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Evaluation of degree of lacunar infarction and carotid atherosclerosis in patients with different severity of OSAS

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ABSTRACT

Objective: To assess the degree of lacunar infarction and carotid atherosclerosis in patients with different severity of obstructive sleep apnea syndrome (OSAS). **Methods:** A total of 198 patients with OSAS were retrospectively studied from case information and test results, and were divided into mild group 84 cases, medium group 70 cases and severe group 44 cases according to apnea-hypopnea index (AHI), and 176 cases of non-OSAS people who received physical examination in our hospital during the same period were selected as healthy control group. Differences in the values of serum lacunar infarction-related indexes, blood viscosity and hemocyte-related indexes, carotid structure and function parameters, serum arteriosclerosis-related indexes and so on were compared among groups. **Results:** t-PA value of healthy control group was higher than those of OSAS group while vWF, PAI-1 and Fg values were lower than those of OSAS group (P<0.05), and with the increase of OSAS severity, t-PA value decreased while vWF, PAI-1 and Fg values increased (P<0.05); blood viscosity, Hct, PDW, RDW and EFR values of healthy control group were lower than those of OSAS group (P<0.05), and with the increase of OSAS severity, blood viscosity, Hct, PDW, RDW and EFR values increased (P<0.05); FMD, NID and DC values of healthy control group were higher than those of OSAS group while Dis, CC and PWV values were lower than those of OSAS group (P<0.05), and with the increase of OSAS severity, FMD, NID and DC values decreased while Dis, CC and PWV values increased (P<0.05); blood uric acid and EF-1 values of healthy control group were lower than those of OSAS group while CGRP and fetuin A levels were higher than those of OSAS group (P<0.05), and with the aggravation of OSAS, blood uric acid and EF-1 levels increased while CGRP and fetuin A levels decreased, and differences among groups were significant (P<0.05). **Conclusions:** With the aggravation of OSAS, patients' microcirculation stability decreases, and the probability of both complicated lacunar infarction and carotid atherosclerosis increases.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is quite common in clinical application, and patients are characterized by intermittent apnea and hypoxemia, which can trigger a series of complications. State of chronic hypoxia can cause oxidative stress, blood viscosity increase and blood vessel endothelial damage[1,2]. A study shows that the probability of OSAS patients complicated with cardiovascular diseases is significantly higher than that of normal people and with the aggravation of OSAS, the incidence of cardiovascular events increases. The occurrence of lacunar infarction and carotid atherosclerosis can significantly increase patients' case fatality rate, and the degree of lacunar infarction and carotid atherosclerosis in patients with different severity of OSAS was mainly analyzed in the research, hereby reported as follows.

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2. Materials and methods

2.1. Case selection

A total of 198 patients with OSAS were retrospectively studied from case information and test results, the hospitalization time range for all patients was from September 2013 to December 2015, and the research was approved by the hospital ethics committee, was consented by patients and their families, and obtained informed consent forms.

Among all OSAS patients, 100 cases were male and 98 cases were female, they were 3-48 years old, the average was (25.18±2.09) years, body mass index (BMI) was 21-27 kg/m^2, and the average was (23.84±2.16) kg/m^2. According to apnea-hypopnea index (AHI), patients were grouped according to disease severity: mild group (AHI5-20 times/h) 84 cases, medium group (AHI21-40 times/h) 70 cases and severe group (AHI > 41 times/h) 44 cases. 176 cases of non-OSAS people who received physical examination in our hospital during the same period were selected as healthy control group, 91 cases were male and 85 cases were female, they were 4-51 years old, the average was (26.91±3.47) years, BMI)was 22-28 kg/m^2, and the average was (23.76±2.33) kg/m^2. Differences in baseline information were not statistical significant among groups (P>0.05).

2.2. Testing methods

Carotid ultrasonography: patients took supine position in resting state, back neck and bilateral common carotid artery sinus inferior border 1.0 cm were exposed, and carotid tubercle relavent function parameters were detected.

A total of 2 mL peripheral fasting venous blood was drawn from patients for blood routine examination, another 2 mL venous blood was collected and centrifuged, and supernatant was collected and preserved in refrigerator at -80 ℃ for subsequent serum factor level detection.

2.3. Observation indexes

Serum lacunar infarction-related indexes: von Willebrand Factor (vWF), tissue-type plasminogen activator (t-PA), plasminogen activator inhibitor-1 (PAI-1) and fibrinogen (Fg).

Blood viscosity and hemocyte-related indexes: blood viscosity, hematokrit (Hct), platelet distribution width (PDW), red blood cell distribution width (RDW) and erythrocyte filtration rate (EFR).

Carotid structure and function parameters: endothelium-dependent flow-mediated dilation (FMD), endothelium-independent nitroglycerin-induced dilation (NID), carotid diameter change (Dis), compliance (CC), dilatancy (DC) and pulse wave velocity (PWV).

Serum arteriosclerosis-related indexes: blood uric acid, endothelin-1 (EF-1), calcitonin gene-related peptide (CGRP) and fetuin A.

2.4. Statistical methods

Data obtained in the research was analyzed by SPSS23.0 software, measurement data was in terms of maen±sd. Comparison between two groups was performed by t test, and P<0.05 was set as the standard of statistical significant differences.

3.Results

3.1. Serum lacunar infarction–related indexes

Differences in vWF, t-PA, PAI-1 and Fg values were statistically significant among groups (P<0.05), and pair wise comparison by LSD method showed that t-PA value of healthy control group was higher than those of OSAS group while vWF, PAI-1 and Fg values were lower than those of OSAS group (P<0.05), and with the increase of OSAS severity, t-PA value decreased while vWF, PAI-1 and Fg values increased, and differences among groups were statistically significant (P<0.05), shown in Table 1.

3.2. Blood viscosity and hemocyte–related indexes

Differences in blood viscosity, Hct, PDW, RDW and EFR values were statistically significant among groups (P<0.05), and pair wise comparison by LSD method showed that blood viscosity, Hct, PDW, RDW and EFR values of healthy control group were lower than those of OSAS group (P<0.05), and with the increase of OSAS severity, blood viscosity, Hct, PDW, RDW and EFR values increased, and differences among groups were significant (P<0.05), shown in Table 2.

3.3. Carotid structure and function parameters

Differences in FMD, NID, Dis, CC, DC and PWV values were statistically significant among groups (P<0.05), and pair wise comparison by LSD method showed that FMD, NID and DC values of healthy control group were higher than those of OSAS group while Dis, CC and PWV values were lower than those of OSAS group (P<0.05), and with the increase of OSAS severity, FMD, NID and DC values decreased while Dis, CC and PWV values increased, and differences among groups were statistically significant (P<0.05), shown in Table 3.

3.4.Serum arteriosclerosis–related indexes

Differences in blood uric acid, EF-1, CGRP and fetuin A values were statistically significant among groups (P<0.05), and pair wise analysis by LSD method showed that blood uric acid and EF-1 values of healthy control group were lower than those of OSAS group while CGRP and fetuin A values were higher than those of OSAS group (P<0.05), and with the aggravation of OSAS, blood uric acid and EF-1 levels increased while CGRP and fetuin A levels decreased, and differences among groups were significant, and differences among groups were significant (P<0.05), shown in Table 4.

4. Discussion

OSAS means that during sleep, upperairway intermittent stenosis or obstruction leads to repeated apnea or hypopnea, which may be accompanied by snoring, hypoxemia, sleepiness and other signs. More and more attention has been paid to OSAS in current clinical practice, and study has shown that patients with severe OSAS may be with a series of important organ complications, of which the ones with the most serious consequences are cerebral infarction

Table 1

Serum lacunar infarction-related indexes.

Groups	vWF (ng/mL)	t-PA (ng/mL)	PAI-1 (AU/mL)	Fg (g/L)
Mild group	45.37±4.32	3.91±0.36	3.12±0.32	2.92±0.25
Medium group	52.47±5.18	3.36±0.32	4.35±0.41	3.76±0.34
Severe group	59.66±5.47	2.64±0.23	5.74±0.49	4.95±0.43
Control group	40.81±3.77	4.25±0.39	2.25±0.23	2.41±0.23
F	7.932	5.182	5.883	6.293
P	<0.05	<0.05	<0.05	<0.05

Table 2

Blood viscosity and hemocyte-related indexes.

Groups	Blood viscosity (mPa s)	Hct (%)	PDW (fl)	RDW (fl)	EFR (s)
Mild group	15.79±1.42	43.28±3.92	12.18±1.09	35.64±3.41	26.29±2.54
Medium group	20.58±2.16	51.67±5.09	13.31±1.28	42.08±4.19	30.16±3.21
Severe group	32.63±3.17	61.27±6.86	14.37±1.54	49.77±4.51	34.28±3.11
Control group	12.17±1.39	38.27±3.28	11.32±1.28	31.28±3.95	21.36±2.09
F	6.394	7.123	5.839	8.394	7.283
P	<0.05	<0.05	<0.05	<0.05	<0.05

Table 3

Carotid structure and function parameters.

Groups	FMD (%)	NID (%)	Dis (μm)	CC (mm2/kPa)	DC (10-/kPa)	PWV (m/s)
Mild group	14.65±1.39	23.15±2.05	346.32±30.15	0.85±0.08	0.20±0.02	7.14±0.73
Medium group	11.37±1.19	19.81±1.76	376.05±34.28	1.03±0.11	0.17±0.01	9.75±0.08
Severe group	9.11±0.87	16.39±1.47	417.95±39.72	1.22±0.13	0.14±0.01	12.17±1.35
Control group	16.27±1.39	25.76±2.49	321.83±29.85	0.81±0.07	0.23±0.02	6.54±0.59
F	6.394	7.293	9.093	5.283	5.873	8.294
P	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4

Srum arteriosclerosis-related indexes.

Groups	Blood uric acid (μmol/L)	EF-1 (ng/L)	CGRP (pg/mL)	Fetuin A (mg/dL)
Mild group	271.55±25.73	43.56±4.19	34.66±3.19	61.25±5.88
Medium group	325.19±30.45	48.71±4.76	29.48±2.76	54.28±5.09
Severe group	417.88±39.85	54.25±5.09	19.74±1.53	40.62±3.76
Control group	231.74±20.48	40.27±3.86	42.83±4.18	69.83±6.11
F	11.294	6.495	7.934	8.394
P	<0.05	<0.05	<0.05	<0.05

and carotid atherosclerosis[3]. The specific mechanism of OSAS to trigger cerebral infarction and carotid atherosclerosis is unknown, and the significance of aggravated OSAS to cerebral infarction and carotid atherosclerosis also needs to be further studied. In the research, patients with different severity of OSAS were included into the study, the changes of lacunar infarction and carotid atherosclerosis-related indicators were mainly analyzed, and thus the correlation between OSAS and complications were analyzed.

Studies have confirmed that OSAS is an independent risk factor for ischemic stroke, long hypoxia state can lead to blood hypercoagulability state as well as various microthrombosis and entering the blood circulation, when emboli enter into the cerebral vessels and produce obstruction, lacunar infarction is produced[4,5]. At first, blood coagulation and fibrinolytic indexes in patients were detected at first, and it was found that there were widespread decreased t-PA value and increased vWF, PAI-1 and Fg values in patients with OSAS, and with OSAS aggravation, the above changes were aggravated. t-PA is the physiological agonist of fibrinolytic system in the body, plays a key role in the process of fibrinolysis and hemolysis balance, and belongs to the new type of thrombolytic agent. vWF, PAI-1 and Fg are involved in blood clotting process and belong to the coagulation-promoting material, high levels of vWF, PAI-1 and Fg mean that blood is in hypercoagulability state, and the probability of all kinds of thrombus-like substances substantially increases[6]. The above results indicated that there was widespread are widespread imbalance in the process of blood coagulation and fibrinolysis, blood was in hypercoagulability state, the hypercoagulability and thrombosis-promoting state was exacerbated with OSAS aggravation and it could directly lead to multiplied risk of the formation of lacunar infarction.

In addition to being associated with high blood hypercoagulability state, the occurrence of lacunar cerebral infarction is also associated with abnormal overall state of blood and blood cells. Blood viscosity is the index reflecting blood viscosity, Hct, aggregation and so on can all directly affect the blood viscosity. PDW reflects platelet volume variation parameter in the blood, increased PDW values suggests platelet size disparity, and it is seen in thrombotic disease[7,8]. RDW reflects the heterogeneity of red blood cell volume, and increased RDW value indicates poor erythrocyte morphology homogeneity. In patients with OSAS long-term anoxia, vascular endothelium is damaged and platelet-activating factors increase, there is local platelet adhesion and aggregation, and increased platelet consumption causes megakaryocytic hyperplasia of bone marrow and releases large volume platelet, leading to increased PDW value. OSAS hypoxemia stimulates the production of a large amount of catecholamine, and can indirectly increase erythropoietin release, erythropoiesis and peripheral blood erythrocyte volume, eventually leading to increased RDW value. EFR represents erythrocyte deformability, and elevated EFR value indicates poorer erythrocyte filtration ability and decreased deformability[9]. Above

research results showed that blood viscosity, Hct, PDW, RDW and EFR values of OSAS patients increased, and with the increase of disease severity, their values increased, indicating that increased blood viscosity as well as changed platelet and red blood cell volume and deformability was the important change in the process of OSAS chronic hypoxia, was also an important reason of lacunar cerebral infarction, and can be used as the important means to judge the risk and treatment guidance of lacunar cerebral infarction.

Carotid atherosclerosis is a common cardiovascular complication of OSAS that can be macroscopically manifested as decreased carotid artery vasomotion function, increased stiffness and so on. Endothelium-dependent FMD, endothelium-independent NID, Dis, CC, DC and pulse wave velocity (PWV) are all effective indicators to judge carotid artery function, and the results are obtained through carotid ultrasonography[10,11]. Above results showed that FMD, NID and DC values of OSAS patients showed different levels of decrease while Dis, CC and PWV values showed different levels of increase, and with the aggravation of OSAS, above carotid artery lesions were aggravated[12]. Above results indicated that in repeated OSAS hypoxia state, carotid artery vasomotion function in patients was weakened gradually, stiffness increased and lumen diameter increased, which might be associated with artery injury and local lipid deposition caused by hypoxia.

Further detection of the values of carotid atherosclerosis-related serum indexes showed that blood uric acid and EF-1 values of OSAS patients increased while CGRP and fetuin A levels decreased, indicating that the significant change of serum carotid atherosclerosis-related factors in the course of OSAS might be the direct cause of the complication. Recurrent apnea-related anoxic events in OSAS patients can start oxidative stress and increase some protein products, protein product adhesion molecules can promote monocytes adhesion to vascular wall and decreased biological activity of NO in patients with OSAS, leading to vascular endothelial function damage[13]. Endothelial dysfunction and increased EF-1 secretion in pathological state can contribute to the development of atherosclerosis. Uric acid is purine metabolite in the body and with both oxidation-resisting and oxidation-promoting effect, studies show that there is hyperuricemia in more than 30% of patients with cerebral infarction, and it indicates that uric acid may play a role of increasing oxidative stress and is an independent risk factor for cardiovascular events. CGRP is the currently known strongest vascular dilation substance, belongs to endogenous protective factor, can promote the prostaglandin release and antagonize endothelin effect, and may inhibit lipid peroxidation. Fetuin A is mainly synthesized and secreted by the liver and can inhibit calcium phosphate deposition and maintain calcium phosphate balance. Angiosteosis is one of the characteristic changes of atherosclerosis, and fetuin A level can effectively predict the severity of carotid atherosclerosis[14,15]. The above results showed that unbalance expression of factors in the body of patients with OSAS was the important factor leading to the occurrence of carotid atherosclerosis, and with OSAS aggravation, the change of the levels of above serum factors was more obvious, and both occurrence rate and severity of atherosclerosis were promoted.

To sum up, it is concluded that with the aggravation of OSAS, patients' microcirculation stability decreases, and the probability of both complicated lacunar infarction and carotid atherosclerosis increases, future clinical treatment of OSAS should pay attention to the probability and severity of lacunar infarction and carotid atherosclerosis, and early prevention and intervention treatment should be done.

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