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Evaluation of cognitive functions in patients with obstructive sleep apnea before and after continuous positive airway pressure treatment

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Abstract

Objectives: The aim of this study is to evaluate the remedial effect of continuous positive airway pressure (CPAP) therapy on neurocognitive function in obstructive sleep apnoea (OSA) patients. *Methods:* The cognitive impairment in OSA patients was evaluated with Montreal Cognitive Assessments (MoCA) before and after CPAP therapy. The study assessed 54 patients who were diagnosed with OSAS seen at the neurology clinic of the Trakya University Medical Faculty. They were given MoCA the day of diagnosis, after one day of CPAP therapy, and after three months of CPAP therapy. *Results:* MoCA scores before treatment showed a statistically significant correlation between disease severity and abstract thinking (Correlation coefficient: 0.270±0.048). There was no significant difference between MoCA scores before treatment and after one day of CPAP therapy (p=0.244). However, there were significant improvements in MoCA scores after three months of treatment, when compared to scores from before treatment and after one day of therapy (p<0.001).
Conclusions: CPAP treatment may improve cognitive function in OSA patients. MoCA is an effective and simple tool for evaluating cognitive function.

Keywords: Obstructive sleep apnea syndrome, continuous positive airway pressure treatment, neurocognitive function, Montreal Cognitive Assessment

INTRODUCTION

Obstructive sleep apnea (OSA) syndrome is caused by repetitive upper airway obstructions during sleep. It is the result of a variety of physiological, anatomical, genetic, and environmental factors.[1] OSA may lead to various cardiovascular, pulmonary, cerebrovascular, and neurocognitive disorders.[2] The prevalence of OSA in adults has been identified as 9% in women and 17% in men.[3] The most common symptoms are snoring, witnessed apneas, excessive daytime sleepiness, and waking up with a feeling of suffocation or insomnia.[4]

Intermittent hypoxemia, sleep fragmentation, and sleep deprivation play a role in the pathogenesis of neurocognitive dysfunction associated with OSA.[5] In OSA patients, two broad areas have been examined: cognitive function and psychomotor performance.[6] OSA has a significant impact on cumulative executive functions such as wisdom, understanding, and learning.[7] Attention is significantly affected by OSA.[8]

In the early stages, in patients that cannot be treated with surgery, most of the neurocognitive complications are reversible with regular use of a continuous positive airway pressure (CPAP) device.[6-8] This study's goal is to evaluate the remedial effect of CPAP therapy on neurocognitive function in OSA patients. This was done by comparing Montreal Cognitive Assessment (MoCA) scores before and after CPAP treatment. The secondary aim of the study was to examine the potential relationship between disease severity and cognitive function subtypes. (This is not clear, clarify or delete).

METHODS

This was a prospective, observational descriptive study. This study included patients between 18 and 65 years of age who were diagnosed with OSA, seen in the neurology clinic of the Medical Faculty, Trakya University between June 2013 and September 2013. Patients aged >65 years, having vitamin deficiency, cerebrovascular, infectious,

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endocrine, or internal diseases that could affect neurocognitive function were excluded. Only newly diagnosed OSA were included.

The demographic characteristics of the patients are shown in Table 1. Thirty-nine patients (72.2%) were male and 15 (27.8%) were female. The average age was 49.1 ± 9.4 with a range of 23–65 years. The average weight was 87.5 with a range of 61–119 kg. Seventeen patients (31.5%) had finished primary school, five (9.3%) had finished secondary school, fourteen (25.9%) had finished high school and 18 (33.3%) had university degrees. Twenty-five patients (46.3%) had co-morbidities of hypertension and 10 (18.5%) had diabetes mellitus.

Polysomnography

Polygraphic sleep tests were performed with a computerized polysomnography (PSG) system (Compumedics 44E). Sleep stages were identified with six electroencephalogram channels (C4-A1, C3-A2, F3-A2, F4-A1, O1-A2, O2-A1), a chin electromyogram, and left and right electrooculograms. Thoracoabdominal movements were monitored by thoracic and abdominal strain gauges. Airflow was monitored by an oronasal thermistor. Arterial oxyhemoglobin saturation was recorded with a pulse oxymeter. Electrocardiogram, snoring, and body position were also recorded. An episode of obstructive apnea was defined as the absence of airflow for at least 10 sec with ribcage and abdominal excursions. Hypopnea was defined as a 50% reduction in airflow compared to the baseline lasting 10 s or more and associated with at least a 4% decrease in arterial oxyhemoglobin saturation, electroencephalographic arousal, or both. The number of episodes of apnea and hypopnea per hour is the apnea–hypopnea index (AHI). AHI was used to diagnosis of patients as follows: 1) if AHI is 0–5, but there is rapid eye movement (REM) during apnea or hypopnea, it is REM-dependent OSA, 2) if AHI is 5–10, it is mild OSA, 3) if AHI is 10–15, it is moderate OSA, and 4) if AHI is >15, it is severe OSA.

CPAP therapy

In patients with moderate to severe OSA, a second PSG was done to determine the pressure for the CPAP device. Patients used the device for three months and the CPAP device memory cards were checked to ensure proper use.

Montreal Cognitive Assessment

The Montreal Cognitive Assessment (MoCA) was created by Dr. Ziad Nasreddine in Montreal in 1996. It was used to evaluate neurocognitive function three times: 1) when first diagnosed with OSA with PSG, 2) after one day of titration with CPAP, the morning after hospitalization, for patients with moderate to severe OSA, and 3) after three months of regular CPAP treatment. The impact of CPAP treatment on cognitive function was evaluated by comparing MoCA scores before and after therapy. MoCA was conducted within 09.00-11.00 AM to all the patients. Patients were asked if they have used any drug, caffeine or felt sleepy, and the MoCA was not administered if any of the conditions existed.

Goldstein *et al*.[9] stated that MOCA was a reliable test for diagnosing Alzheimer and mild cognitive disorder. It's especially effective to differentiate mild cognitive disorder from healthy subjects. A meta-analysis conducted by Ciesielska *et al*.[10] demonstrated that MOCA is superior to Mini-Mental State Examination in population older than 60 years.

Chen *et al*.[11] used MOCA to evaluate the cognitive functions in patients with OSAS and concluded that MOCA was a reliable and valid test. Mu *et al*.[12] also had similar findings.

The MoCA is a simple test that can be administered and scored in about ten minutes. Based on MoCA, sensitivity or detecting mild cognitive impairment is 87%. Out of a total of 30 points, <21 is severe cognitive dysfunction, 21–25 moderate, 26–27 mild, and 28-30 is no cognitive impairment. In order to maintain consistency, the MoCA was performed by the same investigator without specifying participant's name. After explaining the scope and purpose of the study, patients agreed to the study and signed consent forms.

Statistical analysis

Data were expressed as with mean values, standard deviations, and percentages. In the comparison of values of OSAS patients before treatment, after one day of treatment and after three months of treatment, in repeated measurements was used repeated measures analyses of Anova. Compliance with the normal distribution of data was evaluated with Kolmogorov–Smirnov fitness test. MoCA scores were compared from before and after treatment and by AHI subgroup. The presence of a correlation between patients' AHI and MoCA scores was examined with a Spearman correlation analysis. The significance level was $p<0.005$.

Table 1: Demographic characteristics of the patients with OSAS

	Frequency (n)	Percent (%)
Gender, M/F	39/15	72.2/27.8
Education		
Primary	17	31.5
Secondary	5	9.3
High School	14	25.9
University	18	33.3
Hypertension, +/-	25/29	46.3/53.7
Diabetes Mellitus, +/-	10/44	18.5/81.5

RESULTS

During the study period, 75 patients were diagnosed with OSA in our clinic. Six were excluded because they also had vitamin deficiency and cerebrovascular disease. Another 15 patients were excluded for being above 65 years of age. The remaining 54 patients were included in the study and were evaluated with the MoCA when diagnosed with OSA based on PSG. Sixteen of these patients were not given further treatment with CPAP.. Thirty-eight patients had repeat PSG with CPAP to determine the appropriate pressure, and a second MoCA was done after spending a night in the hospital with CPAP. Fourteen patients could not use CPAP because of dry mouth and throat, excess pressure, high cost of treatment, and not feeling comfortable. Twenty-four patients began a three-month CPAP therapy, after which a final MoCA was done. The demographic characteristics of these study patients are shown in Table 1. These patients who received CPAP for 3 months has been cathegorized as the treatment group, while all newly diagnozed OSA patients were classified as control.

There was a statistically significant correlation between AHI and MoCA values before treatment (Correlation Coefficient:0.270±0.048) based on a nonparametric test. The morning after hospitalization, MoCA values dropped but were not significantly correlated with AHI. Finally, after three months of treatment, there was no relationship to the AHI (Table 2). Attention function, abstract thinking, executive functions, verbal and visual memory, visuospatial functions, and language functions were lower in OSA patients before treatment. Abstraction ability was significantly correlated with OSA severity. Other functions had the same tendency, but the correlation was not statistically significant.

Total MoCA scores was used to evaluate severity of cognitive dysfunction secondary to OSA. We used Friedman repeated measures analysis to assess if there is cognitive improvement in OSA patient with one day and three months CPAP treatment compared to baseline level. According to Friedman repeated measures analyses on total MoCA scores (Figure 1A), there were statistically significant differences between the first and third total MoCA scores and the second and third total MoCA scores ($p<0.001$ for both), but not the first and second total MoCA scores ($p=0.244$). When we evaluated the MoCA sub-groups, we found that abtract (Figure 1B) and attention (Figure 1D) sub-items were correlated with total MoCA scores but orientation (Figure 1C) was the least affected sub-item. A multiple comparison procedure was used to isolate the groups.

Table 2: Nonparametric corelation between apnea hypopnea index (AHI) and Montreal Cognitive Assessment (MoCA)

AHI	VSF	NM	ATT	LG	ABS	MM	ORN	TOTAL
Corr Coeff	-,077	,027	-,141	-,128	-,270	-,189	-,023	-,234
P	,581	,847	,309	,357	,048	,172	,870	,089
N	54	54	54	54	54	54	54	54

AHİ: Apnea Hypopnea index, VSF: visuospatial function, NM: naming, ATT: attention, LG: language, ABS: abstract, MM: memory, ORN: orientation, MoCA: Montreal cognitive assessment

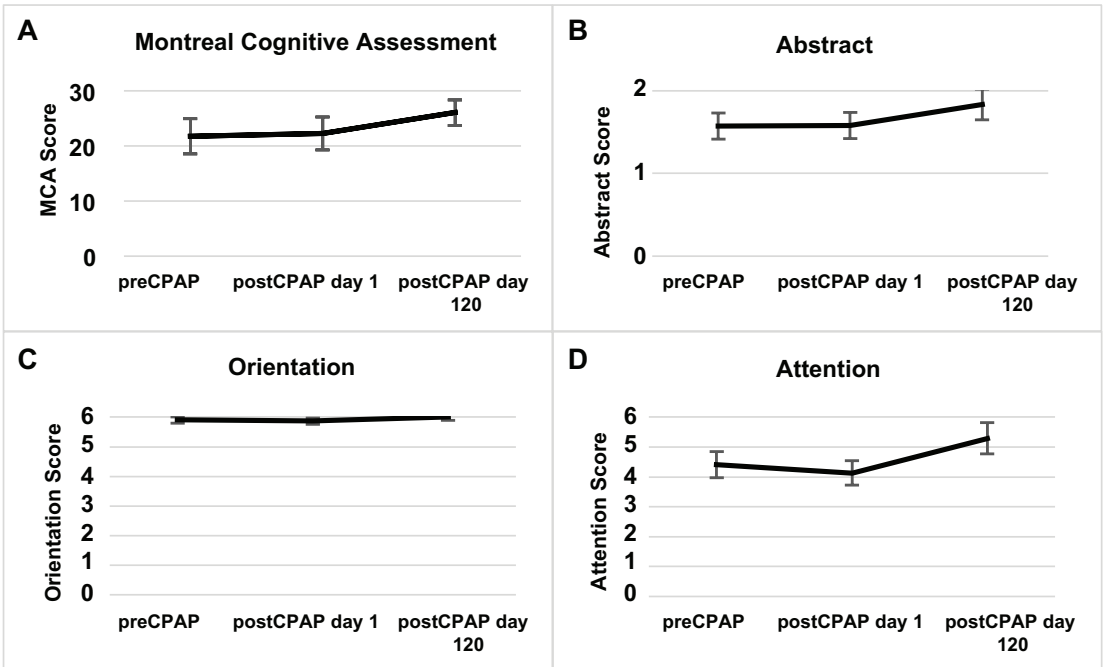

Figure 1. **A**. Cognitive assessment of OSA patients by Montreal Cognitive Assessment (MoCA) before and after CPAP therapy; **B**. Abstract points; **C**. Orientation points; **D**. Attention points

DISCUSSION

The main finding of this study was that there was a statistically significant correlation between MoCA scores and sleep OSA severity as reflected in the AHI. Attention function, abstract thinking, executive functions, verbal and visual memory, visuospatial functions, and language functions were lower in OSA patients before treatment. Abstraction ability was significantly correlated with OSA severity. Other functions had the same tendency, but the correlation was not statistically significant

Romola *et al*.[8] reported that the attention function was impaired in patients with OSA compared to controls, and impairment in attention function increased with increasing disease severity. In four of five studies with OSA patients, worsening of executive function was reported. One study reported deterioration of short-term memory, while four studies found impairment of long-term memory, assessed verbally and visually. A consistent effect of OSA on language ability and psychomotor function was not found. However, in two of the five studies, language abilities and psychomotor functions were affected.[8] Lal *et al*.[6] showed that OSA has a significant effect on reasoning, understanding, and learning functions, known cumulatively as executive functions, and that in OSA patients, wakefulness and attention were significantly affected. Reduced sustained attention in untreated OSA patients can result in motor vehicle accidents.[6]

The study of Nicola *et al*.[13] on untreated OSA patients showed impairments in memory, attention, executive functions, constructional abilities, low scores on the Beck depression test, and increased sleepiness. These impairments were associated with focal gray matter volume reduction in the enthorinal left hippocampal cortex, left posterior parietal cortex, and right superior frontal gyrus.[13] After three months of treatment, significant improvements were observed in all areas. The improvement was associated with a focal gray matter volume increase in the enthorhinal left hippocampal cortex, medial orbitofrontal cortex, and the rostral side of the right superior frontal gyrus. These results provide important clues for the pathogenesis of cognitive impairment in OSA patients. Hypoxemia and sleep fragmentation were proposed as potential contributors. The authors suggested that the pattern of neuropsychological changes in OSA was similar to mild cerebrovascular disease (small vessel disease), hence the deficit could be vasogenic. After treatment, participants showed a significant improvement in all cognitive tests, excluding the Stroop test total time and long-term memory test.[13]

We have also shown in this study that three

months of CPAP therapy resulted in a significant improvement in the cognitive functions of OSA patients. In a randomized controlled study, Pan *et al*.[14] demonstrated improvement of cognitive functions with CPAP treatment. Juraido et al.[15] showed deterioration in the areas of memory and attention in severe OSA patients; with treatment they demonstrated improvement in attention. Ferini *et al*.[16] observed improvements in brain morphology with CPAP treatment. These studies support our findings. Rosenzwieg *et al*.[17] compared two groups of patients with supportive care. One group also had one month of CPAP treatment. The group with CPAP showed significant improvement in daytime sleepiness and verbal repetition memory.[18] On the other hand, Stephanie *et al*.'s[18] review suggested that the effect of CPAP treatment on cognition in OSA patient was not clear and it was not certain that CPAP can greatly reduce cognitive impairment.

As for the pathophysiology mechanism of cognitive improvement from CPAP treatment, There was increase in oxygen saturation, reduction of apnea and sleep fragmentation within one day of CPAP administration. There was no improvement of MoCA one day after CPAP, but improvement was seen after 3 months. We believe that the cytopathology due to low oxygen levels requires time for reversal and regeneration. The process would depends partly on the eradication of proinflammatory agents and free oxygen radicals, with improvement of the oxygen saturation and reduction of sleep fragmentation.

Unlike other studies, our study evaluated cognitive function with the MoCA. The advantages of using MoCA are that results could be obtained in less than ten minutes, and training is not required to administer the test. We have demonstracted that MoCA is could be used to monitor the clinical improvement with CPAP treatment.

One limitation of our study was the insufficient number of patients continuing treatment. Patients often discontinued the treatment because of reasons such as dry mouth and throat, excess pressure, high cost of treatment, and not feeling comfortable. The other limitation of our study was lack of a control group with a sham CPAP. However, leaving severe OSAS patients untreated for three months would be ethically problematic.

In conclusion, we have demonstrated in this study that OSA deteriorates cognitive functions. CPAP is effective in improving the cognitive function, but it requires a sustained treatment period. MoCA is a trustworthy test to monitor the cognitive impairment, and effect of the treatment. OSA mainly affect attention and executive functions. With more severe OSA, cognitive function increasingly deteriorates. The minimum duration of CPAP treatment to ameliorate the cognitive impairment, and when the cognitive impairment become irreversible remains important unknowns.

DISCLOSURE

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