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Original Article

Continuous positive airway pressure improved daytime sleepiness and memory function in patients with obstructive sleep apnea

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Abstract

Objectives: Obstructive sleep apnea (OSA) is a sleep disorder which results in daytime sleepiness and impaired memory function. The aim of this study was to investigate the effect of continuous positive airway pressure (CPAP) on daytime sleepiness and memory function in OSA patients. We also investigated whether CPAP compliance impacted the effect of this treatment. **Materials and Methods:** The nonrandomized, nonblinded clinical trial enrolled 66 patients with moderate-to-severe OSA subjects. All subjects completed a polysomnographic study, daytime sleepiness questionnaires (the Epworth Sleepiness Scale and the Pittsburgh Sleep Quality Index), and four memory function tests (working memory; processing speed [PS]; logical memory [LM]; face memory [FM]). **Results:** Before CPAP treatment, no significant differences ($P < 0.05$) were noted in the demographic data, daytime sleepiness, or memory function between two groups (with/without CPAP). However, OSA patients treated with CPAP for 2 months showed significant improvements in daytime sleepiness, PS, mostly of LM, and FM comparing to 2 months ago. As compared to those who did not receive CPAP treatment, CPAP can improve only parts of LM (delayed LM [DLM] and LM percentage [LMP]). In addition, compared to control group, a significant improvement of daytime sleepiness and LM (LM learning, DLM, and LMP) in good compliance with CPAP treatment group and of DLM and LMP in the low compliance with CPAP treatment group was found. **Conclusion:** CPAP treatment for 2 months could improve some of LM in OSA patients, especially in patients exhibiting good CPAP compliance.

Keywords: *Continuous positive airway pressure therapy, Daytime sleepiness, Memory function, Obstructive sleep apnea*

Introduction

Obstructive sleep apnea (OSA) is characterized by recurrent collapse of the upper airway, leading to episodes of hypoxemia and arousal during sleep [1]. The clinical features of OSA include snoring, daytime sleepiness, and sleep fragmentation [2]. Many studies have reported that OSA patients have significant impairments in cognitive function, attention, and memory function [3-7]. Recently, a large randomized clinical trial of Sleep Apnea Cardiovascular Endpoints (SAVE) study shows improvement of depression and Epworth Sleepiness Scale (ESS) but not anxiety score (hospital anxiety and depression scale) during 48-month follow-up [8]. Other studies have shown that OSA patients have significant impairments in episodic memory, procedural memory, and working memory (WM) [9-11]. Furthermore, in a recent study by Jackson *et al*., OSA patients exhibited greater daytime sleepiness and impairments in the backward digit span test, trail making test, and quality of life compared to a nonsleep apneic community sample [12].

Although there exists significant evidence on memory impairments in OSA patients, the effect of continuous positive airway pressure (CPAP) treatment on these memory impairments remains controversial [13,14]. Indeed, very few studies have investigated the effect of CPAP on memory impairments. A randomized controlled study by Joyeux-Faure *et al*. showed no significant impact of CPAP on memory impairment [15]. However, the drop-out rate of CPAP usage was high and only 10 OSA patients completed the study.

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Therefore, given the limitations of this previous study, we aimed to investigate the effect of CPAP compliance on sleepiness and memory function in OSA patients.

Materials and Methods

Study participants and experimental protocol

This nonrandomized, nonblinded clinical trial was conducted at the Sleep Center of Hualien Tzu Chi General Hospital from 2016 to 2017, and 66 moderate-to-severe adult OSA patients (apnea–hypopnea index [AHI] ≥15/h; age ranging from 20 to 75 years) were enrolled. Patients who had previously been diagnosed with, or treated for, any psychological disease or chronic disease that could have interfered with the accuracy of the neurocognitive tests were excluded from the study. Patients unable to cooperate with the tasks were also excluded. The baseline characteristics of the subjects such as age, sex, and body mass index were recorded. All enrolled subjects underwent polysomnography and completed the ESS, the Pittsburgh Sleep Quality Index (PSQI), and memory tests. The subjects were then divided into two groups – patients in one group received 2 months of CPAP treatment (S8 AutoSet, ResMed Inc., San Diego, CA, USA) and patients in the other did not receive CPAP treatment (controlled group), but rather sleep hygiene education (a program including weight loss, changing sleep position, and avoid of sedative drugs or alcoholic use before sleep) every month. After 2 months, all patients once again completed the ESS, PSQI, and memory tests as well. Data on CPAP compliance were also collected.

Polysomnography

All patients underwent one night of standard Type 1 attended polysomnography (Embla A10, Embla, Broomfield, CO, USA) at our Sleep Center. Sleep and arousals were scored according to the standard criteria. The AHI and 3% oxygen desaturation index (ODI) were determined and utilized as markers of disease severity [2].

Measures

Sleep questionnaires

Sleep questionnaires were conducted before and after 2-month CPAP treatment period. The ESS is an eight-item questionnaire that asks respondents to rate their likelihood of falling asleep during eight different everyday situations. Each question is rated on a scale from 0 (not at all likely to fall asleep) to 3 (very likely to fall asleep), and the total score of the ESS ranges from 0 (minimum) to 24 (maximum) [16]. All enrolled subjects also completed the PSQI, a commonly used instrument designed to measure sleep disturbance and sleep habits within a 1-month period [17]. This questionnaire consists of 19 items including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.

Memory tests

All memory tests were conducted before and after 2-month CPAP treatment period, according to previously published data [18,19]. Here, we employed two components of the Wechsler Memory Scale-Third Edition, namely face memory (FM) and logical memory (LM) subtests. The FM subtest includes (1) immediate FM (IFM), (2) delayed FM (DFM), and (3) FM percentage. The LM subtest includes (1) immediate LM (ILM), (2) LM learning (LML), (3) delayed LM (DLM), (4) LM percentage (LMP), and (5) LM recognition (LMR). All study participants completed the memory tests in the morning in a quiet isolation room at 23°C without any interference.

Continuous positive airway pressure compliance

Although there exists no exact definition of CPAP compliance, we defined good CPAP compliance as the use of CPAP for more than 4 h per night for more than 70% of the days monitored. Low CPAP compliance was defined with those who cannot tolerate more than 4 h CPAP treatment in one night.

Statistical analysis

Independent *t*-tests were used to compare age, sex, body mass index, AHI, ODI, arousal index, ESS, PSQI, and memory test scores between two OSA groups (with/without CPAP treatment) at baseline. Data are presented as mean ± standard deviation (SD). $P < 0.05$ was considered to indicate statistical significance. Paired *t*-tests were used to compare ESS, PSQI, and memory test scores before and after CPAP treatment. Data are presented as mean ± SD. $P < 0.05$ was considered to indicate statistical significance. The subjects were divided into three groups (good compliance group (≥4 h/night), low compliance group (<4 h/night), and control group (denied CPAP used), and the previous test scores were tested by ANCOVA. All statistical analyses were performed using SPSS for Windows Version 14.0 software (SPSS, Chicago, IL, USA).

Ethical statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This study was approved by the Institutional Review Board of Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, and all participants provided informed consent (IRB 105-20-A, dated August 1, 2016). Informed consent was obtained from all individual participants included in the study.

Results

Demographic data

Sixty-six subjects were enrolled in our study – 47 OSA patients received CPAP treatment and 19 did not. The demographic data of these two OSA groups (with/without CPAP treatment) showed no significant differences in age, sex, body mass index, AHI, ODI, arousal index, sleepiness scale (ESS and PSQI), or memory test scores (LM, visual memory [VM], WM, and processing speed [PS]) [Table 1].

Epworth Sleepiness Scale and Pittsburgh Sleep Quality Index questionnaires

The ESS scores of the CPAP and control groups were 10.51 ± 5.09 and 10.53 ± 5.17, respectively, at the baseline. After 2 months of treatment, the ESS score of the CPAP

Table 1: Baseline characteristics of continuous positive airway pressure and control groups

Item	Mean±SD		Pretest (t or χ^2)
	CPAP (n=47)	Control (n=19)	
Characteristics			
Age	52.49±11.48	49.74±12.17	0.87
Male (%)	40±85.11	14±73.68	0.28
BMI	29.70±5.13	33.68±8.29	−1.94
AHI	49.79±20.82	52.80±28.11	−0.42
ODI	40.84±47.93	49.69±37.62	−0.72
AI	35.94±21.25	35.98±24.47	−0.01
ESS	10.51±5.09	10.53±5.71	−0.01
PSQI	10.04±5.43	10.95±5.07	−0.62
WM	2.38±1.23	2.53±1.22	−0.43
PS	66.96±19.19	65.63±24.45	0.23
ILM	38.62±11.78	40.05±16.92	−0.34
LML	4.49±2.59	4.42±1.61	0.13
DLM	23.55±8.77	26.05±11.79	−0.84
LMP	83.24±14.57	86.82±16.22	−0.88
LMR	24.26±3.56	23.95±4.87	0.29
IFM	35.17±4.69	35.11±3.00	0.06
DFM	34.34±4.91	34.47±2.67	−0.14
FMP	94.44±7.25	95.56±6.18	−0.59

*P>0.05 for all tested items. Data: Mean±SD, t: Different of CPAP and control at baseline. AHI: Apnea–hypopnea index, AI: Arousal index, BMI: Body mass index, CPAP: Continuous positive airway pressure, DFM: Delayed face memory, DLM: Delayed logical memory, ESS: Epworth Sleepiness Scale, FMP: Face memory percentage, IFM: Immediate face memory, ILM: Immediate logical memory, LML: Logical memory learning, LMP: Logical memory percentage , LMR: Logical memory recognition, ODI: Oxygen desaturation index, PS: Processing speed of memory, PSQI: Pittsburgh Sleep Quality Index, WM: Working memory

group significantly decreased 3.3 points, compared to its baseline (P = 0.0001). The PSQI scores of the CPAP and control groups were 10.04 ± 5.43 and 10.95 ± 5.07 at the baseline, respectively. After 2 months of treatment, the PSQI score of the CPAP group significantly decreased to 7.13 ± 3.65, compared to its baseline (P = 0.049). Furthermore, PSQI had significant improved in controlled group, compared to its baseline (P = 0.049). However, those two scores of daytime sleepiness at the end of the study showed no significance between these two groups [Table 2].

Memory test

PS (P < 0.001), LM (ILM, DLM, LMP, and LMR), and FM (IFM and DFM) significantly improved after 2 months of CPAP treatment, compared to its baseline. On the other hand, patients who did not undergo CPAP treatment exhibited a significant decrease in LML at the 2-month follow-up, compared to its baseline (P = 0.03). However, compared to the control group, there was only significant improvement on the DML and LMP in the CPAP group at the end of the study [Table 2].

Table 3 shows the association between daytime sleepiness, memory changes, and CPAP compliance, using ANCOVA with the control group as a baseline. The mean CPAP used was 5.5 ± 0.6 h in good compliant group and 3.6 ± 0.4 h in low compliant group. Compared to the control group, a significant improvement of daytime sleepiness and LM (LML, DLM, and LMP) in good compliance with CPAP treatment group and of DLM and LMP in the low compliance with CPAP treatment group was found.

Discussion

In the present study, 2 months of CPAP treatment improved some of memory functions in patients with OSA. Patients exhibiting good CPAP compliance demonstrated greater improvements in daytime sleepiness and some of LM. Although some previous studies showed controversial CPAP effect on memory in OSA patients [12,13], our study showed the effect of CPAP adherence in improving memory in OSA patients.

CPAP treatment in OSA patients improved daytime sleepiness about –3.1 in SAVE study [8]. This value is –3.3 points in our study. The improvement of ESS score was significantly larger than the minimal clinical important difference of ESS (–2 points) in OSA patients [20]. This means that CPAP can significantly decrease daytime sleepiness in OSA patients.

Neurocognitive dysfunction has been well described in OSA patients, and several risk factors for this cognitive impairment have been identified. It has been shown that intermittent hypoxemia affects hippocampal volume, resulting in impairments in memory consolidation and amnesia [21]. In addition, endothelial dysfunction during hypoxemia [22] and daytime sleepiness [23] have both been implicated in neurocognitive dysfunction in OSA patients. In our present study, 2 months of CPAP treatment significantly improved daytime sleepiness and, to a lesser degree, WM and LM that may infer difference from recovery of daytime sleepiness and memory function.

A number of previous studies have shown impairments in episodic memory, procedural memory, and WM in OSA patients [9-11], although the effect of CPAP on WM remains controversial [15,24]. Many of the animal data showed impaired spatial WM under intermittent hypoxemia [25,26], as well as another study in healthy adults [27]. Our study showed that 2 months of CPAP treatment did not have any beneficial effect on WM. WM was found to decrease over the 2-month study period in both groups; however, this decrease was smaller in the CPAP treatment group (–0.08) than in the control group (–0.42). Even adjusted to controlled group, good compliance to 2-month CPAP treatment did not significantly improve WM. This implies that the recovery of intermittent hypoxemia over 2 months with CPAP treatment cannot completely recover WM. In the study by Thomas *et al*., 8 weeks of CPAP therapy was able to achieve complete subjective clinical recovery, but the recovery of neurocognition was still impaired [10]. Further investigation about the recovery time in OSA patients should be studied.

A slow PS was noted in OSA patients, and this was significantly improved by CPAP treatment. A previous pathophysiological study found that white matter integrity was impaired in OSA patients and CPAP treatment reversed this neural injury [28]. In our study, 2 months of CPAP treatment improved the PS of OSA patients, although CPAP compliance did not have an impact on this effect.

Table 2: Changes in daytime sleepiness and memory measures following 2 months of treatment in the continuous positive airway pressure and control groups

Test	CPAP (*n*=47)			Control (*n*=19)			CPAP versus CON *t* (Δ)
	Pretest	Posttest	*t*	Pretest	Posttest	*t*	
Sleep scale							
ESS	10.51 (5.09)	7.21 (4.41)	−4.88*	10.53 (5.71)	9.68 (4.91)	−0.65	−1.82
PSQI	10.04 (5.43)	7.13 (3.65)	−3.90*	10.95 (5.07)	9.42 (4.14)	−1.87*	−1.80
WM	2.38 (1.23)	2.30 (1.47)	−0.40	2.53 (1.22)	2.11 (1.20)	−1.71	0.91
PS	66.96 (19.19)	72.98 (20.79)	5.89*	65.63 (24.45)	65.47 (25.22)	−0.04	1.54
ILM	38.62 (11.78)	47.21 (12.86)	7.08*	40.05 (16.92)	44.32 (16.46)	2.00	1.85
LML	4.49 (2.59)	4.21 (2.29)	−0.49	4.42 (1.61)	2.79 (5.44)	−2.41*	1.36
DLM	23.55 (8.77)	31.62 (9.02)	8.28*	26.05 (11.79)	27.47 (11.44)	0.87	3.59*
LMP	83.24 (14.57)	92.59 (6.76)	4.89*	86.82 (16.22)	86.16 (13.68)	−0.19	2.69*
LMR	24.26 (3.56)	25.32 (3.40)	2.47*	23.95 (4.87)	24.00 (4.4)	0.08	1.28
IFM	35.17 (4.69)	38.83 (3.80)	6.32*	35.11 (3.00)	36.58 (9.54)	0.75	0.53
DFM	34.34 (4.91)	38.00 (4.73)	6.22*	34.47 (2.67)	36.58 (9.78)	0.99	−0.17
FMP	94.44 (7.25)	95.57 (6.61)	0.89	95.56 (6.18)	92.16 (22.76)	−0.61	−0.33

*P<0.05. Data: *t*: Pair *t* of either CPAP or control group, *t*(Δ): Independent *t*-test of difference between from post and pre data by each group, CPAP: Continuous positive airway pressure, DFM: Delayed face memory, DLM: Delayed logical memory, ESS: Epworth Sleepiness Scale, FMP: Face memory percentage, IFM: Immediate face memory, ILM: Immediate logical memory, LML: Logical memory learning, LMP: Logical memory percentage, LMR: Logical memory recognition, PS: Processing speed of memory, PSQI: Pittsburgh Sleep Quality Index, WM: Working memory, CON: Control

Table 3: Associations between daytime sleepiness and memory changes and continuous positive airway pressure compliance by ANCOVA

Test	Good compliance (*n*=32)		Low compliance (*n*=15)	
	β	*P*	β	*P*
Sleep scale				
ESS	−2.637	0.026*	2.096	0.134
PSQI	−2.189	0.026*	1.492	0.199
Memory				
WM	0.069	0.848	0.704	0.103
PS	6.265	0.051	6.277	0.099
ILM	3.918	0.114	4.482	0.131
LML	1.693	0.011*	0.894	0.252
DLM	6.183	0.002*	5.731	0.014*
LMP	7.212	0.004*	7.855	0.010*
LMR	1.096	0.159	1.145	0.216
IFM	2.634	0.101	1.311	0.490
DFM	1.755	0.312	0.984	0.639
FMP	4.055	0.304	2.085	0.665

*P<0.05. β: The difference of post and pre data of each compliance group. DFM: Delayed face memory, DLM: Delayed logical memory, ESS: Epworth Sleepiness Scale, FMP: Face memory percentage, IFM: Immediate face memory, ILM: Immediate logical memory, LML: Logical memory learning, LMP: Logical memory percentage, LMR: Logical memory recognition, PS: Processing speed of memory, PSQI: Pittsburgh Sleep Quality Index, WM: working memory

LM is a useful tool for assessing memory and, along with a verbal test, tests the recall of a short story. A previous study showed that aspects of verbal memory, including immediate and delayed recall scores, were significant lower than in OSA patients than in healthy control groups [5]. Furthermore, in a recent study, CPAP treatment for 1 month improved DLM in OSA patients [29]. Another study showed that 3 months of CPAP treatment also improved LM but did not demonstrate a dose-dependent effect [30]. Similarly, our study demonstrated a significant improvement in LM after 2 months of CPAP treatment in OSA patients. The improvement in the LML subdomain was found to be greater in those exhibiting good CPAP compliance. The DML and LMP subdomains were significantly improved in the CPAP treatment group compared to the control group, irrespective of compliance.

A meta-analysis showed impaired VM in OSA patients compared to normal healthy subjects [30]. A study from Borak *et al*. showed that 3 months of CPAP treatment significantly improved visual and spatial memory in OSA patients [31]. Similarly, our study showed that 2 months of CPAP treatment significantly improved IFM and DFM.

There exists a limitation of our study in that a group of healthy subjects was not included as a control. Although the study provided much information in the impact of CPAP in cognitive improvement in OSA, this was a case–control study rather than randomized trial. Besides, the sample size was too small to investigate the impact of treatment effects in different severity of OSA. Therefore, a future randomized study comprising a large sample size and healthy controls should be considered.

Conclusions

In conclusion, 2 months of CPAP treatment could improve some of LM in OSA patients, especially in patients exhibiting good CPAP compliance. However, daytime sleepiness was not significantly improved after CPAP treatment, compared to control group without CPAP therapy.

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Conflicts of interest

Prof. En-Ting Chang, an editorial board member at *Tzu Chi Medical Journal*, had no role in the peer review process of or decision to publish this article. The other authors decalared no conflicts of interest in writing this paper.

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