



Original Article

Does continuous positive airway pressure treatment affect autonomic nervous system in patients with severe obstructive sleep apnea?



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ARTICLE INFO

Article history:

Received 18 July 2017

Received in revised form

7 September 2017

Accepted 8 September 2017

Available online 23 October 2017

Keywords:

Obstructive sleep apnea

CPAP

SCOPA-Aut

Autonomic nervous system

Cardiovascular reflexes

Tilt test

ABSTRACT

Objective: This study is aimed at evaluating whether Continuous Positive Airway Pressure treatment (CPAP) may affect autonomic nervous system (ANS) in male patients with severe obstructive sleep apnea (OSAS).

Methods: We compared autonomic symptoms of de novo severe OSAS patients, OSAS patients on chronic CPAP treatment and healthy controls, using the Scales for Outcome in Parkinson disease-Autonomic (SCOPA-AUT) questionnaire. All groups underwent cardiovascular function tests including head-up tilt test (HUTT), Valsalva maneuver, deep breathing, hand grip and cold face tests. Statistical significance was set at $p < 0.05$.

Results: Twelve de novo severe OSAS patients, 17 male OSAS on CPAP and 14 controls were studied. The mean SCOPA-AUT total score was significantly higher in de novo OSAS patients compared with controls. Regarding the distinct domains, both de novo OSAS and CPAP group had abnormalities in respect of controls in urinary sphere. In supine rest condition the baseline values of systolic blood pressure were significantly increased in untreated OSAS patients compared with controls, whereas the basal values of diastolic blood pressure were significantly higher in CPAP patients with respect to controls. After ten min of HUTT, diastolic blood pressure changes were significantly higher in controls compared to both OSAS groups. Untreated OSAS patients showed significant different responses at deep breathing compared to controls. Both OSAS groups had a significant reduction of reflex bradycardia at cold face test.

Conclusions: Our study shows that both treated and untreated OSAS patients complain of subjective autonomic symptoms like other sleep disorders reinforcing the close relationship between sleep and autonomic activity. Furthermore, cardiovascular reflexes indicate a tendency to hypertension and a reduced sensitivity to stimuli during wakefulness even in OSA patients on CPAP treatment, suggesting potentially permanent autonomic function deficits.

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1. Introduction

The link between sleep disturbances and autonomic dysfunction stems from the neuroanatomy of the autonomic nervous system (ANS) and the sleep/wake system. Neuronal populations which participate in the transition from wake to sleep are localized near to and reciprocally interconnected with the ANS areas involved in

cardiovascular control [1,2]. As a consequence, it is not uncommon for patients with untreated sleep disorders to complain of symptoms of autonomic impairment, and conversely, the majority of patients with autonomic impairment have some form of sleep disorder [3].

Obstructive Sleep Apnea (OSA) is a common disorder, affecting an estimated 5–10% of the general population [4] characterized by repeated apneas or hypopneas affecting the ANS and leading to significant consequences as hypertension [3]. Many authors reported heart rate (HR) fluctuations as HR decrease at apnoea onset followed by tachycardia on resumption of breathing; moreover sympathetic overactivity has also been documented in relation to

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these respiratory events [5–7]. The autonomic impairment in OSA has been also observed during wakefulness by Cortelli et al., who demonstrated sympathetic overactivity and decreased baroreflex sensitivity in normotensive awake OSA patients compared to controls [8]. The effect of CPAP treatment on ANS during wakefulness has not been yet investigated. The aim of this study is to evaluate possible autonomic complaints assessed through Scales for Outcome in Parkinson disease-Autonomic (SCOPA-AUT) questionnaire [9] and autonomic responses by means of cardiovascular reflexes in severe OSAS patients treated with ventilotherapy CPAP.

2. Methods

Two groups of male severe OSA subjects with AHI >30/h, diagnosed according to American Academy of Sleep Medicine (AASM) criteria [10] were studied: newly diagnosed, de novo, untreated OSA patients and patients under chronic treatment (three months) with nasal continuous positive airway pressure (CPAP). The chronic CPAP subjects were screened for CPAP compliance documented by the ventilator software report and none of them were included if nightly use did not equal or exceeding five h and if residual Apnea-hypopnea index (AHI) was >5/h. OSA patients were compared with healthy subjects comparable for age and sex, screened by a neurologist with expertise in sleep medicine to exclude sleep disorders through a structured interview and polygraphic cardiorespiratory monitoring (AHI < 5/h). Exclusion criteria were the following: diabetes mellitus, hypertension, heart, endocrine, metabolic and renal diseases, smoking habit, mental illnesses, cognitive decline and current therapies or previous use of any neuroleptic agent.

Both patients and controls were assessed for autonomic function using the Scales for Outcome in Parkinson disease-Autonomic (SCOPA-AUT) questionnaire [9]. The SCOPA-AUT questionnaire is divided into subscores for the following domains: gastrointestinal, urinary, cardiovascular, thermoregulatory, pupillomotor, and sexual.

Subjective daytime somnolence was evaluated by means of Epworth Sleepiness Scale (ESS) [11,12].

Finally, all groups underwent AFT in order to assess their cardiovascular reflexes. All subjects gave their informed consent to the procedures and the study was approved by the local ethics committee.

2.1. Sleep studies

All subjects underwent overnight polysomnography whose testing included extraocular and submental electromyogram, airflow, respiratory movements (rib cage and abdominal), oxygen saturation by pulse oximetry (SaO₂), and electrocardiogram. Apnea was defined as cessation of airflow lasting ten s. Hypopnea was defined as 50% decrease in the amplitude of air flow lasting ten s or a 50% reduction associated with either an oxygen desaturation 3% or arousal [10]. AHI is the number of apneas plus hypopneas per hour of sleep as determined by overnight polysomnography.

2.2. Cardiovascular reflexes

The patients were tested in the morning between eight a.m. and ten a.m. in a clinical investigation room (23 ± 1 °C) with a continuous polygraphic recording of systolic blood pressure (SBP) and diastolic blood pressure (DBP) (Finometer, Model-1, TNO Biomedical Instrumentation, Amsterdam, The Netherlands), heart rate (HR), oronasal breathing (Grass model 15-LT). None of the subjects were under medication known to affect autonomic function, and they were asked to abstain from alcohol and caffeine for at least

24 h before the investigations. AFTs were performed using standard procedures [13]. The tests were performed in the order outlined below, allowing a period of rest aimed at restoring basal blood pressure (BP) and heart rate (HR) values between investigations. The results of each test were automatically obtained by means of Light-SNV software (SparkBio Srl, Bologna, Italy) able to visualize, store, and analyse the data, providing a final report with the results [14].

All subjects performed the following tests: HUTT, Valsalva maneuver, deep breathing, handgrip test, and cold face test. After 30 min of supine rest, the subject was tilted up at 65° on HUTT for ten min. At each minute of HUTT, the changes in SBP, DBP, and HR were calculated with respect to basal values. Pre- HUTT supine values (baseline) for SBP, DBP, and HR were set at zero, and changes were expressed as Δ (raw data) from baseline. The Valsalva maneuver was performed by blowing through a mouthpiece attached to a manometer and maintaining a pressure of 40 mmHg for 15 s. The maneuver has four phases. We have considered as indices of autonomic activity the ratio between HR in phases II and IV (VR) and the BP variations during phases II and IV. At the deep breathing test, the sinus arrhythmia calculated in beats per minute was evaluated. The difference between the maximum HR during inspiration and minimum HR during expiration (I–E difference) in an individual respiratory cycle was calculated and expressed as the mean of the differences in ten respiratory cycles.

At the handgrip test, subjects were asked to exert 30% of maximal voluntary contraction of the dominant hand for five min on a dynamometer. BP was measured in the non exercising arm at rest and at the third minute of the test. At the cold face test we compared changes in SBP, DBP, and HR compared to baseline values after 60 s of synthetic ice (0–1 °C) applied to the forehead.

2.3. Statistical analysis

Differences between groups were determined by one-way or two-way analysis of variance (ANOVA) with the post hoc multiple range Tukey–Kramer test. To determine if there were differences in demographic criteria such as age and BMI, groups were compared with the χ^2 test. For all statistical tests, the null hypothesis was rejected at $p > 0.05$. All data are expressed as group means ± standard error of the mean.

3. Results

3.1. Demographic and clinical data

We consecutively enrolled 12 de novo male patients affected by severe OSAS (age 52.75 ± 12.39 y.o.), and 17 male OSAS patients under chronic treatment with CPAP (mean age 54.17 ± 7.58 y.o.). Furthermore, 14 healthy control subjects (mean age 48.5 ± 10 y.o.) were studied.

Subjective daytime somnolence was higher in untreated OSAS compared to CPAP patients and controls.

The mean SCOPA-AUT total score was significantly higher in untreated OSAS patients compared with controls (14.5 ± 12.21 vs 5.7 ± 3.68, $p < 0.05$). CPAP patients showed a trend to an higher SCOPA total score as compared with controls, but the results did not reach statistical significance.

Regarding the distinct domains, both OSAS groups showed significant abnormalities with respect to controls in the genitourinary domain. When comparing individual items both OSAS groups reported nocturia. Conversely, other autonomic symptoms (gastrointestinal, cardiovascular, pupillomotor and sexual domains), were not reported in OSAS patients. All data are reported in Table 1.

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