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Resistant Hypertension and Sleep Duration among Blacks with Metabolic Syndrome MetSO

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Abstract

Introduction—Resistant hypertension (RHTN) is an important condition affecting 29% of the hypertensive population in the U.S., especially among blacks. Sleep disturbances, like obstructive sleep apnea, insomnia, and short sleep duration, are increasingly recognized as underlying modifiable factors for RHTN. We evaluated associations of RHTN with short sleep duration among blacks with metabolic syndrome.

Methods—Data from the Metabolic Syndrome Outcome Study (MetSO), a NIH-funded cohort study characterizing metabolic syndrome (MetS) among blacks were analyzed. MetS was defined according to criteria from the Adult Treatment Panel (ATP III). RHTN was defined according to guidelines from the American Heart Association. Short sleep was defined as self-reported sleep duration <7 hrs experienced during a 24-hour period.

Results—Analysis was based on 1,035 patients (mean age: 62±14years; female: 69.2%). Of the sample, 90.4% were overweight /obese; 61.4% had diabetes; 74.8% had dyslipidemia; 30.2% had a history of heart disease; and 48% were at high risk for obstructive sleep apnea. Overall, 92.6% reported physician-diagnosed hypertension (HTN) and 20.8% met criteria for RHTN. Analyses showed those with RHTN were more likely to be short sleepers (26.8% vs. 14.9%, $p < 0.001$). Based on logistic regression analysis, adjusting for effects of age, sex, and medical comorbidities, patients with metabolic syndrome and RHTN had increased odds of being short sleepers (OR = 1.95, 95% CI: 1.28-2.97, $p = 0.002$).

Conclusion—Among blacks with metabolic syndrome, patients meeting criteria for resistant hypertension showed a twofold greater likelihood of being short sleepers, prompting the need for sleep screening in this vulnerable population.

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Keywords

Resistant hypertension; Sleep duration; Metabolic syndrome

Introduction

The American Heart Association defines resistant hypertension (RHTN) as blood pressure that remains above >140/90 mm Hg or 130/80 mm Hg among patients with diabetes or chronic kidney disease in spite of 3 different classes of antihypertensive medication (one of the three prescribed pharmaceutical agents should be a diuretic and all agents prescribed at optimal dose amounts). Resistant hypertension has escalated as an important clinical problem within this past decade, particularly among racial/ethnic groups [1]. There is an urgent need to focus on blacks, since they have the highest rate (44%) of hypertension in the world and have an increased likelihood of being resistant to treatment [2].

According to the 2002 Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), the prevalence of RHTN in the U.S. was approximately 27% [3]. This is greater than estimates obtained from longitudinal data from National Health and Nutrition Examination Survey (NHANES), which indicated a prevalence of 16% [4]. The growing prevalence of comorbid metabolic syndrome (MetS) (a constellation of medical conditions such as hyperlipidemia, hypertension, insulin resistance, abdominal adiposity and dyslipidemia) and obstructive sleep apnea (OSA), have rendered management of resistant hypertension (RHTN) difficult, particularly among blacks [3].

The literature is unclear about what mechanism[s] might underlie the co-occurrence of RHTN, MetS, and OSA. However, some studies have suggested that resistant hypertension may be due to vasoconstriction from increased sympathetic activation, proinflammatory cytokines, and activation of the renin-angiotensin-aldosterone system, which tend to be present among patients with OSA as well. [5] Compelling evidence that OSA is associated with RHTN and MetS highlights sleep as a novel target that can help explain comorbid RHTN and MetS. In the current study, we examined the association between RHTN and sleep duration among blacks with MetS.

Methods

Study design and participants

Data were collected as part of the Metabolic Syndrome Outcome study (MetSO), an NHLBI funded study of 1035 blacks with metabolic syndrome in a primary-care setting in Four clinics associated with SUNY Downstate Medical Center Brooklyn, NY. Validated questionnaires were administered in order to obtain data on sleep apnea risk, daytime sleepiness, demographic, anthropometric data, and diseases associated with risk for sleep apnea (i.e. hypertension, diabetes, heart disease, and stroke) (Allscripts, Sunrise Enterprise).

Patients were diagnosed with metabolic syndrome using the National Heart, Lung and Blood Institute and the American Heart Association guidelines [1]. According to these guidelines, metabolic syndrome is diagnosed when a patient has at least three of the following five

conditions: 1) fasting glucose ≥ 100 mg/dl or receiving treatment for hyperglycemia, 2) blood pressure $\geq 130/85$ mmHg or receiving drug therapy for hypertension, 3) triglycerides ≥ 150 mg/dl or receiving drug treatment for hypertriglyceridemia, 4) HDL-C <40 mg/dl in men or <50 mg/dl in women or receiving drug therapy for HDL-C and 5) a waist circumference ≥ 102 cm (40 in) in men or ≥ 88 cm (35 in) in women.

Sleep duration was derived from self-reported questionnaire asking participants the average hours of sleep they receive in a 24-hour period. We defined short sleep as sleep duration lasting less than 7 hours in a 24-hour period based. This was referenced to healthy sleep defined as sleep durations between 7-8 hours. RHTN is defined as blood pressure that remains above 140 mmHg in spite of the use of 3 antihypertensive drugs of different classes, one of the three prescribed pharmaceutical agents should be a diuretic and all agents prescribed at optimal dose amounts [6].

Statistical Analysis

Frequency and measures of central tendency were used to describe the sample. Pearson and Spearman correlations were used to explore relationships between variables of interest. To assess association between RHTN and short sleep duration among blacks with MetS, we utilized multivariate logistic regression modeling, adjusting for age, sex, and medical comorbidities.

Ethical Considerations

All participants signed an informed consent form. The study was approved by the institutional review board of SUNY Downstate Medical Center and New York University School of Medicine.

Results

Of the 1,035 participants (mean age of 62 ± 14 years), 90.4% were overweight/obese; 61.4% had diabetes; 74.8% had dyslipidemia; 30.2% had a history of heart disease; 48% were at high OSA risk; 92.6% had HTN; and 20.8% met criteria for RHTN.

Analyses showed no significant difference in HTN prevalence between short (91.4%) and healthy sleepers (93.1%). However, those with RHTN were more likely to be short sleepers compared to non-RHTN patients (26.8% vs. 14.9%, $p < 0.001$). Based on logistic regression analysis, adjusting for effects of age, sex and medical comorbidities, patients with RHTN had a 90% increased odds of being short sleepers (OR=1.95, 95% CI: 1.28-2.97, $p = 0.002$). As expected, individuals with high apnea risk were also likely to be short sleepers (OR=1.85, 95% CI: 1.32-2.57, $p < 0.001$).

Discussion

Our findings indicate that blacks with MetS and meeting criteria for RHTN were almost twice as likely as to without RHTN to report short sleep duration (< 7 hrs.) [See Table 1]. Our findings are consistent with previous evidence that RHTN and MetS are associated [1], although to our knowledge this is the first study suggesting that short sleep duration might

account for the shared risk between these two conditions. Based these findings, we posit that short sleep duration may be common among individuals with MetS and RHTN. However, since the individual etiologies of MetS and RHTN are complex, it remains challenging to argue that short sleep could play a causal role.

Our main finding suggests that sleep duration may be involved in the pathway leading to the development of hypertension and RHTN among individuals with MetS. One well-established pathophysiologic framework suggests that MetS contributes to the development of hypertension via atherosclerosis, endothelial dysfunction, and oxidative stress.[7] Of interest, oxidative stress can alter the vasomotor tone of an arterial vessel leading to inactivation of nitric oxide, and then atherosclerosis [7]. Hardening of arterial vessels through atherosclerosis increases arterial blood pressure and turbulent blood flow, thus increasing risk of hypertension and resistant hypertension [7]. However, the literature is equivocal about what might drive this cascade of biological events. Based on available evidence, it appears that short sleep duration may trigger and/or speed up the pathophysiological trajectory from MetS to RHTN.

Another important finding in our study indicates that apnea risk was independently associated with short sleep duration. Although studies have found that sleep apnea and metabolic syndrome are independently associated with RHTN/HTN, less is known about their shared risk, especially among blacks for whom prevalence is high in both conditions [5,8,9]. A recent study revealed that patients with MetS experience a two-fold increased risk of OSA [10,11,12,13] One plausible pathophysiological explanation is that apneic episodes, which are characterized by restricted airflow while sleeping, cause forced awakenings, decreased total sleep time and poor sleep quality [12,13]. Consequently, this leads to impairment of baroreceptor modulation of sympathetic activity, thus inducing heart rate dysregulation [14] (See Figure 1). Interestingly, the co-occurrence of MetS and OSA, if left untreated, may exacerbate hypertension and potentially lead to RHTN [12,14]. Data indicating that sleep deprivation is linked to increased inflammatory and endothelial dysfunction may provide a novel mechanistic insight into the associations of RHTN and MetS with short sleep duration [15].

Further evidence that sleep is implicated in RHTN is found in recent studies, which highlight that blood pressure among patients with comorbid OSA and RHTN was lowered when treated with continuous positive airway pressure (CPAP) [16]. Long-term use of CPAP tends to suppress the biological sympathetic activity, which in turn promotes normal homeostatic blood pressure dipping among patients with hypertension and RHTN [3,17,18]. A prospective cohort study among patients with resistant hypertension and sleep apnea demonstrated a significant decline of 7.3 mm Hg (95% CI, 3.1– 13.1) in mean systolic blood pressure after 3 months of CPAP therapy [19]. Our findings adds to the growing literature on associations of MetS and RHTN with short sleep duration and highlights the need for studies to delineate the mechanisms linking associations of RHTN and MetS with sleep duration. Further research is needed to investigate whether long-term CPAP treatments can normalize sleep duration and improve blood pressure, especially in vulnerable populations (Figure 2).

Conclusion

Among blacks with metabolic syndrome, patients meeting criteria for RHTN were nearly twice as likely as those without RHTN to report short sleep, independent of the presence of OSA risk and medical comorbidity.

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Figure 1.

Diagrammatic representation of the associations of obstructive sleep apnea with cardiovascular disease via increased pathophysiologic and biologic dysfunctions resulting from repetitive apneic events. Adapted from “Cardiovascular Disease Risk Reduction with Sleep Apnea Treatment” by Jean-Louis, Brown, Zizi, et al. 2010. Copyright 2010 by Expert Reviews Ltd. Adapted with permission.

Figure 2. Association of RHTN and Short Sleep Duration among Blacks with Metabolic Syndrome

Table 1

Relationship between variables and short sleep duration.

	Odds Ratio	Sig	95% C.I.
Age	1.001	.906	.998-1.014
Gender	1.063	.735	.747-1.512
BMI	1.001	.916	.982-1.021
Hypertension	.913	.793	.462-1.804
Dyslipidemia	.965	.851	.665-1.400
Apnea risk	1.845	.000	1.322-2.573
RHTN	1.949	.002	1.279-2.969
ARisk*RHTN	1.122	.876	0.834-1.167