

Sleep Quality and Blood Pressure Dipping in Obstructive Sleep Apnea

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Background: Obstructive sleep apnea (OSA) is associated with poor sleep quality and a high incidence of nondipping. The aim of this study was to determine the association of sleep quality and nocturnal blood pressure (BP) dipping in an OSA population.

Methods: A total of 44 untreated subjects with mild to severe OSA underwent overnight-attended polysomnography and 24-h ambulatory BP monitoring. Subjects were off antihypertensive medication. The percentage of slow wave sleep, percentage of time awake after sleep onset during the sleep period, sleep efficiency, and arousal index were chosen as measurements of sleep quality. Dipping was evaluated using the change in systolic BP, diastolic BP, and mean arterial pressure. Patients were classified as dippers and nondippers based on a nocturnal drop in mean arterial pressure > 10%. Differences between groups were evaluated by independent sample *t* tests. Pearson correlation and linear regression were used to evaluate the association of sleep quality and dipping.

Results: There were no differences between dippers and nondippers with regard to body mass index, age, or respiratory disturbance index. A total of 84% were nondippers. No difference was found between dippers and nondippers in sleep quality. None of the sleep quality measures correlated with the measurements of dipping. In multiple regression analyses, the percentage of slow wave sleep and arousal index each independently predicted only a small percentage of the variance (approximately 10%) of nocturnal DBP dipping.

Conclusions: The prevalence of nondipping was very high in a population of untreated patients with mild to severe OSA. Nonetheless, sleep quality did not appear to be related to BP dipping. Am J Hypertens 2001;14: 887-892 © 2001 American Journal of Hypertension, Ltd.

Key Words: Sleep quality, nocturnal blood pressure dipping, obstructive sleep apnea, hypertension, ambulatory blood pressure monitoring.

Blood pressure normally drops 10% to 15% from its diurnal value during sleep. This circadian drop in blood pressure (BP) has been called dipping. However, there are individuals who do not exhibit a nocturnal drop in BP, and are thus called nondippers. A higher prevalence of nondippers has been reported among subjects with essential hypertension,¹ sodium sensitivity,² chronic renal failure,³ and obstructive sleep apnea.⁴ It has been postulated that the nocturnal drop in BP is a restorative physiologic process,⁵ and that the lack of circadian BP variability may be an important risk factor for hypertensive end-organ damage.⁶⁻⁸

The factors that determine whether an individual is a dipper versus a nondipper are not well known, and the mechanisms for dipping and nondipping have not been fully described. Behavioral factors such as smoking and alcohol intake have been reported to affect the awake-

sleep BP difference.⁹ Impaired sympathetic arterial modulation has been reported in nondipper men and women,¹⁰ and nondipper hypertensives have been reported to have impaired cardiovascular reflexes that might contribute to their lack of circadian BP drop¹¹; however, this finding has been questioned.¹² Also, nondipping has been described in patients with Cushing's syndrome and autonomic nervous system dysfunction.¹³ Some investigators have suggested that the nocturnal drop in BP may be affected by the quantity and quality of sleep.¹⁴⁻¹⁶

One might speculate that poor sleep quality decreases the nocturnal dip in BP (ie, BP does not fall as much during disturbed sleep). However, surprisingly few studies have reported the effects of sleep quality on circadian BP dipping. Table 1 describes the available literature in which dipping has been directly correlated with quality or quantity of sleep. Kario et al¹⁵ and Leary et al¹⁷ indirectly

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Table 1. Sleep quality and nocturnal blood pressure

Reference	Subjects	BP Measurements	Findings
Leary et al ¹⁷	434 subjects, heterogeneous as to age, gender, and BP. Antihypertensive medications were not stopped.	24 h ABPM (Quiet-Track recorder). physical activity (actigraphy).	Increased nighttime activity was associated with a smaller nocturnal dip in BP. Increase in daytime activity was associated with a higher nighttime dip in BP.
Kario et al ¹⁵	160 healthy volunteers. Subjects using antihypertensive medications were excluded.	24 h ABPM (SpaceLabs 90207). Physical activity measurement by actigraphy (ambulatory monitoring).	Nondippers had greater sleep activity than extreme dippers and an increased sleep/awake activity ratio than extreme dippers and dippers (more nocturnal activity = worse sleep quality).
Pedulla et al ¹⁸	19 hypertensive patients (9 nondippers and 10 dippers).	Beat-to-beat BP measurement with Finapres during sleep. PSG to record sleep stages.	Nondippers had more frequent microarousals and less stage 4 sleep than dippers. Nondippers had lighter sleep.
Frisina et al ¹⁹	11 normotensive offspring of hypertensive nondipper parents.	Beat-to-beat BP with Finapres during sleep. PSG to record sleep stages.	Offspring of nondipper hypertensives had more microarousals and more stage 2 sleep than controls (lighter sleep than controls).
Schillaci et al ¹⁶	2042 untreated hypertensive subjects.	24 h outpatient ABPM.	Difference in blood pressure change from day to night increased with reported duration of sleep.
Noda et al ²⁰	26 OSA patients. Patients were not divided by dipping status.	24 h ABPM and PSG.	Movement arousals contribute to elevation of diurnal and nocturnal blood pressure.

BP = blood pressure; PSG = polysomnography; ABPM = ambulatory blood pressure monitoring; OSA = obstructive sleep apnea.

measured sleep quality by measuring physical activity during sleep in healthy volunteers. They reported that nighttime activity was associated with a smaller dip in nocturnal BP. Pedulla et al¹⁸ and Frisina et al¹⁹ evaluated sleep quality directly by polysomnography in hypertensive subjects and their normotensive offspring, respectively. They reported that nondipper hypertensive parents as well as their offspring had more frequent microarousals and less deep sleep than did dippers or controls. In a large epidemiological study, Schillaci et al¹⁶ reported that individuals who reported longer duration of sleep also had greater BP dipping from day to night. We found only one report in which both sleep quality and 24-h BP was evaluated in a population with obstructive sleep apnea (OSA). Noda et al²⁰ reported that movement arousals contributed to the elevation of diurnal and nocturnal BP in sleep apneics. Unfortunately, no attempt was made to correlate sleep quality with dipping status.

Although some investigators have looked at the association of sleep quality and dipping in the normal or hypertensive patient, none have reported the relation of sleep quality and dipping in an OSA sample. In this study we tested the hypothesis that sleep quality correlates with

dipping in patients with mild to severe obstructive sleep apnea, while controlling for hypertension.

Materials and Methods

Subjects

All subjects gave informed consent to the protocol, which was approved by the institutional review board. A total of 44 patients with untreated obstructive sleep apnea (respiratory disturbance index [RDI] > 15) were studied at the University of California San Diego Clinical Research Center. Subjects with symptoms suggestive of obstructive sleep apnea or a previous diagnosis of sleep apnea either responded to public service advertisements or were referred by community physicians or by previous subjects. Shift workers or subjects who normally slept during the day were excluded. Subjects ranged in age from 35 to 65 years, and their weight was between 1.0 and 1.7 times the ideal body weight, as determined from Metropolitan Life tables.²¹ Patients receiving antihypertensive medication had their treatment tapered 3 weeks before the study. A seated screening resting BP was obtained three times on two separate occasions. Subjects with a systolic blood

pressure (SBP) consistently > 140 mm Hg or a diastolic blood pressure (DBP) > 90 mm Hg were considered hypertensive. Subjects were excluded if they were receiving medications known to affect sleep or if they had any of the following: congestive heart failure; symptomatic obstructive pulmonary, coronary, or cerebral vascular disease; history of life-threatening arrhythmias; cardiomyopathy; history of psychosis; narcolepsy; or current alcohol or drug abuse.

Experimental Design

Subjects with untreated obstructive sleep apnea (RDI > 15) based on a recent overnight, unattended home sleep recording (model 203, NightWatch System; Healthdyne Technologies, Marietta, GA) were admitted to the Clinical Research Center at 5 PM and placed on an isocaloric diet providing 170 mEq Na and 100 mEq K/day. Sleep was recorded on the night of admission, with a fully attended overnight polysomnographic instrument (model 4412P; Nihon Kohden, Irvine, CA) that recorded central and occipital electroencephalography, bilateral electro-oculography, submental and tibialis anterior electromyography (EMG), electrocardiogram (ECG), nasal/oral airflow using a thermistor, and respiratory effort using chest and abdominal inductance belts. Pulse oxyhemoglobin saturation (SpO_2) was monitored using a pulse oximeter (Biox 3740; Ohmeda, Boulder, CO) and analyzed using appropriate software (Profox Version PFD 6/97; Profox Associates, Escondido, CA).²² Sleep records were scored according to the criteria of Rechtschaffen and Kales.²³

Apneas were defined as decrements in airflow $\geq 90\%$ from baseline for 10 sec. Hypopneas were defined as a decrement in airflow $\geq 50\%$ but $< 90\%$ from baseline for 10 sec. The number of apneas and hypopneas per hour were calculated to obtain the RDI.

On the evening of admission, a 24-h ambulatory BP measurement was begun using the SpaceLabs ambulatory BP monitoring system (model 90207, SpaceLabs Medical, Redmond, WA). This apparatus was programmed to measure BP every 30 min from 10 PM to 6 AM and every 15 min during the awake period. Daytime and nighttime average systolic, diastolic, and mean arterial pressures (MAP) were recorded.

Dipping Definition

Three measurements of dipping were obtained by subtracting nighttime BP measurements from daytime BP measurements. These included SBP, DBP, and MAP changes. Patients were also divided into dippers and nondippers based on a nocturnal drop in MAP $> 10\%$. Nighttime was arbitrarily denoted as 10 PM to 6 AM, and daytime as 6 AM to 10 PM.

Sleep Quality Definition

We chose four measurements of sleep quality: 1) percentage of total sleep time spent in slow wave sleep (%SWS);

Table 2. Patient characteristics*

	Dipper [†]	Nondipper [†]
<i>n</i>	7	37
Age (y)	48.3 \pm 5.9	47.8 \pm 9.3
Gender (M/F)	7/0	28/9
RDI	55.3 \pm 27.8	48.4 \pm 25.0
BMI	31.9 \pm 6.5	30.9 \pm 5.2
Mean screening SBP (mm Hg)	132 \pm 19	127 \pm 14
Mean screening DBP (mm Hg)	81 \pm 9	81 \pm 8
No. of hypertensive subjects	4	11

RDI = respiratory disturbance index; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure.

* No significant differences were found between dippers and nondippers.

[†] Dipping status based on a nocturnal drop in mean arterial pressure $> 10\%$.

2) percentage of time awake after sleep onset during the sleep period (%WASO); 3) sleep efficiency ([total sleep time/time in bed] $\times 100$); and 4) total arousal index. Arousals were defined as rises in EEG frequency to α or θ activity lasting ≥ 1.5 sec but < 15 sec.

Statistical Analysis

The various sleep quality variables were compared between dippers and nondippers by independent sample *t* tests. Pearson correlations with Bonferoni's correction were performed to examine the association between sleep quality, RDI, and BP dipping using all three dipping measurements. A multiple linear regression procedure was performed to determine the predictive power of the sleep quality variables on dipping after controlling for RDI and screening BP status. Statistical analyses were performed using SPSS for Windows, version 9.0 (SPSS, Chicago, IL).

Results

Table 2 describes the characteristics of the study subjects. The great majority (84.1%) were nondippers. On average, the subjects were moderately obese and had moderate to severe OSA. There was no difference in age, RDI, screening BP, or body mass index (BMI) between dippers and nondippers. A total of 32% of the subjects were classified as hypertensive. In all, 57% of the dippers were hypertensive as compared to 29.7% of the nondippers; however, there was no statistically significant association between hypertension and BP dipping.

Dippers and nondippers were compared with respect to sleep quality measures. There was no difference in sleep efficiency, %WASO, percent time in rapid eye movement (REM) sleep, %SWS, or total arousal frequency between dippers and nondippers.

We also examined the data using a continuous measure

Table 3. Pearson correlation coefficients (r)*

Variable	SBP Dipping	DBP Dipping	MAP Dipping
RDI	−0.018	0.213	0.014
%SWS	0.061	0.195	0.162
Sleep efficiency%	−0.011	−0.024	−0.015
%WASO	−0.080	−0.090	−0.099
Arousal index	0.053	0.280	0.100

%SWS = percentage of slow wave sleep; %WASO = percentage of time awake after sleep onset during sleep period; MAP = mean arterial pressure; other abbreviations as in Table 2.

* None were statistically significant at the 0.01 level.

of dipping (daytime BP minus nocturnal BP) as opposed to the dichotomized “dippers” versus “nondippers.” Table 3 presents the univariate correlations between sleep quality measures and dipping variables. Significance was adjusted using Bonferroni’s correction. Significance was determined at $P < .01$. None of the measurements of dipping correlated significantly with the measurements of sleep quality or RDI.

A multiple linear regression model was used to assess the predictive effects of sleep quality on dipping as assessed by SBP, DBP, and MAP changes. Because of the reported association between RDI and nondipping in patients with sleep apnea, RDI was entered as the initial covariate in the regression model. In the initial step we also controlled for hypertension status using the screening MAP. The %SWS and sleep efficiency were entered next,

based on our hypothesis that deeper and more efficient sleep constituted better quality sleep. The %WASO and total arousal index were entered last in the model as variables that would denote lower quality sleep. None of the sleep quality variables or RDI independently predicted a change in SBP or MAP during sleep. However, %SWS and total arousal index each predicted approximately 10% of the variance of the nocturnal change in DBP (Table 4).

Discussion

The quality and the duration of a night’s sleep is considered essential for proper diurnal cognitive function and overall well-being.²⁴ Given that approximately one third of our life is spent sleeping, it is likely that sleep and its quality influence physiologic functions such as the activity of the sympathetic nervous system and BP.²⁵ Some researchers have suggested that the phenomenon known as BP dipping may be affected by the quality and quantity of sleep, but data are scarce.^{14–16} Patients with OSA are known to have poor sleep quality, characterized by sleep fragmentation and grossly abnormal sleep architecture. Patients with sleep apnea are also known to have a high prevalence of systemic hypertension,²⁶ and a high proportion of these are nondippers.⁴ In this study we set out to test the hypothesis that sleep quality affects the variation in BP normally seen during the night. We recruited a group of untreated OSA patients with various degrees of sleep apnea severity, as these patients have a high prevalence of nondipping and have a wide spectrum of sleep quality.

Table 4. Multiple regression analysis to determine predictors of diastolic blood pressure dipping

Independent Variable Entered	R ²	% Variance Gained	df	F	Significance of F	β	t	P Value
RDI						0.218	1.418	.164
Screening MAP	0.047	4.7	2, 41	1.010	0.373	−0.040	−0.262	.795
RDI						0.355	2.203	.033
Screening MAP						0.015	0.100	.920
%SWS	0.143	9.6	3, 40	2.216	0.101	0.345	2.111	.041
RDI						0.359	2.186	.035
Screening MAP						0.014	0.091	.928
%SWS	0.144	0.1	4, 39	1.634	0.185	0.342	2.056	.047
SLPEFF						−0.032	−0.210	.835
RDI						0.353	2.134	.039
Screening MAP						0.046	0.290	.773
%SWS						0.271	1.428	.161
SLPEFF	0.157	1.3	5, 38	1.418	0.240	−0.267	−0.797	.430
%WASO						−0.267	−0.788	.435
RDI						−0.621	−1.490	.145
Screening MAP						0.140	0.916	.366
%SWS						0.403	2.175	.036*
SLPEFF	0.280	12.3	6, 37	2.403	0.046*	−0.269	−0.860	.395
%WASO						−0.287	−0.907	.370
Arousal index						1.085	2.516	.016*

df = degrees of freedom; SLPEFF = sleep efficiency; Screening MAP = mean arterial pressure (MAP) obtained at screening to determine hypertension status; other abbreviations as in Tables 2 and 3.

* Statistically significant.

In this study, 84.1% of the subjects were nondippers. This is a substantially greater percentage than the 30% to 50% prevalence of nondippers described in the literature.⁴ The reason for the discrepancy in our observations and the reported percentages of nondippers in the literature is unclear. Our sample included a large proportion of patients with severe apnea (mean RDI >50), which could have accounted for the higher prevalence of nondippers, as severity of OSA is associated with nondipping.^{4,27,28} Also, the first night effect could have contributed to the high nondipping prevalence, although the patients had been somewhat acclimatized by a screening overnight home sleep study. Most studies evaluating the association of OSA and dipping have included subjects taking antihypertensive medications or have discontinued antihypertensive medications for a brief period. Antihypertensives have been shown to reduce the nocturnal hypertension in patients with OSA²⁹ and could potentially correct for the nondipping status, thereby reducing the proportion of nondippers in an OSA population. In this study, hypertensive patients were off of their antihypertensive medications for 3 weeks before enrollment in the study protocol.

In this study we chose to define dipping by clock time, using mean daytime (6 AM to 10 PM) and nighttime (10 PM to 6 AM) BP. Some may argue that this definition of dipping may be less sensitive in detecting dipping than if the actual sleep and awake BP were used. We recently reported the reliability of nocturnal BP dipping as measured by clock time, bedtime, and sleep time. We found that no one definition of dipping was demonstrably better than the others.³⁰

We analyzed the data to determine whether dipping/nondipping and hypertension/normotension were associated. A higher percentage of dippers than nondippers were hypertensive, which was opposite to the anticipated positive association between hypertension and nondipping status. However, this association was not statistically significant. These findings are consistent with those reported by Suzuki et al in a sample of sleep apnea patients of similar size, in which no relationship between dipping and BP status was found.⁴

Some researchers have suggested that nondipping may be associated with the quality of sleep.¹⁵⁻¹⁹ They have mostly evaluated normal or hypertensive populations and most studies only indirectly assessed sleep quality.¹⁵⁻¹⁷ We evaluated sleep quality directly by full polysomnography in a population of sleep apnea patients and analyzed the data to determine whether sleep quality was related to dipping. We found no difference between dippers and nondippers as far as the magnitude of %SWS, %WASO, sleep efficiency, and total arousal index. We also found no correlation between any of the sleep quality variables and continuous dipping variables (SBP, DBP, or MAP). In this circumscribed clinical sample, sleep quality was unrelated to dipping.

In a nonapneic group of individuals, there may be a relationship between dipping and sleep quality. Indirect

evidence for this comes from our multiple regression analyses. Once apnea (RDI) was controlled for, %SWS and total arousal index were significant predictors of DBP dipping (Table 4). Each of these variables predicted about 10% of the variance of DBP dipping. Both %SWS and total arousal index were positive predictors (ie, the greater the %SWS and the total arousal index, the greater the DBP dipping). Although it fits our hypothesis that a greater percentage of SWS (implying better sleep quality) would predict more dipping, we do not have a good explanation for the association of a larger total arousal index (more sleep fragmentation, poorer sleep quality) predicting more dipping. This latter finding is contrary to the report of Pedulla et al, in which nondippers had more frequent microarousals and less SWS than did dippers in a small hypertensive sample population.¹⁸ Noda et al also reported that movement arousals contributed to elevation of nocturnal BP in 26 OSA patients.²⁰

It is possible that, in patients without apnea, there is a relationship between sleep quality and BP dipping that may not be found in patients with OSA. However, even the current evidence for a significant role of sleep quality in BP dipping in healthy volunteers is indirect at best. In such studies, sleep quality was measured by actigraphy during sleep. Nondippers exhibited greater sleep movement activity, which was interpreted as worse sleep quality.^{15,17}

In conclusion, in a population of patients with untreated mild to severe obstructive sleep apnea, the prevalence of nondipping was very high and much higher than previously reported. In the same population, sleep quality was unrelated to nocturnal dipping.

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