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Sleep and Biological Rhythms (2022) 20:595–599
https://doi.org/10.1007/s41105-022-00403-7

SHORT PAPER

Sleep duration and lipid metabolism in patients with diabetes mellitus: from the POWER2DM study

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Received: 7 February 2022 / Accepted: 4 July 2022 / Published online: 5 August 2022

Abstract

This study assesses the association between sleep duration and plasma lipid profiles in people with diabetes mellitus (DM). Sleep duration data were obtained in 91 patients from the POWER2DM study (NCT03588104). The patients were divided in tertiles, based on their sleep duration, and blood samples were obtained at the beginning and after 9 months. Significant differences were found, specifically, patients in Tertile 3 (≥ 7.51 h) showed lower plasma levels of high-density lipoprotein cholesterol HDL-c ($p < 0.05$), apolipoprotein A1 (apo-A1; $p < 0.05$) and low HDL-c/apo-A1 ratio ($p < 0.05$). This study shows that sleep duration is associated with plasma lipid profiles in people with DM.

Keywords Diabetes mellitus · Sleep duration · Lipid metabolism · High-density lipoprotein cholesterol

Introduction

Cardiovascular disease (CVD) is currently the leading cause of mortality worldwide, and over half of cardiovascular events are associated to diabetes mellitus (DM) [1] and its related disorders. One of these metabolic disturbances related with lipid metabolism includes low high-density lipoprotein cholesterol (HDL-c) plasma levels, which have been found to be associated to a higher CVD risk. Alterations of sleep duration or sleep timing can directly affect our physiology and cardiovascular health, in fact, extreme sleep duration has shown to be associated to DM, dyslipemia and CVD risk [2]. We aimed to explore whether variability in sleep duration is associated with dyslipemia in people with DM.

Isabel Perez-Corral and Francisco Gomez-Delgado are contributed equally.

Eelco J. P. de Koning and Javier Delgado-Lista are shared joint seniorship.

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Materials and methods

This observational study was part of the POWER2DM Evaluation Campaign study, a European multicenter and multidisciplinary randomized clinical trial of the European H2020 initiative (http://power2dm.org), based on information from several wearable technology devices provided to people with DM; with these data, this project aims to establish a personalized "glycemic profile" that helps us to anticipate periods of hyper and hypoglycemia in people with DM. Through a software for patients (application: App) and another for physicians (personal computer: PC) and supported by decision algorithms made by a team of psychologists and based on the theory of behavior change; the system will give personalized recommendations for lifestyle and treatment. The Spanish cohort of the POWER2DM study included 117 people with DM. In total, 91 people with DM who responded to the sleep questionnaires [3] and had relevant measurements (sleep duration and clinical/biochemical variables at the beginning and after 9 months of follow-up) were included (Type 1 DM: $n = 18$; Type 2 DM: $n = 73$). Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), HDL-c, triglycerides (TG), apolipoprotein A1 (apo-A1) and apolipoprotein B (apo-B) were measured using the Architect c-16000 analyzer (Abbott®, Chicago, Illinois, USA) by oxidation–peroxidation for TC, HDL-c and TG. LDL-c was calculated using the Friedewald formula [4]. Apo-A1 and apo-B levels were determined by immunoturbidimetry. Finally, the HDL-c/apo-A1 ratio was calculated; this is a widely validated clinical and epidemiological measurement for estimating HDL-c size that inversely correlates with CVD risk [5].

The statistical analysis was performed using SPSS® version 25.0 (SPSS Inc., Chicago, IL). For sleep duration analysis, the subjects were grouped into tertiles (T): T-1 ($\leq$ 6.50 h), T-2 (6.51–7.50 h), T-3 ($\geq$ 7.51 h). Data are presented as frequencies and percentages for qualitative variables and mean $\pm$ standard error for quantitative variables. Differences between mean values were explored by univariate analysis of variance (ANOVA). Age, gender, body mass index (BMI), tobacco use, alcohol consumption and lipid lowering treatments were considered and evaluated as potential confounding factors. Qualitative variables were compared using chi-squared test. A p value < 0.05 was considered statistically significant.

Results

Lipid profiles according to tertiles of sleep duration are presented in Table 1. At baseline, people with sleep duration of over 7.51 h (T-3) had lower plasma levels of HDL-c (T-1 = 50mg/dL; T-2 = 49mg/dL; T-3 = 44 mg/dL; $p = 0.03$, Fig. 1A) and apo-A1 (T-1 = 152mg/dL; T-2 = 151mg/dL; T-3 = 141 mg/dL; $p = 0.03$, Fig. 1B). HDL-c/apo-A1 ratio was lower in T-3 (T-1 = 0.33; T-2 = 0.33; T-3 = 0.30; $p = 0.01$, Fig. 1C) than patients in the other two tertiles.

At the end of the study, after 9 months, we confirmed our results, as again persons in T-3 showed lower plasma levels of HDL-c (T-1 = 49mg/dL; T-2 = 50mg/dL; T-3 = 44 mg/dL; $p = 0.03$, Fig. 1A), apo-A1 (T-1 = 146mg/dL; T-2 = 141mg/dL; T-3 = 134 mg/dL; $p = 0.04$, Fig. 1B) and HDL-c/apo-A1 ratio (T-1 = 0.33; T-2 = 0.33; T-3 = 0.31; $p = 0.03$, Fig. 1C) compared with those subjects included in T-1 and T-2 (6.51–7.50 h).

Discussion

Our findings show that in a population of people with DM, sleep duration was associated with lipid metabolism.

Studies such as that published by Mahmood et al. [6] also showed that poor sleep quality was related to high TC and LDL-c plasma levels in 114 people with DM. As regards the relationship of sleep duration to plasma HDL-c levels in people with DM, studies such as published by Shin et al. [7] in over 13,000 subjects, a long sleep duration ($\geq$ 9 h) was associated with low HDL-c levels. As the authors conclude, these results may derive from differences in underlying psychosocial factors in the populations analyzed, such as life expectancy and physical activity / sedentary lifestyle, which interfere with lipid metabolism. Even, these factors should be taken into account and be analyzed in future researches with big sample size and long term follow-up to elucidate the J-shaped association between sleep duration and mortality in people with DM, with evidences showing a reduction in risk at around 7 h, increasing below 5 h and above 8 h [8, 9].

One important, novel finding in our study is the association of sleep duration with the HDL-c/apo-A1 ratio. This ratio is directly associated to HDL-c particle size [10] and subsequently, an increase in this ratio is associated with

Table 1 Baseline characteristics according to tertiles of sleep duration

	Tertiles of sleep duration			*p*
	T-1 ($n=30$)	T-2 ($n=31$)	T-3 ($n=30$)	
Age (years)	53 (1.67)	57 (1.77)	54 (1.74)	0.58
T2DM/T1DM	21/9	28/3	25/5	0.12
Weight (kg)	91 (1.23)	84 (1.30)	83 (1.26)	0.29
WC (cm)	103 (1.06)	97 (1.12)	101 (1.09)	0.37
BMI (kg/m^2)	31 (0.9)	30 (1.02)	31 (1)	0.37
TC (mg/dL)	174 (6.92)	174 (7.06)	170 (6.98)	0.89
LDL-c (mg/dL)	101 (6.03)	95 (5.69)	97 (5.95)	0.35
HDL-c (mg/dL)	50 (1.93)	49 (2.08)	44 (2.05)	0.03*
HDL/apo-A1 ratio	0.33 (0.007)	0.33 (0.008)	0.30 (0.008)	0.01*
TG (mg/dL)	126 (15.24)	121 (15.86)	127 (15.36)	0.79
Lp(a) (mg/dL)	34 (10.76)	44 (9.45)	38 (9.52)	0.68
Apo-B (mg/dL)	78 (3.48)	76 (3.56)	78 (3.59)	0.87
Apo-A1 (mg/dL)	152 (3.65)	151 (3.88)	141 (3.91)	0.03*
Alcohol consumption (%)	35.3	29	15.2	0.16
Tobacco use (%)	26.5	20	15.2	0.52
Lipid lowering treatments				
Statins (%)	47.1	35.1	51.5	0.41
Fibrates (%)	5.9	0	6.1	0.38
Others[a] (%)	0	0	1	0.57

Tertile 1: ≤6.50 h; Tertile 2: 6.51–7.50 h and Tertile 3: ≥7.51 h, Values expressed as mean (SEM). *Apo-A1* apolipoprotein A, *Apo-B* apolipoprotein B, *HDL-c* high-density lipoprotein cholesterol, *Kg* kilograms, *Kg/m^2* kilograms per square meter, *LDL-c* low-density lipoprotein cholesterol, *Lp(a)* lipoprotein a, *mg/dL* milligrams per decilitre, *mg/L* milligrams per liter, *TC* total cholesterol, *TG* triglycerides, *T1DM* type-1 diabetes mellitus, *T2DM* type-2 diabetes mellitus, *WC* waist circumference. Continuous variables calculated using the ANOVA test adjusted by age, gender and BMI. Qualitative variables were compared using chi-squared test.

*$p<0.05$.

[a]Others lipid lowering treatments: Ezetimibe and Gemfibrozil

reduced risk for CVD [5]. The HDL-c/apo-A1 ratio has previously been related with insulin resistance and other glucose metabolism parameters in people with DM, showing an inverse association between this ratio and metabolic control of DM [11]. On the other hand, potential limitations of our research were the absence of physical activity data in all population, a little sample size and a short term follow-up. However, to the best of our knowledge, our study constitutes the first evidence for an association between sleep duration and the HDL-c/apo-A1 ratio.

Conclusion

The present research shows that in a population of people with DM, sleep duration of over 7.51 h is associated with dyslipemia, compared to patients with shorter sleep duration. In the light of these results, modifying sleep duration may create new opportunities, in addition to those offered by nutrition and physical activity, to improve cardiometabolic health in people with DM. Nevertheless, our results derive from an observational study in which we have not carried out any intervention in sleep duration to assess changes in the lipid profile of DM patients from the POWER2DM study.

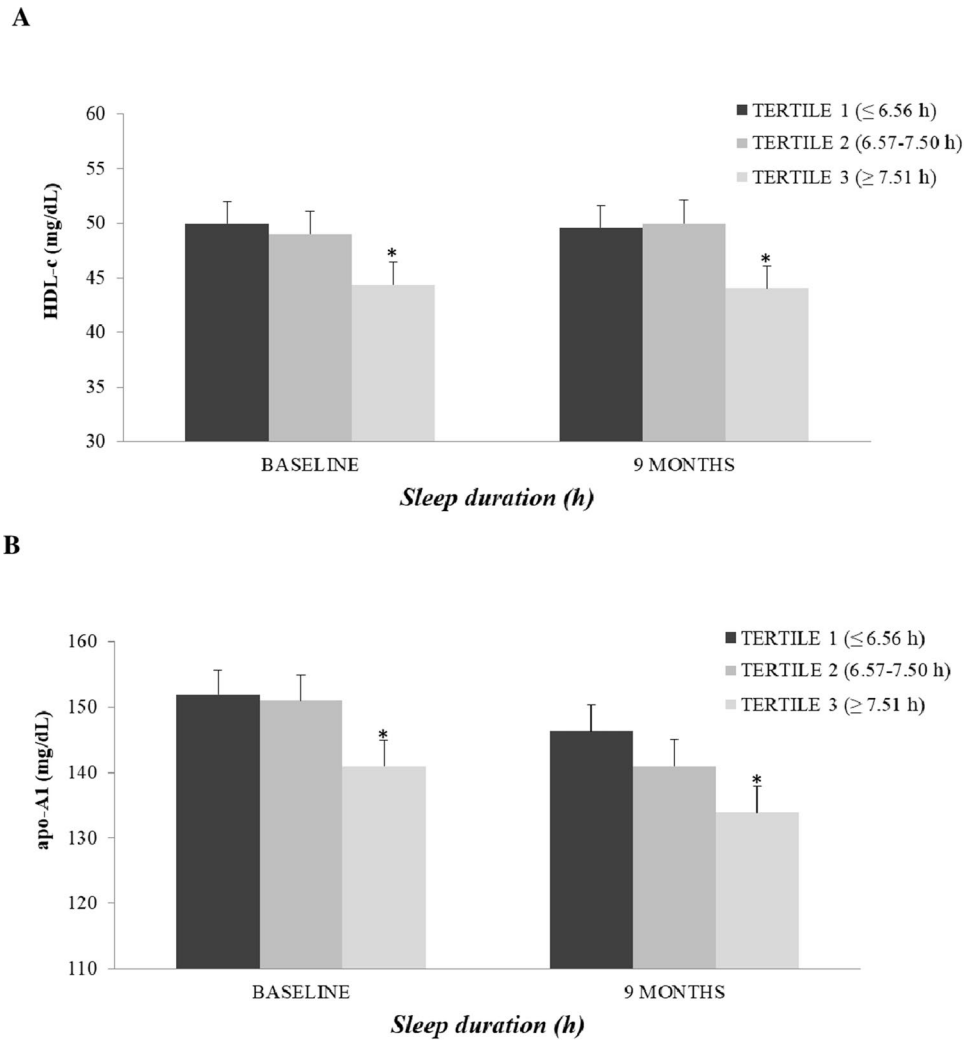

Fig. 1 High-density lipoprotein cholesterol (HDL-c) plasma levels (mg/dL) [A]; Apolipoprotein A1 (apo-A1) plasma levels (mg/dL) [B] and high-density lipoprotein cholesterol (HDL-c) to apolipoprotein A1 (apo-A1) ratio [C] according Tertiles of sleep duration (Tertile 1: ≤ 6.50 h; Tertile 2: 6.51–7.50 h and Tertile 3: ≥ 7.51 h) at baseline and after 9 months of follow-up. Values are means ± SEM. – values were adjusted for age, gender and BMI. $^{*}p < 0.05$

Acknowledgements This study was funded by European Union's Horizon 2020 research and innovation program under grant agreement No. 689444 (POWER2DM).

Author contributions Conceptualization: IP-C, FG-D, MMR and JDT-P; Methodology: IP-C, FG-D, MMR, JDT-P and APAL; Formal analysis and investigation: IP-C, FG-D and AAG; Writing—original draft preparation:: IP-C, FG-D and JD-L; Writing—review and editing: IP-C, FG-D and JD-L Funding acquisition: JD-L and EJPK. Resources: MMR, JDT-P, APAL, JKS, AAG, BSU, EJPK; Supervision: JD-L and EJPK.

Funding This research involving Human Participants and is registered in clinicaltrials.gov: Clinical Trial Registration Number: NCT03588104 (https://clinicaltrials.gov/ct2/show/NCT03588104).

Data availability The data used in the present study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest Isabel Perez-Corral, Francisco Gomez-Delgado, Merel M Ruissen, Jose D Torres-Peña, Antonio P Arenas-de Larriva, Jacob K Sont, Albert A de Graaf, Bas S Uitbeijerse, Eelco J P de Koning and Javier Delgado-Lista declare that they have no conflict of interest.

Ethical committee permission The protocol and all amendments were approved by the local ethic committee of the Reina Sofia University Hospital and were conducted according to the Declaration of Helsinki and its amendments or comparable ethical standards and good clinical practices.

Informed consent Informed consent to participate in this study as well as subsequent scientific dissemination and publication of results in a journal article has been freely-given for all the participants.

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