Biomedical Research 2017; 28 (1): 295-298 *ISSN 0970-938X*
www.biomedres.info

Association of plasma leptin levels with type 2 diabetes in rotating shift work women.

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Abstract

Objective: We aimed to study the association among leptin levels, sleep duration, PSQI and risks of type 2 diabetes in Chinese women nurses.
Methods: We conducted a cross sectional study, 65 diabetics and age matched 72 non-diabetic group were assessed for physical and chemical parameters like Body Mass Index, PSQI, leptin levels, insulin levels and fasting blood glucose. Plasma leptin level was measured by direct sandwich ELISA.
Results: Plasma leptin levels were significantly correlated with age, insulin level, BMI, but not correlated with duration of shift work, sleep duration and PSQI score. Logistic regression analysis showed that a negative association between leptin levels and incidence of diabetes adjusted by age, BMI, sleep duration, PSQI score, duration of shift work and insulin. The odd ratio for diabetes being 0.868 (95% CI 0.597-1.711), 0.793 (95% CI 0.448-0.792), for 2nd tertile and 3rd tertile, respectively. However, we have not found the significant association of sleep duration, PSQI score with diabetes.
Conclusion: An independent negative association was found between leptin levels and the incidence of type 2 diabetes in Chinese women with rotating shift work. However, there were no correlation of sleep duration and PSQI with leptin levels and diabetes.

Keywords: Leptin, Type 2 diabetes, Shift work, Chinese women.

Accepted on June 3, 2016

Introduction

Leptin is a pleiotropic protein involved in body weight regulation, puberty, reproduction and immune function [1,2]. Leptin is produced primarily in adipose tissue and secreted following a circadian rhythm, with a nadir in the early morning, and a peak between 24:00 and 2:00 [3]. Photoperiod can also affect leptin gene expression. An extended day length stimulated leptin release and gene expression in adipose tissue [4,5]. Several studies showed that high levels of leptin are associated with an increased risk of developing diabetes [6,7], whereas conflicting results have been showed in animal models and humans [8-10].

In rotating shift work nurses, the circadian rhythm is disrupted. There is evidence that night shift work increased the risk of type 2 diabetes [11,12]. Night shift work will lead to a variety of health problems, including impairment of glucose tolerance, sleep disturbances and endocrine disorders [13-15]. Tang showed that inadequate sleep, in both quality and quantity, should be regarded as a plausible risk factor for glycaemic control in type 2 diabetes [16]. Recently, Keskin found the association between sleep disorders, HbA1c levels and type 2 diabetes [17]. Up to now, the influence of shift-work on leptin levels remain unknown, and the effect of leptin on developing diaetes controversial. Thus, we performed a cross-sectional study to investigate the association among leptin, sleep duration sleep quality, and risk of type 2 diabetes.

Subjects and Methods

We performed a cross-section study within Affiliated Houjie Hospital of Guangdong Medical College. More than 500 nurses took part in a questionnaire survey, 320 effective questionnaires were returned. On this questionnaire, health status, medications, dietary intake, duration of shift work and lifestyle factors including smoking history and sleeping patterns were ascertained. Women without a history of malignancy and worked at least 3 night shifts per-month were eligible for the current study. The total number of eligible nurses is 289; including 62 with type 2 diabetes. All the eligible nurses were ascertained of diabetes.

Finally, 62 women with type 2 diabetes were compared with 75 non-diabetic women in similar age. This study was approved by the Institutional Review Board at the Affiliated Houjie Hospital of Guangdong Medical College; written informed consent was obtained.

Ascertainment of diabetes

Eligible participants who self-reported diabetes on the questionnaires were asked to ascertain. The diagnosis of diabetes satisfied the criteria of World Health Organization [18]. Type 2 diabetes was defined as a fasting blood glucose ≥ 126 mg/dl [7.0 mmol/l] and/or a 2-h post-load plasma glucose ≥ 200 mg/dl [11.1 mmol/l].

Blood sampling

The 289 participants' fasting blood was sampled from a large antecubital vein before breakfast in the morning. The sample was spun (3000 rpm at 4°C for 10 min) in a chilled centrifuge to obtain plasma, which were stored at -70°C for analysis.

Laboratory measurements

Circulating leptin in plasma was measured in duplicate using a commercially available quantitative enzyme-linked immune-sorbent assay (ELISA) kit (Biorbyt, U.K.). The quantitative determination of human insulin concentrations in serum was estimated by Chemiluminescence enzyme immunoassay [19]. Fasting blood glucose (FBG) was measured by a hexokinase method.

Covariate data collection

Age, gender, duration of shift work, average of sleep duration in the previous 1 month, PSQI, hypertension, family history of diabetes, family history of hypertension, as well as smoking status were determined from the questionnaire. All the patients underwent a physical examination of BMI and blood pressure.

Statistical analysis

Variables are presented in this study as mean ± SD, median (interquartile range), or number (proportion) where appropriate. Differences in variables between the diabetic and non-diabetic group were tested using the non-parametric Mann-Whitney test, or the chi-square test. Spearman correlation statistical analysis was performed to analyse the relationship among variables. We derived leptin levels into three categories; the cut-point for these categories was derived from tertiles of the leptin levels among the 137 participants. Multiple logistic regression analysis was performed to examine the association of three categories of leptin levels with diabetes (adjusted by BMI, insulin levels, age, and duration of shift work, sleep duration and PSQI score).

All p-values in two tailed with 0.05 were used as a significant threshold. All statistical analysis was performed with SPSS 13.0 (Chicago, IL, USA).

Results

Baseline characteristics according to the two groups were shown in Table 1. Because of few samples with hypertension or smoking, the two variables were excluded. The median of leptin levels was significantly higher among non-diabetic group (37.0 ng/mg; 25 to 75%, 20.1-43.2 ng/mg) than among diabetic group (29.5 ng/mg; 25 to 75%, 18.3-42.1 ng/mg). As expected in this matched sample, the mean age (28 ± 3.8) was similar among the two groups. Compared with non-diabetic group, diabetic group had significantly higher insulin levels, FBG, BMI and duration of shift work, whereas much lower leptin levels. The sleep duration, PSQI scores, family history of diabetes and family history of hypertension showed no difference in these two groups.

Table 1. *Characteristics of women who developed type 2 diabetes and their age matched group.*

	Diabetic group (N=62)	Non-diabetic group (N=75)	p-value
Age (years)	28.5 ± 3.2	28.3 ± 4.0	0.905
Leptin (ng/mL)	29.5 (18.3-42.1)	37.0 (20.1-43.2)	0.007
Insulin (uU/mL)	8.4 (2.3-28.9)	6.2 (1.3-12.7)	<0.001
FBG (mmol/L)	6.9 (6.5-7.5)	5.5 (5.0-5.9)	<0.001
BMI (kg/m^2)	25.8 (23.7-27.8)	24.1 (23.0-26.8)	0.039
Duration of shift work (years)	6 (3-6)	5 (2-7)	0.047
sleep duration (hours per night)	6 (6-7)	6 (6-7)	0.897
PSQI score	13.5 (8-18)	9 (8-11)	0.436
Family history of diabetes (%)	19 (30.7)	21 (28)	0.455
Family history of hypertension (%)	21 (33.9)	22(29.3)	0.746

Abbreviations: BMI: Body Mass Index; PSQI: Pittsburgh Sleep Quality Index.

The associations of leptin levels with covariates were showed in Table 2. Plasma leptin levels were significantly correlated with age, insulin level, BMI, but not correlated with duration of shift work, sleep duration and PSQI score.

Table 2. *Spearman correlation coefficients for leptin levels with covariates.*

	Leptin levels	
	r	P value
Age (years)	-0.259	0.027
Insulin (uU/mL)	0.210	0.042
FBG (mmol/L)	-0.122	0.052
BMI (kg/m^2)	0.671	0.024
Duration of shift work (years)	0.032	0.788
sleep duration (hours per night)	0.066	0.578
PSQI score	0.023	0.846
Family history of diabetes (%)	-0.185	0.117
Family history of hypertension (%)	-0.132	0.264

Abbreviations: BMI: Body Mass Index; PSQI: Pittsburgh Sleep Quality Index.

Logistic regression analysis was performed and the results were showed in Table 3.We found a negative association between leptin levels and incident diabetes adjusted by age, BMI, sleep duration, PSQI score, duration of shift work, and insulin. The odd ratios (OR) comparing the highest category of leptin level were 0.868 (95% CI 0.597-1.711), 0.793 (95% CI 0.448-0.792), for 2nd tertile and 3rd tertile, respectively. Duration of shift work was positively correlated with diabetes, and the OR was 1.678 (95% CI 1.459-12.902, P=0.05). However, we have not found the significant association of sleep duration, PSQI score with diabetes.

Table 3. *Logistic regression analysis of leptin levels with incident diabetes.*

	B	S.E.	OR	95% CI	P value
Leptin levels					
<26.1 ng/mL			1		0.026
26.1- 37.8 ng/mL	-0.677	1.534	0.868	0.597-1.711	0.035
>37.8 ng/mL	-0.089	0.089	0.793	0.448-0.792	0.004
Age	0.750	0.311	2.117	1.151-3.892	0.016
BMI	0.028	0.221	1.028	0.667-1.585	0.499
sleep duration	-0.780	0.782	0.458	0.099-0.760	0.318
PSQI score	0.104	0.161	1.109	0.809-1.277	0.519
Duration of shift work	0.389	0.199	1.678	1.459-12.902	0.050
Insulin	1.291	0.730	3.637	2.869-23.987	0.077

Abbreviations: BMI: Body Mass Index; PSQI: Pittsburgh Sleep Quality Index.

Discussion

We found an independent negative association between leptin levels and the incidence of type 2 diabetes in Chinese women nurses with rotating shift work. However, we have not found the correlation of sleep duration and PSQI with leptin levels and diabetes.

A lot of study found high levels of leptin are associated with incidence of diabetes [6,7,20]. However, our study showed a beneficial effect of leptin on diabetes, it was in line with several studies [8-10,21,22]. Schmidt showed that high leptin levels, probably reflecting leptin resistance, predict an increased risk of diabetes, however, after adjusted by factors purportedly related to leptin resistance unveils a protective association of leptin's protective effects against diabetes [9]. Moreover, Rachel found that leptin reverses diabetes by suppression of the hypothalamic-pituitary-adrenal axis in rat models [22]. These inconsistent results may be attributed to variation gender [23], ethnic, study design, length of follow-up, disease identification or other methodological issues.

The circadian rhythms of shift workers are disordered. Several studies showed that the secretion of gastrointestinal hormones was disrupted resulting from the change of circadian rhythms [24,25]. Leptin is a kind of gastrointestinal hormones and highly correlated with sleep and circadian rhythmicity. Lots of studies have found the association of abnormal leptin level and circadian rhythms disorder [26]. However, the associations of leptin with sleep duration and PSQI were not studied before. In this study, we had not found the direct relationship. It suggests that sleep duration or sleep quality cannot completely represent the circadian rhythm, but only one aspect of it. Otherwise, sleep duration or sleep quality may play a role on other parts, for example, fluctuation of leptin secretion and/or the target's sensitivity to leptin. Therefore, future studies assessing associations of leptin with shift work are needed.

Several limitations also merit consideration. First, our study population was limited to Chinese woman. It is unknown whether our findings can be applied to men or to other racial groups. Secondly, the conclusion was based on relatively small amount of study samples. Larger well-designed studies, involving more relevant variables, should be warranted in future to elucidate the mechanism of leptin in incidence of diabetes in rotating shift workers.

Acknowledgements

This study was supported by: The scientific research key project of Dongguan science and technology plan (Grant No. 2012105102025).

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