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Letter to the Editor

LETTER TO THE EDITOR

Deprescribing antihypertensive drugs after starting OSA primary therapy: "first do no net harm?"

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I read with great interest the letter from Revol et al. [1]. These authors focused on the important matter of prescribing and deprescribing antihypertensive agents before and after obstructive sleep apnea (OSA) treatment. They showed insurance-based controlled data highlighting a significant reduction in the median cost of antihypertensive therapy and the use of two drug classes (calcium channels blockers and renin-angiotensin–system-acting agents) and a significant decrease in drug use for the same classes only in the OSA group, suggesting a specific effect related to OSA therapy. The authors correctly highlighted the main study limitations including the absence of BMI, OSA severity (AHI), blood pressure (BP) values, and adherence to OSA therapy. This topic is of great interest but should be treated with caution, particularly with this type of retrospective data. Firstly, the authors reported in table 1 the effect of CPAP or MAD in the non-OSA group. We suppose that this report is a mistake and probably the control non-OSA group was observed with the same time-interval follow-up of OSA treatment.

Furthermore, the authors found that beta-blocking agents and diuretics did not show significant changes before and after OSA treatment. I think that these findings should consider that beta-blocking agents have several indications other than hypertension (i.e., angina pectoris, atrial fibrillation and other arrhythmias, congestive heart failure, essential tremor, glaucoma, migraine prevention, mitral valve prolapse, myocardial infarction, pheochromocytoma with alpha-blockers and symptomatic control of tremor and tachycardia in anxiety and hyperthyroidism) [2]. Similarly, diuretics are widely used for several medical conditions and we should consider different classes. Loop diuretics are mainly used for oedematous disorders and BP and volume control in renal disease, thiazides and related agents are among the most prescribed drugs for hypertension treatment and aldosterone-blockers that are traditionally used for primary or secondary aldosteronism and other diuretic classes with more specific indications [3]. The authors should clarify if their insurance database includes the indications of each drug. This is crucial because the presence of the comorbidities may bias the probability of deprescribing for different indications. Polytherapy may represent a further concern. I suggest evaluating the number of patients with hypertension and monotherapy or polytherapy (independently from the drug classes) to measure the possible effect of OSA treatment on the burden of disease expressed as the number of patients with more than one drug.

Another issue is the controversial effect of CPAP and MAD on BP lacking comparisons between the different treatments in large randomized controlled trials. Revol et al. [1] correctly cited a network meta-analysis comparing CPAP, MADs, and inactive controls on BP in patients with obstructive sleep apnea [4]. Bratton et al. [4] failed to identify statistically significant differences between the BP outcomes associated with MAD and CPAP. However, the authors concluded that CPAP had a different treatment profile significantly reducing BP for longer periods at night or in those with higher baseline BP levels. On the other hand, very recently BP variability was not improved by short-term usage of CPAP and MAD in a randomized controlled study [5]. It may be interesting to compare the number of patients with OSA treated with antihypertensive agents after CPAP or MAD.

Although deprescribing in medical disorders represents a crucial point, if we quantify the literature regarding the term *prescribing* and *deprescribing*, we suppose that the main cause of hypertension overtreating is that physicians are more concerned about the complications of hypertension than overtreating. However, we should not oversimplify this issue, as we "*cannot see the wood for the trees*".

Reducing drug dosages or discontinuing medications overall could be evaluated in patients with BP values below the optimal target, or the case of adverse events [6]. A systematic review highlighted that factors such as monotherapy and lower BP before withdrawal were both predictors of successful long term BP control [7]. Nevertheless, BP values of nearly 40% of patients were found to still be controlled 1 yr after deprescribing. Therefore, frequent follow-ups and BP monitoring should be performed to identify the reappearance of hypertension [6, 7]. Additionally, fast withdrawal of antihypertensive drugs, particularly beta-blockers or clonidine, should be avoided due to the risk of deleterious effects [6].

Overtreatment is a well-known problem in hypertension and usual care of prescription is more expensive than deprescribing. Nevertheless, medication reduction is associated with fewer quality-adjusted life years (QALY) because of a higher risk of cardiovascular events (mainly heart failure) due to quite greater systolic blood pressure in older patients [8]. A randomized, unblinded, noninferiority trial showed that deprescribing should not be attempted in patients with controlled systolic BP as a routine policy. This finding is important for guidelines, encouraging physicians to deprescribe chronic medications where the benefits of antihypertensive agents no longer outweigh the harms. Thus, the crucial question is if and when to consider overtreated a patient with normal BP values for several years with a well-tolerated treatment. I think that OSA treatment may improve BP values and help to reduce antihypertensive overtreatment, although it is still unclear the real impact of OSA treatment on BP variability. Although clear deprescribing guidelines in hypertension are strongly encouraged, balancing harms and benefits is often a complex and time-consuming process. This matter demonstrates that the assessment of risks and benefits is not only a clinical decision based on scientific evidence when available. In a model of precision medicine on OSAS and hypertension, "first do no harm" may not be completely correct, because the patient's risks are never zero and must always be considered concerning the benefits of a decision. "First do no net harm" is better than "first do no harm."

Disclosure Statement

None declared.

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