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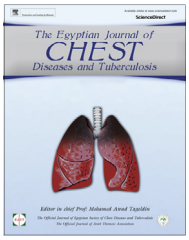

ORIGINAL ARTICLE

Proton magnetic resonance spectroscopy of brain in obstructive sleep apnea in Egyptian subjects

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KEYWORDS

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Abstract *Objective:* The overall objective of this work is to study the cerebral metabolic changes in patients with OSA and to determine the usefulness of MRS as an objective method for evaluation of CNS impairment in these patients.

Materials and methods: This study included two groups; group1 fifteen (15) patients diagnosed with obstructive sleep apnea hypopnea syndrome, and group 2 ten (10) healthy volunteers of comparable age.

Magnetic resonance spectra were obtained from frontal periventricular white matter.

For all subjects, height, body weight, and BMI were assessed. Waist and hip circumference were measured and waist/hip ratio (W/H ratio) was calculated.

Overnight polysomnography (PSG) to identify sleep apnea was done. Daytime sleepiness was evaluated by the Epworth Sleepiness Scale. Symptoms of anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS).

Results: N-acetylaspartate-to-creatine (NAA/Cr) and choline-to-creatine (Cho/Cr) ratios were significantly lower in the frontal white matter of obstructive sleep apnea patients when compared to controls. Absolute concentrations of N-acetylaspartate (NAA) and choline (Cho) were also significantly reduced in the frontal white matter of patients with sleep apnea. Statistically significant negative correlations existed between AHI and metabolites concentrations and ratios in patients with OSAHS. Significant positive correlations existed in patients with OSAHS between Hospital and depression scale for depression (HAD-D) and AHI ($r = 0.764$, $p = 0.001$), ODI ($r = 0.571$,

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$p = 0.026$), and ESS ($r = 0.644$, $p = 0.010$), respectively. Significant positive correlations existed in patients with OSAHS between Hospital and depression scale for anxiety (HAD-A) and AHI ($r = 0.753$, $p = 0.001$), and ESS ($r = 0.537$, $p = 0.039$), respectively. *Multivariate Linear* regression model of factors predictive showed AHI as the main predictor factor for choline to creatine ratio in patients with OSAHS with $t = 5.180$, at $p < 0.001$.

Conclusion: OSA patients show abnormal brain metabolites related to neuronal damage due to intermittent chronic hypoxemia. Anxious and depressive symptoms are highly prevalent in patients with severe untreated OSAS. The severity of depressive and anxious symptoms may be related to excessive daytime sleepiness and to nocturnal hypoxemia both of which are strongly correlated to brain metabolites. AHI seems to be the main predictor factor for choline to creatine ratio in patients with OSAHS.

Introduction

Obstructive sleep apnea is a major public health problem worldwide [1–3]. It is estimated to affect up to 4% of the general adult population [4]. It is associated with several consequences including neurocognitive impairment [5]. To date, the pathophysiology of the cognitive deficits reported in OSA patients has not been determined.

Repeated sleep apneic episodes may lead to CNS impairment in patients with obstructive sleep apnea (OSA). Excessive daytime sleepiness and cognitive and emotional deficits are common daytime symptoms of OSA. Hypoxic brain damage and fragmentation of sleep are generally thought to be causes of these deficits [6].

Some researchers argue that excessive daytime somnolence is the leading cause of the cognitive deficits, while others propose that nocturnal hypoxemia is the main contributing factor [4,7].

Magnetic resonance spectroscopy (MRS) is a non-invasive method, useful for evaluating local metabolic changes in various conditions affecting the central nervous system as in patients with OSAHS [8].

Several studies have shown that executive dysfunction in OSA patients may persist even after nasal continuous positive airway pressure (nCPAP) treatment. Cognitive executive functions are associated with specific prefrontal-subcortical brain circuits, thus it has been proposed that OSAS may promote irreversible anoxic brain damage affecting the prefrontal cortex [8].

Subjects and methods

This study included two groups:

Group 1: fifteen (15) patients newly diagnosed with severe obstructive sleep apnea hypopnea syndrome, and

Group 2: ten (10) healthy volunteers of comparable age.

Fifteen (15) consecutive patients newly diagnosed with severe obstructive sleep apnea hypopnea syndrome who fulfilled the following inclusion criteria were enrolled in this study: apnea/hypopnea index (AHI) >30, age <65 years, Patients' exclusion criteria were: concomitant metabolic disease (DM, hypertension), history of stroke, presence of cardiac disease, neurological disease or history of head injury or CPAP/BiPAP therapy, presence of other sleep disorders, and presence of obstructive lung disease. Patients with claustrophobia or metallic implants were also excluded.

Anthropometric profile

Body weight was recorded in all patients, in erect position without shoes and wearing only light indoor clothes, height was measured and body mass index (BMI) was calculated as body weight/height^2 (kg/m^2) [9,10].

Waist circumference was measured midway between the lower rib cage margin and the anterior superior iliac spine. Hip circumference was measured at the maximum circumference of the buttocks, the subject standing with feet placed together and waist–hip ratio (W–HR) was calculated [11].

Nocturnal sleep studies

All patients underwent overnight polysomnography using Respironics Alice 5 system (RESPIRONICS, Germany Inc.). It is a level I device that records parameters such as body position, effort (thorax and abdomen), nasal flow (canula and/or thermistor), snoring (canula and/or microphone), SpO_2, plethysmogram, pulse rate, ECG, CPAP/BiPAP, and PLM overnight in the hospital. Recordings of at least 5 h were required to validate the sleep study. The analysis was carried out automatically and manually. Respiratory events were scored using standard criteria [12,13].

The apnea hypopnea index (AHI) was defined as the total number of apneas and hypopneas per hour of sleep. As indices of nocturnal hypoxemia we considered the oxygen desaturation index (this is the number of times that the oxygen saturation falls by more than 3 or 4 percent per hour of sleep), T90 (the fraction of sleep time spent below an oxygen saturation of 90 percent) and the minimal value recorded during sleep (minimal SaO_2).

Assessment of daytime sleepiness

The Epworth Sleepiness Scale (ESS) [14,15] was used for assessing daytime sleepiness. This is a commonly used self-administered scale with eight items of about how easily the respondent would fall asleep in different situations. The items are scored on a 0–3 scale, which are added to give an overall score of 0–24. Higher scores indicate more sleepiness. ESS