CPAP Improved Daytime Sleepiness and Memory Function in Patients With Obstructive Sleep Apnea Syndrome

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Speak to the Heart Combined Clinics

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Abstract

Objective: 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 sleepiness and memory function in OSA patients. We also investigated whether CPAP compliance impacted the effect of this treatment.

Methods: The case-control study enrolled sixty-six patients with moderate to severe OSA subjects. All subjects completed a polysomnographic study, sleepiness questionnaires (the Epworth Sleepiness Scale and the Pittsburgh Sleep Quality Index), and four memory function tests (WM: working memory; PS: processing speed; LM: logical memory; FM: face memory).

Results: Prior to CPAP treatment, no significant differences ($p < 0.05$) were noted in the demographic data, daytime sleepiness, or memory function between the two groups (with/without CPAP). However, OSA patients treated with CPAP for two months showed significant improvements in daytime sleepiness, PS, LM, and FM compared to those who did not receive CPAP treatment. A significant improvement in LM was observed in subjects who exhibited good compliance with CPAP treatment compared to those with poor compliance.

Conclusions: In conclusion, CPAP treatment for two months improved daytime sleepiness and memory function in OSA patients. Patients exhibiting good CPAP compliance demonstrated greater improvements in daytime sleepiness and LM function.

Introduction

Obstructive sleep apnea (OSA) syndrome 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 SAVE study shows improvement of depression and Epworth sleep scale but not anxiety score (hospital anxiety and depression scale) during 48 months follow up. [8] Other studies have shown that OSA patients have significant impairments in episodic, procedural and working memory (WM).[9–11] Furthermore, in a recent study by Jackson., OSA patients exhibited greater daytime sleepiness and impairments in the backwards digit span test, trail making test, and quality of life compared to a non-sleep 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 ten OSA

patients completed the study. 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.

Methods

Study participants and experimental protocol

This prospective case-control study 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 /hour) 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 Epworth Sleepiness Scale (ESS), the Pittsburgh Sleep Quality Index (PSQI), and memory tests. The subjects were then divided into two groups - patients in one group received two months of CPAP treatment (S8AutoSet, ResMed Inc., San Diego, CA), and patients in the other did not receive CPAP treatment (controlled group), but rather sleep hygiene education every month. After two months, all patients once again completed the ESS, PSQI, and memory tests as well. Data on CPAP compliance was also collected. 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). This study was funded by Hualien Tzu Chi General Hospital, Taiwan (TCRD 106-19).

Polysomnography

All patients underwent one night of standard type 1 attended polysomnography (Embla A10, Embla, Broomfield, CO) at our Sleep Center. Sleep and arousals were scored according to standard criteria.[2] The AHI and 4% oxygen desaturation index (ODI) were determined and utilized as markers of disease severity.

Measures

Sleep Questionnaires

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

CPAP compliance

Although there exists no exact definition of CPAP compliance, we defined good CPAP compliance as the use of CPAP for more than 4 hours per night for more than 70% of the days monitored.

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 $\pm$ SD. A p value <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 $\pm$ SD. A p value <0.05 was considered to indicate statistical significance. The subjects were divided into 3 groups (high compliance group (≥ 4 hours per night), low compliance group (<4 hours per night) and control group (denied CPAP used), the previous test scores of each group were used as covariance factors performed covariate analysis to examine the therapeutic effect of CPAP on the cognitive function of patients with OSA (Table 3). All statistical analyses were performed using SPSS for Windows Version 14.0 software (SPSS, Chicago, IL).

Results

Demographic data

Sixty-six subjects were enrolled in our study - forty-seven OSA patients received CPAP treatment and nineteen 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 PS) (Table 1).

Table 1
Baseline characteristics of CPAP and control groups

ITEM	CPAP (N=47)	CONTROL (N=19)	PRETEST
Characteristics	MEAN(SD)	MEAN(SD)	t/χ ²
AGE	52.49(11.48)	49.74(12.17)	.87
Male(%):	40(85.11)	14(73.68)	.28
BMI	29.70(5.13)	33.68(8.29)	-1.94
AHI	49.79(20.82)	52.80(28.11)	-.42
ODI	40.84(47.93)	49.69(37.62)	-.72
AI	35.94(21.25)	35.98(24.47)	-.01
ESS	10.51(5.09)	10.53(5.71)	-.01
PSQI	10.04(5.43)	10.95(5.07)	-.62
WM	2.38(1.23)	2.53(1.22)	-.43
PS	66.96(19.19)	65.63(24.45)	.23
ILM	38.62(11.78)	40.05(16.92)	-.34
LML	4.49(2.59)	4.42(1.61)	.13
DLM	23.55(8.77)	26.05(11.79)	-.84
LMP	83.24(14.57)	86.82(16.22)	-.88
LMR	24.26(3.56)	23.95(4.87)	.29
IFM	35.17(4.69)	35.11(3.00)	.06
DFM	34.34(4.91)	34.47(2.67)	-.14
FMP	94.44(7.25)	95.56(6.18)	-.59
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 Sleep Scale; FMP: face memory percentage; IFM: immediate face memory; ILM: immediate logical memory; LML: logical memory learning; LMR: logical memory recognition; ODI: oxygen desaturation index; PS: processing speed of memory; PSQI: Pittsburgh Sleep Quality Index; WM: working memory.			
DATA: MEAN(SD),t: different of cpap & control at baseline, *: Sig.<.05			

ESS and PSQI questionnaires

The ESS scores of the CPAP and control groups were 10.51 ± 5.09 and 10.53 ± 5.17 , respectively. After two months of CPAP treatment, the ESS score of the CPAP group significantly decreased 3.3 points

comparing to 0.85 points in controlled groups. The PSQI scores of the CPAP and control groups were 10.04 ± 5.43 and 10.95 ± 5.07 , respectively. After two months of CPAP treatment, the PSQI score of the former group significantly decreased to 7.13 ± 3.65 . Thus, both ESS and PSQI scores significantly decreased after two months of CPAP treatment (Table 2). Both ESS nor PSQI scores showed significant decrease scores in CPAP group comparing to controlled group, which were decreasing 2.4 difference in ESS and 1.38 in PSQI.

Table 2
Changes in sleep and memory measures following two months of treatment in the CPAP and control groups

TEST	CPAP(n=47)			CONTROL(n=19)			CPAP vs. CON
SLEEP SCALE	pretest	posttest	t	pretest	posttest	t	t(Δ)
ESS	10.51(5.09)	7.21(4.41)	-4.88*	10.53(5.71)	9.68(4.91)	-.65	-1.82
PSQI	10.04(5.43)	7.13(3.65)	-3.90*	10.95(5.07)	9.42(4.14)	-1.87	-1.08
WM	2.38(1.23)	2.30(1.47)	-.40	2.53(1.22)	2.11(1.20)	-1.71	.91
PS	66.96(19.19)	72.98(20.79)	5.89*	65.63(24.45)	65.47(25.22)	-.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)	-.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)	.87	3.59*
LMP	83.24(14.57)	92.59(6.76)	4.89*	86.82(16.22)	86.16(13.68)	-.19	2.69*
LMR	24.26(3.56)	25.32(3.40)	2.47*	23.95(4.87)	24.00(4.47)	.08	1.28
IFM	35.17(4.69)	38.83(3.80)	6.32*	35.11(3.00)	36.58(9.54)	.75	.53
DFM	34.34(4.91)	38.00(4.73)	6.22*	34.47(2.67)	36.58(9.78)	.99	-.17
FMP	94.44(7.25)	95.57(6.61)	0.89	95.56(6.18)	92.16(22.76)	-.61	-.33
CPAP: continuous positive airway pressure; DFM: delayed face memory; DLM: delayed logical memory; ESS: Epworth Sleep Scale; FMP: face memory percentage; IFM: immediate face memory; ILM: immediate logical memory; LML: logical memory learning; LMR: logical memory recognition; PS: processing speed of memory; PSQI: Pittsburgh Sleep Quality Index; WM: working memory.							
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, *:Sig.<.05.							

Memory test

The memory test utilized in this study comprised four parts: working memory (WM), processing speed (PS), LM (ILM, LML, DLM, LMP, and LMR), and VM (IFM, DFM, and FMP). PS, LM (ILM, DLM, LMP, and LMR), and VM (IFM and DFM) significantly improved after two months of CPAP treatment. On the other hand, patients who did not undergo CPAP treatment exhibited a significant decrease in LM at the two-month follow-up (Table 2).

Table 3 shows the association between memory changes and CPAP compliance, using ANCOVA with the control group as a baseline. ESS and PSQI scores were significantly improved in the good compliance group. Those in the good compliance group showed a significant improvement in LM (LML, DLM, and LMP). Those in the poor compliance group also exhibited significant improvements in the DLM and LMP subdomains of LM.

Table 3
Associations between sleep and memory changes and CPAP compliance by ANCOVA

GOOD-COMPLIANCE(N=32)			POOR-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
CPAP: continuous positive airway pressure; DFM: delayed face memory; DLM: delayed logical memory; ESS: Epworth Sleep Scale; FMP: face memory percentage; IFM: immediate face memory; ILM: immediate logical memory; LML: logical memory learning; LMR: logical memory recognition; PS: processing speed of memory; PSQI: Pittsburgh Sleep Quality Index; WM: working memory. * $p < 0.05$; β : the difference of post and pre data of each compliance group.				

Discussion

In the present study, two months of CPAP treatment improved daytime sleepiness and memory function in patients with OSA. Patients exhibiting good CPAP compliance demonstrated greater improvements in daytime sleepiness and LM.

CPAP treatment in OSA patient improved daytime sleepiness about -3.1 in SAVE study[8] as well as -3.3 points in our study as well. The improvement of ESS score was significantly than the minimal clinical important difference of ESS (-2) in OSA patients. [20] This means that CPAP can significant decreased daytime sleepiness in OSA patients.

Neurocognitive dysfunction has been well described in OSA patients, and a number of 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, two 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, procedural, 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 working memory under intermittent hypoxemia[25, 26], as well as another study in healthy adults.[27] Our study showed that two months of CPAP treatment did not have any beneficial effect on WM. WM was found to decrease over the two 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 improved WM. This implies that the recovery of intermittent hypoxemia over two months as a result of CPAP treatment cannot completely recover WM. In the study of Robert J, 8 weeks of CPAP therapy complete subjective clinical recovery but the recovery of neurocognition was still impaired.[28] Further investigation about the recovery time in OSA patient 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.[29] In our study, two months of CPAP treatment improved the PS of OSA patients, although CPAP compliance did not have an impact on this effect.

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 one month improved delayed LM in OSA patients.[30] Another study showed that three months of CPAP treatment also improved LM, but did not demonstrate a dose-dependent effect.[31] Similarly, our study demonstrated a significant improvement in LM after two 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.[32] A study from Borak et al. (1996) showed that three months of CPAP treatment significantly improved visual and spatial memory in OSA patients.[31] Similarly, our study showed that two 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, however, this was a case-control study rather than randomized trial. Therefore, a future study comprising a large sample size and healthy controls should be considered.

In conclusion, two months of CPAP treatment improved daytime sleepiness, PS, LM, and VM in OSA patients. Patients exhibiting good CPAP compliance demonstrated greater improvements in daytime sleepiness and LM function.

Declarations

- Ethics approval and consent to participate: 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). All participants were ensured about the matter of confidentiality and signed the informed consent form. All methods were carried out in accordance with Declarations of Helsinki.
- Consent for publication: Not applicable.
- Availability of data and materials: The datasets analysed during the current study are not publicly available due to limitations of ethical approval involving the participant data and anonymity but are available from the corresponding author on reasonable request.
- Competing interests: None
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- Authors' contributions: CET and HYL: study conception, design, data collection, analysis and writing of the manuscript. KSC: data collection, data analysis and writing the manuscript. SYC: study conception and reviewing the manuscript. The author(s) read and approved the final manuscript.
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