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Original Article

Sleep-disordered breathing and disorders of glucose metabolism

Tomoyuki Kawada^{a,*}, Masao Katsumata^a, Hirofumi Inagaki^a, Takayuki Nakamura^b,
Yoichi Kon^b

^a Department of Hygiene and Public Health, Nippon Medical School, Japan

^b Division of Health Evaluation & Promotion, Ota Memorial Hospital, Japan

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ABSTRACT

Aims: The authors identified the risk of disorders of glucose metabolism (DGM) for sleep-disordered breathing (SDB).

Methods: We conducted a cross-sectional study in 536 men aged 33–84 years. Patients with diabetes medication were excluded for the analysis and DGM were diagnosed by fasting plasma glucose ≥ 100 mg/dl and/or 2 h plasma glucose ≥ 140 mg/dl.

Results: The prevalence of DGM in subjects with and without severe SDB, which was judged by an apnea-hypopnea index (AHI) of 30, were 64.9% and 53.3%, which showed no significant difference. The adjusted odds ratios (ORs) (95% confidence intervals [CIs]) of the logarithmic-transformed AHI and that of C-reactive protein for DGM were 1.3 (0.87–2.0) and 2.3 (1.5–3.6), respectively. When the subjects were categorized by the severity of SDB, the ORs (95% CIs) of subjects with mild, moderate and severe SDB against subjects without SDB were 2.9 (1.8–4.6), 1.2 (0.72–2.1) and 1.5 (0.8–3.0), respectively.

Conclusion: A significant association was observed between mild SDB and the presence of DGM in male subjects of this study.

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1. Introduction

Disorders of glucose metabolism (DGM), as a pre-diabetic state, is considered to be associated with long-term micro- and macrovascular as well as with neurological complications [1]. Lifestyle factors including smoking, drinking, exercise and psychological stress are all related to DGM, and sleep-disordered breathing (SDB) has also been reported to be associated with the risk of DGM [2].

The prevalence of moderate-severe SDB, which is defined as an Apnea-hypopnea index (AHI) of 15 or higher, is 49.7% in men [3]. We previously reported a significant positive associations between SDB and the presence of metabolic syndrome in male subjects [4], but information on the association between SDB and cardiovascular risk was limited [5].

To clarify the relationship between SDB and DGM, we conducted a risk assessment with special reference to the severity of SDB as assessed by determination of the AHI.

2. Subjects and methods

Male subjects (n = 536), aged 33–84 years, were recruited in this study. Subjects who were receiving treatment for diabetes mellitus were initially excluded. Informed consent was obtained from each of the participants and the study was conducted with the approval of the Institutional Review Board of Ota Memorial Hospital, Gunma Prefecture, Japan (April 27, 2015).

Blood samples were collected in the morning after the subjects had fasted overnight and the serum levels of uric acid, high sensitive C-reactive protein, plasma fasting and 2 h plasma glucose after glucose load were determined (AU2700, Olympus Co. Ltd., Japan).

The smoking habit was categorized as “current smoking” or “no current smoking” (including “quit smoking”). The drinking habit was categorized as “daily drinking” or “no daily drinking” (including “no drinking”). Regular exercise was categorized as exercise ≥ 2 times per week for more than one year or not.

DGM was judged by fulfilling fasting plasma glucose ≥ 100 mg/dL (5.6 mmol/L) and/or plasma glucose after 2 h glucose load ≥ 140 mg/dL (7.8 mmol/L).

A portable recording system (SAS-2100, NIHONKOH DEN CO. Ltd., Tokyo) was used for calculating AHI and subjects were classified as not having SDB (AHI < 5), or having mild (AHI of

* Corresponding author.

E-mail address: kawada@nms.ac.jp (T. Kawada).

5–14.9), moderate (AHI of 15–30), or severe (AHI \geq 30) SDB, which was previously described [4].

2.1. Statistical analysis

The subjects were classified into four groups based on the severity of SDB, as described above. The analysis was carried out with the SPSS 21 software package (SPSS Japan, Tokyo). Logistic regression analysis was mainly used for the multivariate analysis and a two-tailed p-value of <0.05 was considered as denoting significance.

3. Results

The mean age (one standard deviation) of the subjects was 53.5 (10.4) years. The prevalence of specific medications, DGM and SDB are shown in Table 1. The prevalence of DGM was 56.7%, and the prevalence of mild, moderate and severe SDB were 35.3%, 20.7% and 14.4%, respectively. The prevalence of DGM in subjects with and without severe SDB was 64.9% and 55.3%, respectively. In addition, the prevalence of DGM in subjects with mild, moderate and severe SDB were 70.4%, 53.2% and 64.9%, respectively.

The geometric means of the serum C-reactive protein and AHI were compared between the patients with and without DGM (Table 2). There were significant differences in the mean values of serum CRP and AHI between two groups, and these two variables increased in subjects with DGM.

The adjusted odds ratio (OR) (95% confidence intervals [CI]) of AHI for DGM was 1.3 (0.87–2.0) (Table 3). When the AHI was categorized into four grades of severity of SDB, the adjusted ORs (95% CIs) of mild, moderate and severe SDB for DGM against no SDB were 2.9 (1.8–4.6), 1.2 (0.72–2.1) and 1.5 (0.80–3.0), respectively (Table 4).

4. Discussion

In this study, mild SDB was found to be significantly associated with the presence of DGM, which was inconsistent with past studies by Punjabi et al. [6,7]. In contrast, body mass index and aging was significantly associated with SDB as previously reported [8]. As our study was a cross-sectional study, the causal association could not be confirmed.

SDB was evaluated by determining the AHI, and a significant increase of the geometric mean of AHI was found in association with the presence of DGM. In addition, there was also a significant difference in the mean value of CRP between two groups. The significant association between serum CRP and DGM was confirmed by multivariate analysis, and mild SDB was only associated with DGM. Punjabi et al. reported that the adjusted

Table 1

The prevalence of hypertension and dyslipidemia treatments, prevalence of disorders of glucose metabolism and SDB (classified by the severity).

Variables	536 men
Hypertension treatment	17.5%
Dyslipidemia treatment	6.5%
Disorders of glucose metabolism	56.7%
SDB	
Mild	35.3%
Moderate	20.7%
Severe	14.4%

SDB, sleep disordered breathing.

Mild, moderate and severe SDB were defined as apnea-hypopnea index of 5–14.9, 15–29.9 and 30-, respectively.

Table 2

The geometric means (geometric standard deviation) of the serum CRP and AHI, stratified by the presence/absence of disorders of glucose metabolism.

Variables	DGM +	DGM –	Significance
CRP	0.068 (2.6)	0.048 (2.7)	$p < 0.001$
AHI	10.1 (2.8)	7.0 (3.6)	$p < 0.01$

CRP, C-reactive protein; AHI, apnea-hypopnea index; DGM, disorders of glucose metabolism.

Table 3

The odds ratios and 95% confidence intervals of each independent variable for disorders of glucose metabolism by multivariate logistic regression analysis.

Age	Odds ratio	95%CI	Significance
Age (one year increase)	1.02	1.00–1.04	$p < 0.05$
BMI (1 unit increase)	1.09	1.02–1.2	$p < 0.05$
Uric acid (1 mg/dL increase)	0.96	0.82 – 1.1	ns
No current smoking	1.08	0.65–1.8	ns
Regular exercise	0.80	0.56–1.2	ns
Not everyday drinking	1.1	0.74–1.7	ns
Log (CRP)	2.3	1.5–3.6	$p < 0.001$
Log (AHI)	1.3	0.87–2.0	ns

ns, not significant; CI, confidence interval; CRP, C-reactive protein; AHI, apnea-hypopnea index.

Table 4

The odds ratios and 95% confidence intervals of each independent variable for disorders of glucose metabolism by multivariate logistic regression analysis.

Age	Odds ratio	95%CI	Significance
Age (one year increase)	1.02	1.00–1.04	$p < 0.05$
BMI (1 unit increase)	1.1	1.04–1.2	$p < 0.01$
Uric acid (1 mg/dL increase)	0.98	0.83–1.1	ns
No current smoking	0.95	0.56–1.6	ns
Regular exercise	0.78	0.54–1.1	ns
Not everyday drinking	1.2	0.76–1.8	ns
Log (CRP)	2.0	1.3–3.2	$p < 0.01$
SDB			ns
Mild	2.9	1.8–4.6	$p < 0.001$
Moderate	1.2	0.72–2.1	ns
Severe	1.5	0.80–3.0	ns

ns, not significant; CI, confidence interval; CRP, C-reactive protein; SDB, sleep disordered breathing.

Mild, moderate and severe SDB were defined as AHI of 5–14.9, 15–29.9 and 30-, respectively.

ORs (95% CIs) of mild and moderate to severe SDB for fasting glucose intolerance were 1.27 (0.98–1.64) and 1.46 (1.09–1.97), respectively [7]. Their study outcome was not in concordance with our present results, presenting highest prevalence of DGM in subjects with mild SDB. Biological mechanism of non-linear association should be specified by further study.

In this study, three lifestyle factors were found to show no significant association with the presence of DGM. Mitchell et al. conducted a systematic review with meta-analysis and weight loss via intensive lifestyle interventions could be encouraged as a treatment for mild to moderate SDB [9]. Causal association between SDB and DGM should be confirmed by a prospective study, as reported on the association between SDB and incident diabetes mellitus [10].

Conflict of interest

We declare that there is no conflict of interest in this study.

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