Effects of Insufficient Sleep on Blood Pressure in Hypertensive Patients
A 24-h Study
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The influence of acute sleep deprivation during the first part of the night on 24-h blood pressure monitoring (ABPM) was studied in 36 never-treated mild to moderate hypertensive patients. According to a crossover design, they were randomized to have either sleep deprivation or a full night’s sleep 1 week apart, during which they were monitored with ABPM. Urine samples for analysis of nocturnal urinary excretion of norepinephrine were collected. During the sleep-deprivation day, both mean 24-h blood pressure and mean 24-h heart rate were higher in comparison with those recorded during the routine workday, the difference being more pronounced during the nighttime ($P < .01$). Urinary excretion of norepinephrine showed a significant increase at night during sleep deprivation ($P < .05$). Blood pressure and heart rate significantly increased in the morning after a sleep-insufficient night ($P < .05$). These data suggest that lack of sleep in hypertensive patients may increase sympathetic nervous activity during the night and the following morning, leading to increased blood pressure and heart rate. This situation might represent an increased risk for both target organ damage and acute cardiovascular diseases. Am J Hypertens 1999;12:63–68 © 1999 American Journal of Hypertension, Ltd.

KEY WORDS: Sleep deprivation, hypertension, ambulatory blood pressure monitoring.

According to a report of the National Commission on Sleep Disorder Research, 30 million adults and teenagers in the United States are chronically sleep deprived.$^{1,2}$ A 9-year follow-up study found that individuals sleeping fewer than 6 h each night experienced poorer health and had a 70% higher mortality rate than those who slept 7 or 8 h each night. This association remains significant even after controlling for age, gender, race, physical health, smoking history, physical activity, alcohol consumption, and social support.$^3$

The relationships among habitual sleep deprivation and premature follow-up mortality,$^{4,5}$ cardiovascular morbidity,$^6$ and functional disability have been reported by either longitudinal or cross-sectional studies.$^7$ Sleep problems and especially being exhausted upon waking are markers of subclinical heart disease and belong to the precursors of myocardial infarction.$^8$ In Japan, “karoshi” (sudden death caused by overwork) is such a serious socioeconomic problem that Tochikubo et al$^9$ recently investigated the effect of sleep deprivation due to overtime work on blood pressure (BP) and on components of the power spectrum of heart rate (HR) variability in normotensive subjects, and found that lack of sleep may increase sympathetic nervous system activity on the following day, leading to increased BP and HR. The same hemodynamic results have been achieved by us in a previous 24-h
ambulatory blood pressure monitoring (ABPM) study of acutely sleep-deprived normotensives.\textsuperscript{10}

The aim of the present study was to evaluate the influence of acute sleep deprivation on blood pressure and heart rate in never-treated hypertensive patients.

**MATERIALS AND METHODS**

Thirty-nine subjects (20 men and 19 women) ranging in age from 34 to 68 years, newly diagnosed as mild to moderate essential hypertensives (diastolic BP \(\geq 95\) mm Hg), gave their informed consent to participate in the study, which was previously approved by the local ethics committee. Diagnosis of arterial hypertension was made after clinical blood pressure measurement with a mercury sphygmomanometer during three visits in 4 weeks. Mean systolic and diastolic blood pressure were 162.3 \(\pm\)10.1 mm Hg and 99.8 \(\pm\)5.4 mm Hg, respectively, after the 4-week period. Secondary hypertension and sleep apnea syndrome were excluded by careful history and through physical and laboratory examinations, including radiologic and endocrinologic studies. The patients affected by organ damage were excluded. All were nonsmokers, without any family history of diabetes mellitus, and had never been treated with any antihypertensive agent or cardiovascular drug. Shift workers and patients affected by major sleep complaints or without a regular sleep-wake schedule (at least 8 h sleep per night) documented by a 4-week diary were excluded. No transmeridian travel was allowed for 3 months before the study. All patients wore white collars at the administrative offices of the University of Pavia, Pavia, Italy.

Subjects underwent three 24-h ambulatory blood pressure monitorings, the first of which aimed to get the patients accustomed to the measurement device, and therefore was excluded from the analysis. Thereafter patients were randomized, according to a cross-over design, to have either sleep deprivation during the first part of the night or a full night’s sleep, 1 week apart, during which they were monitored with ABPM. Recordings were performed with SpaceLabs 90207 monitor (SpaceLabs Inc., Redmond, WA); it was fitted to the patients’ nondominant arm at 2 PM and was programmed to measure blood pressure every 15 min throughout the whole 24-h period. Each time a reading was taken, patients were instructed to remain motionless. On the days of ambulatory monitorings patients followed their daily routine and were asked not to nap, drink caffeinated beverages or alcohol, or to perform any heavy activity.

During the full night’s sleep, the sleep period was scheduled from 11 PM to 7 AM; during the sleep-deprivation night, patients slept from 3 AM to 7 AM, being subjected to a restriction of sleep to the second part of the night (50% of the total amount). To verify that physical activities were generally maintained at a constant level during either the control or the sleep-deprivation day, patients kept a detailed diary. During the sleep-deprivation phase the patients remained at home watching TV, reading, or talking. A relative or a friend prevented their falling asleep for the waking period. Twenty-four–hour recordings were excluded from analysis when more than 10% of all readings or more than one reading per hour were missing or contained error readings. Urine samples for analysis of nocturnal urinary excretion of norepinephrine were collected for 12 h, starting from 7 PM, in urinary sampling devices containing 6 mmol/L HCl. Urinary norepinephrine levels were determined by high-performance liquid chromatography with electrochemical detection.

The statistical analysis of the data was performed using the SAS system version 6.04. Analysis of variance and paired Student’s \(t\) test were used, with \(P < .05\) taken as statistically significant. For all recordings, the first hour of measurements was not included in the statistical analysis to eliminate possible artifacts related to the beginning of the experiment.

**RESULTS**

Thirty-six subjects (20 men and 16 women) completed the study. Three subjects dropped out because they had a 10% or greater loss of the BP data for analysis and withdrew their consent to repeat the 24-h recordings. The main results of the present study are shown in Table 1; Figure 1 shows mean 24-h ambulatory blood pressure and heart rate values during sleep deprivation and the full night’s sleep control conditions. On the whole, during the sleep-deprivation day both mean 24-h BP and mean 24-h HR were higher than during the routine workday (systolic BP [SBP] = +5.2 mm Hg, \(P < .05\); diastolic BP [DBP] = +4.3 mm Hg, NS; HR = 3.8 beats/min, NS); such a difference was to be referred to the nighttime and to the following morning. In fact BP and HR were higher during the sleep-deprivation period (11 PM–3 AM) (SBP = +15 mm Hg, \(P < .001\); DBP = +16 mm Hg, \(P < .001\); HR = +8.3 beats/min, \(P < .001\)) and during the subsequent sleep hour (3 AM–7 AM) (SBP = +5.1 mm Hg, \(P < .01\); DBP = NS; HR = +5.4 beats/min, \(P < .05\)) than during the routine nighttime.

During the morning hours after sleep deprivation (7 AM–12 PM) BP and HR were higher when compared with the values recorded after a full night’s sleep (SBP = +7.1 mm Hg, \(P < .001\); DBP = +4 mm Hg, \(P < .01\); HR = +5.5 beats/min, \(P < .05\)).

When the ABPM of the control day was considered, all patients were “dippers,” but all of them became “nondippers” after the acute sleep deprivation. In fact, nocturnal SBP fall was 14% during the full night’s sleep condition, but only 7% during the sleep-
Subjects,9–11 even though the two groups are not comparable for their different ages, as the hypertensive patients we studied were older. However, we found higher BP and HR values during the sleeping period after the sleep deprivation and higher 24-h HR in comparison with the normotensive group,9 suggesting a greater sympathetic activation in hypertensive subjects.

These results also point out that the nocturnal BP decline is mainly related to sleep itself and to the associated physical inactivity and postural changes rather than to the actual time of day, which confirms previous reports that the timing of the diurnal BP rhythm is determined mainly by extrinsic factors.9–20 Thus, in patients who remained awake BP did not decrease during the first part of the night, although it was time to sleep. Likewise, we observed that, after the sleep deprivation occurring during a westward transmeridian flight, the shift of the sleeping time blunted the BP and HR nocturnal falls in normotensive individuals.19 This might be explained by the fact that an upright position enhances the activity of noradrenergic branches,21 irrespective of the time of day.

The 24-h rhythm of HR seems to reflect modulatory influences that are different from those controlling nycterohemeral changes in BP; according to Van den Meiracker et al22 postural changes have little effect on HR and the nocturnal HR decline appears mainly caused by the sleep condition. As a matter of fact, HR maintained itself higher for all the recovery sleep after the deprivation, in comparison with the control night.

Although we did not perform polysomnographic sleep recordings, we hypothesize that the acute sleep deprivation might have altered the nature of sleep itself, leading to a predominance of rapid eye movement (REM) sleep phases, during which HR reaches higher levels, similar to those during wakefulness, due to sympathetic activation.23–25 Sympathetic activation is likely to contribute also to the significant increase in BP and HR observed in the morning after a night of insufficient sleep, which is supported by the increase in urinary excretion of norepinephrine observed during the sleep-deprivation night. Other authors observed that the normal diurnal variation of urinary catecholamine excretion is easily overridden by sustained sympathoadrenal activity,26 and, in our opinion, sleep deprivation might represent a stressful condition promoting an increased synthesis of catecholamines through the activation of superior centers. Our findings corroborate the observations of Tochikubo et al, who pointed out an altered sympathovagal balance, with a significantly increased low frequency/high frequency (LF/HF) balance at the

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Workday</th>
<th>Sleep Deprivation Day</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean 24h SBP (mm Hg)</td>
<td>145.09 ± 9.40</td>
<td>150.32 ± 7.83</td>
<td>.05</td>
</tr>
<tr>
<td>First part of the night SBP (mm Hg) (23:00–03:00)</td>
<td>131.52 ± 10.36</td>
<td>146.93 ± 9.37</td>
<td>.001</td>
</tr>
<tr>
<td>Second part of the night SBP (mm Hg) (03:00–07:00)</td>
<td>132.84 ± 7.38</td>
<td>137.95 ± 8.04</td>
<td>.01</td>
</tr>
<tr>
<td>Morning SBP (mm Hg) (07:00–12:00)</td>
<td>147.72 ± 6.84</td>
<td>154.86 ± 5.91</td>
<td>.001</td>
</tr>
<tr>
<td>Mean 24h DBP (mm Hg)</td>
<td>86.86 ± 7.25</td>
<td>91.12 ± 7.84</td>
<td>NS</td>
</tr>
<tr>
<td>First part of the night DBP (mm Hg) (23:00–03:00)</td>
<td>75.11 ± 5.68</td>
<td>91.07 ± 6.35</td>
<td>.001</td>
</tr>
<tr>
<td>Second part of the night DBP (mm Hg) (03:00–07:00)</td>
<td>78.76 ± 6.34</td>
<td>80.17 ± 6.42</td>
<td>NS</td>
</tr>
<tr>
<td>Morning DBP (mm Hg) (07:00–12:00)</td>
<td>92.28 ± 7.26</td>
<td>96.29 ± 7.25</td>
<td>.01</td>
</tr>
<tr>
<td>Mean 24h HR (beats/min)</td>
<td>69.79 ± 4.41</td>
<td>73.61 ± 5.23</td>
<td>NS</td>
</tr>
<tr>
<td>First part of the night HR (beats/min) (23:00–03:00)</td>
<td>63.67 ± 10.36</td>
<td>71.93 ± 10.03</td>
<td>.001</td>
</tr>
<tr>
<td>Second part of the night HR (beats/min) (03:00–07:00)</td>
<td>61.11 ± 6.25</td>
<td>66.51 ± 7.48</td>
<td>.05</td>
</tr>
<tr>
<td>Morning HR (beats/min) (07:00–12:00)</td>
<td>69.73 ± 5.26</td>
<td>75.19 ± 6.33</td>
<td>.05</td>
</tr>
<tr>
<td>Urinary excretion of norepinephrine (mmol/min) (19:00–07:00)</td>
<td>1.57 ± 0.26</td>
<td>2.12 ± 0.31</td>
<td>.05</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
FIGURE 1. Ambulatory blood pressure and heart rate monitorings during the sleep deprivation day (■) and the control workday (∗). *P < .05, **P < .01.
spectral analysis of RR intervals, on the day after a sleep-insufficient night.9

Two practical considerations descend from our observations. First, due to the blunted nocturnal BP fall, we might suppose that chronically sleep-deprived hypertensives are presumably nondippers and therefore are at higher risk of target organ damage and cardiovascular morbidity and mortality.27–31 Secondly, the BP and HR increase observed during the morning after sleep deprivation might increase the risk of cardiovascular events, which are known to occur more frequently from early morning to noon.32–34 Thus, in those hypertensives who habitually sleep few hours per night for various reasons, the use of long-acting antihypertensive agents able not only to ensure the nocturnal control of BP but also to blunt the early morning BP rise might be useful. Further studies, however, are needed to confirm such a hypothesis.

REFERENCES


