Bedtime Hypertension Treatment Increases Ambulatory Blood Pressure Control and Reduces Cardiovascular Risk in Resistant Hypertension

To the Editor:

A cross-sectional 24-hour ambulatory blood pressure (BP) monitoring study reported 37.5% incidence of isolated office resistant hypertension (RH), there defined as clinic BP >140/90 mm Hg plus 24-hour BP mean <130/80 mm Hg, and it was even higher (44.1%) when defined on the basis of a daytime BP mean <135/85 mm Hg. These findings constitute an overestimation, because, first, among their so-defined isolated office hypertensives, 34.4% ingested ≥4 medications per day; by definition, ≥3 medications per day is true RH, regardless of BP values; exclusion of patients treated with ≥4 medications per day would decrease the reported prevalence to 24.6%; and, second, nocturnal hypertension and abnormal nondipper per BP pattern are prevalent in RH; current guidelines designate separate diagnostic thresholds for daytime and nighttime BP means; mean nighttime BP ≥120/70 mm Hg designates hypertension, regardless of mean daytime and clinic BP.

The investigator-promoted, government-funded Hygia Project (www.clinicaltrials.gov, NCT00741585), designed to prospectively evaluate cardiovascular disease risk, involving primary care centers of Northwest Spain and highly reproducible 48-hour ambulatory BP monitoring, substantiates significantly higher prevalence of elevated sleep time than daytime BP in diabetes mellitus, chronic kidney disease, and RH. Consequently, isolated-office hypertension was up to 3-fold higher when defined only by daytime BP mean than daytime and nighttime BP means jointly. Despite current guidelines, reliance on the 24-hour BP mean to diagnose isolated office hypertension, as done by de la Sierra et al., is inadequate: a “normal” 24-hour BP mean is not a guarantee of a normal nighttime BP mean; moreover, BP patterns ranging from extreme dipping to rising (asleep BP mean >awake BP mean), with potentially markedly different cardiovascular disease risk, might show the same 24-hour BP mean. Elevated sleep time BP is a better predictor of cardiovascular disease risk than awake or 24-hour BP means, and treatment-targeted reduction of sleep time BP in hypertension was prospectively shown to be the most significant independent predictor of event-free survival.

de la Sierra et al. also reported comparable prevalence of isolated office RH, whether patients ingested all of their BP medications with breakfast or ≥1 medication with dinner, stating that “switching a part of the medication from morning to bedtime does not improve ambulatory BP control.” This sweeping conclusion is unjustified. First, their study was not a randomized, prospective trial and did not evaluate whether “switching medications to bedtime” actually affected ambulatory BP regulation. Second, the proportion of subjects taking medications in the evening was too low, at 25%; further, authors did not report which medications were ingested in the evening, the clinical criteria for prescribing evening dosing, and if medication(s) ingested in the evening were the same ones as ingested in the morning. Prescribing the same hypertension medications multiple times per day to achieve homogeneous 24-hour BP lowering is common, especially for medications with <24-hour sustained therapeutic coverage; however, this approach would hardly affect sleep time relative BP decline. Thus, morning-evening splitting of daily doses is not recommended for nondipper hypertension. Third, multiple prospective randomized trials systematically demonstrated that ingestion of medications of 6 different classes, as monotherapies or combination therapies, at bedtime (versus upon awakening) lowers nighttime BP significantly better, enhances sleep time relative BP decline, increases the proportion of fully controlled patients (daytime and nighttime BP), and, most importantly, reduces cardiovascular disease risk, including among RH patients.

Disclosures

None.

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