



LETTER TO THE EDITOR

Impact of OSA primary therapy on antihypertensive drugs use

Bruno Revol^{1,2,3,◉}, Christel Castelli^{4,5}, Marie Joyeux-Faure^{1,2,†} and Jean-Louis Pépin^{1,2,†,◉}

¹HP2 Laboratory, Inserm U1300, Grenoble Alpes University, Grenoble, France, ²EFCR Laboratory, Pole Thorax and vessels, Grenoble Alpes University Hospital, Grenoble, France, ³Pharmacovigilance Department, Grenoble Alpes University Hospital, Grenoble, France, ⁴UMR 5815, Laboratory of law and health economics, University of Montpellier, Montpellier, France and ⁵Department of Languedoc Mutualité Nouvelles Technologies, Montpellier Beausoleil Clinic, Montpellier, France

†These authors contributed equally to this work

*Corresponding author. Jean-Louis PEPIN, Laboratoire EFCR, CHU Grenoble Alpes, CS 10217, 38043 Grenoble cedex 09, France. Email: JPepin@chu-grenoble.fr

We appreciated the letter to the editor from Romigi et al. in response to our work dealing with the impact of obstructive sleep apnea (OSA) primary therapies on antihypertensive drug use [1]. This letter gives us the opportunity to clarify the methodology we used. Based on a random sample of the French population (representative for age and sex) affiliated to the main public health-insurance scheme (Echantillon généraliste des bénéficiaires), we analyzed data on adult patients with OSA starting treatment with continuous positive airway pressure (CPAP) or a mandibular advancement device (MAD) for the first time in 2017 and being concurrently treated with antihypertensive drugs. To limit selection bias, we excluded those who had received less than 3 months of antihypertensive treatment in the year preceding OSA treatment initiation. A total of 1153 patients were included, 61.9% of whom were men, the mean age was 65.1 years, and they had the following frequent comorbidities: diabetes (28%), arrhythmias (15.5%), and a history of stroke (6.7%). Their care consumption during the 12 months before and 12 months after the date of initiation of OSA treatment was extracted. In order to limit potential confounding factors, a cohort of controls was selected by matching each OSA subject with a beneficiary without OSA but with antihypertensive treatment and the same profile of age, sex, and associated comorbidities over the same period. The date of initiation of CPAP or MAD for each OSA patient was used

as the index date applied to each matched non-OSA control subject, in order to compare the 1-year periods before and after between the two cohorts (OSA and non-OSA), thereby limiting temporality bias. Finally, 1151 beneficiaries without OSA were matched.

We acknowledge the absence of the exact indication for each drug is a limitation of our data. However, this is an inherent limitation of any study using claims reimbursement databases. The main attribute of our data was the decrease in the use of two specific drug classes (calcium channels blockers and renin-angiotensin-system-acting agents). These are the most widely used medications for hypertension and associated complications, whereas diuretics and beta-blocking agents have much broader indications, as pointed out by Romigi et al. A concern of Romigi et al. was that comorbidities may have biased the deprescription rate. This was probably not the case as in our work non-OSA and OSA cohorts were matched for morbidities.

Romigi et al. also discuss the respective effects of CPAP or MAD on blood pressure (BP) in a short-term randomized controlled trial [2]. The mean duration of the randomized controlled trials in the field is limited to less than four months of follow-up [3]. They do not inform on the long-term impact of CPAP on incident hypertension and mortality [4]. Studies in real-life conditions and in unselected OSA populations are providing important complementary results. In this context,

our data on the representative sample of the French population provide new insights, as they reflect the real use of antihypertensive drugs in a large cohort of OSA patients over the long term.

In addition, our results might be partly explained by other factors than an isolated effect of CPAP or MAD on BP. Weight loss and exercise, alcohol avoidance, or sodium restriction [5] are recommended for multimorbid OSA patients on primary therapy [6, 7]. In the general field of hypertension, higher success rates for cessation of antihypertensive therapy are observed in individuals who initiate and adhere to lifestyle modifications [8]. While in OSA, weight loss and CPAP have been demonstrated to have a synergistic effect for improving cardiometabolic health [9]. Finally, almost all national and international recommendations include dietary sodium reduction as part of the nonpharmacologic therapy for hypertension. In parallel, the potential role of sodium in the pathogenesis of OSA has been recently shown in hypertensive patients [10], suggesting that interventions to reduce bodily fluid content (e.g., low sodium intake or diuretics) may have the potential to both reduce OSA severity and treat OSA-related hypertension [11].

Whatever the exact mechanisms, our results are consistent with those of an online survey commissioned by the American Academy of Sleep Medicine, revealing that 17% of patients had reduced their use of antihypertensive drugs and 3% had permanently stopped taking them after starting OSA primary therapy [12]. Further studies are therefore needed to characterize this specific population and highlight the underlying mechanisms leading to antihypertensive drug discontinuation, in order to move toward personalized and precision medicine for OSA.

Acknowledgment

We thank Alison Foote (Grenoble Alpes University Hospital, France) for critically reading and editing the manuscript.

Disclosure Statement

None declared.

References

1. Revol B, et al. Deprescribing antihypertensive drugs after starting OSA primary therapy? *Sleep*. 2022;45(5). doi:10.1093/sleep/zsac060
2. Dissanayake HU, et al. Comparative effects of CPAP and mandibular advancement splint therapy on blood pressure variability in moderate to severe obstructive sleep apnoea. *Sleep Med*. 2021;80:294–300. doi:10.1016/j.sleep.2021.01.059
3. Bratton DJ, et al. CPAP vs Mandibular advancement devices and blood pressure in patients with obstructive sleep apnea: a systematic review and meta-analysis. *JAMA*. 2015;314:2280–2293. doi:10.1001/jama.2015.16303
4. Pépin J-L, et al. Relationship between cpap termination and all-cause mortality: a French nationwide database analysis. *Chest*. 2022;161:1657–1665. doi:10.1016/j.chest.2022.02.013
5. Revol B, et al. Who may benefit from diuretics in OSA? A propensity score-match observational study. *Chest*. 2020;158:359–364. doi:10.1016/j.chest.2020.01.050
6. Hudgel DW, et al. The role of weight management in the treatment of adult obstructive sleep apnea. An official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med*. 2018;198:e70–e87. doi:10.1164/rccm.201807-1326ST
7. Mendelson M, et al. Obstructive sleep apnea syndrome, objectively measured physical activity and exercise training interventions: a systematic review and meta-analysis. *Front Neurol*. 2018;9:73. doi:10.3389/fneur.2018.00073
8. Stamler R, et al. Nutritional therapy for high blood pressure. Final report of a four-year randomized controlled trial—the Hypertension Control Program. *JAMA*. 1987;257:1484–1491. doi:10.1001/jama.257.11.1484
9. Chirinos JA, et al. CPAP, weight loss, or both for obstructive sleep apnea. *N Engl J Med*. 2014;370:2265–2275. doi:10.1056/NEJMoa1306187
10. Giatti S, et al. Association of sodium with obstructive sleep apnea. The ELSA-Brasil Study. *Ann Am Thorac Soc*. 2021;18:502–510. doi:10.1513/AnnalsATS.202005-498OC
11. Revol B, et al. Diuretics in patients with obstructive sleep apnea and concomitant hypertension. *Ann Am Thorac Soc*. 2021;18:2101–2102. doi:10.1513/AnnalsATS.202104-496LE
12. Frost & Sullivan. *In an Age of Constant Activity, the Solution to Improving the Nation's Health May Lie in Helping It Sleep Better. What Benefits Do Patients Experience in Treating Their Obstructive Sleep Apnea?* American Academy of Sleep Medicine; 2016. <http://www.aasmnet.org/sleep-apnea-economic-impact.aspx>.