Sleepers Versus Nonsleepers: Another Twist to the Dipper/Nondipper Concept

Eoin O'Brien

Hypertension 2007;49;769-770; originally published online Feb 5, 2007;
DOI: 10.1161/01.HYP.0000258152.29476.de
Hypertension is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0194-911X. Online ISSN: 1524-4563

Editorial Commentary

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There is growing evidence that an elevated nocturnal blood pressure is associated with an adverse cardiovascular outcome. In the Dublin Outcome Study, for each 10-mm Hg increase in mean nighttime systolic blood pressure, the mortality risk increased by 21%.[1] At present, ambulatory blood pressure measurement is the only technique that permits close examination of the circadian profile and identification of patterns that may be associated with risk.

Much happens to the cardiovascular system at nighttime, especially in relation to blood pressure. The patterns of nocturnal blood pressure–nocturnal hypertension, nocturnal hypotension, dipping and nondipping, reverse dipping, and autonomic failure–have been largely ignored in clinical practice. Many studies evaluating morbidity and dipping status have supported the concept that a diminished nocturnal blood pressure fall is associated with a worse prognosis.[2] However, despite compelling evidence that changes in nighttime blood pressure may hold many secrets that, if unlocked, might benefit the clinical management of hypertension, there has been reluctance to focus on nocturnal blood pressure both clinically and in hypertension research.[3]

The nocturnal period of the 24-hour blood pressure profile, which is surprisingly complex, can be divided into a number of windows in which discrete phenomena may occur. These windows are the retiring (or perhaps more aptly named vesperal) window, the nighttime (or basal) window during which sleep is most likely, and the preawakening (or matinal) window, which precedes rising. In the normal individual there is a decline in blood pressure in the vesperal window from daytime levels of blood pressure to reach a plateau during the basal window (the "dipping" pattern), with a modest rise in the matinal window to regain daytime levels of blood pressure.[4] In hypertensive patients (or some normotensive patients with cardiovascular disease), the decline in the vesperal window may be absent (nondipping) so that blood pressures do not reach basal levels, or blood pressure may even rise above daytime levels (reverse dipping).[5] Alternatively, there may be a marked fall in basal blood pressure (extreme dipping). Patients with a marked nocturnal fall in blood pressure are at risk for nonfatal ischemic stroke and silent myocardial ischemia. This is particularly likely in extreme dippers, who already have atherosclerotic disease and in whom excessive blood pressure reduction is induced by injudicious antihypertensive medication.[5] This possibility was originally enunciated by Floras[6] as long ago as 1988, when he postulated that patients with critical coronary stenoses or hypertrophied ventricles might have impaired coronary vasodilator reserve and would, therefore, be at greatest risk of myocardial ischemia or infarction if subendocardial perfusion pressure fell below the lower threshold of blood flow autoregulation. This was most likely to occur during sleep, when excessive antihypertensive treatment might cause unrecognized nocturnal hypotension leading to coronary artery hypoperfusion, which might explain why treatment had not diminished the risk of myocardial infarction in patients with hypertension.[6] Also, in hypertensive patients, the matinal rise in blood pressure may soar above the daytime average, the preawakening or morning surge, which may be excessive in extreme dippers leading to a high-risk of future stroke.[5]

I have applied the term "basal" to the window between the vesperal and matinal windows in acknowledgement of the seminal article written by Horace Smirk in 1964.[7] In this article, Smirk outlines the technique for obtaining basal blood pressure under standardized conditions with sedation using oral pentobarbitone, which he differentiates from casual blood pressure as obtained in hospital or elsewhere without special precautions; the term supplemental blood pressure was applied to the difference between the casual and basal blood pressures. Smirk[7] observed that the basal blood pressure was practically a physiological constant in normotensive subjects and, although more variable in hypertensive patients, was much less variable than the casual blood pressure. Moreover, he observed that the casual blood pressure of an individual was a "most unreliable" guide to the basal blood pressure and that basal and supplemental pressures were almost independent variables. The compelling conclusion from Smirk's analysis[7] was that basal blood pressure was superior to casual pressure in predicting outcome. I believe that the growing evidence for the superiority of nocturnal blood pressure measured with ambulatory blood pressure monitors is that we are measuring blood pressure when it is most stable or basal, in contrast to daytime measurements, which are subject to so many influences, not the least of which is activity. This reasoning is supported by evidence that administering a mild sedative during ambulatory blood pressure monitoring may help to identify the patients with a high cardiovascular risk, namely, those patients who continue to manifest a blunted nocturnal dip despite sedation.[8]

Valuable though the information derived from nocturnal blood pressure may be, there are several methodologic

From the Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin, Ireland.

Correspondence to Eoin O'Brien, Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin 4, Ireland. E-mail eobrien@iol.ie

(*Hypertension*. 2007;49:769-770.)

Hypertension **is available at http://www.hypertensionaha.org**
DOI: 10.1161/01.HYP.0000258152.29476.de

limitations to recording blood pressure at night. These include poor reproducibility, different criteria for defining dipping/nondipping status, and the influence of daytime physical activity on the dipping phenomenon.[9] Now Verdecchia et al[10] have added a further caveat to the measurement of nocturnal blood pressure, namely, the influence of sleep disturbance. A review of the literature on the effect of the quality of sleep on blood pressure measurement at night is nonconclusive, with some (but not all) studies suggesting that nocturnal blood pressure may be affected by the noise and disturbance caused by repeated cuff inflations, but none have assessed the prognostic significance of such sleep disturbance.[10] In the Italian study there were 356 major cardiovascular events and 184 all-cause deaths over a mean 7-year follow-up period in 2934 hypertensive subjects. Sleep quality was assessed by questionnaire according to the number of estimated hours of sleep deprivation. The interesting finding from the study is that nighttime blood pressure significantly rises and loses its prognostic significance in a sizeable minority (≈14% of untreated hypertensive subjects) who perceived sleep deprivation of ≥2 hours during overnight blood pressure monitoring. On the other hand, 86.4% of subjects did not report any significant disturbance of sleep in spite of having measurements every 15 minutes throughout the night. The number of cardiovascular events in the subset without significant perceived sleep disturbance compared with that with significant perceived sleep disturbance was 300 and 56, respectively, and the total number of deaths in the 2 groups was 157 and 27, respectively.

Although the results of this study are interesting and important in that they provide outcome data suggesting that sleep disturbance may affect the prognostic value of nocturnal blood pressure, they must be interpreted with some caution. Apart from the potential unreliability of questionnaires to assess sleep quality and the fact that the group with more severe sleep deprivation was smaller than the group without sleep deprivation, my main concern is that the methodology of nocturnal measurement may have influenced the results. Firstly, there is the issue of the frequency of measurement. I would argue that the potential disturbance to sleep induced by recording blood pressure every 15 rather than every 30 minutes outweighs the advantage of increasing the number of measurements. This is an issue that should be decided by consensus among researchers and experts; the Guideline of the Working Party on Blood Pressure Monitoring of the European Society of Hypertension recommends a minimum number of measurements for the day and nighttime periods and, although it does not recommend the precise frequency of measurement, the minimum requirements can usually be easily achieved with measurement every 30 minutes throughout the day and night.[11] Second, there is the issue of the amount of sleep disturbance caused by the ambulatory device used, and there is a clear message here for manufacturers of ambulatory devices. Interestingly, the older device used in the Italian study, the SpaceLabs 5200 model, was associated with more sleep deprivation and lesser day–night blood pressure reduction then the newer models, the SpaceLabs 90202 and 90207, indicating that the bigger size and louder noise of the pump during inflation in the early model might have induced more sleep disturbance. It behoves manufacturers, therefore, to look critically at the design of devices for ambulatory blood pressure measurement. Although both the size of monitors and the noise of pumps have improved in recent times, it is fair to say that manufacturers have shown little innovative flair over the past 30 years in providing a device for ambulatory measurement that is not dependent on a relatively heavy and cumbersome recorder being connected to an inflatable arm cuff.

Disclosures

None.

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