COMMENTARY

Evidence for the Pathophysiology of Insomnia

Commentary on Vgontzas et al. Insomnia with objective short sleep duration is associated with a high risk for hypertension. Sleep 2009;32:491-497.

Michael H. Bonnet, PhD

Dayton Department of Veterans Affairs Medical Center, Wright State University, and the Wallace Kettering Neuroscience Institute, Dayton, OH

THIS ISSUE OF SLEEP FEATURES THE FIRST LARGE STUDY OF THE RELATIONSHIP BETWEEN INSOMNIA AND HYPERTENSION BASED UPON POLYSOMNOGRAPHIC results.[1] Numerous studies have shown that patients with primary insomnia have physiological activation as measured by heart rate, spectral EEG, hormone secretion, and whole body and brain metabolic rate. A review by the National Institutes of Health has also concluded that insomnia is a chronic disorder.[2] If physiological activation is chronic in insomnia patients, then these patients should be at increased risk for abnormalities associated with elevated sympathetic nervous system or hypothalamic-pituitary-adrenal activity such as hypertension and other cardiovascular disorders.

A previous questionnaire study in Japanese telecommunication workers[3] and the Atherosclerosis Risk in Communities Study[4] have shown significant odds ratios between reported difficulty falling asleep and/or staying asleep and the development of hypertension at a later date, although these results were not replicated in a smaller study that used data from the Cardiovascular Health Study.[5] At least fifteen questionnaire studies (see reviews[6,7]) have shown significant relationships between difficulty falling asleep or poor sleep and cardiac outcomes such as myocardial infarction, cardiac death, or other cardiac pathology. Many of these studies have examined large groups and many have controlled for important variables such as BMI, depression, personality, age, gender, race, and alcohol use but none has objectively controlled for sleep apnea or objective sleep times by using polysomnography in a large sample. Consequently, the significant previous research has been casually dismissed by many observers as artifact or severely flawed secondary to unmeasured but probable sleep disordered breathing in the populations questioned.

As a result, the current study, with polysomnography from 1741 subjects and subsequent risk ratios controlled for age, race, gender, BMI, diabetes, smoking, alcohol use, depression and sleep disordered breathing, does much to establish the independent link between insomnia and hypertension. The use of polysomnography in addition to subjective report further allowed the investigators to conclude that the link between insomnia and hypertension required both the subjective report of insomnia and objectively decreased total sleep time. Insomnia patients who slept for more than 6 hours did not have an increased risk for hypertension compared with controls. Of equal importance, patients without insomnia but with a short total sleep time did not have an increased risk of hypertension unless they slept for less than 5 hours per night, and the risk in these subjects was much less than in insomnia patients with the same sleep length.

These results are an important confirmation of our understanding of chronic arousal in insomnia patients. However, these data have more significant implications for all sleep disorders specialists. If one accepts the link between chronic insomnia and hypertension, it implies a medical need for chronic treatment of either the insomnia or the hypertension that it will produce. Unfortunately, we know very little about long-term treatment of insomnia and do not know if treatment of insomnia will reduce the risk of hypertension later. Much work has described physiological abnormalities in these patients but very few studies have described the effect of insomnia treatments on any variables that are not simple sleep outcomes. For example, we know that insomnia patients have increased 24-hour whole metabolic rate but do not know if standard therapy reduces or normalizes metabolic rate. The few published studies available do suggest that treatment with doxepin 25 mg reduces elevated cortisol[8] in insomnia patients and that 8 weeks of behavioral therapy reduces EEG beta activity in patients.[9] However these improvements did not return the respective patients to control levels of cortisol or beta activity. Obviously, it is important that future multicenter pharmacological trials track blood pressure and other suspected risk factors. Perhaps effective treatment of insomnia at a younger age might reduce the need for specific treatment of hypertension(and other negative outcomes) at a later age.

An equally important implication of the data is that insomnia is a real medical problem and not a merely a disorder of mood or inappropriate learning. As such, treatment requires the same attention that physicians provide for hypertension and other medical problems. As with hypertension itself, some patients will respond to behavioral treatments with improved sleep and physiological function. However, many other patients will not respond to simple behavioral intervention, and, as patients with hypertension are put on medication and carefully monitored for the rest of their life, many insomnia patients may require similar care. It cannot be denied that the emphasis of sleep medicine on treatment of sleep apnea has provided great benefit to many patients. The current study foretells a larger group of patients with sleep pathology and associated medical complications that remains to be addressed with equal emphasis.

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Address correspondence to: Michael H. Bonnet, Ph.D., Dayton Department of Veterans Affairs Medical Center, 4100 West Third Street, Dayton, OH 45228; Tel: (937) 267-3910 ; Fax : (937) 267-5317 ; E-mail: bonnetmichael@yahoo.com

DISCLOSURE STATEMENT

Dr. Bonnet has participated in speaking engagements and consulted for Somaxon, Sanofi-Aventis, Takeda, and Cephalon

RESOURCES

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