



## LETTER TO THE EDITOR

# Deprescribing antihypertensive drugs after starting OSA primary therapy?

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Dear Editor,

Obstructive sleep apnea (OSA) syndrome corresponds to the repetition of complete or partial collapses of the upper airway during sleep. Its prevalence is high in Europe and North America, varying from 9% to 38% (depending on the study). Approximately 50% of patients with OSA have coexisting hypertension, usually diastolic and nocturnal. The prevalence of OSA is as high as 80% in patients with resistant hypertension [1]. Evidence that OSA may be a cause of secondary hypertension includes the high prevalence and incidence of hypertension among patients with OSA, and an observed dose-response effect between the severity of OSA and the likelihood of hypertension.

It has been shown that the health costs of patients with OSA are higher than those of individuals without OSA [2]. More extensive treatment of OSA would make it possible to reduce the consumption of care and drug usage related to the comorbidities of OSA. Continuous positive airway pressure (CPAP) is considered the gold standard for effective treatment, even if mandibular advancement devices (MAD) are also widely prescribed.

Only a few studies have investigated medication withdrawal after CPAP or MAD initiation. Delbarre *et al.* showed that CPAP therapy does not result in an earlier decrease in psychotropic drug use in OSA patients compared to non-OSA matched controls after a 3-year follow-up [3]. Assuming that CPAP might be particularly effective with regard to the most commonly reported comorbidity (hypertension) an online survey was commissioned by the American Academy of Sleep Medicine. It revealed that 17% of patients had reduced their antihypertensive drug consumption and 3% had permanently stopped taking antihypertensives [4]. However, this survey was not designed to evaluate changes in the use of the specific classes of antihypertensive drugs and was based on declarative data, without a control group. No large healthcare database based study is available, despite the fact that the number of CPAP prescriptions is growing very rapidly, especially in France.

For this purpose, we explored data on the consumption of hypertensive drugs in OSA patients in a random sample of the French population representative in age and sex. Data from the permanent sample of health insurance beneficiaries (Echantillon

généraliste des bénéficiaires (EGB)) comprising 1/97th of individuals affiliated to the main public health-insurance scheme in France were analyzed.

The objectives were (1) to compare the median cumulative cost of antihypertensive therapy before and after CPAP or MAD initiation, (2) to compare the use of the various classes of antihypertensive drugs before and after CPAP or MAD initiation, and (3) to compare overall observed trends in antihypertensive drug prescriptions in non-OSA matched controls across the same period.

The study population was OSA patients included in the EGB starting treatment with CPAP or MAD for the first time in 2017. We extracted data on 2231 patients, including 2210 adults, of whom 1153 were also treated for hypertension. Their annual consumption of care before and after the date of initiation of OSA treatment was extracted. Associated comorbidities such as diabetes, arrhythmias, and/or a history of stroke were also sought. A cohort of controls was selected from the EGB by matching the 1153 patients to beneficiaries without OSA but with declared hypertension and the same profile of age, sex, and associated comorbidities over the same period. A paired Wilcoxon test was used to compare the cumulative costs in the two cohorts. A paired MacNemar test was used to compare the number of patients, 1 year before and 1 year after OSA treatment initiation.

Concerning the median cumulative cost of antihypertensive therapy before and after starting CPAP or MAD, a significant decrease occurred: 89.8 [48–161] and 84.7 [45–151] €/year/patient, respectively ( $p < 0.0001$ ). At the same time, a significant decrease in drug use was observed for calcium channels blockers ( $p = .0150$ ) and renin-angiotensin-system-acting agents ( $p = .0133$ ). Neither of these trends occurred in the control group suggesting a specific effect related to OSA primary therapy (Table 1).

To the best of our knowledge, this is the first study to evaluate trends in antihypertensive drug use before and after initiation of therapy for OSA. Significant decreases in the median cost of antihypertensive therapy and in the use of two drug classes are highlighted: calcium channels blockers (C08) and renin-angiotensin-system-acting agents (C09). However, our analysis is exposed to limitations, such as the absence of data on body mass index (BMI), apnea-hypopnea index (AHI), blood pressure values, or compliance with OSA therapy.

Randomized trials and meta-analyses have found that effective treatment of OSA using CPAP reduces systemic blood pressure, regardless of whether the patients are hypertensive at baseline [5]. Although this reduction is usually modest, and

appears to be less than that due to antihypertensive medication [6], its clinical relevance is supported by data demonstrating that a 2 mmHg reduction in blood pressure is enough to significantly reduce cardiovascular risk [7]. However, the reduction may not occur in subgroups of non-responders even when they are well adherent to CPAP, highlighting the challenges of biomarkers of response in personalized medicine for OSA [8].

The term “deprescribing” refers to a process of medication withdrawal, supervised by a health care professional, which is an essential part of good prescribing. Diminishing or discontinuing antihypertensive medication is observed in certain subgroups of hypertensive patients [9], although there is no international recommendation to support deprescribing. Even if the large majority will require lifelong drug therapy to control their blood pressure, our results suggest that the initiation of CPAP or MAD could be an opportunity for medication reduction. Particularly as the use of antihypertensive medications is associated with some harms, including the development of adverse drug reactions (eg, falls), drug-drug interactions, and an increase in the medication burden, resulting in reduced adherence. In a recent systematic review evaluating the withdrawal of antihypertensive drugs in older people, rates of adverse events attributed to drug withdrawal remained low, and some metabolic disorders improved once therapy was withdrawn [10]. Thus, blood pressure should be carefully monitored after CPAP or MAD initiation and discontinuation of antihypertensive drugs should be considered if blood pressure falls below the thresholds for their use.

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**Table 1.** Number of OSA patients treated with the different classes of antihypertensive drugs before and after initiation of CPAP or MAD compared with matched controls (non-OSA) over the same period

	OSA (n = 1153)				NON OSA (n = 1151)			
	Before CPAP or MAD (n)	after CPAP or MAD (n)	delta (%)	p	before CPAP or MAD (n)	after CPAP or MAD (n)	delta (%)	p
C03	342	344	+0.17	.9306	236	255	+1.65	.0402*
C07	551	551	0	/	525	538	+1.13	.1120
C08	387	357	-2.60	.0150*	295	306	+0.96	.2724
C09	896	873	-1.99	.0133*	829	832	+0.26	.8011
C02	106	93	-1.12	.0609	59	59	0	/

C03 = diuretics; C07 = betablocking agents; C08 = calcium channel blockers; C09 = agents acting on the renin-angiotensin system; C02 = other antihypertensive drugs; CPAP = continuous positive airway pressure; MAD = mandibular advancement device; OSA = obstructive sleep apnea.

\*Significantly different from the value before CPAP or MAD initiation.

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