World Journal of Urology (2019) 37:1449–1453
https://doi.org/10.1007/s00345-018-2485-2

ORIGINAL ARTICLE

Impaired sleep is associated with low testosterone in US adult males: results from the National Health and Nutrition Examination Survey

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Received: 10 July 2018 / Accepted: 10 September 2018 / Published online: 17 September 2018

Abstract

Purpose Testosterone deficiency has been linked to several adverse health outcomes and recent data have suggested that abnormal sleep quality may result in lower testosterone levels. We assessed the effect of self-reported sleep patterns on serum testosterone while controlling for co-morbidities, and baseline demographics.

Materials and methods Using data collected from the 2011–2012 National Health and Nutrition Examination Survey (NHANES), we extracted serum total testosterone level, sleep duration, demographic, and co-morbidities for men aged 16 years and older. Univariate and multivariate linear regression was used to estimate the association of number of hours slept, co-morbidities, and demographics with serum testosterone.

Results Among the 9756 individuals in the NHANES dataset, 2295 (23.5%) were males 16 years and older with a median (interquartile range) age of 46 years (29–62) who also had serum testosterone levels drawn. Median serum testosterone level was 377 ng/dL (IQR: 279–492 ng/dL). Median number of hours slept was 7 h (IQR: 6–8 h). On multivariate linear regression, we found serum testosterone decreased by 0.49 ng/dL per year of age ($p = 0.04$), 5.85 ng/dL per hour loss of sleep ($p < 0.01$) and 6.18 ng/dL per unit of body mass index (BMI) increase ($p < 0.01$).

Conclusions Among men aged 16–80 in the United States, we found increasing age, impaired sleep and elevated BMI is associated with low testosterone. It is important, therefore, that evaluation and treatment of reduced serum testosterone should also include improving sleep duration in combination with weight management.

Keywords Sleep · Testosterone · National Health and Nutrition Examination Survey · Male · Hormones

Introduction

Sleep is a critical factor in human health. However, sleep deprivation has become endemic in modern societies. In 2015, the American Academy of Sleep Medicine and Sleep Research Society released a reached a joint consensus that 7–9 h of sleep were appropriate to reach optimal health in adults [1]. However, surveys conducted by the Behavioral Risk Factor Surveillance System under the Center for Disease Control and Prevention in 2014 found that 35.2% of all adults in the United States reported short sleep duration, defined as less than 7 h of sleep per night [2]. A survey of Americans in 2012 found 29.2% reported insufficient sleep duration (defined as < 6 h) as compared to 22.3% in 1985, representing a 31% increase [3]. Short sleep duration has been associated with numerous adverse metabolic and endocrinologic health effects. A recent literature review found that insufficient sleep is a risk factor for obesity and type 2 diabetes [4]. Additionally, 2 meta-analyses by Cappuccio et al. found that short sleep duration is associated with increased risk of coronary heart disease and stroke, as well as an overall increased risk of death [5, 6]. These results substantiate the importance of sufficient sleep duration.

Although the diurnal variation of testosterone was first observed in 1965 [7], the specific association between sleep and testosterone was first examined in 1971 by Evans et al., who found that testosterone peaks occurred in conjunction with periods of rapid eye movement (REM) sleep [8]. In the years since, numerous studies have corroborated the

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association between sleep and testosterone. In the past decade, several sleep deprivation studies have demonstrated some aspect of reduction in testosterone levels in response to short sleep duration or periods of prolonged awakening [9–12]. However, these studies have been small in nature, with the largest consisting of only 77 subjects in a study conducted by Abu-Samak et al. [12]. To date, there have been no population-level studies examining the association between sleep and testosterone. In this study, we report the first population-based study that evaluated the association number of hours slept and serum testosterone levels.

Methods

The National Health and Nutrition Examination Survey (NHANES) is a program of studies that took place in the early 1960 s and is designed to assess the health and nutritional status of adults and children in the United States. It became continuous in 1999, and now examines a nationally representative sample of ~ 5000 persons each year. These cross-sectional surveys are conducted by the National Center for Health Statistics of the Center for Disease Control. The NHANES sampling procedure oversamples targeted populations, such as Hispanics, non-Hispanic blacks, non-Hispanic Asians, older adults, and low-income persons, to obtain adequate samples for meaningful subgroup analyses and more reliable variable estimates [13].

NHANES 2011–2012 included several questions regarding sleep as well as laboratory measurement of serum testosterone levels. It, therefore, provides an ideal opportunity to examine the relationship between sleep and testosterone. Biospecimen collection took place in the mobile examination center which were open 5 days per week. The centers had a controlled environment to ensure an identical condition at each survey location. Participants were randomly assigned for their scheduled appointment. Questionnaires were administered both at home and in the mobile examination center. With regard to questions pertaining to sleep, participants were asked "how much sleep {do you/does sample persons} usually get at night on weekdays or workdays?" and "{have you/has sample persons} ever been told by a doctor or other health professional that {you have s/he has} a sleep disorder?".

Routine quantification of serum total testosterone was based on the National Institute for Standards and Technology's reference method. A minimal of 150 µL of fresh or frozen serum required with a sample volume of 100 µL is used for analysis. Morning fasting samples (8:30–11:30 am) were conducted to minimize biologic variability with samples subsequently centrifuged with serum aliquoted and stored at – 70 °C. The lowest detection limits by the electrochemiluminescence immunoassays on the 2010 Elecsys autoanalyzer for the samples were 0.02 ng/mL [14].

We retrieved demographic information, past medical, social history, serum testosterone levels as well as questions regarding hours of sleep per night. Using a univariate and multivariate linear regression models, we evaluated the association between baseline patient demographics, past medical history, questionings pertaining to sleep and serum testosterone. All analyses were performed using R 3.3.3 (R Foundation for Statistical Computing) [15].

Results

A total of 2295 men were included in our analysis. Table 1 illustrates patient age (median: 46; IQR: 29–62), numbers of hours slept (median: 7; IQR: 6–8), Body Mass Index (BMI) (median: 27.2; IQR: 24.2–31.7), serum testosterone levels (median: 377.26; IQR: 279.18–492.70), alcohol intake per day (median: 1; IQR: 0–3, history of a diagnosed sleep

Table 1 Baseline Patient Characteristics

Variables	Median (IQR)
Men included	2295
Age (years)	46 (29–62)
Hours of sleep	7 (6–8)
BMI (kg/m^2)	27.2 (24.2–31.7)
Testosterone (ng/dL)	377 (279–493)
Diagnosed by medical doctor with a sleep disorder, yes	193/2293 (8.4%)
Education	
College graduate or above	517 (24.1%)
Some college or AA degree	568 (26.5%)
High school graduate	519 (24.2%)
9–11th grade	317 (14.8%)
Less than 9th grade	220 (10.3%)
Marital status	
Divorced	189 (9.1%)
Living with partner	174 (8.4%)
Married	1108 (53.4%)
Never married	460 (22.2%)
Separated	55 (2.7%)
Widowed	89 (4.3%)
Alcoholic drinks per day	1 (0–3)
Diabetes, yes	291/2241 (13%)
Nocturia, yes	1 (0–1)
Coronary artery disease, yes	97/2064 (4.7%)
Angina, yes	48/2065 (2.3%)
Prior MI, yes	97/2069 (4.7%)
Prior stroke, yes	79/2071 (3.8%)
History of cancer, yes	170/2070 (8.2%)

disorder, education level, marital status, and past medical history (diabetes mellitus, nocturia, coronary artery disease, etc.).

Table 2 represents the results from our univariate and multivariate linear regression. On univariate linear regression, we found increasing age, reduction of hours slept, marital status, increasing amount of drinks per day, nocturia, BMI and a history of diabetes mellitus, coronary heart disease, angina, myocardial infarction, stroke and malignancy to be associated with decreasing serum testosterone levels. On multivariate linear regression, we found increasing age (estimate: − 0.45 ng/dL per year of life, $p = 0.03$), reduction of hours slept (estimate: − 5.85 ng/dL per hour loss of sleep, $p = 0.01$) and increasing BMI (− 6.18 ng/dL per unit

Table 2 Univariate and Multivariate Linear Regression

Variable	Univariate linear regression			Multivariate linear regression		
	Difference in Testosterone level (ng/dL)	SE	*p* value	Difference in Testosterone level (ng/dL)	SE	*p* value
Age	− 0.78	0.16	**< 0.001**	− 0.49	0.24	**0.038**
Hours of sleep	− 5.46	2.22	**0.014**	− 5.85	2.26	**0.001**
Diagnosed with sleep disorder						
Yes	− 21.3	87.1	0.137	–	–	–
No	Ref.	86.5				
Education						
College graduate or above	19.9	13.7		–	–	–
Some college or AA degree	19.6	13.6	0.117			
High School Graduate	31.0	13.7				
9–11th grade	8.87	14.7				
< 9th grade	Ref.	15.7				
Marital status						
Widowed	− 18.3	18.7		− 4.88	141.9	0.364
Divorced	32.1	14.8		37.5	141.4	0.226
Separated	− 7.94	22.5	**< 0.001**	11.8	142.4	0.307
Living with partner	11.5	15.1		4.28	141.6	0.330
Never married	26.3	12.2		7.35	141.2	0.319
Married	Ref.	11.0		Ref.	133.7	0.343
Drinks per day	2.97	0.90	**< 0.001**	2.99	0.98	**0.002**
Nocturia	− 8.82	2.87	**0.002**	− 0.71	3.09	NS
BMI	− 5.94	0.50	**< 0.001**	− 6.18	0.53	**< 0.001**
History of diabetes						
Yes	− 44.6	23.7	**< 0.001**	− 16.8	23.2	0.819
No	Ref.	22.2		Ref.	22.0	
History of CAD						
Yes	− 42.7	18.0	**< 0.001**	− 19.4	58.5	0.067
No	Ref.	10.4		Ref.	58.8	0.132
History of angina						
Yes	− 71.1	23.6	**< 0.001**	− 44.6	70.6	0.676
No	Ref.	10.4		Ref.	67.7	0.824
Prior myocardial infarction						
Yes	− 38.3	18.1	**< 0.001**	− 15.5	101.4	0.387
No	Ref.	10.5		Ref.	99.8	0.468
Prior stroke						
Yes	− 16.0	19.5	**< 0.001**	− 5.91	187.1	0.655
No	Ref.	10.5		Ref.	187.8	0.634
History of malignancy						
Yes	− 14.5	15.2	**< 0.001**	− 14.6	141.1	0.972
No	Ref.	10.5		Ref.	140.6	0.946

BMI) to be associated with declining serum testosterone levels. Increasing drinks per day was associated with elevated serum testosterone levels (2.99 ng/dL per alcoholic drink per day, $p = 0.002$).

Discussion

Our results using the large NHANES database demonstrate that on multivariate linear regression shorter sleep duration, increasing age and BMI are associated with a decrease in serum testosterone. The results of our study require further evaluation with prospective data but provide additional support to the negative consequences of altered sleep habits and suggest that improving sleep duration and proper weight management may lead to improved serum testosterone levels.

Studies examining the relationship between sleep and testosterone over the past decade have been largely interventional in design. Leproult et al. examined the effect of 1 week of sleep restriction to 5 h per night and found that daytime testosterone levels were decreased by 10–15% compared to pre-restriction levels [9]. Another study by Schmid et al. investigated whether sleep duration as well as timing differentially affected the male pituitary–gonadal axis. They found that sleep restriction in the first half of the night did not result in reduced testosterone compared to 8-h sleep, while testosterone was indeed reduced after both total sleep deprivation and sleep restriction in the second half of the night [10]. Their findings suggest that testosterone may be more impacted by sleep timing rather than sleep duration. To further delineate the temporal impact of sleep on testosterone, Arnal et al. assessed whether a period of extended sleep (10 h in bed) prior to a period of sleep deprivation mitigated the hormonal reduction previously described. They found that the testosterone reduction persisted despite prior sleep extension, but levels rebounded after only a single night of recovery sleep [11]. Though the evidence for a relationship between sleep and testosterone is undoubtedly compelling, the mechanism by which this relationship operates is not well understood. Judd et al. theorized that this may be related to increases in testicular blood flow or increased Leydig cell sensitivity to luteinizing hormone in an early 1974 study. In a more recent paper, Cooke et al. suspected that the increase in free testosterone levels that is seen with sleep is largely related to postural changes in serum protein concentrations. Lying supine such as during sleep results in shift of fluid into the vascular compartment due to a decrease in hydrostatic pressure. This results in a decrease in the concentration of non-diffusible blood proteins such as albumin and sex hormone binding globulin that bind testosterone, leading to an increase in free testosterone levels [16]. Other studies have shown that the rise in testosterone with sleep is related to the appearance of the first REM episode, though it remains unclear whether testosterone is causally related to REM or if they both reflect a common underlying factor [17, 18].

We provide further support for the well-established relationship between both aging and obesity and testosterone levels. Several large cohort and cross-sectional studies have identified longitudinal age-related decreases in testosterone [19–22]. Most of these studies also show a negative association between body mass index (BMI) and total testosterone, though there is mixed evidence for a similar association between BMI and free testosterone [19, 21, 22]. While the direction of causation for this association has been debated, a recent study by Eriksson et al. determined that BMI was indeed the causal factor using a bi-directional Mendelian randomization analysis [23]. The association seen in the present study between alcohol consumption and serum testosterone levels is in contrast with previous research. In a 2006 study, Maneesh et al. found that alcohol abusers had significantly lower plasma testosterone than healthy controls [24]. This was also shown in an earlier study by Castilla-Garcia et al., who also found that testosterone levels increased during alcohol withdrawal in heavy alcohol users [25]. Moderate alcohol consumption has been shown to lower testosterone levels as well [26].

Our study has several strengths and limitations. Prior studies assessing testosterone and sleep have been large experimental in nature with small cohorts. We use a large database that utilizes thorough data collection with standardized laboratory measurements of a representative sample of US males. Nonetheless, several limitations need to be highlighted. First, as is the nature of cross-sectional study designs, we are unable to draw causality with respect to decreased number of hours slept and its association with declining serum testosterone levels but rather a compelling association does exist. Second, the clinical impact of our findings needs to be taken under consideration, as it is unlikely that a reduction in testosterone by 5.85 ng/dL per hour loss of sleep will have a detrimental health impact. Nonetheless, it is common for patients to inquire as to methods to improve their own endogenous testosterone levels or whether they are required to remain on testosterone therapy for life. Our findings do prompt the attempt of conservative measures by means of improving sleep duration and weight loss. For patients presenting with signs of hypogonadism and low testosterone, our initial evaluation includes assessment of sleep habits, nutrition and weight loss with an emphasis to ensure continuous evaluation of these factors for those electing testosterone replacement.

Conclusion

Analysis of the 2011–2012 NHANES data demonstrates an association between testosterone and sleep, increasing age, alcohol consumption and BMI. The present study represents by far the largest study to date showing that short sleep duration is associated with reduced testosterone levels. Further research is needed in order to determine the mechanism by which sleep and testosterone are related, as well as the clinical impact of this association.

Author contributions Protocol/project development: PP, TK, RR. Data collection or management: PP, TK. Data analysis: PP, TK. Manuscript writing/editing: PP, BS, TK, RR.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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