Night Shift Work, Sleep Quality, and Obesity

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Background: The aims of this study were to examine the relationship between night shift work and sleep, to investigate the correlations with various biomarkers that show the influence of sleep on obesity, and ultimately, to analyze factors that have an impact on obesity.

Methods: This study used data from the National Survey of Midlife Development in the United States II (MIDUS II study) and the MIDUS II Biomarker Project. After connecting the MIDUS II study data with the MIDUS II Biomarker Project data, we analyzed data from 883 subjects to investigate the relationship between night shift work and sleep quality. We also examined the correlations with biomarkers and sleep quality. Lastly, we performed logistic regression analyses to investigate factors that had an impact on obesity.

Results: Sleep quality was found to be low among night shift workers. Sleep quality was positively correlated with HbA1c, total cholesterol, and triglyceride levels, and inversely correlated with DHEA levels. Sleep quality was highly correlated with inflammatory markers and inversely correlated with antioxidant markers. Sleep quality was significantly associated with obesity (OR: 1.10, 95% CI: 1.03-1.18). Biomarkers that had an influence on obesity included diastolic blood pressure, HbA1c and triglyceride levels, inflammatory markers, and antioxidant values.

Conclusion: Poor sleep quality due to night shift work disturbs the circadian rhythm, causing negative changes in metabolic, inflammatory, neuroendocrine, and antioxidant biomarkers. These changes may eventually play a role in increasing the incidence of obesity.

Key Words: Shift work, Sleep, Obesity, Biomarker

INTRODUCTION

Shift work that occurs primarily outside of conventional daytime working hours has become more common as industrial processes have diversified in modern society. In the US, at least 20% of the working population is engaged in shift work. Companies have implemented shift work systems for reasons of work continuity, work efficiency, and economic benefit; however, shift work can disturb a worker's circadian rhythm and induce physiological malfunction. In particular, night shift workers may have more difficulty in falling asleep than day shift workers. They may experience a shortage of sleeping hours and poor quality of sleep, and could develop obesity and various health problems due to chronic fatigue [1,2].

Shift work and lack of sleep are associated with obesity. Recently, there has been an increase in the number of people experiencing sleep deprivation around the world [3]. Over the past several decades, the obesity epidemic in the US has been related to a decrease in the number of Americans sleeping for eight hours or more, as reported by the National Sleep Foundation [4].

Many epidemiological studies have demonstrated that lack

of sleep is related to the incidence of obesity. The findings in 31 cross-sectional and 5 cohort studies suggest that short sleep duration is strongly and consistently associated with concurrent and future obesity [4]. Sleep deprivation has an influence on obesity because workers tend to have more chances to eat during their night shift, which leads to an increase in caloric intake and fatigue, and a resulting decrease in physical activity [5].

The biological mechanism through which lack of sleep results in obesity can be explained by the circadian cycle disruption that is attributable to day and night reversal. In particular, a major function of the circadian system is to regulate the physiological function of the human body with the help of the clock center that is located in the suprachiasmatic nucleus (SCN), at the intersection with the optic nerve. This internal control is synchronized to the exogenous environment through signals, such as the transient night and day cycle, where light is captured by the retina [6]. Activator proteins such as CLOCK and BMAL-1, which play a core function in the neural circadian master clock, exist not only in the SCN, but also in adipose tissue. The peripheral clocks are synchronized by the central SCN clock and control the secretion of glucocorticoids, melatonin, and other mediators [7]. Therefore, if there is a lack of sleep, activation of the hypothalamus-pituitary-adrenal (HPA) axis and dysregulation of the autonomic nervous system cause hormonal changes, which lead to a decrease in melatonin. Consequently, metabolic dysfunction occurs, leading to an increase in insulin resistance, pro-inflammatory cytokines, and oxidative stress. This eventually results in a greater incidence of obesity [8-10].

Many of the studies mentioned above examined the relationships between shift work and sleep, shift work and obesity, and sleep and obesity; however, no single study has covered all of these processes (shift work, sleep, biomarkers, and obesity). The aims of this study were thus to examine the relationship between night shift work and sleep, to investigate the correlations between various biomarkers and quality of sleep, and ultimately, to analyze factors that have an impact on obesity.

MATERIALS AND METHODS

1. Study subjects

This study used data from the National Survey of Midlife Development in the United States II (MIDUS II study) and the MIDUS II Biomarker Project [11]. The total number of study subjects was 4,693 for the MIDUS II study and 1,255 for the MIDUS II Biomarker Project. After connecting the two data sets, the information for 1,255 subjects was extracted. Among them, 372 patients who were diagnosed with or treated for cardiovascular disease were excluded, which brought the final number of study subjects to 883.

2. Survey variables

- A night shift worker was defined as a person who reportedly works more than one night per month, with 'night' defined as any time between 9:30 pm and 4:30 am, or overnight.

- Sleep quality was examined using the Pittsburgh Sleep Quality Inventory (PSQI) questionnaire that was developed by Buysee et al. [12]. The questionnaire has 19 questions in 7 components and includes subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance range, use of sleeping medication, and daytime dysfunction. The questions were scored from 0-3 points. In the questionnaire, 0 points indicated "no problems" while 3 points indicated a serious problem. The scores for the 7 components were added to form one global score.

- As for biomarkers, we used data from the MIDUS II Biomarker Project. They classified biomarkers into 5 categories:

Cholesterol panel - Total cholesterol, HDL cholesterol, Triglycerides

Glycosylated hemoglobin

Neuroendocrine - dehydroepiandrosterone (DHEA)

Inflammatory - Interleukin 6 (IL 6), C-reactive protein (CRP), Intracellular adhesion molecule (ICAM), Fibrinogen, E-Selectin

Antioxidant - all-trans-beta-carotene, 13-cis-beta-carotene, alpha-carotene, beta-cryptoxanthin, lutein, zeaxantin, lycopene, retinol, gamma-tocopherol

- Obesity was defined as a body mass index of 30 kg/m^2 or higher, based on measured height and weight.

3. Analysis method

To investigate the relationship between night shift work and sleep quality, a *t*-test was conducted. To assess the correlations between biomarkers and sleep quality, a correlation analysis was conducted. Logistic regression analyses were performed to examine the factors influencing obesity. Independent variables were PSQI and biomarkers, while the dependent variable was BMI. In regard to confounding variables, model 1 was adjusted for age and sex, while model 2 was adjusted for age, sex, income, smoking, and drinking.

RESULTS

The study subjects averaged 53.95 years of age and included 495 women (56.1%) and 388 men (43.9%); thus, the women outnumbered the men by a significant margin. Current smokers made up 11.2% of the population, 41.6% never smoked, and 47.2% were non-smokers. Sixty-five percent of the population drank alcohol, while 35% did not. With respect to employment status, 65.3% of the subjects were full-time workers, while 19.3% were unemployed. There were 110 (20.9%) night shift workers in the study population (Table 1).

The relation between night shift work and sleep quality was examined. The global score representing quality of sleep was significantly higher in the night shift workers. Moreover, the scores for subjective sleep quality, sleep duration, habitual sleep efficiency, and daytime dysfunction were also significantly higher in the night shift workers (Table 2).

Table 1. General subject characteristics, including occurrence of night shift work, pittsburgh sleep quality inventory scores, and incidence of obesity

Variable	N (%), Mean ± SD
Age (years)	53.95 ± 11.45
Sex	
Women	495 (56.1)
Men	388 (43.9)
Smoking	
Current smoker	99 (11.2)
Never smoked	367 (41.6)
Non-smoker	417 (47.2)
Alcohol drinking	
Yes	574 (65.0)
No	309 (35.0)
Income ($1,000/year)	17.08 ± 11.64
Employment status	
Full time	528 (65.3)
Part time	110 (13.6)
Other	170 (19.3)
Night shift work	
Yes	110 (20.9)
No	764 (79.1)
Pittsburgh sleep quality inventory	
Global score	5.82 ± 3.37
Subjective sleep quality	0.95 ± 0.67
Sleep latency	0.86 ± 0.90
Sleep duration	0.78 ± 0.74
Habitual sleep efficiency	0.71 ± 1.16
Sleep disturbance range	1.27 ± 0.56
Use of sleep medicine	0.54 ± 1.03
Daytime dysfunction	0.78 ± 0.65
Obesity	
BMI < 30	555 (62.8)
BMI ≥ 30	328 (37.2)

Table 2. Association between PSQI and night shift work

PSQI	Night shift work		p-value
	No	Yes	
Global score	5.42 ± 3.05	6.27 ± 3.21	0.01
Subjective sleep quality	0.73 ± 0.63	0.95 ± 0.65	0.02
Sleep latency	0.79 ± 0.85	0.84 ± 0.87	0.58
Sleep duration	0.77 ± 0.70	0.98 ± 0.78	0.01
Habitual sleep efficiency	0.55 ± 1.05	0.83 ± 1.28	0.02
Sleep disturbance range	1.23 ± 0.52	1.24 ± 0.59	0.77
Use of sleep medicine	0.45 ± 0.96	0.55 ± 1.08	0.37
Daytime dysfunction	0.75 ± 0.63	0.97 ± 0.68	0.03

PSQI: Pittsburgh sleep quality inventory.

According to our results, sleep quality appears to be positively correlated with HbA1c levels (a marker for insulin resistance) and with total cholesterol and triglyceride levels (markers for hyperlipidemia). In addition, sleep quality was inversely correlated with DHEA levels (a neuroendocrine marker). With respect to relationships with inflammatory markers, sleep quality showed the highest correlation with IL6, CRP, and ICAM levels. Sleep quality was inversely correlated with all-trans-beta-carotene, 13-cis-beta-carotene, alpha-carotene, and lutein (antioxidant markers) (Table 3).

According to our logistic regression analyses, sleep quality had a significant influence on obesity, with an odds ratio of 1.10 (1.03-1.18). The specific factors that were influenced were subjective sleep quality, sleeping duration, sleep disturbance, and daytime dysfunction (Table 4).

Diastolic blood pressure and HbA1c levels were both significantly correlated with sleep quality with odds ratios of 1.03 (1.02-1.05) and 1.86 (1.28-2.70), respectively. With respect to the cholesterol panel, triglyceride levels were also significantly correlated with sleep quality with an odds ratio of 1.01 (1.00-1.01); inflammatory markers showed the same correlation with an odds ratio of 1.25 (1.11-1.39) for IL6, 1.12 (1.04-1.21) for CRP, and 1.02 (1.01-1.04) for E-selection. Antioxidants were also similarly correlated for all-trans-beta-carotene, 13-cis-beta-carotene, alpha-carotene, beta-cryptoxanthin, and lutein (Table 5).

DISCUSSION

In general, shift work lowers quality of sleep compared to daytime work. Many researchers have used the PSQI to measure sleep quality. They have also reported that sleep quality is consistently lower among shift workers [13,14].

Night shift workers have difficulties in falling asleep due to circadian cycle disruptions and their sleeping hours are reduced by 2-3 hours a night compared to their sleeping

Table 3. Correlation between sleep global score and biomarkers

Variable	Correlation coefficient	p-value
SBP (mmHg)	0.01	0.78
DBP (mmHg)	0.03	0.43
HbA1c (mg/dl)	0.07	0.04
Total C (mg/dl)	0.09	0.01
Triglycerides (mg/dl)	0.16	0.00
HDL C (mg/dl)	−0.03	0.44
DHEA (ng/dl)	−0.11	0.00
IL6 (pg/ml)	0.12	0.00
CRP (ug/ml)	0.10	0.01
ICAM (ng/ml)	0.13	0.00
Fibrinogen (mg/dl)	0.04	0.23
E-Selectin (ng/ml)	0.06	0.11
All trans-beta-carotenes (uM)	−0.08	0.04
13-cis-beta-carotene (uM)	−0.07	0.04
Alpha-carotene (uM)	−0.07	0.04
Beta-cryptoxanthin (uM)	0.01	0.91
Lutein (uM)	−0.08	0.03
Zeaxanthin (uM)	−0.05	0.14
Lycopene (uM)	−0.06	0.08
Retinol (uM)	0.06	0.08
Alpha-tocopherol (uM)	0.03	0.38
Gamma-tocopherol (uM)	0.15	0.00

SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: hemoglobin A1c, Total C: total cholesterol, HDL C: HDL cholesterol, DHEA: dehydroepiandrosterone, IL6: interleukin 6, CRP: C-reactive protein, ICAM: Intracellular adhesion molecule.

Table 4. Odds ratio (95% confidence interval) of PSQI for obesity (body mass index ≥ 30)

PSQI	Model 1		Model 2	
	Adjusted OR	95% CI	Adjusted OR	95% CI
Global score	1.07	1.03-1.12	1.10	1.03-1.18
Subjective sleep quality	1.38	1.12-1.69	1.46	1.04-2.05
Sleep latency	1.14	0.98-1.33	1.14	0.89-1.48
Sleep duration	1.23	1.03-1.48	1.22	1.01-1.50
Habitual sleep efficiency	1.07	0.95-1.20	0.96	0.79-1.16
Sleep disturbance range	1.51	1.18-1.93	1.69	1.12-2.57
Use of sleep medicine	1.17	1.03-1.33	1.09	0.65-1.83
Daytime dysfunction	1.30	1.05-1.60	1.42	1.01-2.03

PSQI: Pittsburgh sleep quality inventory, OR: odds ratio, 95% CI: 95% confidence interval, Model 1: adjusted for age and sex, Model 2: adjusted for age, sex, income, smoking, and drinking.

Table 5. Odds ratio (95% confidence interval) of biomarkers for obesity (body mass index ≥ 30)

Variable	Model 1		Model 2	
	Adjusted OR	95% CI	Adjusted OR	95% CI
SBP (mmHg)	1.02	1.01-1.02	1.02	0.49-1.04
DBP (mmHg)	1.03	1.01-1.04	1.03	1.02-1.05
HbA1c (mg/dl)	1.44	1.21-1.72	1.86	1.28-2.70
Total cholesterol (mg/dl)	1.01	0.99-1.01	1.00	0.98-1.02
Triglycerides (mg/dl)	1.01	1.01-1.02	1.01	1.00-1.01
HDL cholesterol (mg/dl)	0.96	0.94-0.97	0.95	0.93-0.97
DHEA (ng/dl)	0.98	0.95-1.01	0.96	0.90-1.02
IL6 (pg//ml)	1.16	1.09-1.23	1.25	1.11-1.39
CRP (ug/ml)	1.16	1.10-1.22	1.12	1.04-1.21
ICAM (ng/ml)	1.01	1.00-1.01	1.00	0.99-1.01
Fibrinogen (mg/dl)	1.01	1.00-1.01	1.00	0.99-1.02
E-Selectin (ng/ml)	1.03	1.02-1.04	1.02	1.01-1.04
All trans-beta-carotene (uM)	0.31	0.22-0.45	0.29	0.15-0.54
13-cis-beta-carotene (uM)	0.02	0.01-0.10	0.01	0.00-0.12
Alpha-carotene (uM)	0.01	0.00-0.11	0.01	0.00-0.13
Beta-cryptoxanthin (uM)	0.04	0.01-0.13	0.02	0.00-0.17
Lutein (uM)	0.11	0.05-0.27	0.12	0.03-0.46
Zeaxantin (uM)	0.01	0.00-0.15	0.20	0.50-3.08
Lycopene (uM)	0.59	0.31-1.08	0.43	0.16-1.17
Retinol (uM)	1.29	1.05-1.59	1.22	0.87-1.71
Alpha-tocopherol (uM)	1.00	0.99-1.02	0.99	0.97-1.02

SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: hemoglobin A1c, DHEA: dehydroepiandrosterone, IL6: interleukin 6, CRP: C-reactive protein, ICAM: intracellular adhesion molecule.

hours when they work in the daytime [15,16]. In particular, night shift workers reportedly slept four or more fewer hours per week, even though they slept more in order to make up for their sleep debt when they were off work [6]. Workers who are required to sleep in the daytime also face difficulties in their everyday lives because they experience sleep disruptions, decreased vigilance, general feelings of malaise, and decreased mental efficiency [17]. This study also found that night shift workers had a decrease in sleeping hours, a decline in subjective sleep quality, and significantly high daytime dysfunction.

Why is it that short sleep duration and poor sleep quality increase the risk of obesity? First, shift work causes disturbances to the circadian rhythm; in particular, sleep rhythm and sleep duration both play a critical role. Second, dysregulation of the autonomic nervous system and activation of the HPA axis have an impact on the incidence of obesity [8,18]. Third, sleep has a major influence on metabolic hormones that regulate energy balance; sleep restriction decreases blood leptin levels that suppress appetite

and increases ghrelin levels that promote appetite [19,20]. Fourth, lack of sleep decreases melatonin levels, causing metabolic dysfunction, which results in increasing insulin resistance, pro-inflammatory cytokine levels, oxidative stress, and hormonal changes, ultimately leading to obesity [8-10,20].

This study intended to investigate the mechanism linking poor sleep quality and obesity. We analyzed the relationships between sleep quality and diverse biomarkers such as hypertension, cholesterol panel levels, insulin resistance, inflammatory biomarkers, neuroendocrine biomarkers, and anti-oxidant biomarkers, and their influence on obesity. We found a significant correlation between sleep quality and HbA1c levels, a marker for insulin resistance. Sleep quality also showed a positive correlation with total cholesterol and triglyceride (TG) levels, which are markers for diastolic blood pressure and hyperlipidemia. As explained above, metabolic dysfunction that is attributable to short sleep duration and poor sleep quality may lead to increases in blood pressure, insulin resistance, blood glucose levels, and hyper-

lipidemia [21-23].

In this study, DHEA level, a neuroendocrine marker, had an inverse correlation with obesity. DHEA was found to help prevent persons from developing obesity or fatty liver disease. Consequently, a decrease in DHEA levels can be directly related to obesity. Tchernof and Labrie [24] reviewed human studies and reported that DHEA levels had a negative correlation with obesity.

In this study, sleep quality was highly correlated with levels of the inflammatory markers IL6, CRP, and ICAM. Other studies have also shown a close relationship between IL6 and sleep [25]. Sleep deprivation has been reported to influence CRP and inflammatory marker levels, which reportedly have an impact on obesity [26]. E-Selection and ICAM had a high correlation with total fat volume [27].

This study demonstrated that the antioxidant markers of all-trans-beta-carotene, 13-cis-beta-carotene, alpha-carotene, and lutein are inversely correlated with sleep and obesity. In general, systematic oxidative stress is known to be correlated with obesity [28]. As a result, an increase in oxidative stress leads to a decrease in total antioxidants. Chrysohoou et al. [29] also reported that a decrease in total antioxidants had a high relation with obesity.

Epidemiological studies often focus on the relationship between shift work and obesity, or between sleep and obesity; however, there have been few studies analyzing such relationships alongside the mechanisms of obesity. Some studies on the mechanisms of obesity have been conducted in the laboratory, while those that have targeted humans have been limited to a small number of study subjects or a specific field. The current study is meaningful in that it is a large-scale epidemiological study that targeted American adults, combined with a biomarker study that enabled the investigation of various mechanisms of obesity.

In conclusion, poor sleep quality due to night shift work disturbs the circadian rhythm, causing negative changes in metabolic, inflammatory, neuroendocrine, and antioxidant biomarkers. Such negative changes may eventually play a role in increasing the incidence of obesity.

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