Med Clin (Barc). 2016;xxx(xx):xxx–xxx

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Original article

Long-term effects of continuous positive airway pressure treatment on subclinical atherosclerosis in obstructive sleep apnoea syndrome☆

Raquel Català[a,*], Raimon Ferré[b], Anna Cabré[b], Josefa Girona[b], María Porto[a], Anna Texidó[a], Lluís Masana[b]

[a] Unidad del Sueño, Sección de Neumología, Hospital Universitari Sant Joan, Institut d'Investigació Sanitària Pere Virgili, Reus, Tarragona, Spain
[b] Unitat de Recerca de Lípids i Arteriosclerosi (URLA), Hospital Universitari Sant Joan, Institut d'Investigació Sanitària Pere Virgili, Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Reus, Tarragona, Spain

ARTICLE INFO

Article history:
Received 12 January 2016
Accepted 31 March 2016
Available online xxx

Keywords:
Obstructive sleep apnea
Carotid intima-media thickness
Continuous positive airway pressure
Atherosclerosis

ABSTRACT

Background and objective: Obstructive sleep apnoea (OSA) is associated with an increased risk of cardiovascular disease. Our objective was to evaluate subclinical atherosclerosis in OSA patients and the effect of continuous positive airway pressure (CPAP) treatment on carotid intima-media thickness (cIMT).
Patients and method: We included 125 patients with suspected OSA. After polysomnography, 107 patients were diagnosed with OSA; 58 of these met the criteria for CPAP treatment. cIMT was measured by ultrasonography at baseline in all patients and after 2 years of follow up in 50 patients on CPAP and 35 without CPAP treatment.
Results: The average cIMT was significantly thicker in OSA than in non-OSA patients (665 ± 120 vs. 581 ± 78 μm, $p = .005$) and did not differ according to OSA severity. Atheromatous carotid plaque was more prevalent in OSA than non-OSA patients (48 vs. 2%, $p = .004$). Among OSA patients, the mean cIMT remained stable over time in the group without CPAP, whereas cIMT decreased markedly in the CPAP group (679 ± 122 vs. 631 ± 117 μm, $p < .0001$).
Conclusions: Increased cIMT was associated with presence of OSA, but not with its severity. Carotid ultrasound in OSA is a reliable marker of atherosclerosis. CPAP treatment with CPAP in OSA reduces cIMT and cardiovascular risk.

Efecto a largo plazo del tratamiento con presión positiva continua de la vía aérea sobre la arteriosclerosis subclínica en el síndrome de apnea-hipopnea durante el sueño

Palabras clave:
Apnea del sueño
Grosor íntima-media carotídeo
Presión positiva continua de vías aéreas
Arteriosclerosis

RESUMEN

Antecedentes y objetivo: El síndrome de apnea-hipopnea durante el sueño (SAHS) es un factor de riesgo de arteriosclerosis. Nuestro objetivo fue evaluar la arteriosclerosis subclínica en los pacientes con SAHS y el efecto del tratamiento con *continuous positive airway pressure* (CPAP, «presión positiva continua de la vía aérea superior») sobre el grosor íntima-media carotídeo (GIMc).
Pacientes y método: Se incluyeron 125 pacientes con sospecha de SAHS. Después de la polisomnografía, 107 pacientes fueron diagnosticados de SAHS; 58 cumplían criterios de tratamiento con CPAP. El GIMc se midió mediante ecografía a nivel basal y a los 2 años de seguimiento en 50 pacientes con SAHS en tratamiento con CPAP y 35 SAHS sin criterio de CPAP.

☆ Please cite this article as: Català R, Ferré R, Cabré A, Girona J, Porto M, Texidó A, et al. Efecto a largo plazo del tratamiento con presión positiva continua de la vía aérea sobre la arteriosclerosis subclínica en el síndrome de apnea-hipopnea durante el sueño. Med Clin (Barc). 2016. http://dx.doi.org/10.1016/j.medcli.2016.03.032

* Corresponding author.
E-mail address: raqcatala@hotmail.com (R. Català).

Resultados: Los valores del GIMc fueron superiores en los pacientes con SAHS respecto a los que no tenían SAHS (665 ± 120 frente a 581 ± 78 μm, p = 0,005), sin asociarse con su nivel de gravedad. La presencia de placas de ateroma fue más prevalente en los SAHS que en los no SAHS (48 frente a 2%, p = 0,004). En los pacientes con SAHS, la media del GIMc permaneció estable durante el seguimiento en el grupo sin CPAP, y en el grupo tratado con CPAP disminuyó significativamente (679 ± 122 frente a 631 ± 117 μm, p < 0,0001).
Conclusiones: Los pacientes con SAHS presentan un mayor grado de arteriosclerosis subclínica y no se asocia con su gravedad. La ecografía carotídea en el SAHS es un marcador fiable de arteriosclerosis. El tratamiento con CPAP en el SAHS disminuye el GIMc y el riesgo cardiovascular.

Introduction

Sleep apnoea-hypopnoea syndrome (SAHS) is a public health problem that affects 3–7% of the general adult population.[1,2] Sleep apnoea generates intermittent hypoxia and sleep fragmentation that results in cardiovascular and metabolic consequences.[3–5]

Continuous positive airway pressure (CPAP) is a first-line treatment for SAHS, it improves daytime sleepiness and quality of life for these patients.[6] CPAP has a major impact on reducing cholesterol levels, insulin resistance and blood pressure, and, therefore, on cardiovascular risk reduction.[7,8]

Previous studies have shown that repeated episodes of hypoxia and re-oxygenation and increased sympathetic activity during sleep with SAHS could activate different pathways that promote atherosclerosis, such as: oxidative stress, endothelial dysfunction and systemic inflammation.[9] The association between SAHS and atherosclerosis is independent, despite the many risk factors for atherosclerosis that sleep apnoea patients have.[10] In the early stages, the morphological abnormalities of arterial walls can be visualised by B-mode ultrasound by measuring the carotid intima-media thickness (CIMT). CIMT is a non-invasive and reproducible degree marker of subclinical atherosclerosis, which correlates directly with the incidence of cardiovascular events.[11,12] The presence of atherosclerotic plaques is also an independent predictor of future cardiovascular disease.[13] Recent studies in SAHS patients have shown that CIMT is increased and correlates with SAHS, especially if it is accompanied by a marked nocturnal hypoxaemia.[10,14,15] Treatment with CPAP in sleep apnoea for months improves early signs of atherosclerosis, and results in a decrease in CIMT.[16]

The aim of this study is to assess subclinical atherosclerosis in SAHS patients and the long-term effect of CPAP treatment on CIMT.

Materials and methods

Population and study design

A prospective observational study of cases and controls which includes 125 subjects aged 18–75 who were referred to the Sleep Unit (SU) because of suspected sleep apnoea. SAHS was diagnosed by polysomnography (PSG) monitored in 107 patients; 85 SAHS were followed for 2.1 (1.6–2.4) years (50 being treated with CPAP and 35 without CPAP treatment). Exclusion criteria were: the need for invasive mechanical ventilation, recent myocardial infarction, unstable angina, chronic renal failure, severe psychiatric disorders and alcoholism. SAHS patients monitored in the SU underwent no changes in the chronic medication prescribed to them and that information was obtained from medical visits. The study was approved by our hospital's Ethics Committee. No. 09-10-29/10proj3) and informed consent was obtained from each patient.

Clinical parameters and laboratory analysis

Anthropometric parameters and blood pressure were measured at baseline and end of the monitoring period. The forced expiratory volume in one second (FEV_1), the forced vital capacity (FVC) and the FEV_1/FVC determined by simple spirometry when the sample was collected. The Spanish version of the Epworth Sleepiness Scale (ESS) was calculated at baseline (ESS_0) and at follow-up (ESS_1); a score greater than 10 was considered indicative of excessive daytime sleepiness.

Venous blood samples were collected under standardised conditions for all participants after 12 h of fasting for, lipid profile, glucose, HbA_{1c}, renal and liver function, blood count and coagulation parameters.

Polysomnography

The diagnosis of SAHS was carried out by conventional, monitored PSG (eXea; BITMED, Zaragoza, Spain) overnight in the SU in accordance with international standard regulations.[17] SAHS was defined as an apnoea-hypopnoea index (AHI) of five or more episodes per hour. The variables analysed were: AHI, oxygen desaturation index, medium and minimum arterial oxygen saturation (SaO_2) and percentage of time that SaO_2 was lower than 90% (CT90). The severity of SAHS was established by AHI: mild ≥5 and <15; moderate ≥15 and <30; severe ≥30.[18]

Setting the continuous positive pressure of the airway

A CPAP adjustment was conducted on all patients with severe SAHS and those with moderate SAHS with excessive daytime sleepiness ($ESS_0 > 12$) and/or associated cardiovascular disease, by using an automatic pressure device (Goodknight 420G CPAP, Covidien-Nellcor and Puritan Bennett, Boulder, USA). They entered the SU for one night after between three and ten days of being diagnosed. Adherence to treatment was estimated by using the hour meter generator. Completion was considered good if the CPAP was used ≥4 h/night for 75% of the nights.

Vascular study: ultrasound of carotid arteries

The CIMT was determined by ultrasound in the deep wall of the left and right common carotid arteries, 1 cm next to its bifurcation, at baseline and at the end of follow-up.[19] The ultrasound equipment used was the MyLab 60 X-Vision ultrasound (Esaote S. p. A, USA.) with a linear 7–12 MHz probe, and was performed live by radiofrequency (QAS software images, Esaote S. p. A, USA). The average CIMT of the right and left common carotid arteries were calculated to obtain the average of both carotids (mGIMc). Measurements were calculated by the same blinded researcher who calculated the rest of the data, who had previous experience in the implementation of these measures, avoiding inter and intra-operator variability. A plate was sonographically defined as a focal