

Time to rethink the management of underlying sleep disturbances in nondippers?

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See original paper on page 448

The most recent guidelines on the management of hypertension [1] once again reinforce the concept that the evaluation of out-of-office blood pressure (BP) through modalities, such as ambulatory BP monitoring (ABPM) and home BP monitoring is superior to clinic BP monitoring in predicting outcome. In this context, nocturnal BP has now been recognized as an important out-of-office BP parameter for optimizing cardiovascular risk stratification. As a matter of fact, a systematic review by Hansen *et al.* [2] of 23 856 hypertensive patients and 9641 participants from Asian, European and South-American population cohorts showed that nocturnal BP predicts mortality and cardiovascular morbidity in both hypertensive patients and the general population, even when adjustments were made for daytime BP.

Despite this evidence, it is still unknown how to adequately manage elevated nocturnal BP, most of all when it does not fall compared with daytime BP: the so called 'nocturnal nondipping'. Even though this definition is largely arbitrary, a decrease of 10–20% in nocturnal BP relative to daytime BP is considered normal. In 1988, O'Brien [3] introduced the novel concept of 'nondippers' to describe a subgroup of hypertensive patients in whom the nocturnal SBP/DBP decline was less than 10/5 mmHg and the stroke risk was high.

Although a nondipping profile is frequently accompanied by high nocturnal BP, these two phenotypes are not always concomitantly present, and therefore, the pathophysiological and clinical implications of each of them may differ.

Several possible determinants of an increase in nocturnal BP were identified: risk factors like ageing or obesity, behavioural factors, such as high salt intake, underlying

autonomic nervous system dysfunction, and last but not least, sleep disorders [4].

Obstructive sleep apnea is known to alter the physiological nocturnal BP dipping because of the repetitive airway obstruction and related BP and heart rate surges, but the role of other sleep disorders is rarely taken into account in the evaluation of the patient's circadian BP profile. Insomnia, in particular, the most prevalent sleep disorder, has been associated with the development of hypertension: a recent systematic review confirmed that insomnia is related to hypertension and BP nondipping [5]. This association was stronger with more frequent insomnia symptoms and objective short sleep duration. However, studies on the role of insomnia as a predictor of future nondipping status are currently lacking.

On this background, the article by Lyu *et al.* [6] published in the current issue of *Journal of Hypertension* provides further interesting evidence on the association between BP dipping, sleep quality and clinical features of insomnia. The authors analyzed a subset (399 patients) of the Wisconsin Sleep Cohort, one of the largest prospective population-based studies on the natural history of sleep disorders, in particular, sleep-disordered breathing. In a cross-sectional analysis, features of insomnia, such as difficulty in falling asleep, longer waking after sleep onset (WASO), shorter sleep time and lower sleep efficiency were associated with greater probability of both SBP and DBP nondipping. Furthermore, the authors performed a longitudinal analysis confirming the association between incident nondipping status at follow-up and polysomnographic features of insomnia and poor sleep, such as sleep efficiency lower than 80% and WASO greater than 60 min.

This study has several strengths: firstly, patients have been comprehensively assessed with both full-polysomnography and ABPM, which, despite the limited reproducibility of the dipping status [7], offers the most adequate and standardized method of BP assessment in patients with sleep disorders and hypertension. Secondly, the longitudinal nature of the study and the long follow-up allow to understand the potential predictive value of some objective sleep features, such as WASO and sleep efficiency, which are not routinely analyzed in clinical practice.

The results are in line with previous studies confirming the association between insomnia and hypertension. In

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particular, the association between shorter sleep time and features of insomnia with SBP and DBP nondipping status is consistent with the results of the studies by Vgontzas *et al.* [8] who found that insomnia with short sleep duration was associated with increased risk of hypertension, to a degree comparable with that of other common sleep disorders, for example, sleep disordered breathing. The same group confirmed the complex relationship between sleep quality and hypertension by evaluating polysomnographic features of 219 chronic insomniacs and 96 normal sleepers who underwent polysomnography followed by a multiple sleep latency test (MSLT) to assess the degree of vigilance. They found that insomnia combined with MSLT greater than 14 min increased the odds of hypertension by 300% (odds ratio = 3.27; 95% confidence interval = 1.20–8.96), whereas insomnia combined with MSLT greater than 17 min increased even further the odds of hypertension by 400% (odds ratio = 4.33; 95% confidence interval = 1.48–12.68) compared with normal sleepers with MSLT 14 min or less [9].

Taken together, these data on one hand reinforce the role of both objective features of insomnia and subjective symptoms of the disease as important players in the link between insomnia and hypertension. On the other hand, they support the presence of the so-called physiological hyperarousal as a possible determinant of an enhanced sympathetic activation, and therefore, of an increased risk of developing hypertension [9].

Another interesting aspect of the article by Lyu *et al.* [6] is the assessment of the longitudinal relationship between certain objective polysomnographic features of poor sleep and insomnia, such as reduced sleep efficiency and increased WASO with incident nondipping status, performed in a subset of participants. This is so far the first study evaluating this relationship with a proper methodology and adequate follow-up of 7.4 years. The authors report that the odds of incident nondipping were about twice as high in participants with longer WASO, longer total sleep time and lower sleep efficiency. These findings support the presence of cause–effect relationship between poor sleep quality and nondipping.

A possible limitation of the study by Lyu *et al.* [6] is that it did not include elderly participants. Considering that the prevalence of both insomnia and hypertension increases with ageing it would be particularly important to confirm the study findings also in older patients.

The clinical relevance of the reported findings is very clear: we, clinicians, should put more effort in investigating sleep quality and symptoms suggesting sleep disorders in hypertensive patients seen routinely during our clinic visits. In particular, the presence of a nondipping status should at

least require a thorough investigation of sleep complaints, if not an objective assessment to evaluate the basic sleep quality indexes. Considering the reported association with poor sleep quality and adverse cardiovascular outcomes [10], a more careful diagnostic approach may improve risk stratification and ensure that potential contributing factors to an increased risk of cardiovascular complications are properly assessed and treated.

Clearly, the study by Lyu *et al.* [6] while offering a convincing proof of the link between sleep disturbances and nondipping status cannot demonstrate the reversibility of such association. Therefore, given the complexity of the relationship between sleep disturbances, insomnia and hypertension, interventional studies on comorbid insomnia and hypertension are needed to document the impact of treating insomnia on circadian BP profile and, possibly, long-term cardiovascular morbidity.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, *et al.* 2018 ESC/ESH Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens* 2018; 36:1953–2041.
- Hansen TW, Li Y, Boggia J, Thijs L, Richart T, Staessen JA. Predictive role of the nighttime blood pressure. *Hypertension* 2011; 57:3–10.
- O'Brien E, Sheridan J, O'Malley K. Dippers and nondippers. *Lancet* 1988; 2:397.
- Kario K. Nocturnal hypertension: new technology and evidence. *Hypertension* 2018; 71:997–1009.
- Jarrin DC, Alvaro PK, Bouchard MA, Jarrin SD, Drake CL, Morin CM. Insomnia and hypertension: a systematic review. *Sleep Med Rev* 2018; 41:3–38.
- Lyu B, Hagen EW, Ravelo LA, Peppard PE. Blood pressure dipping and sleep quality in the Wisconsin Sleep Cohort. *J Hypertens* 2020; 38:448–455.
- Omboni S, Parati G, Palatini P, Vanasia A, Muiesan ML, Cuspidi C, Mancia G. Reproducibility and clinical value of nocturnal hypotension: prospective evidence from the SAMPLE Study. *J Hypertens* 1998; 16:733–738.
- Vgontzas AN, Liao D, Bixler EO, Chrousos GP, Vela-Bueno A. Insomnia with objective short sleep duration is associated with a high risk for hypertension. *Sleep* 2009; 32:491–497.
- Li Y, Vgontzas AN, Fernandez-Mendoza J, Bixler EO, Sun Y, Zhou J, *et al.* Insomnia with physiological hyperarousal is associated with hypertension. *Hypertension* 2015; 65:644–650.
- Hoeveraar-Blom MP, Spijkerman AM, Kromhout D, van den Berg JF, Verschuren WM. Sleep duration and sleep quality in relation to 12-year cardiovascular disease incidence: the MORGEN study. *Sleep* 2011; 34:1487–1492.