

Control Test (ACT) was used to evaluate the level of asthma control. This is a practical and simple instrument widely used for this purpose and has been previously translated and validated for use in Brazil [15]. It is composed of five questions with five possible answers each, individually scored from 1 to 5. Total score may thus range from 5 (worst control) to 25 points (optimal control), and a score ≥ 20 is considered indicative of well-controlled asthma [16].

Depressive symptoms were assessed by the Brazilian-Portuguese language version of the Beck Depression Inventory (BDI) [17]. This instrument consists of 21 items rated on a Likert-type scale, from 0 (neutral) to 3 (maximum intensity). The final score can thus range from 0 to 63 points, corresponding to normal (0 to 9), mild (10 to 18), moderate (19 to 29), and severe (30 to 63) symptoms [18].

Quality of sleep was assessed by the Brazilian-Portuguese version of the Pittsburgh Sleep Quality Index (PSQI). This questionnaire comprises 19 items that compose seven scoring components, each one related to a specific aspect of sleep: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of hypnotics or sedative drugs, and daytime dysfunction. The score of each component is added so that the global score can range from 0 to 21 points. Overall global score higher than 5 is considered indicative of poor quality sleep [19].

The degree of daytime sleepiness was assessed by the Epworth Sleepiness Scale (ESS), a questionnaire widely used for this purpose, which has been previously translated and validated for use by Brazilian subjects [20]. It is composed of eight questions that ask for the likelihood of falling asleep in eight hypothetical situations, quantified as 0 (no chance), 1 (small chance), 2 (moderate chance), or 3 (high chance). The final score ranges from 0 to 24 points, and scores ≥ 10 are considered indicative of excessive daytime sleepiness [21].

Statistical analysis

Data are expressed as mean, standard deviation (SD), and/or frequency. Chi-squared test was used for analysis of dichotomous variables. The Kolmogorov-Smirnov test was used to assess normality. In between-group comparisons, Student's *t* test or Mann-Whitney test were used, as appropriate. To measure the association between variables, we used the Pearson correlation coefficient. Multiple regression analysis (stepwise) was used to identify the factors more strongly related to the degree of asthma control. In this analysis, the dependent variable was ACT score; BDI and PSQI were the independent variables, adjusted for the covariates age, body mass index (BMI), and ESS score. The selection of independent variables was done according to their clinical and statistical significance in previous analyses. Two-tailed tests were used throughout the study, with alpha set at 5 % probability ($p < 0.05$).

Analyses were performed using the Statistic Package for Social Sciences (SPSS) version 20.0 for Windows.

Results

The patients were aged between 18 and 83 (mean $\pm$ SD = 50.8 ± 12.2) years. A combination of inhaled corticosteroids and long-acting beta agonists was used by 118 (95.9 %) individuals and systemic corticosteroids by 10 (8.1 %). All the subjects reported the use of inhaled short-acting beta agonists on an as-needed basis. Antidepressants were used by 16 (13.0 %) patients, antihypertensives by 48 (39.0 %), proton-pump inhibitors by 23 (18.7 %), lipid-lowering drugs by 15 (12.2 %), and oral antidiabetic agents by 7 (5.7 %). One subject was a current smoker and 38 (30.9 %) were ex-smokers. Data on asthma control, sleep quality, daytime sleepiness, and depressive symptoms are summarized in Table 1.

The severity of depressive symptoms was classified as mild ($20 \geq \text{BDI} > 10$) in 53 (43.09 %) cases, moderate ($30 \geq \text{BDI} > 20$) in 28 (22.77 %), and severe ($\text{BDI} > 30$) in 11 (8.94 %). Of the 39 subjects with moderate or severe depressive symptoms, 8 (20.5 %) were on antidepressants. On average, the patients with depressive symptoms, as compared to those without, had poorer control of asthma, worse quality of sleep, and a higher sleepiness score (Fig. 1). Correlation analysis showed that cases with lower BDI, i.e., less

Fig. 1 Women with asthma and depressive symptoms showed lower levels of disease control, poorer sleep quality, and more daytime sleepiness than those without depressive symptoms. *ACT* Asthma Control Test, *ESS* Epworth Sleepiness Scale, *PSQI* Pittsburgh Sleep Quality Index, 95%CI 95 % confidence interval

depressive symptoms, had higher ACT scores, indicating better asthma control ($R = -0.299$; $p = 0.001$) as well as lower PSQI scores, indicating better quality sleep ($R = 0.326$; $p < 0.001$).

Asthma control was worse in patients with poor quality sleep in comparison to that in those with good quality sleep (Fig. 2). A negative correlation was found between PSQI and ACT scores, suggesting that patients with better quality sleep present higher levels of asthma control ($R = -0.315$; $p < 0.001$). On average, participants with excessive daytime

Table 1 General characteristics, sleep quality, daytime sleepiness, and depressive symptoms in 123 women with asthma, according to the level of disease control

	All patients (<i>N</i> = 123)	Poorly controlled asthma (<i>N</i> = 94)	Well-controlled asthma (<i>N</i> = 29)	<i>p</i> value*
Age (years)	50.8 $\pm$ 12.2	49.6 $\pm$ 11.6	54.5 $\pm$ 13.6	0.058 ^a
BMI (kg/m ²)	28.4 $\pm$ 5.2	28.9 $\pm$ 5.5	26.9 $\pm$ 3.4	0.045 ^a
PSQI, global score	9.9 $\pm$ 4.6	10.6 $\pm$ 4.4	7.4 $\pm$ 4.4	0.001 ^b
Poor quality sleep				0.004 ^c
Present	99 (80.4 %)	81 (86.2 %)	18 (62.1 %)	
Absent	24 (19.6 %)	13 (13.8 %)	11 (37.9 %)	
ESS score	7.3 $\pm$ 4.4	7.5 $\pm$ 4.5	6.7 $\pm$ 4.1	0.347 ^b
Hypersomnolence				0.152 ^c
Present	34 (27.6 %)	29 (30.9 %)	5 (17.2 %)	
Absent	89 (72.4 %)	65 (69.1 %)	24 (82.8 %)	
BDI score	17.0 $\pm$ 8.6	17.7 $\pm$ 8.8	14.8 $\pm$ 7.7	0.079 ^b
Depressive symptoms				0.408 ^c
Present	92 (74.7 %)	72 (76.6 %)	20 (69.0 %)	
Absent	31 (25.3 %)	22 (23.4 %)	9 (31.0 %)	

BMI body mass index, *PSQI* Pittsburgh Sleep Quality Index, *ESS* Epworth Sleepiness Scale, *BDI* Beck Depression Inventory

**p* values are for comparisons between controlled and poorly controlled asthma groups

^a Student's *t* test

^b Mann-Whitney

^c Chi-squared test

Fig. 2 Women with asthma who presented poor quality sleep exhibited lower level of disease control, relative to those with good quality sleep. *ACT* Asthma Control Test, *BDI* Beck Depression Inventory, *ESS* Epworth Sleepiness Scale, *PSQI* Pittsburgh Sleep Quality Index, 95%CI 95 % confidence interval

sleepiness ($ESS \geq 10$) had worse levels of asthma control ($p = 0.02$).

Multiple regression analysis showed that depressive symptoms, as measured by the BDI, and subjective sleep quality, as measured by PSQI, were independent predictors of the level of asthma control (Table 2).

Discussion

This study shows that asthma control in women is independently associated with depressive symptoms and quality of sleep. Less than a quarter of the study participants exhibited, at least, partially controlled asthma, as assessed by the ACT. In a recent study, Al-Zahrani et al. also using the ACT reported an overall rate of uncontrolled disease of 39.8 % in 400 patients from a primary care center. Female participants, however, presented a rate of uncontrolled asthma of 78.6 %, i.e., close to the present study and more than four times higher than men [22]. Mintz et al. in a cross-sectional evaluation of 2238 adults in primary care units reported a general frequency of 58 % of uncontrolled asthma, also measured by ACT. But when asthma was the main reason for seeking medical

assistance, that rate rose to 72 %, slightly lower than that in the present study. Interestingly, according to Mintz et al., 48 % of the patients who attended the health center for medical problems other than asthma had uncontrolled disease [23].

A European multinational study found poorly controlled disease in more than 50 % of patients treated for asthma and more often in women, assessed by ACT. There was substantial variation in the rate of asthma control among various countries, which was attributed to differences in the level of organization of health care systems [24]. In Brazil, Vieira et al. investigated 78 patients with previous diagnosis of moderate to severe asthma from an outpatient clinic at a university hospital, and found that about 60 % of the subjects had uncontrolled asthma, as assessed by ACT, with no difference between genders [5]. This set of results shows clearly that a major proportion of asthma patients suffer from inadequate disease control, particularly women, despite significant advances in the knowledge of asthma pathophysiology and pharmacotherapy, thus highlighting the need for a better assessment and control of individual risk factors [25].

Depressive symptoms were observed in most participants of this study. Previously, depression rates consistently higher than those observed in the general population have been reported in patients with asthma [4]. Moreover, asthma patients show depressive symptoms more often than patients with other chronic diseases, which also significantly interfere with the activities of daily living [26, 27]. In a cohort of 439 adults with asthma, mostly of female gender, Katz et al. observed a depression rate twice as high as for the general population. Low perception of asthma control was associated with the presence of depression in that study [28]. Depression was reported in 25 % of the participants of a retrospective cohort study, involving 1812 patients with moderate and severe persistent asthma [29]. Recently, Bruner et al. conducted a longitudinal study with a 20-year follow-up, involving 3614 adults, initially free from asthma, classified according to the presence of depressive symptoms, and found that depression is a risk factor for the incidence of asthma. By contrast, there was no increased incidence of depression in 3016 adults with asthma, also included in the same study [30].

Table 2 Multiple regression analysis of Asthma Control Test (ACT) score and other characteristics of 123 women with asthma

Predictors	Coefficients	SE	Student's <i>t</i> test	<i>p</i> value	95%CI
Constant	19.239	3.29	0.83	0.00	12.68–25.78
BDI	−0.119	0.054	−2.19	0.03	−0.227–−0.011
PSQI	−0.255	0.105	−2.43	0.01	−0.46–−0.04

95%CI 95 % confidence interval, *BDI* Beck Depression Inventory, *PSQI* Pittsburgh Sleep Quality Index, *ACT* Asthma Control Test, *SE* Standard Error

In this study, there was an association between depressive symptoms and level of asthma control. Previously, Di Marco et al. reported an association between depression and inadequate asthma control, measured by ACT. Those investigators suggested that an increase in awareness of asthma symptoms caused by depression could be negatively affecting the level of control, as perceived by the patient [31]. However, there are many additional factors that might contribute to the relationship between depressive symptoms and poor asthma control, including low adherence to drug therapy [32] and increased use of emergency services for asthma patients with depressive symptoms, compared to individuals who do not present these symptoms [33]. The high frequency of depressive symptoms in asthma, confirmed by the present study, assumes even greater relevance in view of the fact that psychiatric comorbidities, although common in chronic respiratory diseases, still remain largely undiagnosed and untreated. This is also evident from our finding that only one fifth of the patients with moderate or severe depressive symptoms were receiving specific treatment.

Poor sleep quality was observed in the majority of the participants of this study, particularly in those with depressive symptoms or poorly controlled disease. Excessive daytime sleepiness was present in just under a third of our cases. Impaired sleep and its negative daytime consequences have been previously reported in asthma, even in patients with mild and relatively stable disease [7–12]. Insomnia-related symptoms have been described in almost half of the subjects with asthma in a large population-based survey, with higher frequencies being found in females and asthmatics with nocturnal symptoms [34]. Obstructive sleep apnea (OSA), a common cause of disturbed sleep, particularly in middle-aged adults, has been frequently reported in asthma [35] and may also have contributed to worsen sleep quality in our subjects.

One of the main findings of the present study is that asthma control is independently related to subjective sleep quality, regardless of the presence of depressive symptoms. Previously, the relationship between asthma control and quality of sleep was examined in a very limited number of studies, and the potential confounding effect of depression has not been accounted for [7, 9, 10]. Luyster et al. investigated the effects of gastroesophageal reflux disease, allergic rhinitis, and obstructive sleep apnea, but not depressive symptoms, on asthma control, and observed an association between low level of asthma control and poor sleep quality. In the same study, it was found that patients without nocturnal symptoms of asthma almost always presented poor sleep quality, indicating that the high frequency of sleep problems in asthma cannot be secondary only to the presence of

nocturnal symptoms [36]. Additionally, the possibility of a mutual relationship between asthma control and quality of sleep should be considered. In fact, negative effects of insufficient sleep on pulmonary function were previously described in patients with chronic obstructive pulmonary disease [37]. In experimental animals, sleep deprivation can exacerbate acute lung inflammation, an effect that can be attenuated by melatonin, which has a powerful antioxidant action [38]. Interestingly, nocturnal melatonin administration can reportedly improve the quality of sleep in women with mild to moderate stable asthma [12].

The present study has several limitations. First, as no male patients were included, these results cannot be immediately extrapolated to the entire asthmatic population. On the other hand, because of well-recognized effects of gender on clinical manifestations and disease control in asthma [2], recruiting only female subjects allowed for the exclusion of a potentially relevant confounding factor. In this study, quality of sleep was evaluated subjectively by the PSQI, an instrument widely used for this purpose. Previous reports indicate that subjective criteria are superior to polysomnography in identifying individuals with insomnia, and laboratory records add little relevant information to confirm or exclude this condition [39]. Finally, because of its cross-sectional design, causality cannot be inferred from the relationships described.

In conclusion, depressive symptoms are present in the majority of female outpatients with asthma and are associated with impaired quality of sleep and inadequate disease control. These findings, added to the observation that in asthmatic subjects, depressive symptoms remain largely untreated, reinforce the need to evaluate these patients more routinely for the presence of depression and possibly indicate that adequate measures to treat this problem could have a positive effect on asthma control. Our demonstration of an independent association between poor quality sleep and inadequate asthma control, regardless of depressive symptoms, is relevant and suggests that simple measures to promote healthy sleep behavior and adequate sleep hygiene could be beneficial in this clinical context. New prospective studies involving asthmatic patients of both genders are needed to further characterize these relationships and to evaluate the efficacy of the proposed interventions.

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Compliance with ethical standards

Funding No funding was received for this research.

Conflict of interest The authors declare that they have no competing interests.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent Informed consent was obtained from all the individual participants included in the study.

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