Sleep Medicine 15 (2014) 1398–1404

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Night-time sleep duration and the incidence of obesity and type 2 diabetes. Findings from the prospective Pizarra study

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ARTICLE INFO

Article history:
Received 13 February 2014
Received in revised form 9 June 2014
Accepted 12 June 2014
Available online 11 August 2014

Keywords:
Night-time sleep duration
Prospective study
Weight gain
Obesity
Type 2 diabetes
Southern Spain

ABSTRACT

Background: Several recent studies have related short sleep duration with different health problems, though the results related with the risk of obesity and type 2 diabetes (T2D) are far from conclusive. The aim of this study was to investigate the association between night-time sleep duration and the incidence of obesity and T2D in a prospective study with a follow-up of 11 years.
Material and methods: The study comprised 1145 people evaluated in 1997–1998 and re-evaluated after 6 years and 11 years. At the three study points, subjects without known diabetes mellitus (KDM) were given an oral glucose tolerance test (OGTT). Anthropometric and biochemical variables were measured. The subjects were asked about their number of hours of night-time sleep.
Results: After adjustment, the OR of becoming obese was significantly higher in subjects who slept ≤7 hours per night, at both the 6-year follow-up (OR = 1.99; 95% CI = 1.12–3.55) and the 11-year follow-up (OR = 2.73; 95% CI = 1.47–5.04). The incidence of T2D at the 6-year follow-up in subjects without T2D at baseline was higher in those who slept ≤7 hours per night (OR = 1.96; 95% CI = 1.10–3.50). However, this association was not independent of obesity, weight gain or abnormal glucose regulation at baseline. At the 11-year follow-up however there was no association between night-time sleep duration and the incidence of T2D.
Conclusions: The incidence of obesity over the 11-year follow-up increased in subjects with fewer hours of night-time sleep. The incidence of T2D according to the hours of night-time sleep depended on obesity and the carbohydrate metabolism phenotype.

1. Introduction

In those countries where sleep duration has been studied, the number of hours of sleep has decreased over recent years [1,2]. This decrease has been related to changes in lifestyle [3]. In recent years, several studies have related short sleep duration with different health problems, in cross-sectional [4–7], prospective [8–10], and intervention studies [11]. However, the particular results related to the risk of obesity and type 2 diabetes (T2D) are far from conclusive [12].

A large cross-sectional study of 375,653 US adults aged ≥18 years (the Behavioral Risk Factor Surveillance System) undertaken in 2009 found a positive association between short sleep duration and the likelihood of having chronic diseases (coronary heart disease, stroke, high blood pressure, asthma, arthritis, T2D and obesity). This association became weaker but did not disappear after adjustment for frequent mental distress (FMD) (FMD ≥14 days during the past 30 days) [4]. Other recent cross-sectional studies found an association between poor sleep quality and short sleep duration and prediabetes and T2D [7,13].

In a large prospective study, the Nurses' Health Study, the authors concluded that the association between a reduced self-reported sleep duration and a diagnosis of T2D could be due to confounding by

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http://dx.doi.org/10.1016/j.sleep.2014.06.014
1389-9457/

body mass index (BMI), or that sleep restriction may mediate its effects on T2D through weight gain [8]. A recently published systematic review of 13 prospective studies in adults failed to detect a clear association between sleep duration and weight gain [14].

The aim, therefore, of this study was to seek a possible association between night-time sleep duration and the incidence of obesity and T2D at the 6- and 11-year follow-up points in the Pizarra study, a prospective study in progress since 1995 in southern Spain. We examined the hypothesis that those subjects with short night-time sleep duration have a higher risk of becoming obese and/or diabetic.

2. Methods

2.1. Baseline and follow-up studies

This study formed part of the Pizarra cohort study, the characteristics of which have been published previously [15]. In 1997, 1226 subjects were randomly selected from the adult population of Pizarra, a village in the province of Malaga (Spain). The inclusion age was 18–65 years, and individuals were excluded from the study if they were institutionalized for any reason, pregnant, or had a severe clinical or psychological disorder. The final sample distribution, by age and sex, was not significantly different from the population distribution.

The study was approved by the Ethics and Clinical Investigation Committee of Carlos Haya Hospital, and written informed consent was obtained from all participants.

The night-time sleep duration for 1145 subjects was obtained from a self-report questionnaire. Phenotyping of the carbohydrate metabolism was carried out according to the World Health Organization [16] in 1051 of these subjects, performing an oral glucose tolerance test (OGTT) in those subjects who were unaware of their diabetic status.

The cohort was re-evaluated in 2003–2004 (6-year follow-up study). All those who had completed the baseline study were invited by letter or by phone to attend for another clinical and anthropometric examination and another OGTT. In total, 968 of these subjects completed this 6-year follow-up study. In 2009–2010, 673 subjects were re-evaluated (11-year follow-up study).

2.2. Procedures

The protocol was the same at all three study points. The anthropometric study was carried out following a standardized method [17]. At all three study points, measurements were made of weight and height, and the BMI was calculated (weight/height^2). Subjects with BMI >30 kg/m^2 were considered as obese.

The blood glucose level was measured at the three study points using the glucose oxidase method (Accu-Chek, Roche Diagnostics, Barcelona, Spain) at fasting and 120 min after an OGTT with 75 g of glucose. The fasting serum insulin level was measured at baseline and at the 6-year follow-up by radioimmunoassay (Coat a Count RIA kit, DPC, Los Angeles, CA, USA). Insulin resistance was estimated with the HOMA equation (homeostatic model assessment – insulin resistance), as follows: HOMA-IR = [fasting insulin (μU/mL) × fasting glucose (mmol/L)]/22.5.

At all three study points, the blood pressure was measured twice with a sphygmomanometer, with an interval of 5 min between measurements, and the average of the two measurements was used in the analyses. Participants were considered to have hypertension if their blood pressure was ≥140/90 mmHg or if they were receiving antihypertensive treatment.

At all three study points, information on physical activity level, smoking habit, educational level, and other lifestyle habits was obtained using a self-administered questionnaire. Subjects were also asked about night-time sleep duration. The average night-time sleep duration was assessed by asking 'On average, how many hours do you usually sleep at night?' Subjects were divided into two groups according to the night-time sleep duration: those who slept ≤7 h per night and those who slept ≥8 h per night. The cut-off points were the 25th percentile (7 h) and the 50th percentile (8 h) of the frequency distribution. A food frequency questionnaire was completed at baseline and at the 6-year follow-up [18]. The transformation to energy and macronutrients was done by a computer program that included the composition of local foods based on food composition studies [19].

Baseline measurements were made of leptin and interleukin-6 (IL-6). Additional proinflammatory cytokines and adipokines were measured at the 6-year follow-up study: tumor necrosis factor-α (TNF-α) receptors R60KDa (R1) and R80KDa (R2), IL-6, leptin, adiponectin, fatty acid binding protein 4 (FABP4) and high-sensitivity C-reactive protein (hs-CRP). At the 6-year follow-up study, ferritin and resistin were also measured. Ferritin was measured by immunoturbidimetry (ATOM S.A., Barcelona, Spain) using an A15 autoanalyzer from Biosystems S.A. (Barcelona, Spain). Resistin was measured using an enzyme-immunoassay commercial kit (SPI Bio Bertin, York, UK).

Measurements of cytokines were performed using enzyme-immunoassay commercial kits: TNF-α receptors R1 and R2 (BLK Diagnostics, Barcelona, Spain); IL-6 (R&D Systems, Inc., Minneapolis, MN, USA); adiponectin (DRG Diagnostics GmbH, Marburg, Germany); leptin (Mediagnost, Reutlingen, Germany); FABP4 (SPI Bio, Montigny le Bretonneux, France); hs-CRP (BLK Diagnostics).

2.3. Statistical analysis

Data are presented as the mean and standard deviation. Differences between means were calculated using Student's *t*-test or one-way or multivariate analysis of variance. The correlation between variables was measured using Spearman's test. The strength of association between dependent variables and the explanatory variables was measured using logistic regression analysis, calculating the odds ratio (OR) and the 95% confidence interval (CI). In all cases, a rejection level of $\alpha = 0.05$ was used. Analyses were done with SPSS v10 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Population variables according to night-time sleep

The number of hours of night-time sleep decreased over the 11-year follow-up: 8.23 ± 1.30 h (median, 8 h) at baseline, 8.01 ± 1.38 h (median, 7.9 h) at the 6-year follow-up, and 7.18 ± 1.48 h (median, 7 h) at the 11-year follow-up.

Sex, educational level, smoking habit, daily energy consumed, intake of carbohydrates, proteins and lipids, proportion of fatty acids in the diet, hours watching television (TV), dietary habits watching TV, number of meals per day, snacking habits, and alcohol intake (all variables studied on at least one of the three study points) did not vary according to the number of hours of night-time sleep (Table 1).

Subjects who rested ≤7 h per night practised sport in their leisure time less often at both the 6-year ($P = 0.01$) and the 11-year follow-up ($P = 0.02$) (Table 1). On the other hand, daily work activity was described as more intense in those subjects who rested ≤7 h per night at both the 6-year ($P = 0.01$) and the 11-year follow-up ($P = 0.02$), adjusted for age, sex, and obesity (Table 1).

Subjects who drank coffee at least once per day were more likely to sleep fewer hours per night, both at baseline (8.11 ± 1.17 vs 8.43 ± 1.35 h; $P = 0.005$ adjusted for age, sex and obesity) and at the 6-year follow-up (7.82 ± 1.35 vs 8.15 ± 1.40 h; $P = 0.005$ adjusted for