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ORIGINAL ARTICLE

Effects of positive airway pressure therapy on cardiovascular and metabolic markers in males with obstructive sleep apnea

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Abstract
Introduction: Obstructive sleep apnea syndrome (OSAS) is associated with cardiovascular/metabolic complications. Some analytical parameters (homocysteine, glycemic and lipidic profiles) are recognized markers of these consequences. Limited data is available on the association of these markers and OSAS's severity/response to positive airway pressure therapy (PAP).
Material and methods: In this prospective study we analyzed polysomnographic and analytical data of male patients admitted to sleep laboratory. The aim was to evaluate metabolic/cardiovascular markers in snorers and OSAS patients, to relate with sleep parameters and PAP response. One-hundred and three patients were included, and 73 (71%) were OSAS patients. OSAS patients were similar to snorers except for higher body mass index (BMI) and dyslipidemia. Severe OSAS patients showed higher glycemia, HbA1c, insulin, and insulin resistance, and lower HDL cholesterol in comparison to mild–moderate ($p < 0.05$, $p < 0.05$, $p < 0.001$, $p < 0.001$, $p < 0.05$, respectively). Glycemic profile and triglycerides were slightly correlated with OSAS severity. 46 OSAS patients were submitted to 6 months of PAP,

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with a statistical decrease in mean values of homocysteine, glycemia, total and LDL cholesterol ($p < 0.05$, $p < 0.05$, $p < 0.05$, respectively), and in glycemia and LDL cholesterol in severe group only ($p < 0.05$, $p < 0.05$, respectively).

Results: This study demonstrated an association between glucose metabolism parameters and triglycerides with OSAS severity underlying the complexity of the process leading to cardiovascular/metabolic complications in this disorder. Moreover, homocysteine, glycemic and lipidic profiles changed significantly after 6 months of PAP therapy in OSAS, supporting its cardiovascular and metabolic protective effect.

Conclusion: Our study has reinforced the importance of analytical cardiovascular/metabolic evaluation as complementary tool of diagnosis/treatment response in OSAS.

Introduction

Obstructive sleep apnea syndrome (OSAS) is a common sleep and chronic respiratory disorder,[1,2] associated with cardiovascular[3–5] and metabolic (such as obesity,[6] dyslipidemia[7] and type 2 diabetes)[8] complications. It has been difficult to determine if these are due to OSAS or to associated risk factors. Sleep fragmentation and intermittent hypoxia are some mechanisms contributing to OSAS complications,[9,10] which improve with positive airway pressure treatment (PAP). However, the impact of PAP on other mechanisms involved is still not well characterized. Some oxidative stress biomarkers have been associated to OSAS morbidity.[11] Still controversy remains regarding the best diagnostic/prognostic marker. An example is homocysteine (Hcy), which is considered a ''promising'' marker.[12] Hcy is an intermediate product in the biosynthesis of methionine and cysteine,[13] and is determinant of the methylation cycle.[14] Hcy levels in adults follow a circadian variation,[15] being lower in the morning. Studies reported Hcy as an independent risk factor for atherosclerosis,[16,17] cerebral, and cardiovascular diseases (CVD),[13,18–24] being related with their prognosis.[18] The proposed mechanisms are its adverse effects on vascular structure and function,[25] hypercoagulability state,[23] and depletion of nitric oxide.[26] Moreover, dyslipidemia, diabetes, cancer, renal, and thyroid dysfunction[13,23] are associated with elevated Hcy. Also, older age, male gender, various drugs, tobacco/coffee/alcohol, and vitamins deficiency.[13,23] Hcy has been proposed as an OSAS biomarker regarding its relationship with CVD. Studies show higher levels of Hcy in OSAS with[27–30] or without[31,32] pre-existing cardiac disease. Moreover there are contradictory studies reporting the effect of PAP on Hcy levels.[29,33–37]

The aim of this study was to analyze Hcy levels in snorers and OSAS patients, its correlation with OSAS severity, and response to PAP. Additionally, glycemic and lipid parameters were also evaluated.

Material and methods

This prospective study included one hundred three consecutive male subjects with suspicion of OSAS, who were evaluated at a Sleep Clinic. Demographic data included age, body mass index (BMI), Epworth sleepiness scale, and medical history. Exclusion criteria were female gender (to avoid hormonal influence), other sleep disorders, neuromuscular, renal, and thyroid disease, heart failure, cancer, acute disease, and previous PAP.

All patients underwent an overnight polysomnography (PSG) using Embla S7000 System (Embla, USA) with a technician monitoring. Sleep recording and events were manually analyzed according to standard criteria.[38] The respiratory disturbance index (RDI), oxygen desaturation index (ODI), percentage of time with saturation under 90% (T90) and lowest oxygen saturation (SpO_2) were calculated. Based on RDI ≥ 5 obstructive events/h of sleep, patients were diagnosed as OSAS ($n = 73$) and grouped into mild (RDI 5–14.9), moderate (RDI 15–29.9), and severe (RDI ≥ 30). Later, in pre/post OSAS treatment analysis, mild and moderate patients were combined (RDI < 30), in order to evaluate the extreme of disease spectrum.

To calculate the sample size we focused in the main objective, that is Hcy analysis before/after PAP treatment. The sample size was calculated with PS software, version 3.1.2. It was planned a study of a continuous response variable from matched pairs of study subjects. Prior data indicated that the difference in the response of matched pairs was normally distributed with standard deviation 2. If the true difference in the mean response of matched pairs is 0.95, the sample size need to be of 37 pairs of subjects to be able to reject the null hypothesis that this response difference is zero with probability (power) 0.8 (i.e. beta 0.20). The type I error probability associated with this test of this null hypothesis is 0.05 (i.e. alfa 0.05).

According to criteria,[39] PAP therapy with automatic devices (S9, Resmed, Australia) was prescribed for 46 patients in severe disease or in disease of any severity when associated with excessive diurnal sleepiness and/or cardio/cerebrovascular complications. These patients were evaluated at six months for compliance registration. As described,[41] more than 4 h use/night for at least 70% of nights was considered as acceptable compliance. After PAP initiation, no more indications (excluding healthy lifestyle) were given, assuming a real life scenario.

Venous blood samples were collected after PSG and a 12-h fasting period, into EDTA-coated polypropylene tubes. At six months of PAP a second morning blood sample was collected. The collected blood was processed between 1 and 2 h to determine Hcy (chemiluminescence

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