Dipping Status May Be Determined by Nocturnal Urination

Gila Perk, Liora Ben-Arie, Judith Mekler, Michael Bursztyn

Abstract—Nondipping, ie, failure to reduce blood pressure by \( \geq 10\% \) during the night, is considered an important prognostic variable of 24-hour ambulatory blood pressure monitoring. However, some people wake up at night to urinate. Usually, 24-hour ambulatory blood pressure monitoring–derived blood pressure includes these rises in the nighttime blood pressure mean. We identified 97 subjects undergoing 24-hour ambulatory blood pressure monitoring who reported waking up at night to urinate. We assessed the 24-hour ambulatory blood pressure monitoring first using total daytime and total nighttime means and then using actual daytime awake and nighttime asleep (as reported by the patient) means. Nocturnal decline in blood pressure was \( 14.4 \pm 8.5/11.8 \pm 6.1 \) mm Hg with the first method and \( 17.1 \pm 8.3/13.8 \pm 5.9 \) mm Hg with the second one \( (P<0.00001) \). Although the absolute difference between the nocturnal blood pressure declines calculated by the 2 methods was small, the effect on nocturnal dip was profound. Average systolic blood pressure dipping was \( 10.1\% \) by the total day–total night method and \( 12.0\% \) by the actual day awake–night asleep method \( (P=0.00001) \), and that of diastolic blood pressure was \( 14.2\% \) and \( 16.7\% \), respectively \( (P=0.00001) \). The prevalence of systolic blood pressure nondipping decreased from \( 42.2\% \) by the first method to \( 31.9\% \) by the second method \( (P=0.0056) \), and that of diastolic blood pressure nondipping decreased from \( 22.6\% \) to \( 11.3\% \) \( (P=0.00001) \). Inclusion of awake blood pressure measurements during the night obscured the normal dipping pattern in people who woke up to urinate. Thus, taking into account people’s actual behavior increases the accuracy of the results.

\[ (Hypertension. 2001;37[part 2]:749-752.) \]

Key Words: blood pressure, ambulatory \( \bullet \) urination \( \bullet \) dipping \( \bullet \) nondipping

Ambulatory blood pressure monitoring has become an important tool in the diagnosis and management of hypertension. It has been shown that compared with clinic blood pressure, ambulatory blood pressure is more closely associated with target organ damage and prognosis.\(^1\)\(^2\) It has been observed that in normotensive and most hypertensive people, there is a nocturnal decline in blood pressure. Normally, it is a decline of \( 10\% \) to \( 15\% \) of daytime values (“dipping”). However, some people do not show this nighttime change in blood pressure (nondippers). It has been shown that lack of nocturnal decline in blood pressure is associated with increased target organ damage.\(^3\)\(^-\)\(^8\) Also, lack of nocturnal decline in blood pressure, ie, nondipping, has been found to be associated with adverse prognosis in women.\(^9\)\(^10\)

However, the criteria used to define day and nighttime in the course of ambulatory blood pressure monitoring are multiple. Some researchers used an arbitrary division (eg, day from \( 6 \) AM to \( 10 \) PM and night from \( 10 \) PM to \( 6 \) AM), while others used the actual awake and asleep hours reported by the patients. It has been shown that using an arbitrary definition of nighttime as opposed to actual asleep and awake hours can result in misclassification of patients in regard to their “dipping” status.\(^11\)\(^-\)\(^13\) A behavioral factor that can influence the interpretation of the results of the ambulatory blood pressure monitoring is the afternoon nap. Including the nap time in the calculation of daytime blood pressure can artificially lower the daytime average and thus result in incorrectly classifying patients as nondippers.\(^14\)\(^-\)\(^16\)

Defining daytime and nighttime solely on the basis of the reported time of retiring to bed may also be a possible misclassification. People may have different patterns of behaviors during the night; some people wake up several times a night. These different modes of nighttime activity can influence the results of the ambulatory blood pressure monitoring and cause misclassification of patients as nondippers. We undertook this study to verify the importance of considering the individualized patterns of nighttime “sleep.” We studied subjects who underwent 24-hour ambulatory blood pressure monitoring and reported waking up at night to urinate.

Methods

Subjects

During a period of 4 months (November 1999 to March 2000), a prospective evaluation of consecutive 24-hour ambulatory blood pressure monitorings at our unit was done. During this period, 374 monitoring sessions were performed. Subjects were referred to our unit by primary care physicians to confirm the presence of hyper-
Ambulatory Blood Pressure Monitoring
Ambulatory blood pressure was monitored with the Spacelab model 90207 monitor. The monitor was mounted on the nondominant arm between 8 and 10 AM and removed 24 hours later. Calibration was checked twice (at the beginning and the end of the session) with a Y adapter and was verified to be in close agreement with the auscultatory findings (<5 mm Hg). Blood pressure was recorded 3 times per hour during the day, 2 times per hour during the night, and on request by the patients when they woke up in the night. The patients were instructed to immobilize their arm during cuff inflation. They were asked to keep a diary of their activities and asleep hours and, in particular, to record any asleep time during the day and every awake period during the night. The nocturnal awake blood pressure was taken from the manual activation when present or from the nearest recorded awake time during the session. Thus, 34% of all recordings were associated with nighttime awakenings.

Statistical Analysis
Two analyses were performed on the results of the ambulatory blood pressure monitoring. One was done using total daytime (from waking in the morning until retiring to sleep at night) and total nighttime (from retiring to sleep until waking up in the morning). The second was done using the actual asleep (excluding nighttime awake hours) and actual awake (excluding daytime naps) times as reported by the patient and by the ordered measurements by the monitor. Dippers (by both methods) were defined as the subjects whose nocturnal blood pressure decline was >50% of their mean daytime blood pressure.

Results
There was no difference between daytime awake and nighttime awake (when waking up to urinate at night) blood pressure (141.8 ± 13.7/81.9 ± 10.7 versus 140.3 ± 15.7/80.3 ± 11.0 mm Hg).

Mean nocturnal blood pressure was significantly higher than mean actual nighttime asleep blood pressure (Table 1). The differences between mean day and night ambulatory blood pressure and heart rate, ie, the nocturnal blood pressure and heart rate decline, were significantly greater (P<0.00001) when the measurements of night awake blood pressure (on waking up to urinate) and daytime asleep blood pressure (during afternoon nap) were not taken into account (Table 2). Average dipping was also significantly greater with this method of calculation (Table 2).

Although the blood pressure differences calculated by the 2 methods were highly significant, the absolute differences were rather modest. Nevertheless, these modest differences had a profound effect on dipping status as evident from Figure 1. Prevalence of systolic blood pressure nondipping was about 25% lower and that of diastolic blood pressure was 50% lower when the actual daytime awake and nighttime asleep means were used. The blood pressure differences between daytime and nighttime mean ambulatory blood pressure were also significantly greater when nighttime means were calculated excluding the measurements on waking up and daytime means were calculated as the total daytime means without excluding daytime naps (16.16 ± 3.2/13.17 ± 4.0 mm Hg; P<0.00001).

Of the 97 participants, 58 awoke once at night to urinate, 33 awoke twice, and 6 awoke ≥3 times. With each way of calculating the nocturnal pressure differences, the nocturnal awake blood pressure and heart rate were significantly greater (P<0.00001) than the awake awake blood pressure and heart rate.

Table 1: Average Nocturnal Blood Pressure and Heart Rate of 24-Hour Monitoring Calculated for Total Night or Actual Night Sleep Measurements in 97 Subjects Who Wake up at Night to Urinate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Night</th>
<th>Actual Night Asleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, mm Hg</td>
<td>126.4 ± 13.4</td>
<td>124.7 ± 13.4*</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>69.5 ± 9.4</td>
<td>68.1 ± 9.5*</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>63.3 ± 8.3</td>
<td>62.4 ± 8.2*</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; and HR, heart rate.

*P<0.0001.

Figure 1. Prevalence of systolic blood pressure nondipping calculated by total day–total night and actual daytime awake–nighttime asleep measurements in 97 subjects who wake up at night to urinate. SBP indicates systolic blood pressure; DBP, diastolic blood pressure. *McNemar’s χ² = 7.68, df = 1, P = 0.0056; **McNemar’s χ² = 36.44, df = 1, P = 0.0001.

Table 2: Difference Between Daytime and Nighttime Ambulatory Blood Pressures and Heart Rate Calculated According to Total Day–Total Night and Actual Daytime Awake–Nighttime Asleep Measurements in 97 Subjects Who Wake up to Urinate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Day–Total Night</th>
<th>Awake Day–Asleep Night</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocturnal SBP decline, mm Hg</td>
<td>14.4 ± 8.5</td>
<td>17.1 ± 8.3*</td>
</tr>
<tr>
<td>Nocturnal DBP decline, mm Hg</td>
<td>11.8 ± 6.1</td>
<td>13.8 ± 5.9*</td>
</tr>
<tr>
<td>Nocturnal HR decline, bpm</td>
<td>10.3 ± 5.8</td>
<td>11.4 ± 6.1*</td>
</tr>
<tr>
<td>Nocturnal SBP dip, %</td>
<td>10.1 ± 5.7</td>
<td>12.0 ± 5.1*</td>
</tr>
<tr>
<td>Nocturnal DBP dip, %</td>
<td>14.2 ± 6.8</td>
<td>16.7 ± 6.4*</td>
</tr>
<tr>
<td>Nocturnal HR dip, %</td>
<td>13.6 ± 6.5</td>
<td>14.9 ± 6.9*</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

*P<0.0001.
monitoring, waking up to urinate at night was common and in the dipping status of the subject. We found that among the ambulatory blood pressure monitoring can cause a change into account the activity level and using it in the analysis of

calculation, more frequent nocturnal urination was associated with a higher nondipping rate: $\chi^2$ for trend = 6.7, $df = 2$, $P = 0.035$ for systolic, and $\chi^2 = 8.4$, $df = 2$, $P = 0.015$ for diastolic blood pressure by the total day–total night method; $\chi^2 = 7.6$, $df = 2$, $P = 0.022$ for systolic, and $\chi^2 = 6.0$, $df = 2$, $P = 0.05$ for diastolic blood pressure by the awake day–asleep night method (Figure 2). Again, with the actual daytime awake–nighttime asleep method, the prevalence of nondipping was substantially lower.

The average difference between the dip as calculated by the 2 methods increased from (systolic/diastolic blood pressure) 2.2±1.8/1.5±1.1 mm Hg in the 58 subjects who woke up only once at night to 3.6±2.5/2.6±2.2 mm Hg in the 39 who woke up ≥2 times ($P<0.01$ for systolic and $P<0.003$ for diastolic blood pressures).

**Discussion**

We have shown that disregarding common patterns of behavior, like nighttime awakenings for urination, can result in misclassification of people as nondippers. Our results show that there is significant importance for accuracy in analyzing the results of 24-hour ambulatory blood pressure monitoring. Determining whether a patient is a dipper or nondipper is partially dependent on the daytime and nighttime definitions used. Previous studies have focused on the differences between using an arbitrary definition of day and night and using the actual reported time of going to sleep and getting up. There have been no studies yet that addressed the question of actual nighttime activities. Previous works studied the interaction between physical activity (as quantified objectively by an electronic activity meter) and ambulatory blood pressure. These showed that physical activity contributes significantly to the blood pressure variation. Taking into account the activity level and using it in the analysis of the ambulatory blood pressure monitoring can cause a change in the dipping status of the subject. We found that among patients referred for 24-hour ambulatory blood pressure monitoring, waking up to urinate at night was common and occurred in more than a third of all monitorings. We believe that analyses need to be individualized. Arbitrary definition of sleep time as the time between when the patient decided to go to sleep and the time when he decided to get up actually ignores patterns of behaviors that can cause a falsely elevated average sleep-time blood pressure. This can make the difference between average day and night blood pressures smaller and thus can result in erroneously defining a patient as a nondipper.

One study has tried to check the reliability and reproducibility of the nocturnal dipping. It has shown that there is considerable variability in the dipping status during 24-hour ambulatory blood pressure monitoring performed twice in a row. We believe that at least part of this problem can be resolved by relating the results of the monitoring to the actual nighttime activity. As shown in Figure 2, there is considerable difference in the prevalence of nondipping between the people who wake up once at night and those who wake up more frequently. The number of awakenings can change from night to night and can cause poor reproducibility of the dipping status.

Numerous studies have shown that nondipping is a poor prognostic sign. It has been shown to be associated with greater target organ damage, including left ventricular hypertrophy, microalbuminuria, and lacunar infarcts. Thus, it is not surprising that nondipping was also shown to be a poor prognostic sign associated with increased cardiovascular morbidity. However, in the study by Verdecchia et al, which was the first to establish the prognostic value of 24-hour ambulatory blood pressure monitoring, nondipping had an adverse effect only on women. It may well be that men who are more likely to wake up at night to urinate because of prostatism and were more likely to nap in the afternoon (as we found in an elderly population survey). This could have resulted in misclassification of more men as nondippers when in fact the blunted nocturnal fall in blood pressure was related to higher mean nighttime blood pressure and lower mean daytime blood pressure because of the factors suggested. Men who are classified as nondippers because they arise to urinate might not be at the same risk for cardiovascular events as those who are nondippers but do not arise to urinate. Counting the former as nondippers might obscure the relation between nondipping and cardiovascular risk in men.

It is not yet clear whether the associated increase in cardiovascular morbidity and target organ damage is related to the inability of the patient to lower blood pressure during the night or to the increased load of hypertension. It has been shown that nondipping is common in people with diabetes and secondary forms of hypertension, such as preeclampsia, chronic renal failure, and adrenocortical hypertension. However, there is minimal information on whether this is related to physiological alterations and an inability to lower blood pressure or to different modes of behavior that alter the calculated differences (eg, nocturia in diabetic patients). We found previously that diabetic patients have a blunted decline in blood pressure during afternoon naps compared with matched, non diabetic subjects. Nap time is usually short enough to be devoid of waking periods; thus, this suggests
that diabetics actually lack the mechanism required to lower blood pressure during sleep.

Our results show that actual activity during the night has a significant meaning in the interpretation of results of ambulatory blood pressure monitoring. There is reason to believe that an inability to lower blood pressure during the night, or nondipping, is a marker of pathology that is related to increased morbidity. However, to study this more accurately, we first need more precision in the analysis of the results of ambulatory blood pressure monitoring, with consideration given to the individual patterns of behavior.

References
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Hypertension. 2001;37:749-752
doi: 10.1161/01.HYP.37.2.749

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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