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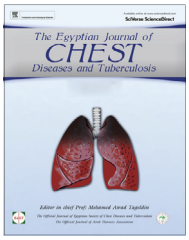

ORIGINAL ARTICLE

Assessment of the prevalence of obstructive sleep apnea in patients with stable uncontrolled asthma, impact of continuous positive airway pressure treatment

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KEYWORDS

Bronchial asthma;
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Abstract There are increasing data about the association between bronchial asthma and obstructive sleep apnea (OSA) is an important contributor to asthma control and can aggravate asthma exacerbation, continuous positive airway pressure (CPAP) which is the main line of treatment in OSA can improve asthma outcomes.

Aim of the present study: To assess the prevalence of OSA in patients with stable uncontrolled asthma and to study the effect of CPAP treatment on the asthma condition.

Subjects and methods: Sixty subjects with uncontrolled bronchial asthma were included in the study, mean age was 46 ± 13 years, there were female predominance (75%), all patients were not smokers, pregnancy and patients in acute exacerbation were excluded, after detailed history taking and physical examination pulmonary function tests and asthma control test were applied to all patients to assess the asthma control, then polysomnography was done to all patients and those proved to have OSA were offered CPAP treatment and followed up for 6 weeks then assessed again for asthma control test, pulmonary function tests and day – time sleepiness.

Results: Fifteen patients out of the 60 patients included in the study proved to have OSA, Apnea Hypopnea Index (AHI) was 23.5 ± 10.9/h of sleep, CPAP treatment improved significantly the AHI (from 23.5 ± 10.9 to 2.3 ± 2.1/h of sleep, $p < 0.01$), but there was no significant improvement in asthma control test or in the pulmonary functions (ACT was 13.97 ± 3.52 before CPAP and became 14.1 ± 3.97, $p > 0.05$ after CPAP, FEV1% pred. was 60.1 ± 6.9 before CPAP and became 61.2 ± 6.2, $p > 0.05$ after CPAP.

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Conclusion: Obstructive sleep apnea should be screened for in all patients with uncontrolled bronchial asthma, CPAP treatment may improve asthma quality of life but not improving the pulmonary function tests. Larger studies are needed to fully address the impact of CPAP on asthma condition in patient with both asthma and OSA.

Introduction

Bronchial asthma is a world – wide problem affecting about 300 million people of all ages [1], current guidelines for the management of asthma recommend that therapy be targeted to achieve asthma control which involves multiple components of subjective and objective measures [1–3]. Asthma control has been shown to improve health-related quality of life [4]. However, large community-based surveys show that this goal is rarely achieved [5,6].

here are many reasons that can contribute in preventing optimal control of asthma such as: non-compliance on treatment, persistent exposure to certain allergen, alternative diagnosis as COPD or bronchiectasis, psychological disturbances, presence of comorbid disease as allergic rhinitis or gastro-oesophageal reflux, in this respect; there is growing data that obstructive sleep apnea (OSA) is an important contributor to asthma control, OSA is characterized by intermittent upper airway constriction during sleep and was recently identified as an important risk factor for frequent exacerbations in patients with difficult-to-treat asthma [7]. The National Asthma Education and Prevention Program guidelines recommend evaluation for OSA in patients with asthma with suboptimal control [1]. On the other hand continuous positive airway pressure (CPAP) which is the main line of treatment of OSA in patients with asthma improves outcomes, including asthma symptoms [8–10], rescue bronchodilator use [8], peak expiratory flow rates (PEFRs) [8] and asthma-specific quality of life assessed with validated instruments [7,11]. The aim of the present study is to assess the prevalence of OSA in patients with stable bronchial asthma who are not well controlled and the effect of CPAP on the outcomes of these patients.

Subjects and methods

The present study was done in AlRashed center for allergy and respiratory diseases, Ministry of health, Kuwait. It included 60 patients with proven diagnosis of bronchial asthma on treatment and follow up in the outpatient clinic.

Inclusion criteria

(1) Long history of bronchial asthma.
(2) Proven reversible airway obstruction with spirometry pre- and post-bronchodilatation.
(3) Asthma state is not controlled in spite of optimal treatment with inhaled corticosteroids, inhaled bronchodilators and bursts of oral steroids.

Exclusion criteria

(1) Current smoking or history of smoking.
(2) Pregnancy.
(3) Any patient who is in acute exacerbation.

All patients were subjected to

(1) History taking and physical examination.
(2) Asthma control test (ACT), it is consisted of five items; for each item, five options were provided pertaining to asthma control during the past 4 weeks. Each item was scored according to a 5-point scale, and the item scores were totaled for assessing asthma control, with higher total scores indicating better asthma control, a score of 20 or more denotes controlled asthma, a score of 18, 19 denotes partially controlled asthma, and a score of 17 or less denotes uncontrolled asthma [12,13].
(3) Chest X-ray.
(4) Electrocardiogram (ECG).
(5) Full pulmonary function testing including spirometry pre- and post-bronchodilatation, lung volumes and diffusing capacity using Care Fusion master screen MS. IOS 733-765.
(6) Body mass index derived from the weight and height formula [14].
(7) Epworth sleepiness scale to assess presence of day-time sleepiness [15].
(8) Over night polysomnography to screen for OSA, OSA is diagnosed if the apnea/hypopnea index is more than 5 events per hour of sleep associated with symptoms like: day time sleepiness, snoring, attacks of suffocation during sleep.
(9) For those who proved to have OSA another night is recorded with titration of nasal CPAP to treat the OSA, then patient is followed up for 6 weeks for any problem with the CPAP use, after 6 weeks patient is assessed again for ESS, pulmonary function testing and the asthma control test.

Data analysis

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) software version 9, all data will be tabulated and presented as mean ± SD, paired student *t* test will be done to compare data of the asthmatic patients proved to have OSA before and after 6 weeks from CPAP use, and sensitivity at 0.05 is accepted.

Results

From the Table 1 the demographic data of the patients showed that the mean age of patients was 46 ± 13 years, female patient constituted about 75% of all patients, body mass index was 30 ± 6.1 Kg/m^2, none of our patients had morbid obesity, asthma score test score was 13.97 ± 3.52, all of our patients

Table 1 Demographic and physiologic characteristics and medical history of all patients.

Characteristic	Data
Age in years	46 ± 13
Female gender	45 (75%)
Body mass index	30 ± 6.1
ACT score	13.97 ± 3.52
FEV1% pred.	60 ± 7.8
FVC% pred.	81.2 ± 3.5
FEV1/FVC	69.5 ± 6.2
FEF_{25-75}% pred.	50.2 ± 9.4
History of chronic sinusitis	15 (25%)
History of rhinitis	48 (80%)
History of GERD	30 (50%)
ESS	9.2 ± 6.5
Snoring	45 (75%)

FEV1, forced expiratory volume in first second; FVC, forced vital capacity; FEF, forced expiratory flow; GERD, gastroesophageal reflux disease; ESS, Epworth Sleepiness Scale.

Table 2 Sleep history, polysomnography data and asthma condition before and 6 weeks after CPAP use in group 2 patients.

Characteristic	Before CPAP use	After CPAP use
ESS	10.5 ± 4.3	6.4 ± 2.3*
AHI	23.5 ± 10.9	2.3 ± 2.1**
Oxygen desaturation index	25.8 ± 7.4	4.2 ± 3.2**
Arousal index	32.5 ± 6.4	10.7 ± 3.2**
FEV1% pred.	60.1 ± 6.9	61.2 ± 6.2***
FVC% pred.	79.3 ± 5.3	80.9 ± 4.8***
FEV1/FVC	70.3 ± 8.2	72.5 ± 8.5***
ACT score	13.97 ± 3.52	14.1 ± 3.97***

* Significant difference $p < 0.05$.
** Highly significant difference $p < 0.01$.
*** Insignificant difference $p > 0.05$.

had ACT score of 17 or less denoting uncontrolled asthma condition in the last 4 weeks, As regard pulmonary function testing forced expiratory volume in the first second was 60 ± 7.8% pred., forced vital capacity was 81.2 ± 3.5% pred., FEV1/FVC was 69.5 ± 6.2, FEF_{25-75} was 50.2 ± 9.4% pred. As regard the medical history of the patients: 15 patients had chronic sinusitis (25%), 48 patients had history of rhinitis (80%) and 30 patients had history of GERD (50%), Epworth Sleepiness Scale was 9.2 ± 6.5, and snoring was present in 45 patients (75%).

Polysomnography was done for all patients, and according to the results of polysomnography the patients were divided into 2 groups: group 1 without obstructive sleep apnea with apnea/hypopnea index (AHI) < 5/h of sleep and group 2 with proved OSA and AHI more than 5/h of sleep, CPAP with titrated in second night polysomnography for all patients in group 2 to define the most tolerable pressure by the patient that makes the AHI to return to normal, then the patients of group 2 were followed up for 6 weeks then reassessed again for sleep history and for the asthma condition, OSA was proved by polysomnography in 15 patients, all patients accepted the CPAP trial and completed the follow up period for 6 weeks.

From the Table 2 there was significant improvement in daytime sleepiness after the use of CPAP, ESS was 10.5 ± 4.3 and became 6.4 ± 2.3 ($p < 0.05$), there was highly significant improvement in all parameters of polysomnography after CPAP use, AHI was 23.5 ± 10.9/h of sleep before CPAP and after use of CPAP it became 2.3 ± 2.1/h of sleep ($p < 0.01$), oxygen desaturation index was 25.8 ± 7.4/h of sleep before CPAP use and it became 4.2 ± 3.2/h of sleep after CPAP use ($p < 0.01$), arousal index was 32.5 ± 6.4/h of sleep before CPAP use and became 10.7 ± 3.2/h of sleep ($p < 0.01$). As regard the asthma condition there was no significant difference before and after CPAP use, FEV1% pred. was 60.1 ± 6.9 before CPAP use and after CPAP use it was 61.2 ± 6.2 ($p > 0.05$), FVC% pred. was 79.3 ± 5.3 before CPAP use and became 80.9 ± 4.8 after CPAP use ($p > 0.05$), FEV1/FVC was 70.3 ± 8.2 before CPAP use and after CPAP use it became 72.5 ± 8.5 ($p > 0.05$), although there was increase in numbers of pulmonary function testing after CPAP use the difference was not statistically significant. As regard the ACT it

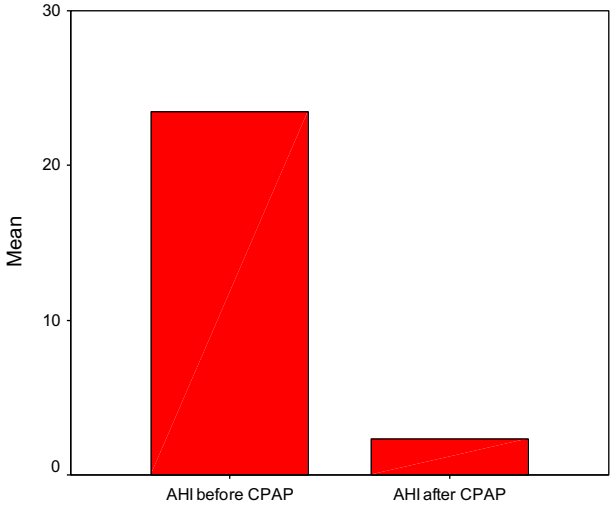

Figure 1 AHI before and after CPAP use.

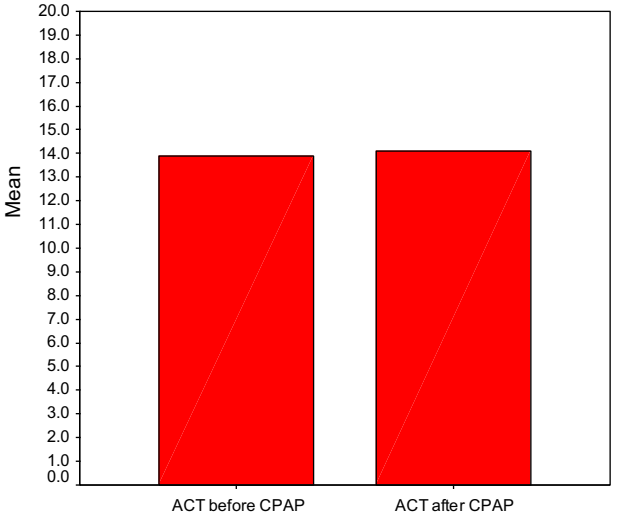

Figure 2 ACT before and after CPAP use.

was 13.97 ± 3.52 before the use of CPAP and it became 14.1 ± 3.97 after the use of CPAP, although it was increased the difference was not significant ($p > 0.05$) and the score remained 17 or below denoting non improvement in the control of asthma Figs. 1 and 2.

Discussion

The present study had 2 objectives; the first was to assess the prevalence of OSA in patients with uncontrolled bronchial asthma, 15 patients out of the 60 patients included in the study were proved to have OSA, the AHI was 23.5 ± 10.9 events/h of sleep, the association between bronchial asthma and OSA has many consequences on the patient, both of the 2 diseases affect the airway of the patient, OSA affects the upper airway by intermittent obstruction during sleep while asthma affects mainly the medium sized and small bronchial branches of the airways by inflammation of the wall, smooth muscle contraction and viscid secretions inside the lumen leading to partial obstruction and embarrassment of respiration, many patients with bronchial asthma have their symptoms to be exaggerated during night with a lot of explanations were postulated for this exaggeration like GERD, increased humidity, bed mite, decreased level of cortisone during night and increases level of acetylcholine, this exaggeration of symptoms during night has its impact on the quality of sleep of the patient and in a study done by Janson et al. in 1996 [16] they studied 2202 patients from 3 different European countries and they concluded that Asthma is associated with decreased subjective quality of sleep and increased daytime sleepiness. The net result of both diseases (OSA and asthma) will be more affection of the respiratory system and poor quality of sleep with its impact on day-time activity and concentration leading to poor quality of life of the patient. Many researchers studied this association between OSA and bronchial asthma from different points: Yigla et al. in 2003 [17] studied 22 patients with uncontrolled asthma on oral steroids either continuous or in purists, study was prospective cohort study and polysomnography was done for all patients and they found that 21 out of the 22 patients were having OSA and they concluded that It may be assumed that prolonged and especially continuous oral corticosteroid therapy in asthma increases airway collapsibility leading to development of OSA. ten Brinke et al. in 2005 [7] studied 136 patients with difficult to control asthma searching for clinical and environmental factors potentially associated with recurrent exacerbations, they found that factors significantly associated with frequent exacerbations include: severe nasal sinus disease; gastro-oesophageal reflux; recurrent respiratory infections; psychological dysfunctioning; and obstructive sleep apnoea, they concluded that recurrent exacerbations in asthma are associated with specific co-morbid factors that are easy to detect and that they are treatable. Therapeutic interventions aimed at correcting these factors are likely to reduce morbidity and medical expenditure in these patients. Teodorescu et al. in 2009 [18] studied 244 bronchial asthma patients to evaluate factors associated with habitual snoring and OSA risk, from the 244 patients 37% had habitual snoring and 40% of patients had high risk of OSA, they concluded that symptoms of OSA in patients with asthma are predicted by asthma severity, coexistent GERD, and use of an ICS in a dose-dependent fashion. The well-recognized male gender predominance for OSA symptoms is not apparent in these patients. Further exploration of these relationships may help to explain the increased prevalence of OSA in asthma and provide new insights into the reported female predominance of asthma morbidity. The study gave high prevalence of OSA in patients with asthma (40%) but the problem is that the authors did not use polysomnography to prove the diagnosis of OSA in the high risk patients making a weak point in the study. Teodorescu et al. in 2010 [19] studied 427 subjects with asthma to evaluate the relationship between OSA risk and level of asthma control in adults, the study was done using multiple questionnaires to assess for the OSA risk and on the other hand to assess for asthma control in the studied group, polysomnography was used to support the results in large group of sleep patients, the authors concluded that high OSA risk is significantly associated with not-well-controlled asthma independent of known asthma aggravators and regardless of the asthma control questionnaire version used. Patients who have difficulty achieving adequate asthma control should be screened for OSA. From the above mentioned studies and from the results of the present study there are a lot points of association between bronchial asthma and OSA, asthma may have a causative relationship to OSA through prolonged use of steroids and female asthmatic patients are more liable to have OSA reversing the predominance of OSA in male gender, while on the other hand OSA can be a potential cause of inadequate control of bronchial asthma and increases frequency of exacerbations through possible mechanisms such as obesity, GERD, airway inflammation, or increased resistive loading on the lower airway by partial obstruction of upper airway, a lot of points that needs further studies, but most important to be put in mind for clinicians that OSA must be suspected in patients with uncontrolled bronchial asthma as presence of OSA in addition to bronchial asthma increases the burden on the patient. The second objective of the present study was to assess the impact of using CPAP on the OSA and the asthma condition of the patient, all 15 patients proved to have OSA in the present study accepted the CPAP treatment and were followed up for 6 weeks before re-assessment, CPAP improved significantly all the sleep parameters as AHI, oxygen desaturation index and arousal index, also use of CPAP improved the day time sleepiness be significant reduction in ESS, improvement in arousal index and day-time sleepiness means improved day-time activity and quality of life of the patient, on the other hand there was no significant improvement in pulmonary function testing as regard FEV1% pred., FVC% pred., and FEV1/FVC, although ACT was increased after CPAP use the difference was insignificant in comparison to values before the use of CPAP, the above mentioned results indicate that there was improvement in OSA state and some improvement in quality of life of the patient but without improvement in the asthma control, Ciftci et al., in 2005 [9] studied 43 patients with nocturnal asthma for the presence of OSA, patients who were found to have OSA were treated with CPAP and then followed again after 2 months, they found that there was no improvement in pulmonary function tests after CPAP use while asthma night time symptom scores were improved significantly after CPAP treatment. Lafond et al. in 2007 [10] studied 20 patients (11 males and 9 females) with stable asthma and OSA, they compared airway responsiveness before and after 6 weeks from CPAP use and they concluded that nocturnal continuous positive airway pressure treatment did

not alter airway responsiveness or forced expiratory volume in one second in subjects with stable mild-to moderate asthma and newly diagnosed obstructive sleep apnoea. However, nocturnal continuous positive airway pressure treatment did improve asthma quality of life. The results of the above mentioned studies and the results of the present study support the hypothesis that asthma control has multiple potentials and asthmatic patients have many co-morbidities that can aggravate the asthma condition and preventing optimal control these co-morbidities include rhinitis, sinusitis, obesity and GERD. So, controlling one aggravating factor can help in improving symptoms or quality of life but not improving the pulmonary function testing.

Conclusion

Obstructive sleep apnea should be screened for in all patients with uncontrolled bronchial asthma, CPAP treatment may improve asthma quality of life but not improving the pulmonary function tests.

Recommendation

Larger studies are needed to fully address the impact of CPAP on asthma condition in patient with both asthma and OSA.

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