Blood Pressure Changes During Daytime Sleep and Comparison of Daytime and Nighttime Sleep-Related Blood Pressure Changes in Patients With Chronic Renal Failure\textsuperscript{1,2}

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ABSTRACT
Blood pressure has a diurnal pattern primarily related to activity and sleep. Chronic renal failure patients may lack the normal nocturnal decline in blood pressure during sleep. In 33 subjects (14 with normal renal function and 19 with renal dysfunction), the relationship between depth of daytime sleep, as determined by electroencephalographic sleep phase, and change in mean arterial blood pressure (MAP) and heart rate measured oscillometrically, was correlated. In 15 chronic renal failure patients, the effect of daytime and nighttime sleep on MAP and heart rate was compared. The percent change in night asleep versus day awake MAP and heart rate was measured (with Space Labs ambulatory blood pressure monitors) and compared with the percent change in daytime sleep-related MAP and heart rate measured during a daytime sleep electroencephalographic study. During daytime sleep, MAP changes are not significantly different in the normal versus renal dysfunction groups. In the 33 study subjects, MAP declines progressively from the upright to recumbent position, before sleep. Heart rate declines moving from the upright to recumbent position, 76 ± 2.3 to 70 ± 2.1 beats/min, but does not decline further with sleep. In 15 chronic renal failure patients, heart rate (10.8 ± 2.8\% \( P < 0.05 \)) declines during nighttime sleep. Both MAP (7.7 ± 3.3\%) and heart rate (5.4 ± 1.9\%) decline significantly during daytime sleep. The responses of MAP and heart rate to daytime and nighttime sleep were in opposite directions in 3 of 15 subjects. In conclusion, MAP declines progressively during daytime sleep with successively deeper levels of sleep. Movement from the upright to the recumbent position accounts for a large part of the decline. In patients with chronic renal failure, MAP and heart rate responses to daytime and nighttime sleep may be in opposite directions. Future physiologic studies are needed to explore the mechanisms of daytime and nighttime sleep-related hemodynamic changes.

Key Words: Diurnal, blood pressure, electroencephalogram, sleep

Blood pressure has a circadian rhythm that is primarily related to activity. During nocturnal sleep, blood pressure normally declines. This decrease in blood pressure may correlate with depth of sleep, as documented by electroencephalogram (EEG), although reports to date give conflicting results (1-5). The prevention of nighttime sleep removes the bimodal pattern of blood pressure in normal subjects (6).

The absence of the normal nocturnal decline in blood pressure during sleep has been documented in patients with chronic renal failure, autonomic dysfunction, and diabetes mellitus (7-9). The relationship between daytime sleep (as documented by EEG) and blood pressure has not been studied. In addition, the relationship between blood pressure decline during nighttime sleep versus daytime sleep in the same patient has not been evaluated.

This study addresses the following questions. (1) Does daytime sleep result in a decline in blood pressure proportional to the depth of sleep as measured by EEG sleep phases? Is this response different in
subjects with normal versus abnormal renal function? (2) Is there a relationship between blood pressure changes during daytime and nighttime sleep in patients with chronic renal failure?

METHODS

Subjects

Included in the study are 33 male veteran hypertensive outpatients from the W.J.B. Dorn VA Hospital (Columbia, SC), 11 stable chronic hemodialysis patients, 8 patients with varying degrees of chronic renal failure (serum creatinine, 1.8 to 4 mg/dL) and 14 patients with normal renal function (serum creatinine, <1 mg/dL). All dialysis patients were hypertensive, and none were diabetic. The primary causes of renal failure included 24 patients with hypertensive nephropathy, 7 with chronic glomerulonephritis, and 2 with cystic kidney disease. The normal renal function group included nonhypertensive, nondiabetic subjects who received a sleep EEG study as part of a routine seizure evaluation.

Informed consent was obtained after all procedures were explained to the subjects. All 33 patients underwent a 1.5-h EEG study between 8:00 a.m. and 12:00 p.m. Before the EEG study, patients were asked to wake up 2 h earlier than usual. Subjects withheld all medications the morning of the study until the study was completed. A Nihon-Khoden model 1347D, 17-channel EEG machine was used. A Datascopes Accutor-2 was used to monitor systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), and heart rate. These hemodynamic parameters were monitored for three readings at 2.5-min intervals with the patient (1) in a sitting position after the placement of the EEG electrodes (baseline upright [BU]) and (2) in bed recumbent before the EEG recording started (baseline down [BD]). Next, these parameters were recorded every 5 min while the patient was awake and until the patient entered Phase 1 sleep. Once the patient entered Phase 1 sleep, the parameters were measured every minute. Phases of sleep were recorded as Phase 1, 2, 3, or 4 according to the criteria of Dement and Kleitman (10). Data from Phases 1 and 2 were combined, and data from Phases 3 and 4 were combined for data analysis. Because rapid eye movement sleep may be associated with either an increase or a decrease in MAP, periods of rapid eye movement sleep were excluded from the analysis (3).

Fifteen of the 33 patients (11 with end-stage renal failure, 8 of whom were on chronic hemodialysis, and 4 patients with moderate renal failure) underwent 24-h ambulatory blood pressure monitoring with Space Labs 90202 and 90207 blood pressure monitors. After the completion of the nighttime monitoring, patients filled out a sleep diary to indicate times they fell asleep and were awake during the nighttime and daytime hours.

Data Analysis

The mean percent change (±SE) for systolic and diastolic blood pressure, MAP, and heart rate for each sequential period of the EEG study (BU, BD, Phase 1/2 sleep, Phase 3/4 sleep) was calculated. If a patient had fewer than 5 min in Phase 1/2 or 3/4 sleep, then the data for the respective period were excluded from the analysis. Paired and unpaired t tests were used to determine if there was a significant change in hemodynamic parameters at the P = 0.05 level. The percent change in day awake versus night asleep MAP and heart rate during 24-h monitoring was calculated as follows:

\[
\text{Percent change} = \left( \frac{\text{day awake} - \text{night asleep}}{\text{day awake}} \right) \times 100
\]

Awake and asleep intervals were obtained from 24-h sleep diaries. Night asleep includes only those intervals between first going to sleep and waking up in the morning. Day awake intervals exclude any data during daytime sleep. MAP was chosen for analysis because this parameter is the most accurately determined blood pressure with the oscilometric blood pressure instrument (11).

RESULTS

Change in MAP and Heart Rate During Daytime Sleep

Patients slept an average of 6.4 h the evening before the EEG study. The mean (±SE) control period (baseline upright) systolic/diastolic blood pressure and MAP for the normal renal function and renal dysfunction groups were 144 (±5.0)/94 (±3.8) and 116 (±5.0) mm Hg and 149 (±4.2)/97 (±3.7) and 120 (±3.8) mm Hg, respectively. The baseline heart rate was 71 (±2.6) beats/min in the normal renal function group compared with 79 (±3.3) beats/min in the renal dysfunction group (Table 1). None of the baseline blood pressure measurements were significantly different in the normal versus renal dysfunction groups (i.e., P > 0.05 for all). Heart rate was significantly greater (P < 0.01) in the renal dysfunction group.

As seen in Table 2, 25 of the 33 subjects entered Phase 3/4 sleep for a minimum of 5 min. All 33 subjects entered Phase 1/2 sleep for at least 5 min. Although slightly higher in the renal dysfunction group, MAP was not significantly different in any phase of the EEG sleep study in subjects with renal dysfunction compared to subjects with normal renal function. MAP declined from 120 (±3.8) to 107 (±4.1) mm Hg and from 116 (±5.0) to 105 (±5.8) mm Hg (P < 0.05 for each), whereas heart rate decreased from
TABLE 1. MAP and heart rate during daytime sleep EEG³

<table>
<thead>
<tr>
<th>Sleep Phase</th>
<th>Total Group</th>
<th>Normal Renal Function⁶</th>
<th>Renal Dysfunction⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MAP (mm Hg)</td>
<td>HR (beats/min)</td>
<td>N</td>
</tr>
<tr>
<td>BU</td>
<td>118 (±3.3)</td>
<td>76 (±2.3)</td>
<td>33</td>
</tr>
<tr>
<td>BD</td>
<td>113 (±3.2)</td>
<td>70 (±2.1)</td>
<td>33</td>
</tr>
<tr>
<td>Phase 1/2 sleep</td>
<td>109 (±2.8)</td>
<td>70 (±1.9)</td>
<td>33</td>
</tr>
<tr>
<td>Phase 3/4 sleep</td>
<td>106 (±3.6)</td>
<td>70 (±2.6)</td>
<td>25</td>
</tr>
</tbody>
</table>

Values are mean (±SE). HR, heart rate in beats per minute.

Normal renal function defined as serum creatinine ≤ 1.5 mg/dL.
Renal dysfunction defined as serum creatinine > 1.5 mg/dL.
BU, sitting position after EEG electrode placement.
BD, in bed before the start of EEG.
C, Combined Phases 1 and 2 of sleep EEG.
D, Combined Phases 3 and 4 of sleep EEG.

Table 2 gives the percent change in MAP during the sleep EEG study. As with absolute MAP, percent change in MAP was not significantly different at any stage of the sleep EEG study in the normal renal function versus renal dysfunction groups. Thus, these two groups were combined (all subjects). For all subjects, there is a progressive and significant decline in MAP with each phase of the sleep EEG study. The greatest absolute, although not statistically significant, percent decline occurred before sleep, when subjects moved from the BU to the BD position (−3.9 ± 1.3).

The percent decline in heart rate was not significantly different in the two groups, except for the movement from the BU to the BD position. The decline was significantly greater in the normal renal function group (−9.6 ± 2.0) versus the renal dysfunction group (−4.9 ± 1.6) (P < 0.05). As seen with MAP, the greatest percent change in heart rate occurred before sleep, when subjects moved from the upright to the recumbent position (−6.9 ± 1.3) for all subjects; P < 0.05.

Comparison of Daytime Sleep and Nighttime Sleep Associated MAP Changes in Patients with Chronic Renal Failure

Table 3 compares the percent change in MAP during sleep in 15 chronic renal failure subjects who underwent daytime EEG and 24-h ambulatory blood
TABLE 3. Comparison of percent change in MAP and heart rate during daytime and nighttime sleep in patients with chronic renal failure

<table>
<thead>
<tr>
<th>Subject</th>
<th>MAP BU → 1/2 (Day Sleep)</th>
<th>% Change DA → NS</th>
<th>HR BU → 1/2 (Day Sleep)</th>
<th>% Change DA → NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-29.5</td>
<td>-7.2</td>
<td>-18.3</td>
<td>-24.7</td>
</tr>
<tr>
<td>2a</td>
<td>3.1</td>
<td>-12.4</td>
<td>-17.7</td>
<td>-23.0</td>
</tr>
<tr>
<td>3</td>
<td>-7.1</td>
<td>-2.0</td>
<td>-1.7</td>
<td>-23.7</td>
</tr>
<tr>
<td>4</td>
<td>-7.1</td>
<td>-22.0</td>
<td>-4.6</td>
<td>-4.1</td>
</tr>
<tr>
<td>5</td>
<td>-14.1</td>
<td>-2.2</td>
<td>-1.5</td>
<td>-5.1</td>
</tr>
<tr>
<td>6</td>
<td>-23.4</td>
<td>-13.5</td>
<td>1.7</td>
<td>-0.8</td>
</tr>
<tr>
<td>7</td>
<td>5.3</td>
<td>0.0</td>
<td>-8.0</td>
<td>-15.3</td>
</tr>
<tr>
<td>8a</td>
<td>15.4</td>
<td>-13.7</td>
<td>-8.2</td>
<td>-21.1</td>
</tr>
<tr>
<td>9</td>
<td>-6.4</td>
<td>-5.4</td>
<td>-7.8</td>
<td>2.3</td>
</tr>
<tr>
<td>10</td>
<td>-23.6</td>
<td>-25.0</td>
<td>-2.4</td>
<td>-24.2</td>
</tr>
<tr>
<td>11a</td>
<td>-23.5</td>
<td>21.3</td>
<td>-10.9</td>
<td>3.4</td>
</tr>
<tr>
<td>12</td>
<td>-7.1</td>
<td>-8.9</td>
<td>-14.3</td>
<td>-22.8</td>
</tr>
<tr>
<td>13a</td>
<td>-12.4</td>
<td>14.9</td>
<td>2.7</td>
<td>-4.9</td>
</tr>
<tr>
<td>14</td>
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<td>-1.1</td>
<td>5.6</td>
<td>-1.2</td>
</tr>
<tr>
<td>15</td>
<td>-2.5</td>
<td>0.9</td>
<td>4.3</td>
<td>2.4</td>
</tr>
<tr>
<td>Mean</td>
<td>-7.7</td>
<td>-5.1</td>
<td>-5.4</td>
<td>-10.8</td>
</tr>
<tr>
<td>SE</td>
<td>3.3</td>
<td>3.1</td>
<td>1.9</td>
<td>2.8</td>
</tr>
<tr>
<td>P &lt; 0.05*</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Subjects ordered according to level of renal function. Subjects 1 to 4, creatinine, 0.8 to 4.1 mg/dL; Subjects 5 and 6, end-stage renal failure not yet on dialysis; Subjects 7 to 15, dialysis subjects.

b Percent change in MAP or heart rate (HR) from BU sitting position to Phase 1/2 daytime sleep (daytime upright blood pressure is used as representation of average day awake (DA) blood pressure).

c Percent change in MAP or HR recorded by 24-h ambulatory blood pressure, calculated as in Table 2.

d Day and night sleep associated with inverse MAP responses.

Pressure monitoring. Eleven of the 15 subjects entered Phase 3/4 sleep (data not included in Table 3). BU MAP during the EEG study (Table 3) is used as a representation of average daytime awake blood pressure. The percent change in MAP from BU to Phase 1/2 sleep is -7.7 (±3.3) (P < 0.05).

In contrast to the significant decline in MAP during daytime sleep, nighttime sleep is not associated with a significant change in MAP (-5.1 ±3.1); P > 0.05; Table 3). Heart rate declines more during nighttime sleep than during daytime sleep (-10.8 versus -5.4%), although this difference is not statistically significant.

In Table 3, Subjects 1 to 4 had mild renal insufficiency (serum creatinine, 1.8 to 4.1 mg/dL). Subjects 5 and 6 had end-stage renal failure but were not yet receiving dialysis, and Subjects 7 to 15 were stable chronic hemodialysis patients. These patients are ordered according to level of renal function (Table 3). There is no apparent relationship between renal function and blood pressure change during daytime or nighttime sleep.

In several subjects (Table 3), the percent change in MAP during daytime and nighttime sleep is inverse. For example, Subject 2 has a 3% increase in daytime sleep MAP and a 12.4% decrease in nighttime sleep MAP. Subject 8 has a 13.7% decline in nocturnal sleep blood pressure versus a 15.4% rise in MAP associated with daytime sleep. Subject 11 has a 21% rise in nocturnal sleep blood pressure and a similar percent decline in daytime sleep blood pressure. Subject 13 has an increase of approximately 15% in nighttime sleep MAP and a similar percent decline in daytime sleep MAP. Subject 1 had a much greater percent decline in daytime sleep MAP than in nighttime sleep MAP. Many subjects have significantly different heart rate responses to daytime versus nighttime sleep.

DISCUSSION

To our knowledge, this is the first attempt to evaluate the relationship between daytime sleep, as determined by EEG, and changes in blood pressure. As well, this is the first report that compares daytime and nighttime sleep-related blood pressure changes in patients with chronic renal failure.

Unfortunately, we were unable to compare the daytime and nighttime MAP and heart rate changes in a normal renal function control population. Also, the normal renal function group studied was composed of subjects who required an EEG study and thus could not be considered a true control group. We also lack nighttime sleep EEG blood pressure data that...
could confirm the nocturnal automated sleep blood pressure results. We used a patient "sleep diary" to document intervals of wakefulness after going to sleep and sleep intervals during the day. The sleep diary data were not validated, and thus, the accuracy of the data cannot be ascertained.

In the two groups studied, absolute MAP and MAP percent change were not significantly different for any phase of the EEG study (Tables 1 and 2). Thus, the two groups were combined (all subjects). The combined group demonstrates a statistically significant progressive decline in MAP with successively deeper levels of sleep. Also, significant changes in both MAP and heart rate occurred when patients moved from the upright to recumbent position in preparation for sleep (Table 2). The largest absolute percent change in MAP and heart rate occurred with movement from the upright to recumbent position. This change, in preparation for sleep, parallels the early morning increase in blood pressure after nocturnal sleep that is reportedly determined by movement from the recumbent position in bed to the upright awake position (12).

Very few studies have examined MAP and heart rate change during nocturnal sleep, and none have evaluated changes with daytime sleep. Hornyak et al. studied sympathetic nerve activity during daytime sleep but did not obtain useful blood pressure data (13). Other available studies give conflicting results. In two studies, in normal subjects, the decline in MAP during sleep was attributed to a decline in cardiac output secondary to a decrease in heart rate (2) or stroke volume (14). Total peripheral resistance was unchanged (2). Nevertheless, in patients with fixed-rate pacemakers, nocturnal MAP declined despite a fixed heart rate (15). Another study showed that the decline in MAP during sleep was due to a decline in total peripheral resistance without a change in cardiac output (16). In monkeys, Talon and Engel found that cardiac output fell but total peripheral resistance rose during sleep (17). Talon and Engel attributed the decline in MAP during sleep to nocturnal shift of intravascular volume. More recently, Somers et al. found a reduction of blood pressure during nighttime sleep, accompanied by a reduction in heart rate and sympathetic nerve activity (18). Thus, the hemodynamic mechanism responsible for the nocturnal decline in blood pressure with sleep in normal subjects needs further study.

The study population presented here includes 19 patients with varying degrees of chronic renal failure. These subjects did not show the normal nocturnal decline in sleep-associated MAP. Their level of renal function did not seem to be related to the change in daytime or nighttime sleep-associated blood pressures (Table 3). Although we adjusted for awake periods by the use of the sleep diary (Table 3), without observing these renal failure patients in a sleep laboratory at night, we cannot be certain that they were asleep. Nevertheless, several subjects had multiple 24-h blood pressure studies with very similar changes in day awake versus night asleep blood pressures. In addition, several prior studies report that chronic renal failure patients have a blunted nocturnal decline in blood pressure or a rise in nocturnal blood pressure (7–9). For example, Portaluppi et al. found 2.7 and 3.7% increases in nocturnal systolic and diastolic blood pressure, respectively, in 30 hypertensive patients with chronic renal failure (8). Although nocturnal blood pressure rose, nocturnal heart rate declined, albeit less than in a matched control population. As in our study, no relationship was seen between renal function and day-night blood pressure changes (Table 3). The physiologic mechanisms responsible for this response have not been explored.

In contrast to the abnormal nocturnal blood pressure changes reported in chronic renal failure patients, this study demonstrates a similar decline in MAP during daytime sleep in renal failure and nonrenal failure subjects (Table 2). One may postulate that anxiety related to EEG electrode placement artificially raised BU MAP. This explanation is unlikely because all subjects relaxed for 10 min after EEG electrode placement and before BU MAP monitoring. Although the normal renal function groups were nonhypertensive, it was not a normal control group because these subjects had EEG performed (primarily for seizure disorders). If this group had a normal nocturnal decline in blood pressure with sleep, then one could postulate that different physiologic mechanisms are responsible for blood pressure declines during daytime versus nighttime sleep.

The renal dysfunction group had a greater baseline heart rate at each phase of the EEG study compared with the normal renal function group (Table 1). In addition, during daytime sleep, heart rate failed to decline in the renal dysfunction group, whereas it declined significantly in the normal renal function group. This abnormality of heart rate response to sleep may relate to the association of autonomic dysfunction and chronic renal failure. Nevertheless, similar to the normal renal function group, the chronic renal failure patients showed a significant decline in heart rate when moving from the BU to the BD position in preparation for sleep. Most of the decline in blood pressure and heart rate with sleep appears to occur in preparation for sleep when subjects move from the upright to the recumbent position (Table 2). During sleep, heart rate remained unchanged.

Several chronic renal failure patients had remarkably different MAP responses to daytime and nighttime sleep (Table 3). When interpreting these results,
one must realize that the techniques used to acquire the data and the data themselves are not equivalent. We equate BU EEG study data with mean day awake ambulatory monitored data and daytime sleep EEG data with unobserved nocturnal sleep data, as obtained from 24-h monitoring and sleep diaries. We recently showed that 24-h ambulatory blood pressure studies that fail to adjust for nocturnal awake periods overestimate the frequency of "nocturnal hypertension" (lack of nocturnal decline of blood pressure) (19). The use of sleep diaries that adjust for nocturnal awake periods, in this study, may decrease this problem. Because sleep diary data are not confirmed and because chronic renal failure patients have abnormal sleep patterns, the differences between daytime and nighttime sleep-related blood pressure changes may not be real. Against this possibility is the fact that several of these chronic renal failure patients had subsequent 24-h studies that confirmed their nocturnal hypertension.

In conclusion, daytime sleep is associated with a progressive decline in MAP with deeper levels of sleep. Movement from the upright to the recumbent position accounts for a large part of the decline in heart rate and MAP that accompanies daytime sleep. The physiologic mechanisms associated with daytime and nighttime sleep-associated heart rate and MAP changes may be different. Further, studies are needed to explore the mechanisms of daytime and nighttime sleep-related hemodynamic changes. An elucidation of the mechanisms responsible for blood pressure decline during daytime and nighttime sleep may be useful when treating patients with absent nocturnal blood pressure decline who may be at increased risk of hypertension-related end-organ damage.

REFERENCES