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SHORT REPORT

Continuous positive air pressure treatment reduces serum advanced glycation end products in patients with obstructive sleep apnoea syndrome: a pilot study

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Abstract

Nasal continuous positive air pressure (nCPAP) treatment may favourably affect serum levels of advanced glycation end products (AGEs) in patients with obstructive sleep apnoea syndrome (OSAS). At baseline, OSAS patients had significantly higher levels of AGEs than controls. Six months after nCPAP initiation, AGEs decreased significantly. nCPAP treatment could lower AGEs in patients with OSAS.

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Introduction

Advanced glycation end products (AGEs) are implicated in the pathogenesis of diabetic complications as well as kidney failure, with an important role in atherogenesis.[1-3] Enhanced production of reactive oxygen species (ROS) by the mitochondrial electron transport chain leads to formation of intracellular AGEs that can be blocked by normalising mitochondrial superoxide production.[3] AGEs are formed not only in conditions of hyperglycaemia but also in states of enhanced oxidative stress.[3] A recent report has shown that the serum AGE concentration is increased in subjects with obstructive sleep apnoea syndrome (OSAS), which is considered a condition with oxidative stress.[4] In OSAS, frequent episodes of upper airway obstruction occur during sleep and lead to significant hypoxia.[5] The ensuing recurring changes in arterial oxygen saturation and hypoxia/reoxygenation tilts the oxidative balance towards an excess of oxygen-free radicals. Biomarkers of oxidative stress may thus be consistently elevated in this type of patient.

OSAS is a common disease and is strongly associated with the risk of cardiovascular disease (CVD); recognition of the pathophysiology of OSAS is therefore crucial in the primary care setting.[5,6] Treatment with nasal continuous positive airway pressure (nCPAP) improves sleep and daytime sleepiness by reducing the hypoxic cycles (reducing ROS production),[7] but its effects on CVD risk – while promising – remain incompletely established.[5,8] We hypothesised that nCPAP has a beneficial effect on the oxidative phase of advanced glycation and therefore on serum AGE levels as biomarkers. In this preliminary study we measured AGE levels in a cohort of patients with OSAS at baseline and 6 months after initiation of nCPAP treatment compared with age- and sex-matched control subjects.

Methods

Ten Japanese patients with OSAS (5 men/5 women; mean±SE age 52±4 years) and 30 age- and sex-matched controls (mean 52±4 years) were studied. We included the patients with characteristic symptoms such as daytime somnolence, chronic fatigue and restless sleep as well as an apnoea plus hypopnoea score (apnoea-hypopnoea index) of ≥20/hr of sleep on polysomnography. All patients were non-diabetics and they did not change their exercise

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habits or medication during the study. Subjects with a history of cardiovascular, cerebrovascular, renal, thyroid, psychiatric or infectious diseases were excluded. In control subjects, OSAS was clinically excluded by Kapuniai's criteria.[9] The study was approved by the institutional ethics committees and each subject gave informed consent.

At baseline, after an overnight fast, body weight, serum AGEs and lipid panels were measured. For AGEs, fluorescence intensity was recorded at the emission maximum (440nm) upon excitation at 350nm and at 335/385 for pentosidine fluorescence.[1,2,10] Fluorescence intensity is expressed in arbitrary units (AU). We used a SPECTRAmax Gemini XPS spectrofluorometer with SOFTmax PRO software (Molecular Devices, Sunnyvale, CA, USA). The measurements in the OSAS patients were repeated after 6 months of nCPAP treatment.

Differences between groups were compared by paired or unpaired t test. The correlations between bivariables were examined by Spearman's rank correlation. A p value of <0.05 was considered significant.

Results

The mean baseline characteristics of the patients with OSAS were: weight 72.7±2.9kg, total cholesterol 5.74±0.25mmol/L, triglycerides 1.74±0.22mmol/L, high-density lipoprotein cholesterol 1.40±0.14mmol/L. At baseline, AGE levels in patients with OSAS were higher than in controls (82.8±26.0 vs. 64.2±12.2 AU, p=0.001) and pentosidine fluorescence was similar to controls (37.4±10.5 vs. 36.1±9.2 AU, p>0.05). AGEs were 29% higher in OSAS patients than in control subjects.

After nCPAP treatment the patients consistently and significantly showed decreased levels of AGEs (68.9±4.2 vs. 82.8±26.0 AU at baseline, p=0.03). Similar changes were found for pentosidine fluorescence (28.3±10.2 vs. 37.4±10.5 AU at baseline, p=0.01) – that is, after nCPAP treatment, AGEs decreased by 17% (range 1–42%) and pentosidine fluorescence decreased by 24% (range 1–40%). No significant correlations were found with other parameters measured.

Discussion

In this study, AGE levels were significantly higher in patients with OSAS than in controls; this is in agreement with the only previous paper published on this subject.[5] More importantly, our data strongly suggest that nCPAP treatment could lower serum AGE levels in OSAS patients. To our knowledge, this is the first report showing this beneficial effect of nCPAP. This finding may be partly explained by the fact that nCPAP (which could minimise the cycles of hypoxia/reoxygenation) has favourable effects on the production of ROS and oxidative stress.[7] The interaction of AGEs with their main receptors is largely a pro-inflammatory process; accordingly, therapies that lower the AGE burden may prove to be beneficial in the prevention of OSAS-related complications. AGEs are candidate factors in the enhanced risk of CVD development in OSAS patients, so our results may partly support this mechanism. A limitation of this study is the small number of patients studied; nevertheless, it serves as proof-of-principle evidence for an effect of nCPAP treatment in lowering serum levels of AGEs. More research on the effects of nCPAP and the role of AGEs in a larger cohort of OSAS patients using more sensitive and specific AGE biomarkers is warranted.

Conflicts of interest

There are no conflicts of interest in relation to the research presented.

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