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CLINICAL REVIEW

Sleep disturbances compared to traditional risk factors for diabetes development: Systematic review and meta-analysis

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SUMMARY

Sleep disturbances [short (<6 h) and long (>8 h) sleeping time, insomnia (initiating or maintaining sleep), obstructive sleep apnea (OSA) and abnormal sleep timing] have been associated with increased diabetes risk but the effect size relative to that of traditional risk factors is unknown. We conducted a systematic review and meta-analysis to compare the risk associated with sleep disturbances to traditional risk factors. Studies were identified from Medline and Scopus. Cohort studies measuring the association between sleep disturbances and incident diabetes were eligible. For traditional risk factors (i.e., overweight, family history, and physical inactivity), systematic reviews with or without meta-analysis were included. Thirty-six studies (1,061,555 participants) were included. Pooled relative risks (RRs) of sleep variables were estimated using a random-effect model. Pooled RRs of sleeping ≤5 h, 6 h, and ≥9 h/d were respectively 1.48 (95%CI:1.25,1.76), 1.18 (1.10,1.26) and 1.36 (1.12,1.65). Poor sleep quality, OSA and shift work were associated with diabetes with a pooled RR of 1.40 (1.21,1.63), 2.02 (1.57, 2.61) and 1.40 (1.18,1.66), respectively. The pooled RRs of being overweight, having a family history of diabetes, and being physically inactive were 2.99 (2.42,3.72), 2.33 (1.79,2.79), and 1.20 (1.11,1.32), respectively. In conclusion, the risk of developing diabetes associated with sleep disturbances is comparable to that of traditional risk factors. Sleep disturbances should be considered in clinical guidelines for type 2 diabetes screening.

Introduction

Sleep is affected by demographic variables, behaviors (including those dictated by social pressures) and pathological conditions. According to the National Heart, Lung and Blood Institute, “sleep deficiency” occurs when an individual has insufficient sleep, poor sleep, a diagnosed sleep disorder or abnormal timing of sleep [1]. Multiple reviews [2–4] have elected to use the term “sleep disturbances” to designate insufficient or excessive sleep duration, poor self-reported sleep quality, or a diagnosed sleep disorder such as obstructive sleep apnea (OSA). There is increasing evidence linking these very common types of sleep disturbances to abnormal glucose metabolism and elevated diabetes risk.

Findings from laboratory studies manipulating sleep duration and/or quality in healthy adults indicate that a few days of sleep restriction and/or fragmentation are sufficient to cause a marked reduction of insulin sensitivity, without adequate compensation by increased insulin release, resulting in decreased glucose tolerance [5–7]. These findings are consistent with the results of prospective cohort studies that revealed that short sleep (generally ≤6 h/d) and poor sleep quality are both associated with an increased risk of incident diabetes after adjusting for confounders [8–12]. In addition, there is evidence that individuals who report being long sleepers (i.e., ≥9 h/night) are also at increased risk of developing diabetes [13]. It is important to note that the amount of sleep that

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Abbreviations

AHI	apnea hypopnea index
BMI	body mass index
CPAP	continuous positive airway pressure
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4th edition
DSM-V	Diagnostic and Statistical Manual of Mental Disorders 5th edition
FPG	fasting plasma glucose
GAD Ab	glutamate decarboxylase antibody
HbA1c	hemoglobin A1c
ODI	oxygen desaturation index
OGTT	oral glucose tolerance test
OSA	obstructive sleep apnea
PSG	polysomnography
RDI	respiratory disturbance index
RR	relative risk

optimizes physical and mental health is an individual characteristic that tends to decrease with age. However, it is generally considered that 7–8 h of sleep nightly is adequate for most adults [14].

OSA is a complex sleep disorder characterized by repetitive episodes of upper airway closures or partial collapse during sleep, resulting in intermittent hypoxia, fragmented sleep, and generally reduced total sleep time. Experimental intermittent hypoxia during the daytime in fully awake healthy volunteers results in a reduction in insulin sensitivity without simultaneous increase in insulin secretion [15,16]. Longitudinal studies indicate that the presence of OSA is associated with an increased risk of developing diabetes, even after adjusting for adiposity [17,18].

Shift workers generally have eating and sleeping schedules that are not synchronized with their own internal circadian rhythms, a condition called “circadian misalignment”. In well-controlled laboratory studies in healthy adults, experimentally induced circadian misalignment between eight days to five weeks resulted in elevated glucose levels, insulin resistance and increased systemic inflammation [19–21]. These metabolic derangements returned to baseline levels after a period of sleep recovery [20]. In agreement with these findings, several cohort studies revealed that shift work was associated with increased risk for incident diabetes [22,23], although the findings were not entirely consistent [24].

Despite the increasing body of evidence linking sleep disturbances with an adverse effect on glucose tolerance, they are not yet recognized by the medical community as novel risk factors for type 2 diabetes. Clinical practice recommendations issued yearly by the American Diabetes Association recommend screening for diabetes in all adults who are overweight (body mass index [BMI] $\geq$ 25 kg/m^2) with additional risk factors (e.g., hypertension, dyslipidemia, physical inactivity or a family history of diabetes) [25] without considering sleep disturbances as additional risk factors. The International Diabetes Federation recognizes a similar set of risk factors, but also includes unhealthy diet, ethnicity and poor nutrition during pregnancy [26]. The centers for disease control and prevention (CDC) also list advanced age (65 y or older) as a risk factor for prediabetes, in addition to other factors [27]. None of the 94 diabetes risk scores developed by multiple international groups of investigators have included sleep in their models of diabetes prediction [28]. With diabetes estimated to affect 387 million people around the world in 2014, 29 million of whom residing in the United States (9.3% of the US population), it has become a major chronic disease with significant morbidity (micro and macrovascular complications) and mortality, along with increased health care costs [29,30]. Diabetes was the 7th leading cause of death in the US in 2013 and cost 245 billion dollars in 2012 [29]. It is therefore crucial that we understand diabetes risk factors, especially the modifiable ones, in order to properly screen and attempt to prevent or reduce the severity and complications of this important disease.

We hypothesized that the impact of sleep disturbances on diabetes risk may be comparable to that of well-recognized traditional risk factors. We therefore conducted a systematic review and meta-analysis aiming to compare the diabetes risk imparted by different types of sleep disturbances to those considered as well-accepted traditional risk factors. For traditional risk factors, we have chosen family history of diabetes, overweight and physical inactivity to represent a set of universally accepted non-modifiable and modifiable risk factors. Our selection of overweight and physical inactivity was guided by the fact that intensive lifestyle modifications focusing on weight loss and exercise have resulted in clear reductions in diabetes risk [31].

Methods

Data sources and searches

Investigators identified relevant studies from searches of Medline and Scopus databases since their inception through November 2013. Reference lists of included studies were explored for identifying additional relevant studies. Search terms and search strategies are described in Appendix 1 and 2, respectively.

Study selection

Two reviewers (T.A., S.R.) independently selected studies. Disagreements between the two reviewers were resolved by discussion and consultation with a senior advisor (A.T.).

For sleep variables, cohort studies published in English were eligible if they met all of the following criteria: participants were 18 y or older; studied variables were any of the following: sleep duration, sleep quality (presence of an insomnia symptom as defined by the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-V) criteria [32] versus absence), OSA (presence or absence), shift work versus non-shift work; incidence of diabetes was the outcome of interest; and reported data were sufficient for extraction.

For traditional risk factors for diabetes, we focused on family history (yes versus no), overweight (BMI 25.0–29.9 kg/m^2 versus normal weight), and physical inactivity (inactive versus active) in adult subjects. Reviews with or without meta-analysis published in English were selected if they provided pooled effects of at least one of these risk factors.

Data extraction

Two reviewers independently extracted the data using a standardized data record form. Discrepancies were resolved by discussion and consensus with a third party (A.T.). The corresponding authors were contacted if there were missing data.

Sleep variables

These included sleep duration, sleep quality, OSA and shift work. Sleep duration was obtained by self-report and was categorized into short ($\leq$5 or = 6 h/d), normal (7–8 h/d), and long ($\geq$9 h/d). The studies by Kita [33] and Mallon [34] had classified sleep durations of 7 h and 6–8 h/d as normal, respectively. Thus, these sleep