CORRELATION OF SERUM 8-HYDROXYDEOXYGUANYLATE LEVEL WITH DISEASE SEVERITY AND OXIDATIVE STRESS IN OSAHS PATIENTS

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ABSTRACT

Objective*: To study the correlation between serum 8-hydroxydeoxyguanylate levels, disease severity, and oxidative stress in patients with obstructive sleep apnea-hypopnea syndrome.*

Methods: *Sixty OSAHS patients – treated at our department of respiratory medicine from July 2018 to July 2019 – were selected for the study group. According to their sleep apnea-hypopnea index (AHI) and minimum blood oxygen saturation (SaO2min), OSAHS patients were divided into three groups: mild group (n=24), moderate group (n = 20), and severe group (n=16). Healthy people were collected in the hospitals' physical examination centre as the control group (n=30). Five millilitres of fasting blood of all the subjects were taken and tested, and the serum 8-hydroxydeoxyguanylate (8-OHdG), brain hemoglobin (NGB), malondialdehyde (MDA), supertrophic disproportion Enzyme (SOD), and glutathione peroxidase (GSH-Px) levels were compared to investigate the relationship between serum 8-OHdG levels, disease severity, and oxidative stress in OSAHS patients.*

Results: *There were significant differences in 8-OHdG, NGB, and MDA levels in each group: the severe group>the moderate group>the mild group >the control group (P<0.05). There were also significant differences in SOD and GSH-Px levels: the severe group <the moderate group <the mild group <the control group (P<0.05). Through Pearson linear analysis, it was found that 8-OHdG was directly proportional to AHI and NGB (r=5.112, 3.251, 2.436, P<0.05), and inversely proportional to SaO_2min (r=–5.243, P<0.05). 8-OHdG was negatively correlated to SOD and GSH-Px (r=–6.221, –5.489, P<0.05), and was positively correlated to MDA (r=3.251, P <0.05).*

Conclusion: *The level of serum 8-OHdG in OSAHS patients is higher than that in healthy people, and it is positively correlated to the disease severity and oxidative stress.*

Keywords: *OSAHS, 8-hydroxydeoxyguanylic acid, disease severity, oxidative stress, correlation.*

DOI: 10.19193/0393-6384_2020_6_556

Received *November 30, 2019;* ***Accepted*** *January 20, 2020*

Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a breathing disorder that occurs during sleep. It is a disease with a high incident rate and several associated potential dangers, but its pathogenesis is not clear[(1)]. Studies have shown that narrowing and obstruction of the upper airway through nasal septum flexion, tonsil hypertrophy, megatonia, and mandibular retraction malformations could be the cause of OSAHS[(2)]. Clinical symptoms such as nocturnal sleep snoring, repeated apnea, nocturnal hypoxemia, increased nocturia, headache, superficial breathing, and daytime drowsiness could occur. Long-term apnea can induce nocturnal hypoxia and hypercapnia, leading to high blood pressure. Complications such as blood pressure, diabetes, coronary heart disease, and cerebrovascular disease can cause sudden death (at night) in severe cases[(3, 4)]. 8-hydroxydeoxyguanosine (8-hydroxydeoxyguanosine, 8-OHdG) is a specific product of guanine oxidative damage in DNA, which can predict oxidative DNA

damage in the body[5]. Studies have shown that the abnormal expression of 8-OHdG is closely related to the onset of OSAHS[6]. Our hospital conducted this trial to study the correlation between serum 8-OHdG levels, the severity of the disease, and oxidative stress in patients with OSAHS.

Materials and methods

General information

A total of 60 patients with OSAHS – treated at the Department of Respiratory Medicine of our hospital from July 2018 to July 2019 – were utilized as the study group. There were 60 patients in the study group, including 32 males and 28 females. The average age was 46.15±7.35 years. The average BMI was 20.10±1.12 kg/m^2.

The inclusion criteria were as follows:

• All patients met the diagnostic criteria for OSAHS outlined in the 'Diagnostic Guidelines for Obstructive Sleep Apnea/Hypopnea Syndrome', formulated by the Sleep Respiratory Diseases Group of the Chinese Medical Association Respiratory Branch in 2002; the patients – to varying degrees – exhibited night snoring, apnea, and daytime drowsiness;

• Patients were willing to undergo polysomnography (PSG) testing during 7 hours of sleep per night, with apnea and hypopnea episodes >30 or the sleep apnea-hypopnea index (AHI) ≥5 h;

• Their blood pressure was normal before going to bed and after waking up;

• No history of hypertension.

The exclusion criteria included the following:

• The patient had cardiovascular disease;

• The patient had chronic lung diseases such as emphysema and empyema;

• The patient had an autoimmune disease;

• The patient had severe hepatic and renal dysfunction;

• The patient had a malignant tumour;

• The patient suffered from ocular diseases;

• The patient had severe brain diseases, such as acute cerebral infarction;

• The patient had thyroid disease, diabetes, or other endocrine diseases.

According to the AHI and the lowest oxygen saturation (SaO_2min) of patients, OSAHS patients were divided into a mild group (AHI 5-20 times/h; SaO_2min ≥86 %), a moderately ill group (AHI 21-50 times/h; SaO_2min 80%-85%), and a severe group (AHI >51 times/h; SaO_2min ≤79%). The mild group had a total of 24 patients (12 male and 12 female), with an average age of 46.28±8.26 years and an average BMI of 20.13±1.06 kg/m^2; the moderately ill group had 20 patients (11 male and 9 female), with an average age of 45.98±8.46 years and an average BMI of 20.09±1.11 kg/m^2; the severe group had 16 patients (9 male and 7 female), with an average age of 46.34±7.22 years and an average BMI of 20.11±1.11 kg/m^2. A healthy population – collected in the physical examination centre of our hospital – acted as the control group, with 30 patients (16 male and 14 female), with an average age of 46.22±7.86 years and an average BMI of 20.15±1.03 kg/m^2.

There was no significant difference in the general information, including age, gender, and BMI among the subjects in each group (P>0.05). This information can be found in table 1.

Group	Age (years)	Gender (case)		BMI (kg/m^2)
		male	female	
Study group (n=60)	46.15±7.35	32	28	20.10±1.12
Control group (n=30)	46.22±7.86	16	14	20.15±1.03
t/χ^2	0.042	0.000		0.205
P	0.967	1.000		0.838

Table 1: Comparison of general information of subjects in each group ($\bar{x}\pm s$).

Observation indicators

Ten millilitres of fasting venous blood were collected from all subjects who woke up in the morning after monitoring, left at room temperature for 30 minutes, and centrifuged at 2000 r/min. Next, the upper serum was carefully separated and refrigerated at –80°C for subsequent inspection. Enzyme-linked immunosorbent assay was used to detect 8-OHdG, malondialdehyde (MDA), supertrophic dismutase (SOD), brain red protein (NGB), and glutamate in the serum of all subjects. Glutathione peroxidase (GSH-Px) levels, compared with the levels of 8-OHdG, NGB, MDA, SOD, and GSH-Px in the serum of each group of subjects, was used to explore the serum 8-OHdG levels and disease conditions of OSAHS patients.

Statistical methods

The SPSS 20.0 software package was used for statistical data analysis. Measurement data were compared using single-factor analysis of variance and the LSD t-test. Counting data were compared using the χ^2 test. Grade data comparison was performed using the Ridit test. The correlation between the 8-OHdG

level, disease severity, and oxidative stress was analysed by Pearson linear analysis. Statistical results are statistically significant, with P<0.05.

Results

Comparison of 8-OHdG and NGB levels of subjects in each group

The levels of 8-OHdG and NGB in the severe group were significantly higher than those in the moderate group, the mild group, and the control group.

The levels of 8-OHdG and NGB were significantly higher in patients in the moderate group than in the mild group and the control group. Further, the levels of 8-OHdG and NGB were significantly higher in the mild group than those in the control group; the difference was statistically significant (P<0.05). See Table 2 for these results.

Group	Cases	8-OHdG (ng/ml)	MDA (nmol/L)
Control group	30	2.46±1.12	10.46±2.13
Mild group	24	16.43±1.21[a]	12.46±2.41[a]
Moderate group	20	23.51± 1.45[ab]	15.26±2.36[ab]
Severe group	16	71.56±12.26[abc]	17.14±2.84[abc]

Table 2: Comparison of 8-OHdG and NGB levels of subjects in each group ($\bar{x}\pm s$).
Note: Compared with the control group, [a]P<0.05; compared with the mild group, [b]P<0.05; compared with the moderate group, [c]P<0.05.

Comparison of MDA, SOD, and GSH-Px levels of subjects in each group

The MDA level of patients in the severe group was significantly higher than that of patients in the mild group, the mild group, and the control group. The MDA level of patients in the moderate group was significantly higher than that of patients in the mild group and the control group.

Further, the MDA level of patients in the mild group was significantly higher than that of patients in the control group (P<0.05). The levels of SOD and GSH-Px in patients with severe disease were significantly lower than those in the moderate, mild, and control groups.

The levels of SOD and GSH-Px in patients with moderate disease were significantly lower than those of patients in the mild and control groups. The levels of SOD and GSH-Px in patients in the mild group were significantly lower than those of patients in the control group; the difference was statistically significant (P <0.05). Please check the results in Table 3.

Group	Cases	MDA (ng/ml)	SOD (ug/ml)	GSH-Px (ng/ml)
Control group	30	27.46±5.12	2.46±0.26	18.25±2.63
Mild group	24	29.36±5.36[a]	2.26±0.21[a]	17.16±2.41[a]
Moderate group	20	31.26±5.85[ab]	2.12±0.16[ab]	16.28±2.13[ab]
Severe group	16	33.41±6.10[abc]	2.03±0.12[abc]	15.36±2.10[abc]

Table 3: Comparison of MDA, SOD, and GSH-Px levels of subjects in each group ($\bar{x}\pm s$).
Note: Compared with the control group, [a]P<0.05; compared with the mild group, [b]P<0.05; compared with the moderate group, [c]P<0.05.

Analysis of the correlation between serum 8-OHdG level, disease severity, and oxidative stress in OSAHS

Through Pearson linear analysis, it was concluded that 8-OHdG was positively correlated with AHI and NGB (r=5.112, 3.251, 2.436, P<0.05), and negatively correlated with SaO2min (r=–5.243, P<0.05). 8-OHdG was negatively correlated with SOD and GSH-Px (r=–6.221, –5.489, P<0.05); it was positively correlated with MDA (r=3.251, P<0.05). Please see Tables 4 and 5 for more information.

Indicator	AHI		SaO_2min		NGB	
	r	*P*	*r*	*P*	*r*	*P*
8-OHdG	5.112	0.025	-5.243	0.016	2.436	0.034

Table 4: Correlation between serum 8-OHdG levels and disease severity in patients with OSAHS.

Indicator	MDA		SOD		GSH-Px	
	P	*r*	*P*	*r*	*P*	*P*
8-OHdG	0.011	-6.221	0.041	-5.489	0.036	0.034

Table 5: Correlation between serum 8-OHdG levels and oxidative stress in patients with OSAHS.

Conclusions

The long-term onset of OSAHS can affect multiple organs and systems throughout the body, causing serious harm to human health related to a reduction in oxidative stress levels[7]. 8-OHDG, a biomarker that responds to oxidative DNA damage, can assess the degree of oxidative damage and repair in the body, which is of great significance to study the mechanism of carcinogenesis, degenerative diseases, ageing, and the relationship between

environmental toxins and oxidative stress. It can also be used to reflect the effect of antioxidants in treating oxidative DNA damage[8, 9]. Further, owing to its high sensitivity and high selectivity, it is widely used in clinical applications[10].

NGB is an oxygen-carrying protein that has been discovered recently. It is mainly expressed in brain tissue and has a high affinity for oxygen. It can also reversibly bind oxygen and transport oxygen across the blood–brain barrier, which is important to maintain the normal function of nerve cells[11].

In this study, the levels of 8-OHdG and NGB in the severe group were significantly higher than those in the moderate group, the mild group, and the control group. The levels of 8-OHdG and NGB in the moderate group were significantly higher than those in the mild group and the control group ($P<0.05$). It is suggested that serum 8-OHdG and NGB levels are related to the level of oxidative stress and the severity of OSAHS in patients. Hypoxemia and hypercapnia are the most significant pathophysiological changes caused by OSAHS. Studies have found that repeated increases and decreases in oxygen saturation can induce high levels of living oxidative clusters in the body, leading to oxidative and anti-oxidative disorders[12]. MDA is one of the most important products of membrane lipid peroxidation, and increases in MDA levels reflect the damage to membranes in the body. Therefore, the degree of membrane lipid peroxidation can be understood through MDA to indirectly measure the degree of membrane system damage[13]. SOD is a metalloenzyme that is widely present in animals, plants, and microorganisms. It can catalyse the disproportionation of superoxide radicals in living organisms and is a natural eliminator of superoxide radicals in the body[14].

GSH-Px is an important peroxolytic enzyme that is prevalent throughout the body, which can protect the structure and function of cell membranes from interference and damage by peroxides[15]. In this study, the levels of MDA, SOD, and GSH-Px in the serum of subjects in each group reflect the degree of oxidative stress in the body. The MDA level of patients in the severe group was significantly higher than that in the moderate group, the mild group, and the control group. The MDA level of patients in the moderate group was significantly higher than that in the mild group and the control group. The MDA level of patients in the mild group was significantly higher than that in the control group ($P<0.05$). The levels of SOD and GSH-Px in the severe group were significantly lower than those in the moderate, mild, and control groups. The levels of SOD and GSH-Px in the moderate group were significantly lower than those in the mild and control groups. The levels of SOD and GSH-Px in the mild group were significantly lower than those in the control group ($P<0.05$). It is suggested that oxidative stress exists in patients with OSAHS, and with the exacerbation of the disease, the body's oxidative and anti-oxidant reactions are imbalanced, aggravating the degree of cell damage.

The changes in AHI, SaO_2min, and NGB levels reflect the severity of OSAHS in patients, and the levels of MDA, SOD, and GSH-Px in serum reflect the degree of oxidative stress in the body. According to Pearson linear analysis, it was found that 8-OHdG was positively correlated to AHI and NGB ($r=5.112$, 3.251, 2.436, $P<0.05$) and negatively correlated to SaO_2min ($r=–5.243$, $P<0.05$). 8-OHdG was negatively correlated to SOD and GSH-Px ($r=–6.221$, –5.489, $P<0.05$) and positively correlated to MDA ($r=3.251$, $P<0.05$). This indicates that the level of 8-OHdG is positively related to the severity of the disease and the level of oxidative stress, which is of great significance in assessing the condition of patients with OSAHS, formulating treatment plans, and understanding the prognosis.

In summary, the level of 8-OHdG in serum of OSAHS patients is highly expressed, which is positively correlated with the severity of the disease and oxidative stress. This information can be used as a test standard for assessing the condition of OSAHS patients, formulating treatment plans, and prognosis.

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Acknowledgements:
This paper was supported by the NSFC (Youth Fund): 81300064.

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