Biomedical Research 2016; 27 (2): 537-542 *ISSN 0970-938X*
www.biomedres.info

Effects of sleep disorders and 25-OH Vitamin D levels on HbA1c levels in geriatric type 2 diabetic patients.

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Abstract

Introduction: Sleep disorders and insufficient vitamin D levels can impair control of diabetes mellitus. The aim of this study was to determine the prevalence of sleep disorders by using Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI) and by comparing them with a control group, and to investigate the possible relationship among sleep disorders, scores, 25-OH Vitamin D levels (25VD) and HbA1C levels.

Materials and method: This study was conducted in type 2 diabetic patients who attended to the family medicine outpatient clinic for routine controls. One hundred and six geriatric patients having type 2 diabetes were included in the study, and simultaneously selected 102 adult age group patients were taken as controls. Blood analyses for routine diabetes control parameters (HbA1c, fasting blood glucose, lipid profile) were performed. Target value for HbA1C was accepted as below %7. Demographic form, the Pittsburgh Sleep Quality Index, and Epworth Sleepiness Scale were used as the data collection instruments.

Results: There are significant differences in PSQI and ESS scores between adult and geriatric diabetic patients (6.16 ± 3.62 vs 6.96 ± 3.42, p=0.070 and 7.84 ± 5.37, p <0.001, respectively). 25VD levels were found as 22.40 ± 13.85 ng/ml in the adult group, 18.65 ± 14.17 ng/ml in the geriatric group. There is a significant difference between the groups in terms of vitamin D levels (p=0.007). Epworth categories were found to have an effect on HbA1c levels in geriatric patients. Changes in levels of ESS scores were found to be related with 4.784 fold increase in HbA1c levels. Vitamin D levels and ESS scores have major effects on HbA1C levels in elderly population (p=0.007, 0.001, respectively).

Conclusion: In elderly patients, low 25VD levels and daytime sleepiness are associated with abnormal HbA1c levels. These results are important indicators of roles of sleep quality and VD deficiency in glycemic control for elderly patients. In elderly diabetic patients, with difficult blood glucose regulation, sleep problems and VD deficiency must be considered.

Keywords: 25-OH-Vitamin D, Sleep disorders, Type 2 diabetes mellitus.

Accepted on February 15, 2016

Introduction

Diabetes mellitus is a metabolic disorder that negatively affects the quality and duration of life of the patients. Besides the deterioration of carbohydrate metabolism, in particular causing hyperglycemia, protein and lipid metabolisms are also affected. Although it is considered as a disease of developed countries, in recent years it became a very important and costly disease in the health care systems of developing countries. Incidence and prevalence of diabetes mellitus progressively increase with age. Diabetic patients over sixty-five years of age constitute almost 40% of all diabetics. Also, impaired glucose tolerance is common in geriatric population [1,2]. As a result of physiological changes caused by aging, alterations in the sleep cycle and a decrease in duration of sleep may be seen. Also,

the incidence of sleep disorders causing deterioration in the quality of life increases with advanced age [3].

Insomnia and hypersomnia are common in the elderly, but when these complaints become chronic they may need medical and psychosocial support because of impaired quality of life [4,5]. It is well known that insomnia can develop secondary to chronic health problems and it is also frequently associated with depression. Sleep disorders can also impair control of chronic diseases such as diabetes mellitus and hypertension. The frequently seen symptom in depressive elderly patients is waking up early in the morning. Rarely, prolonged sleeping and daytime sleepiness can be seen [3,4]. In diabetic patients, sleep disorders may be responsible for poor glycemic control, diabetic neuropathy and night hypoglycemia. According to studies, there is a bidirectional relationship between sleep disorders and diabetes. In other words, diabetes can cause sleep disorders, sleep disorders can cause diabetes and complicate the control of diabetes [5].

The production of vitamin D in the skin is reduced with age. Also, dietary intake of vitamin D is usually inadequate in elderly [6]. 25-OH VD is the main indicator of VD level of the body. Also, Vitamin D has an effect on sleep disorders [7]. The aim of this study was to determine the prevalence of sleep disorders in geriatric patients by using Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index and by comparing them with a control group, and to investigate the possible relationship among sleep disorders, scores, 25-OH Vitamin D levels (25VD) and HbA1C levels.

Material and Methods

This is a multicenter study which was conducted in the family medicine clinics of Yıldırım Beyazıt University Faculty of Medicine, Eskişehir Osmangazi University Faculty of Medicine, İnönü University Faculty of Medicine, and internal medicine clinic of Eskisehir Osmangazi University Faculty of Medicine. This study was conducted in type 2 diabetic patients who attended to outpatient clinics for routine controls. Patients who had cognitive impairment and patients who were under 18 years old were excluded. To the study, 106 geriatric patients (≥ 65 years old) and simultaneously selected 102 adult patients, who attended between May-October 2014, were included on a voluntary basis. Patients' sleep, sleep quality, and sleep scores were taken as the independent variables and HbA1C was taken as dependent variable. Blood analyses for routine diabetes control parameters (HbA1c, fasting blood glucose, low density lipoprotein, triglyceride) were taken. Target value for HbA1C was accepted as below 7% [8]. Complete blood cell count, liver function test values and TSH values were within normal limits. Body Mass Index (BMI) was defined as a person's weight in kilograms divided by the square of his height in meters (kg/m^2) by World Health Organization and BMI levels greater than or equal to 30 were accepted as obesity. The original study was approved by the local university ethics committee in Malatya İnönü University. Demographic form, the Pittsburgh Sleep Quality Index, and Epworth Sleepiness Scale were used as the data collection instruments. Sociodemographic characteristics of the patients were recorded.

Pittsburgh Sleep Quality Index (PSQI)

Pittsburgh Sleep Quality Index (PSQI) is a questionnaire evaluating the quality of sleep by measuring 7 domains as subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. Scoring of the answers is based on a 0 to 3 scale, whereby high scores reflect poor sleep quality. First, each of the 7 domains was considered in itself. Then, a calculated global sum of 7 domains as "5" or greater indicates "poor" sleep quality [9].

Epworth Sleepiness Scale (ESS)

Epworth Sleepiness Scale (ESS) is a scale intended to measure daytime sleepiness that is measured by use of a very short questionnaire. It was introduced in 1991 by Johns. Four ratings to a total of 8 questions were made. A score within the 10-24 range indicates daytime sleepiness [10].

25-OH-Vitamin D (25VD) levels

25VD results of last 3 months were retrospectively reviewed in patients who did not receive any VD support for the last 6 months. Vitamin D insufficiency was defined as serum 25VD level of <30 ng/ml [11].

Statistical analysis

Continuous data are given as mean ± standard deviation. The categorical data are given as percent (%). Shapiro-Wilk test was used to test for normality of data. The Mann-Whitney U-test was used for comparison of non-normally distributed variables between 2 groups. In the analysis of cross tables, Pearson Chi-square analyzes were used. A multivariate regression analysis was used to determine the risk factors. IBM SPSS Statistics 21.0 software was used for implementation of analyzes. $P<0.05$ was accepted as statistical significance. The ethical approval was obtained from Turgut Özal Medical Center Clinical Research Ethics Committee of Inonu University.

Results

A total of 208 patients, of whom106 were geriatric (36 female, 70 male), 102 were adult patients (25 male, 77 female), were included in study. There was no significant difference in terms of gender ($x^2=2.241$, $p=0.134$), smoking and obesity ratios ($x^2=1.366$, 2.187; $p=0.242$, 0.139, respectively) between the groups (Summarized in table 1). When the groups were evaluated for sleep disorders, there was a significant difference between Epworth and Pittsburgh scores ($x^2=9.997$, 5.075; $p=0.002$, 0.024, respectively). According to the ESS; excessive daytime sleepiness was seen in 57.4% in the geriatric group, whereas 35.3% in the adult group ($x^2=9.997$, $p=0.002$).In elderly patients, excessive sleepiness was found 2.473 times more than the adult group (OR=2.473; 95% CI 1.404-4.356).

According to Pittsburgh scale, poor sleep quality was seen in 72.8% in the geriatric group, whereas 57.8% in the adult group (x^2=5.075; p=0.024). In elderly patients, the risk of having poor sleep quality was found 1.952 times more than the adult group (OR=1.952; 95% CI 1.087-3.506).

Table 1. *Summary of the results.*

Categories		Groups		χ^2; p
		Adult n (%)	Geriatric n (%)	
Gender	Male	25 (%24.5)	36 (%34.0)	2.241; 0.134*
	Female	77 (%75.5)	70 (%66.0)	
SmokingStatus	Non-Smoker	87 (%85.3)	96 (%90.6)	1.366; 0.242**
	Smoker	15 (%14.7)	10 (%9.4)	
BMI	(Non-obese)	42 (%41.2)	54 (%51.4)	2.187; 0.139*
	Obese	60 (%58.8)	51 (%48.6)	
Epworth Sleepiness Scale	Normal	66 (%64.7)	43 (%42.6)	9.997; 0.002*
	Daytime Sleepiness	36 (%35.3)	58 (%57.4)	
Pittsburgh Sleep Quality Index	Good Sleeping Quality	43 (%42.2)	28 (%27.2)	5.075; 0.024*
	Poor Sleeping Quality	59 (%57.8)	75 (%72.8)	

*Pearson Chi-Square Test

**Yates's Chi-Square Test

25VD levels were found as 22.40 ± 13.85 ng/ml in the adult group, 18.65 ± 14.17 ng/ml in the geriatric group. There is a significant difference between the groups in terms of VD levels (p=0.007). When target fasting blood glucose value was taken as less than 100 mg/dl, target achievement rates for Fasting Plasma Glucose (FPG) were found as 24% in the adult group and 12.2% in the geriatric group (x^2=4.372; p=0.037). When target LDL (Low Density Lipoprotein) value was taken as less than 100 mg/dl, goal attainment rates for LDL were found as 21.6% in the adult group, 26.7% in the geriatric group (x^2=0.734; p=0.392) (Table 2).

Table 2. *Summary of theResults.*

Categories	Adult	Elderly	p
	Mean ± SD Median (Q1-Q3)	Mean ± SD Median (Q1-Q3)	
Age (years)	52.63 ± 8.56 54.00 (48.00-59.00)	71.16 ± 4.98 70.50 (68.00-74.00)	<0.001
25 (OH) Vitamin D (ng/ml)	22.40 ± 13.85 20.50 (11.30-28.55)	18.65 ± 14.17 12.85 (6.76-20.05)	0.007
Body Mass Index (kg/m2)	31.93 ± 6.36 31.17 (27.63-35.29)	30.15 ± 4.67 29.41 (27.31-32.72)	0.046
HbA1c (%)	7.23 ± 1.83 6.60 (6.02-7.75)	7.45 ± 1.42 7.25 (6.40-8.20)	0.021
Low-density lipoprotein (mg/dl)	127.62 ± 34.19 130.00 (104.00-147.25)	123.98 ± 39.26 118.00 (97.00-145.00)	0.357
Triglycerides (mg/dl)	161.31 ± 97.88 150.00 (96.00-195.75)	160.95 ± 77.97 146.50 (111.00-192.00)	0.702
ESS Scores	7.84 ± 5.37 7.00 (3.00-12.00)	10.96 ± 6.38 11.00 (6.00-15.25)	<0.001

PSQI Scores	6.16 ± 3.62 6.00 (3.00-9.00)	6.96 ± 3.42 7.00 (4.00-9.00)	0.070

Mann-Whitney U test

ESS: Epworth Sleepiness Scale; PSQI: Pittsburgh Sleep Quality Index.

According to multivariate regression analysis; the confounding variables thought to influence HbA1c levels are gender, 25VD levels, ESS scores and Pittsburgh scores. Binary logistic regression analysis was used to examine the impact on the patient and the adult groups. While gender, 25VD levels, ESS scores, and Pittsburgh scores had no significant effect on HbA1c levels in the adult group (p=0.380, 0.482, 0.468, 0.862, respectively), ESS categories were found to have an effect on HbA1c levels in elderly population. The risk of not achieving target HbA1c in elderly patients with excessive daytime sleepiness according to the ESS results was almost 5 times more than the geriatric group who have normal sleep quality (OR=4.784; 95% CI 2.041-11.235). 25VD levels, ESS scores, and Pittsburgh scores were analyzed by the logistic regression model to evaluate their effects on HbA1c levels. VD levels and ESS scores have major effects on HbA1C levels in elderly population (p=0.007, 0.001, respectively).When target HbA1c level was taken as 7%, target levels were achieved in 58.8% of the adult group, 45.7% of the geriatric group (x^2=3.563; p=0.059).

Discussion

Sleep quality and daytime sleepiness are important parameters that affect the sleep alertness function. The aging process causes many changes on sleep. Sleep problems, increasing with age, adversely affect the quality of life of the elderly. However, depending on the poor quality of life, sleep problems are important risk factors for mortality especially in elderly, and there is a strong link between sleep problems and premature death [12]. Excessive daytime sleepiness is a common condition that occurs in the sleep deprivation, irregular sleep, intrinsic sleep disorders and other medical problems [4,5]. According to the results of our study, in comparison to adult patients, geriatric patients have increased disturbances in sleep quality and daytime sleepiness; according to ESS, daytime sleepiness negatively affect HbA1c levels and makes it difficult to reach target HbA1c levels. These findings are parallel to the findings of other studies. Impaired sleep quality and daytime sleepiness are factors that complicate the control of type 2 DM [13].

Studies show that sleep disorders are associated with cardiovascular diseases, hypertension, metabolic syndrome, impaired glucose tolerance, type 2 diabetes and quality of life. Knowing the factors associated with sleep quality and daytime sleepiness may provide better diagnostics and treatment of sleep problems. Therefore, it is important to assess sleep problems and take precautions [13,14]. Diabetic patients with excessive daytime sleepiness have higher HbA1c and Body Mass Index (BMI) levels [15]. Poor sleep quality and daytime sleepiness affect diabetes care profile. According to studies, daytime sleepiness complicates control of the diabetes and it is recommended that patients should be screened for sleep disorders [16].

Nowadays, VD deficiency has become a more common problem [17]. Deficiency of VD levels causes increased bone turnover rate, osteoporosis and osteomalacia. It also causes diabetes, hypertension, cancer and autoimmune diseases, most of which lead to hip and other bone fractures. Therefore, it is effective in mortality and has become a major health problem in the world [18]. Obesity is common in type 2 diabetic patients; since it is stored in fat tissue, the bioavailability of VD is reduced and can cause VD deficiency. In this study, despite the absence of significant differences in BMI and obesity levels between elderly and adult groups, levels of 25VD was lower in elderly patients. Due to lack of VD synthesis, its deficiency is expected to be seen more common in elderly [19].

When HbA1c target value was accepted as ≤ 7%, in the control group 58.8%, in the elderly group 45.7% of patients were within normal limits (x^2=3563, p=0.059). Statistical analysis revealed that, besides ESS score, also 25VD levels affect HbA1c levels in elderly patients. According to longitudinal follow-up study, low VD levels are effective on all-cause mortality and cardiovascular mortality; also, this effect is valid for type 2 diabetic patients (VD-DM mortality). According to studies, type 2 DM and metabolic syndrome-related conditions are associated with adverse VD status [20,21]. According to another study, when VD is given to deficient individuals moderate improvement was seen in insulin resistance [22].

HbA1c is the most important indicator of glycemic control and recently it is used in the diagnosis of early stages of DM [23]. It is known that, there is an inverse relationship between HbA1c and 25VD. In our study, there was a statistically significant negative effect of 25VD on HbA1c [24,25]. VD deficiency leads to decreased insulin secretion by causing calcium deficit in islet beta cells. Also, VD can cause insulin resistance and glucose intolerance by increasing insulin sensitivity [26]. The mechanistic role of insulin therapy in mediating the functional responses has been recently proved in elderly patients [27]. Also it was shown that reduced β(2)AR expression can be the reason of age-related decline of glucose tolerance [28]. Limitations of the study were the lack of family history, pre-diabetes history. As we could not evaluate the pre-diabetic or family history of our subjects which are the important factors for cardiovascular morbidity and mortality in diabetic patients [29].

Conclusion

In conclusion, in geriatric patients, low 25VD levels and daytime sleepiness are associated with abnormal HbA1c levels. These results are important indicators of roles of sleep quality and VD deficiency in glycemic control for elderly patients. In geriatric diabetic patients, with difficult blood glucose regulation, sleep problems and VD deficiency must be considered.

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