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The efficiency of continuous positive airway pressure therapy in reducing cardiovascular dysfunction in a patient with arterial hypertension and obstructive sleep apnea

Eficiența terapiei cu presiune pozitivă continuă în reducerea disfuncției cardiovasculare la un pacient cu hipertensiune arterială și apnee în somn obstructivă

Abstract

Obstructive sleep apnea (OSA) has been included by European and American hypertension therapy guidelines as a common cause of high blood pressure. Recent studies have demonstrated a strong link between OSA and HBP and the treatment thereof should consist of combination therapy, especially in patients with refractory AHT and a non-dipping profile. We present the case of a patient with high grade hypertension, with secondary organ damage and severe OSA. The ultimate method for controlling blood pressure and reversing subclinical cardiac and cerebrovascular dysfunction of this patient was the specific therapy with continuous positive airway pressure (cPAP).
Keywords: *obstructive sleep apnea, arterial hypertension, cardiovascular dysfunction, continuous positive pressure*

Rezumat

Apneea în somn obstructivă (OSA) a fost inclusă ca și cauză frecventă de hipertensiune arterială (HTA) atât în ghidurile europene, cât și în cele americane de management al hipertensiunii arteriale. Studii recente indică faptul că OSA și HTA sunt strâns asociate și că tratamentul în cazul acestei asocieri trebuie să fie unul combinat, mai ales la pacienți cu HTA refractară și profil de non-dipping. Prezentăm cazul unui pacient mare hipertensiv, cu afectare secundară de organ și cu OSA severă, la care singura modalitate de control a valorilor tensionale și de reversie a afectării subclinice cardio- și cerebrovasculare a fost reprezentată de terapia specifică cu presiune pozitivă continuă (cPAP).
Cuvinte-cheie: *apnee în somn obstructivă, hipertensiune arterială, disfuncție cardiovasculară, presiune pozitivă continuă*

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Introduction:

Obstructive sleep apnea (OSA) has been included by European and American therapy guidelines as a common cause of arterial hypertension (AHT). Recent studies have demonstrated a strong association between OSA and AHT and it has been suggested that the treatment thereof should consist of combination therapy, especially in patients with refractory AHT and a non-dipping profile [1-3].

Although parts of such association can be mediated by coexisting risk factors such as obesity, there is a lot of evidence that supports the independent role of OSA in the pathology of daytime AHT [5-7]. AHT prevalence in patients with OSA ranges from 35 to 80% and seems to be influenced by the severity of the OSA.

Also, about 40% of hypertensive subjects are diagnosed with OSA [1] .

Case presentation

We present the case of a 53 year old man, living in an urban area, with a higher education, without any documented pathological medical history, slightly overweight (BMI 26.5 kg/m^2; waist circumference 95 cm; waist-hip index 0.96, neck circumference 41 cm), smoker (5PA), referred to a sleep laboratory by the family doctor for episodes of drowsiness at the wheel, without nocturnal snoring.

Upon pulmonary evaluation, the patient had an oxygen saturation of 98% on air and ventilation was normal. A diagnosis of obstructive sleep apnea is established based on the daytime sleepiness, with a score of 12 out of 24 on the Epworth Sleepiness Scale and also based on the ventilatory poligraphy, that detects an Apnea Hypopnea Index (AHI) of ~ 46/hour (mostly obstructive apnea) and a Desaturation Index (DI) of ~ 31/hour (at a 3% threshold for

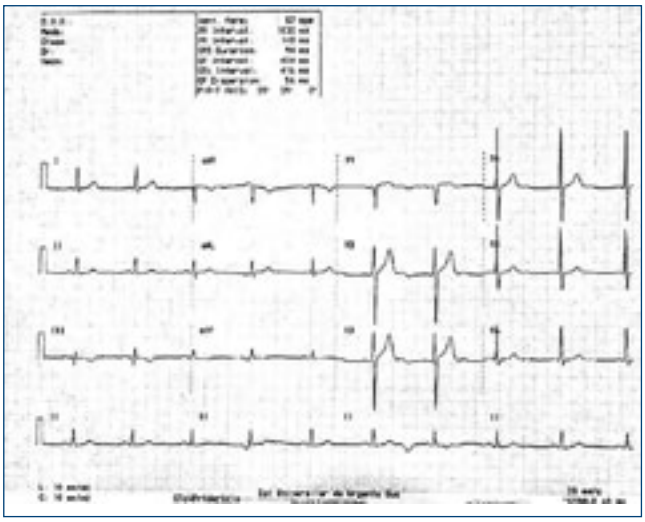

Figura 1. *Resting ECG*

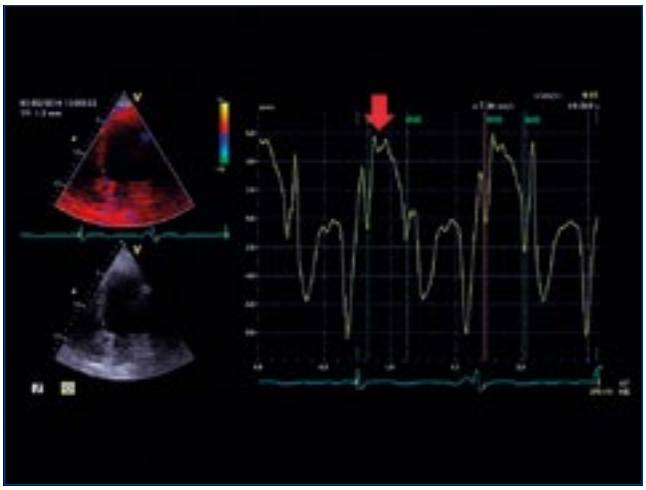

Figura 2a. *Tissue Doppler echocardiography (systolic velocities marked by red arrow)*

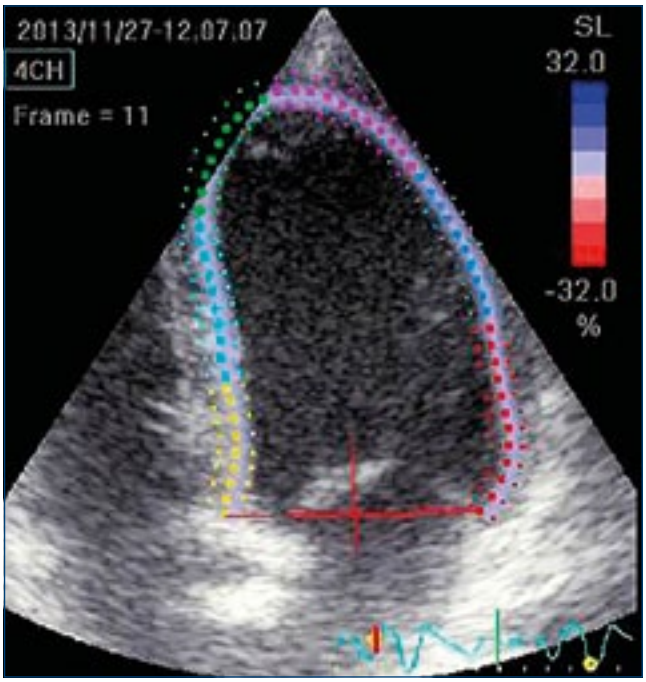

Figura 2b. *2D Speckle Tracking echocardiography*

individual desaturation), not related to sleeping position and without persistent snoring, with an average saturation of 95% (a minimum saturation of 74%; in the 546 minutes of recording of the pulse oximetry curve, the saturation was below 90% for 30 minutes).

Due to a severe OSA, cPAP titration is performed and patient is advised to quit smoking. Under a pulse oximetry control, the auto-cPAP titration shows a significant improvement, both in the residual AHI and in the nocturnal saturation to the pressures shown below; thus, the maximum average pressure is of 14.3 cm H_2O, the average pressure is of 11 cm H_2O with residual AHI of ~ 7/hour (of which 3 obstructive apnea, 2 hypopnea). The average oxygen saturation is 98%, DI <1/hour. The pressure is higher than 13 cm H_2O 10% of the time.

The patient is referred to the cardiology department for a study of evaluation of the subclinical cardiovascular dysfunction in patients with OSA.

The cardiac examination is normal, except for blood pressure with values of 170/80 mm Hg on both arms. From a biological point of view, the total cholesterol is of 270 mg/dl, with the HDL cholesterol at 45 mg/dl, LDL at 150 mg/dl, and triglycerides at 88 mg/dl. The NT-proBNP was determined, a biological marker for subclinical myocardial dysfunction, with a value of 128 pg/ml (at upper normal limit).

A sinus rhythm with a AV 57 bpm is recorded on the resting electrocardiogram (Figure 1) positive index of left ventricular hypertrophy (Sokolow Lyon index of 2.7 mV, modified Sokolow Lyon index of 3.7 mV and Cornell index of 24mV), without any changes in repolarization.

24-hour ambulatory blood pressure monitoring is performed (ABPM) in order to track the blood pressure values for the proposed study, as the patient is not known to suffer from AHT; the ABPM indicates high BP values over 24 hours (188/114 mmHg), both during the day (195/117 mmHg), as well as during the night (172/106 mmHg), with a dipping profile at its limit (nocturnal/diurnal BP ratio of 0.9).

Standard cardiac ultrasound reveals a mild left ventricular hypertrophy (LVH) (interventricular septum and LV posterior wall of 12 mm) with a normal left ventricular systolic function (with an ejection fraction of 60%), a higher than normal ventricular mass index (118 g/m^2), a mild diastolic dysfunction (E/A ratio of 1.5, E-wave deceleration time of 220 ms), without any notable changes to the right side of the heart.

The Tissue Dopple cardiac ultrasound (Figure 2a), performed to assess subclinical cardiac dysfunction, shows lower myocardial systolic parietal basal speed at the LV level (6 cm/s, compared to the normal 7cm/s), with maximum threshold values for the diastolic function parameter, while the 2D Speckle tracking echocardiography (Figure 2b) shows a reduction of the LV global longitudinal strain (-18%, normally above -20%).

The investigation continues, in order to determine the arterial stiffness parameters. The carotid artery ultrasonography shows an intima-media thickness (IMT) of 1.07

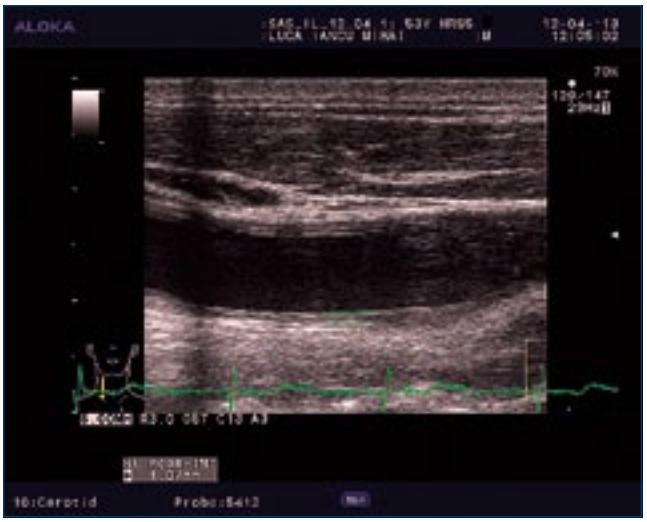

Figura 3a. *Common carotid artery ultrasound to determine IMT*

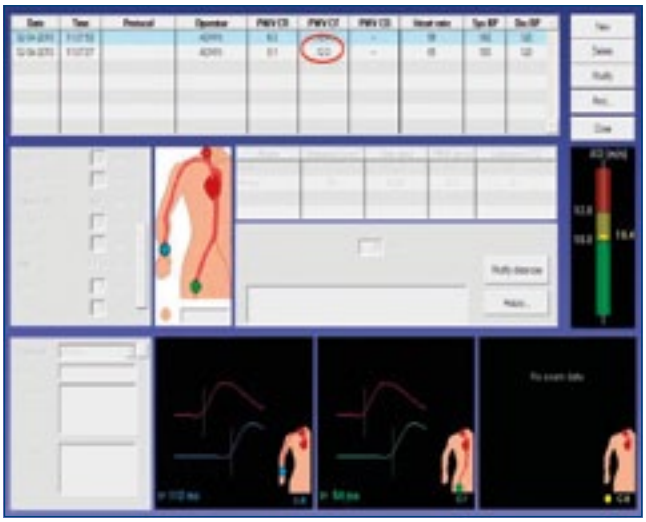

Figura 3b. *Carotid–femoral PWV with COMPLIOR method*

mm (over the 1 mm marker for atherosclerosis) with discrete, non-stenotic, atherosclerotic plaques on the common internal and external carotid arteries (Figure 3a). The carotid femoral pulse wave velocity (PWV), as determined by the Complior method (Figure 3b), has a value indicated by the current AHT guidelines [2,3] as suggestive of subclinical organ dysfunction (12 m/s).

The final diagnosis, established by the cardiology and pulmonary examinations is: AHT stage III ESC/ESH, very high additional risk group; Dyslipidemia hypercholesterolemia; Severe obstructive sleep apnea syndrome with recommended non-invasive cPAP ventilation treatment. According to the European guide for AHT management, the cardiovascular risk criteria [2]are: male gender, smoking, dyslipidemia, EKG criteria for LVH, echocardiographic evidence of subclinical cardiac dysfunction, over 1mm IMT and 12 m/s PWV.

The patient is first recommended a change in lifestyle. Secondly, we aim at reducing blood pressure below 140/90 mmHg. Because of the LVH and asymptomatic carotid atherosclerosis we're prescribing a combination of ARBs (Telmisartan 80 mg) with calcium channel blocker (Amlodipine 10 mg). Also, the patient must receive aspirin and statin, while the cardiologist maintains the indication for cPAP.

After 6 months, the patient returns with an urgent episode of paroxysmal vertigo. He quit smoking, respected the drug therapy, but DID NOT comply with the hygienic-dietary regime and DID NOT use cPAP. Upon arrival, a cerebral CT scan is performed, which turns out normal, an ultrasound for the cervical and cerebral arteries with IMT, which turns out similar to the first one, and a PWV, which is still 12 m/s. The lipid profile has improved, but a stage II hypertensive angiopathy was detected during a fundus examination. The standard and special echocardiographies remain unchanged. The renal ultrasound and the renal artery vascular ultrasound are both normal.

The 24-hour ABPM indicates a significant reduction in blood pressure (medium BP of 156/95 mmHg, 162/101 mmHG diurnal, 145/87 mmHG nocturnal, mild dipping nocturnal/diurnal ratio), but with average values above the therapeutic target.

The cerebral MRI, performed on the recommendation of the neurologist, reveals a small ischemic area, in the right cerebellar hemisphere (Figure 4).

This time, the final diagnosis is: EAHT stage III ESC/ESH, very high additional risk group; Right cerebellar ischemic stroke; Dyslipidemia hypercholesterolemia partially controlled with therapy; Severe obstructive sleep apnea syndrome with a recommended non-invasive cPAP ventilation treatment.

The treatment includes 3 antihypertensives (Candesartan 32 mg/day, Amplodipine 10 mg/day, Indapamide 1.5 mg/day) dual antiplatelet therapy (Clopidogrel 75 mg/day and Aspirine 75 mg/day), the maximum dose of statin (Rosuvastatin 40 mg), while the need for a hygienic-dietary regime and cPAP treatment is reiterated.

At the 1 month follow-up, the patient confirms that he has followed all the recommendations regarding his lifestyle and the sporadic use of cPAP; the neurological exam is normal, but pressure values are still over 140/90 (150/85 mmHg). The recommendations remain the same, with a great emphasis on non-invasive cPAP ventilation.

After another 3 months of daily auto-cPAP use, the patient reports improvement in his general condition, but especially in his daytime sleepiness (5 out of 24, Epworth). While at home, the values are constantly below 130/80 mmHg, which is confirmed by the 24-hour ABPM, with normal values (average BP/24h of 127/75 mmHg, 135/78 mmHg diurnal, 115/70 mmHg nocturnal). In addition, the 2D Speckle Tracking ultrasound shows overall improvement in the LV longitudinal deformation (-20% vs. -18% at the first measurement) and a decreased PVW of 11 m/s. Note that reading the information from the cPAP machine's compliance card showed an average usage of at least 4 hours/day and a average residual AHI of 5, without significant air loss. A high tolerance to the pressure mask and quality sleep, without snoring.

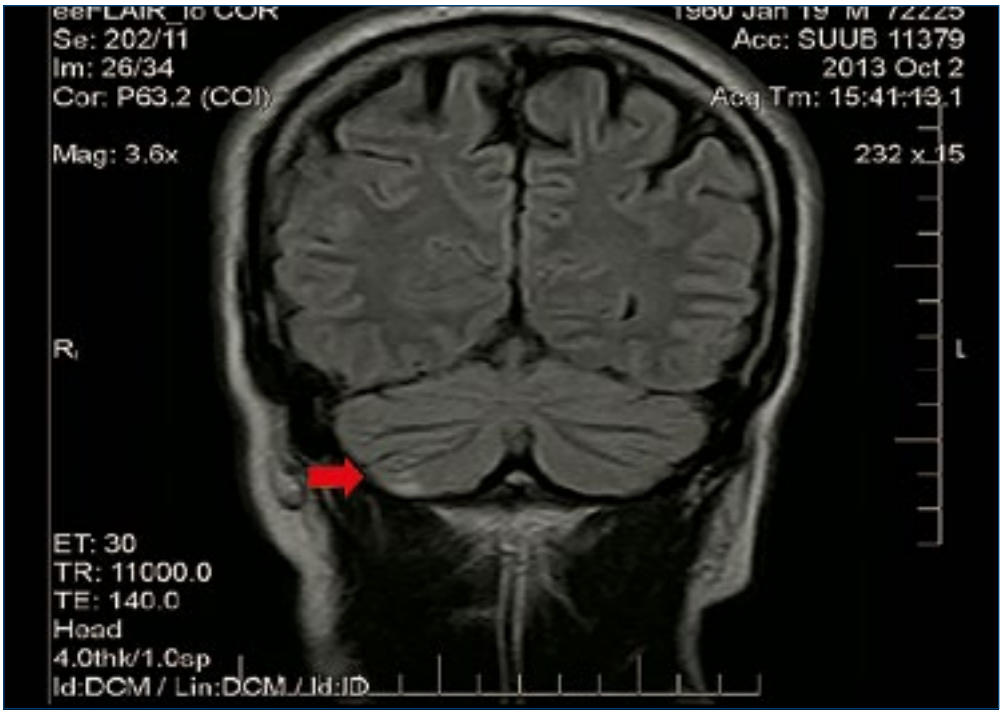

Figura 4. *MRI brain with cerebellar ischemia indicated by the red arrow*

Discussions and conclusions

Current guidelines define the treatment-resistant AHT as a form that cannot be reduced below 140/90 mmHg, despite changes in lifestyle or using a diuretic treatment with two other antihypertensive drugs. Resistant AHT has a prevalence between 5 and 30%, depending on the test subjects, and is associated with a very high risk of cardiovascular and renal events [2,8] . Resistant AHT in patients with OSA is generally systolic and increased nocturnally. The evaluation of patients with OSA and resistant AHT should be based on identifying the aggravating factors and excluding other secondary or resistant AHT factors.

The treatment for AHT associated with OSA involves a change in lifestyle, medication and cPAP therapy. The studies conducted so far on the influence cPAP has in reducing blood pressure in OSA patients have shown that cPAP helps reduce systolic and diastolic blood pressure, nocturnal and diurnal, especially in patients with severe OSA that use cPAP every night, for at least 5 hours [1, 2] . However, the reduction of blood pressure is minimal, varying between 1 and 2.5 mmHg [2, 9-11] .

This case is highly relevant for OSA-AHT association, especially for the decisive effects that the cPAP therapy has here. It is the case of a patient who suffers from both OSA and severe AHT, with a high cardiovascular risk and a diagnosis of subclinical cardiovascular dysfunction, with later target organ damage, for which a triple anti-hypertensive therapy was recommended, maintaining the supernormal BP values. After 3 months of continuous cPAP treatment, the therapeutic targets have been achieved without additional therapy and the subclinical cardiovascular dysfunction has improved.

In conclusion we should note the following: Any patient with treatment-resistant AHT should be evaluated for OSA. There is clear evidence of the benefit of cPAP treatment in the OSA-AHT association, but patient compliance is crucial. ■

Conflict of interest: The authors declare that there is no conflict of interest

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