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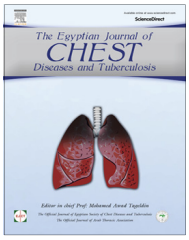

ORIGINAL ARTICLE

Sleep pattern changes in patients with connective tissue diseases

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KEYWORDS

Sleep disorders;
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Apnea hypopnea index;
C-reactive protein and rheumatic disorders

Abstract *Objectives:* To assess sleep pattern changes in patients with connective tissue diseases.

Background: There is evidence that patients with rheumatic disorders may be at an increased risk for sleep disorders, particularly obstructive sleep apnea (OSA). Sleep abnormalities have also been linked to increased pain and fatigue perception, which are common concerns in rheumatology patients. Untreated OSA with intermittent hypoxia is associated with elevated levels of systemic inflammatory markers: C-reactive protein (CRP) and pro-inflammatory cytokines.

Methods: Thirty patients diagnosed as connective tissue diseases (CTD), and 30 apparent healthy control subjects were invited to participate in the study. All the patients were subjected to full medical history, Epworth sleepiness score (ESS), thorough clinical examination with evaluation of the disease activity, laboratory assessment of CRP, and Complete overnight polysomnography.

Results: In the current work, the prevalence of Sleep apnea in CTD patients was 18/30(60%). Sleep apnea was obstructive. Mean AHI (apnea–hypopnea index) was 23.42 ± 26.27/h. Among these OSA patients, 36.7% had severe, 10% had moderate, and 36.7% had mild OSA. The study showed a significant correlation between AHI and BMI, Neck circumference, ESS, erythrocyte sedimentation rate (ESR), CRP, and hematocrit (HCT).

Conclusion: Obstructive sleep apnea is commonly associated with CTD patients. Co-existence of OSA in CTD patients may influence the disease activity and the level of circulating inflammatory markers.

Introduction

Connective tissue disorders (CTDs) are defined as a group of acquired diseases resulting from persistent immune mediated inflammation. In most CTDs there is immune dysregulation resulting in generation of autoreactive T cells or autoantibodies [1].

Sleep abnormalities have been recognized in a number of different rheumatic diseases, including rheumatoid arthritis, osteoarthritis, fibromyalgia, juvenile idiopathic arthritis, Sjögren's syndrome, systemic lupus erythematosus, scleroderma, spondyloarthritis, sarcoidosis and Behcet's syndrome [2].

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Obstructive sleep apnea is a common disorder, characterized by recurrent narrowing and closure of the upper airway accompanied by intermittent oxyhemoglobin desaturation and sympathetic activation [3]. The presence of sleep apnea as a comorbidity may interfere with the evaluation of rheumatic disease activity and responsiveness to therapy [4].

Aim of the work

The aim of our study is to assess sleep pattern changes in patients with connective tissue diseases.

Patients and methods

Thirty patients diagnosed as CTDs attending to outpatient Immunology and Rheumatology clinic of Internal Medicine Department and outpatient clinic of Rheumatology Department of Menoufia University Hospital, and 30 apparent healthy control subjects were invited to participate in the study.

This study included 60 subjects; they were divided into two groups:

Group 1: consists of 30 patients who were diagnosed as CTD patients and on a regular medication regimen for CTD.

Group 2: consists of 30 apparent healthy subjects. Complete medical history was obtained; they were clinically free from any known CTDs.

Health Research Ethics Board of Menoufia University approved the study. Informed consent was obtained from all participants, each patient underwent:

1. Detailed clinical evaluation including history talking, general and local rheumatological examination.
2. Disease activity scores [the systemic lupus erythematosus (SLE) Disease Activity Index (SLEDAI) [5] and Disease Activity Score 28 (DAS28) [6]] for SLE & RA respectively.
3. Epworth sleepiness score (ESS).
4. Investigations:
    1. Chest X-ray (posteroanterior and lateral views).
    2. Electrocardiogram (ECG), echocardiography and High-resolution CT chest if needed.
    3. Routine laboratory investigations and immunological profile.
    4. Complete overnight polysomnography (PSG):

It was conducted in the sleep laboratory unit, Chest Department, Menoufia University Hospital over a whole night (8 h sleep). We started the study at 10 P.M. until 6 A.M. using EMBLA S 4000 system (Iceland).

The PSG consisted of Somnologica studio software, electroencephalography sensor with its cables, electrooculography electrodes, electromyography electrodes for the chin and anterior tibialis muscle, Nasal canula and nasal thermistor, Thoracic and abdominal belt, Pulse oximetry sensor, electrocardiography electrodes with their cables, Snoring microphone, and Body position sensor (see Graph 5).

Data obtained from this study were:

- *Apnea index (AI):* Complete cessation of airflow breathing at the nostrils and mouth for at least 10 s or longer.
- *Hypopnea index (HI):* A decrease in rate and depth of breathing by 50% for 10 s or longer.
- *Apnea–hypopnea index (AHI):* Average number of apnea and hypopnea per hour of sleep. Persons with an AHI < 5 are not considered to have OSA. In contrast, an AHI $\geqslant 5$ and < 15, AHI $\geqslant 15$ and < 30, and an AHI $\geqslant 30$ are classified as mild, moderate, and severe respectively [7].

Results

Table 1 shows that:

Group 1 (cases): included 11 males (36.7%) and 19 females (63.3%), the age ranged from 23 to 74 years with a mean ± SD value of 41.87 ± 15.01 years, the Body mass index (BMI) of the patients ranged from 19.1 to 58.6 kg/m^2 with a mean ± SD value of 35.74 ± 11.20 kg/m^2.

Group 2 (control): included 12 males (40.0%) and 18 females (60.0%), the age ranged from 33 to 83 years with a mean ± SD value of 52.50 ± 12.39 years, the BMI of the subjects ranged from 20 to 60 kg/m^2 with a mean ± SD value of 31.0 ± 9.39 kg/m^2.

Table 2 shows a statistical significant difference between all patients & control group as regard Epworth sleepiness scale (ESS) and significant difference between them as regard Neck circumference and smoking.

Table 3 displays Polysomnography parameters across the studied groups that shows:

Total sleep time (TST), Sleep efficiency, REM Latency from Sleep Onset, Spontaneous Arousals Index, PLMS sequences, AHI, Oxygen Desaturation Events (OD), percentage of Snoring Time in TST, and Total AHI in NREM were significantly different in the cases compared with control group. There were no significant differences in Sleep Onset, flow limitation index,% of sleep in supine position, A + H/h in supine position, Average Oxygen Saturation, (%) of Lowest Oxygen Saturation, % of REM in TST, and Total AHI in REM across two groups.

Table 4 shows Sleep disorders by AHI, cases were subdivided according to results of polysomnography into:

Mild OSA (AHI $\geqslant 5$ and < 15): consisted of 4/30(13.3%) patients, moderate OSA (AHI $\geqslant 15$ and < 30): consisted of 3/30(10%) patients, severe OSA (AHI $\geqslant 30$): consisted of 11/30(36.7%) patients, negative (AHI < 5): consisted of 12/30(40%) patients without OSA.

Table 5 shows a significant positive correlation between AHI in patients and age, uric acid, and creatinine. In addition, there were highly significant positive correlations between AHI in patients and BMI, Neck circumference, ESS, ESR, CRP, and HCT.

Table 6 shows a significant positive correlation between OD in patients and age and Neck circumference. In addition, there were highly significant positive correlations between OD in patients and BMI, ESS, ESR, CRP, and HCT.

Table 7 shows the binary logistic regression model for risk factors of sleep related breathing disorders (SRBD), which demonstrates that ESR is independent risk factors for, SRBD with odds ratio 1.90 and CI (1.01–4.55).

Discussion

Sleep disorders have been described in more than 75% of subjects suffering from various forms of rheumatic diseases [8].