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Effect of an Anti-Inflammatory Dietary Pattern on the Risk of the Common Chronic Sleep Disorder Comorbidities

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Abstract

Objective: The objective of this study is to explore the relationship between an anti-inflammatory dietary pattern (AID) and common chronic sleep disorder comorbidities.

Methods: This study analyzed data from the National Health and Nutrition Survey of the United States from 2009 to 2018. The anti-inflammatory dietary patterns of 5093 subjects were assessed using the dietary inflammatory index. The index was calculated as the intake of nutrients and other food components that were collected via a 24-hour dietary recall for two consecutive days. A questionnaire survey was administered to determine the chronic comorbidities of the subjects. A logistic regression was used to analyze the relationship between an AID and common chronic sleep disorder comorbidities.

Results: The average age of the subjects was 53 (16) years old, and the P25, P50, and P75 of the scores of the dietary inflammation index were 0.29, 2.39, and 4.17, respectively. Among the subjects, 58.2% had common chronic sleep disorder comorbidities. The logistic regression results showed that after controlling the demographic characteristics, the AID reduced the risk of common chronic sleep disorder comorbidities, and the model was stable.

Conclusion: The higher the adherence to an anti-inflammatory dietary pattern, the lower the risk of the common chronic sleep disorder comorbidities. An AID can be implemented among patient populations with sleep disorders to prevent the occurrence of common chronic sleep disorder comorbidities.

Keywords: Anti-Inflammatory Dietary; Sleep Disorder; insomnia

Introduction

Sleep can eliminate fatigue, improve immunity, recover physical strength, and relieve mood. When an individual's sleep-wake homeostasis mechanism and internal biological clock are abnormal, various types of sleep disorders, such as psychophysiological insomnia, idiopathic insomnia, and contradictory insomnia, can be triggered [1]. Sleep disorders can cause inflammation, oxidative stress, insulin resistance, endothelial dysfunction, circadian rhythm disorder, and autonomic nervous dysfunction. These are the underlying mechanisms that can lead to cardiovascular disease, metabolic system disease, nervous system disease, hypertension, diabetes, and depression [2-4]. Due to the high prevalence of sleep disorders worldwide and the close relationship between hypertension, diabetes, depression, and sleep disorders, it is of great significance to control these common chronic sleep disorder comorbidities and slow down the secondary deterioration due to these comorbidities. In addition, such comorbidities may easily lead to more serious health problems than those only caused by sleep disorders.

Some inflammatory processes are risk factors of depression [5]. Therefore anti-inflammation may help control depressive symptoms among people with sleep disorders. Diet can moderate the concentrations of inflammatory mediators [6]. For instance, there is an association between high intake levels of whole grains, vegetables, fruit, fish, and yogurt and low levels of inflammatory mediators [7, 8]. In addition, a study has shown that a dietary pattern like the Mediterranean dietary pattern might have a protective effect and decline inflammatory mediator concentrations [9]. Studies have shown that an anti-inflammatory dietary pattern (AID) might decrease the risk of hypertension, diabetes, and depressive symptoms among healthy adults [10-12].

There is a limitation in the exploration of the association between adherence to an AID and the onset of these the common chronic sleep disorder comorbidities. Therefore, in this study, the aim is to evaluate whether adherence to an AID can decrease common chronic sleep disorder comorbidities in sleep disorder patients.

Methods

The subjects were collected from the National Health and Nutrition Examination Survey (NHAENS) from 2009 to 2018.

We excluded those with incomplete data (including sociodemographic characteristics, diet, lifestyle behaviors characteristics, and health characteristics), those below 20 years of age, those pregnant, and those without sleep disorders. As a result, 5093 subjects were included in the study (Table 1).

The survey obtained the approval of the ethics committee of the National Center for Health Statistics in the USA. All of the subjects signed informed consents prior to the investigation.

Assessment of the Adherence to an Anti-Inflammatory Dietary Pattern

The adherence to an AID was assessed using the dietary inflammatory index (DII). Two consecutive days of 24-hour dietary recalls were utilized to collect the subjects' food consumption. The DII was then calculated. $DII = \sum((Component\ intake - Global\ standard\ mean)/Global\ standard\ deviation)$ Total inflammatory effect score. Details regarding the DII are available in a previous publication [13]. Subjects with higher DIIs had lower adherences to an AID.

Assessment of the Common Chronic Comorbidities of Sleep Disorders among Sleep Disorder Patients

In this study, the prevalence of hypertension and the prevalence of diabetes were divided into two parts according to whether the subjects were diagnosed by doctors. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 score ranged from 0 to 27. When the PHQ-9 score ranged from 10 to 27, this meant the individual had moderate or severe depressive symptoms. The higher the PHQ-9 score, the higher the symptoms of depression. Details regarding PHQ-9 are available in a previous publication [14]. The common chronic sleep disorder comorbidities were classified as binary variables of yes or no according to whether the subjects had at least one type of hypertension, diabetes, or moderate or severe depression symptoms.

The other variables in the study were sociodemographic characteristics, lifestyle behaviors characteristics, and other health characteristics. The sociodemographic characteristics included age, gender, marital status, education level, and the family poverty-to-income ratio (PIR). The lifestyle behavior characteristics included smoking status and weekly sedentary time. Other health characteristics included the body mass index (BMI), hypertension status, and diabetes status. We classified

the smoking status into two types, namely, smoked at least 100 cigarettes in their life and smoked less than 100 cigarettes in their life. We classified the hypertension status and diabetes status into two types, namely, having a diagnosis or not. See Table 1 for details.

The descriptive statistics for the continuous variables (age, PIR, PHQ-9 score, and BMI) were estimated as the mean (standard deviation). We calculated the frequency (proportion) for the categorical variables (gender, marital status, education level, smoking status, moderate or severe depressive symptoms, hypertension status, and diabetes status). A logistics regression with robust standard errors was used to determine the association between adherence to an AID and the common chronic sleep disorder comorbidities among sleep disorders across the DII quartile (-P25, P25-P50, P50-P75, P75-) when controlling the covariates. In the sensitivity analyses, we additionally controlled for (1) health conditions and (2) lifestyle behaviors (Table 2). The significance of all of the tests was based on two-sided tests, and the confidence interval was 95%.

Results

The subject characteristics are presented in Table 1. Approximately half of the subjects were female (58.4%), and individuals were an average of 53.03 years of age (standard error [SD] = 16.08). The P_{25} , P_{50} , and P_{75} scores of the DII were 0.61, 2.79, and 4.55.

Individuals with the lowest DII score (Q_1) compared to other DII scores (Q_2 , Q_3 , and Q_4) were somewhat younger and had higher BMIs. Individuals with the lowest DII score (Q_1) compared to higher DII scores (Q_3 and Q_4) had family PIR scores. Additionally, there was an association between the DII scores and the common chronic sleep disorder comorbidities with $\chi^2 = 48.47$ ($P < 0.001$).

The association between adherence to an AID and the common chronic sleep disorder comorbidities is detailed in Table 2. In the unadjusted model, compared with the subjects with a DII score in Q_4 , those with a lower DII score had a 22.9% to 38.3% lower probability of having the common chronic sleep disorder comorbidities (Q_1 OR = 0.617, 95% CI: 0.5260.723; Q_2 OR = 0.697, 95% CI: 0.5940.818; Q_3 OR = 0.771, 95% CI: 0.6570.905).

Table 2 shows the sensitivity analysis results. In the primary model that only controlled demographic variables, each OR value (Q_1 OR = 0.715, 95% CI: 0.9560.858; Q_2 OR = 0.748, 95% CI: 0.6260.895; Q_3 OR = 0.792, 95% CI: 0.6640.944) had a statistical significance ($P < 0.05$) similar with additional controlled physical characteristics (Q_1 OR = 0.760, 95% CI: 0.6280.920; Q_2 OR = 0.742, 95% CI: 0.6280.920; Q_3 OR = 0.800, 95% CI: 0.6650.961) or additional controlled lifestyle characteristics (Q_1 OR = 0.719, 95% CI: 0.5990.863; Q_2 OR = 0.750, 95% CI: 0.6260.897; Q_3 OR = 0.800, 95% CI: 0.6710.955).

Table 1: Characteristics of adults with sleep disorder and by DII quartile

	N(%) or Mean (Standard Error)				
	Overall	Q_1 DII, $-P_{25}^{\wedge}$	Q_2 DII, P_{25-P50}^{\wedge}	Q_3 DII, P_{50-P75}^{\wedge}	Q_4 DII, P_{75}^{\wedge}
	(n=5093)	(n=1274)	(n=1273)	(n=1277)	(n=1269)
Sociodemographic					
Mean age	53.027(16.077)	51.490(16.067)	53.452(15.648)	53.517(16.333)	53.650(16.171)
Females	2972(58.4)	530(41.6)	687(54.0)	822(64.4)	933(73.5)
Marital status					
Married	2437(47.8)	650(51.0)	662(52.0)	601(47.1)	524(41.3)
Widowed	471(9.2)	84(6.6)	105(8.2)	127(9.9)	155(12.2)
Divorced	772(15.2)	169(13.3)	172(13.5)	207(16.2)	224(17.7)
Separated	211(4.1)	48(3.8)	45(3.5)	51(4.0)	67(5.3)

Never married	821(16.1)	228(17.9)	193(15.2)	190(14.9)	210(16.5)
Living with partner	381(7.5)	95(7.5)	96(7.5)	101(7.9)	89(7.0)
Education level					
Less than 9th grade	319(6.3)	47(3.7)	62(4.9)	98(7.7)	112(8.8)
9-11th grade	642(12.6)	112(8.8)	119(9.3)	184(14.4)	227(17.9)
High school graduate/GED or equivalent	1186(23.3)	235(18.4)	315(24.7)	305(23.9)	331(26.1)
Some college or AA degree	1755(34.5)	456(35.8)	416(32.7)	445(34.8)	438(34.5)
College graduate or above	1191(23.4)	424(33.3)	361(28.4)	245(19.2)	161(12.7)
Mean family PIR	2.488(1.643)	2.803(1.685)	2.750(1.667)	2.389(1.593)	2.010(1.497)
Lifestyle Behaviors					
Smoked less than 100 cigarettes in life	2362(46.4)	576(45.2)	637(50.0)	610(47.8)	539(42.5)
Sedentary time weekly	386.343(204.814)	397.005(206.342)	397.320(210.985)	375.863(196.532)	375.173(204.250)
Health					
BMI	30.918(7.974)	30.112(7.867)	30.967(7.883)	30.954(7.820)	31.644(204.250)
Diagnose with hypertension	2553(50.1)	595(46.7)	624(49.0)	639(50.0)	695(54.8)
Diagnose with diabetes	999(19.6)	203(15.9)	241(18.9)	261(20.4)	294(23.2)
Moderate or severe depressive symptoms	419(8.2)	81(6.4)	81(6.4)	107(8.4)	150(11.8)
Having the common chronic comorbidities of sleep disorders	2963(58.2)	677(53.1)	715(56.2)	749(58.7)	447(35.2)

$$^{\wedge}P_{25} \leq 0.29; P_{25}-P_{50} 0.30-2.39; P_{50}-P_{75} 2.40-4.17; P_{75} > 4.18;$$

Q=Quartile; DII=Dietary Inflammatory Index; GED=General Educational Development; family PIR=family Poverty- to -income ratio.

Table 2: Association between DII and depression

	Odds Ratio (95% Confidence Interval)		
	Q ₁	Q ₂	Q ₃
Unadjusted Model	0.617(0.526,0.723) ^{***}	0.697(0.594,0.818) ^{***}	0.771(0.657,0.905) [†]
Primary Model ¹	0.715(0.956,0.858) ^{***}	0.748(0.626,0.895) ^{**}	0.792(0.664,0.944) [†]
Sensitivity Analyses			
+ control for physical characteristics ^{1,2}	0.760(0.628,0.920) ^{**}	0.742(0.628,0.920) ^{**}	0.800(0.665,0.961) [†]
+ control for other lifestyle characteristics ^{1,3}	0.719(0.599,0.863) ^{***}	0.750(0.626,0.897) ^{**}	0.800(0.671,0.955) [†]

¹Estimated using Logistic regression with robust standard errors. Model control for age, educational level, marital status, family PIR. ² Models additionally control for BMI. ³ Models additionally control for smoking status and sedentary time weekly. [†]- P_{25} , ≤ 0.29 , P_{25} - P_{50} , 0.30-2.39, P_{50} - P_{75} , 2.40-4.17, P_{75} , > 4.18 . * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Discussion

The purpose of this study was to investigate whether an AID can reduce the risk of common chronic sleep disorder comorbidities. We found that whether due to physical characteristics or the adjustment of other lifestyle characteristics, there was a negative correlation between the adherence to an AID and the risk of common chronic sleep disorder comorbidities. Patients with higher adherence to an AID had a lower risk of common chronic sleep disorder comorbidities.

According to the current research, studies regarding the relationship between an AID and sleep disorder comorbidities are limited. Hence, we can only refer to the relevant research regarding an AID and single chronic disease in the general population. A prospective study from a large sample population in France (2020) evaluated the relationship between an AID and hypertension risk in the general population and found that a pro-inflammatory diet pattern had the effect of increasing the prevalence of hypertension $HR_{Q1-Q5} = 1.07$ (95% CI: 1.021.13) [15]. Another review by Aslani et al. (2020) showed that in some studies, an AID had the effect of reducing hypertension risk [16]. A study regarding the relationship between an AID and diabetes risk in the general population in Mexico found that Q₅ with the highest DII score had a higher risk of diabetes than Q₁ with the lowest DII score and was approximately 66.9% higher [17]. Researchers from China, South Korea, Ireland, the United Kingdom, and Australia found that in a study of typical adults, those with higher DII scores had a higher risk of depression than those with lower

DII scores. Among Australian female adults, those with the highest DII score in Q₄ had a higher risk of depression than those with the lowest DII score in Q₁ by approximately 20% [18-22]. These results were similar to our research results. This study found that an AID can also reduce the risk of the common chronic comorbidities in patients with sleep disorders. The risk of the common chronic sleep disorder comorbidities in Q₄ with the highest DII score was approximately 20%30% higher than that in Q₁ with the lowest DII score.

The possible reasons for the protective effect of an AID on common chronic sleep disorder comorbidities are as follows. First, an AID reduces the level of inflammatory factors caused by sleep disorders, thereby reducing the risk of the common chronic sleep disorder comorbidities. Previous studies have found that sleep disorders can cause the body to present a chronic inflammatory state. Chronic inflammation of the body can cause blood pressure to rise by affecting the permeability of blood vessels [23] and activate proteins β antibodies that can cause insulin resistance by blocking insulin signal transmission [24]. It can also activate inflammatory mediators, such as *TLR4* signaling pathways, to cause inflammatory reactions in the brain [25], leading to an increased risk of hypertension, diabetes, and depression. An AID can reduce the inflammation level in the body, thus reducing the risk of these the common chronic sleep disorder comorbidities. Second, an AID reduces the level of body oxidative stress caused by sleep disorders, thus reducing the risk of common chronic sleep disorder comorbidities. Previous studies have found that sleep disorders can cause the body to present

oxidative stress, and this can increase blood pressure by affecting vascular inflammation, increasing the permeability of the vascular endothelium, and changing the redox state of the body [26]. This can cause the body's islets of pancreas β insulin resistance that is caused by cell dysfunction, the down-regulation of *GLUT-4* expression, mitochondrial dysfunction, and impairment of the insulin signaling pathway [27]. These will change the function of nerve cells and cause neuronal degeneration, neuronal apoptosis, and neuronal plasticity [28], leading to increased risks of hypertension, diabetes, and depression. An AID is a common plant-based dietary pattern. Aleksandrova et al. (2021) found that a plant-based dietary pattern has the effect of reducing the level of oxidative stress biomarkers by reducing the body's oxidative stress response (such as lipid oxidation) [29]. An AID can reduce the level of oxidative stress in the body, thus reducing the risk of these the common chronic comorbidities of sleep disorders. Third, an AID reduces the level of insulin resistance caused by sleep disorders, thus reducing the risk of the common chronic sleep disorder comorbidities. Previous studies have found that sleep disorders will make the body present with insulin resistance, and insulin resistance will increase kidney sodium retention and sympathetic nervous system activity. These will lead to increased blood pressure [30], dysfunction of the body's mitochondria and various neurotransmitters, and neuronal cell damage [31], thus leading to increased risks of hypertension, diabetes, and depression. Inflammatory factors can affect the function of insulin by interfering with multiple sites of the insulin signal pathway, causing insulin resistance. An AID can reduce inflammatory factors in the body, such as *IL-6*, *TNF- α* , and *CRP*, to reduce the level of insulin resistance, thereby reducing the risk of these the common chronic sleep disorder comorbidities [32, 33]. Fourth, an AID improves the circadian rhythm disorder caused by sleep disorders, thus reducing the risk of common chronic sleep disorder comorbidities. Previous studies have found that sleep disorders will lead to circadian rhythm disorder in the body, and this will lead to an abnormal peripheral clock function in the body's smooth muscle, perivascular adipose tissue, liver, adrenal glands, and kidneys, leading to increased blood pressure [34]. The body's brain glucose utilization is reduced, the adrenal cortex axis is over activated, and leptin and ghrelin and other satiety hormone disorders lead to an increase in blood sugar [35], creating an increased risk of hypertension and diabetes. Although the mechanism of depression caused by circadian rhythm disorder is not clear, existing research shows

that depression can be reduced by improving circadian rhythm disorder [36]. The composition ratio of macronutrients and micronutrients in an AID is conducive to improving the circadian rhythm disorder in terms of gene expression and intestinal flora composition [37], thereby reducing the risk of these the common chronic sleep disorder comorbidities.

There are some limitations in this study. First, this study is a cross-sectional study that cannot directly deduce the causal relationship between an AID and common chronic sleep disorder comorbidities. Second, compared with the food frequency method, the 24-hour meal review method for two consecutive days and the 24-hour meal review method for one day, the systematic error of the 24-hour meal review method for two non-consecutive days is smaller, but the systematic error of the 24-hour meal review method is larger than that of the 30-day meal diary method. Finally, due to data source limitations, other sleep disorder comorbidities were not considered in this study. The results still need to be verified using a large sample of a cohort population.

Conclusion

In summary, an AID may be a healthy dietary pattern to reduce the risk of developing common chronic sleep disorder comorbidities. An AID should be promoted among patients with sleep disorders to guide individuals to eat foods that will help to reduce DII scores, such as foods that are rich in B vitamins and fat-soluble vitamins. Since the impact of an AID on chronic diseases may lag behind, future research should increase the development of an AID compliance scale to explore the causal relationship between AIDs and common chronic sleep disorder comorbidities.

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