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Original Article

The relationship between serum irisin and sleep apnea syndrome

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Abstract: One of the main predisposing factors of obstructive sleep apnea hypopnea syndrome (OSAHS) is obesity. Current study confirmed that irisin can increase insulin sensitivity, reduce weight, and improve glucose tolerance. This study is to investigate the relationship between serum irisin and sleep apnea syndrome. Enzyme-linked immunosorbent (ELISA) was applied to determine irisin level in 100 cases of sleep apnea syndrome and 30 cases of healthy control. The group was divided into three groups according to illness degree. Serum irisin expression level in sleep apnea syndrome (SAS) group (1.45±0.30 ng/ml) was significantly lower than that in healthy control (2.6±0.50 ng/ml) ($P<0.05$). Its level in severe group (0.55±0.05 ng/ml) was obviously lower than in moderate (1.01±0.04 ng/ml) and mild group (1.85±0.03 ng/ml) ($P<0.05$). Serum irisin level showed certain correlativity with OSAHS. Serum irisin level can provide auxiliary support for OSAHS diagnosis and severity evaluation.

Keywords: Irisin, OSAHS, ELISA

Introduction

Sleep apnea syndrome (SAS) presents as respiratory tract obstruction caused by obesity, older age, or disease. It is a kind of complicated disease performed as apnea, snoring, doldrums, and anoxia. Patients in sleep may appear more than 30 times apnea and sustain for more than 10 s during 7 hours' sleep, or apnea more than 5 times in each hour. The pathogenesis includes deviation of nasal septum, nasal polyps, nasopharyngeal adenoid hypertrophy, giant tongue, tonsil hypertrophy, mandibular malformation, chronic obstructive pulmonary disease (COPD), pulmonary heart disease, obesity dyspnea sleepiness syndrome, acromegaly, mucous edema, high altitude polycythemia, drug-induced respiratory depression, and medulla oblongata polio, etc. Generally, SAS can be divided into three types in clinic: (1) block type, (2) central type, and (3) hybrid type, of which obstructive sleep apnea hypopnea syndrome (OSAHS) is common. Its pathogenesis is upper respiratory tract obstruction caused by the soft tissue relaxation near throat, leading to vagus nerve active at night, and resulting in sleep apnea induced by airway narrowing. Such patients generally exist insomnia, snoring, and hypophrenia. Long-time sustaining will cause harm to the cardiopulmonary function, and severe cases can appear sudden death. The patients are often accompanied by hypertension, abnormal voice, and obesity. Its pathogenesis is quite complicated and associated with both anatomical and neural elements. It seriously affects patients' life and work, and may even threaten the patients' life [1-3]. Some studies showed that SAS is the inducing factor of cerebral infarction, coronary heart disease, and cardiac insufficiency [4, 5]. Thus, its diagnosis and treatment is the hot spot of the clinical and basic research. Irisin is a kind of membrane protein, which production needs peroxisome proliferator-activated receptor activation. It also can be induced by the movement and increase the heat production. It plays a preventive and protective role on metabolic disorders since it can induce white fat cells to produce brown fat cells phenotype, whereas the later can improve a variety of metabolic parameters by increasing the heat production. Therefore, irisin can protect cardiovascular disease, type 2

Table 1. Serum irisin level comparison

Group	Cases	Serum irisin level (ng/ml)
SAS	100	1.45±0.30*
Healthy control	30	2.6±0.50

*P<0.05.

Table 2. Serum irisin level in different degree of SAS

Group	Cases	Serum irisin level (ng/ml)
Mild	30	1.85±0.03
Moderate	30	1.01±0.04
Severe	40	0.55±0.05

Table 3. The value of serum irisin in OSAHS diagnosis

Group	Cases	Positive rate
Mild	30	20.0 (6/30)
Moderate	30	10.0 (3/30)
Severe	40	5.0 (2/40)

diabetes, and fatty liver [6-8], and some studies found that serum irisin level was related to SAS [9]. This study observed serum irisin level in 100 patients diagnosed with SAS and 30 cases of healthy control to explore its meaning in SAS.

Materials and methods

Research object

(1) Experimental group: 100 cases of patients between January 2014 and May 2015 in the otolaryngology of our hospital were enrolled. The patients were diagnosed as SAS according to the American academy of sleep medicine diagnostic criteria [10], including 30 cases of mild (5 times/h ≤ AHI <20 times/h), 30 cases of moderate (20 times/h ≤ AHI <40 times/h), and 40 cases of severe (AHI ≥ 40 times/h). AHI represented for sleep apnea hypoventilation index; male and female ratio was 3:2, and the average age was 40.0±10.0 years old. (2) Control group: 30 cases of healthy examined subjects in our hospital medical center. Male and female ratio was 1:1, and the average age was 45.0±9.0 years old. All patients underwent overnight polysomnography (PSG) monitoring using the Embletta 9 (Embla, Bloomfield, CO, USA) at the sleep laboratory of the Geriatrics Department of the Second Xiangya Hospital of Central South University,

Methods

4 ml peripheral blood was extracted from elbow vein in the morning (fasting for 8~12 h), and centrifuged at 1000 rpm for 20 min after 2 hours' standing at room temperature to reduce red blood cells and serum adhesion and the incidence of hemolysis. The serum was stored at -20°C refrigerator for irisin detection. Irisin concentration was determined by enzyme-linked immuno sorbent assay (ELISA) according to the manual. ELISA kit was bought from Wuhan yoel Biotech Company. Inter assay index of variation (CV) <12%, whereas intra-assay index of variation (CV) <10%.

Statistical analysis

All statistical analyses were performed using SPSS17.0 software (Chicago, IL). Numerical data were presented as means and standard deviation (Mean ± SD). Differences between multiple groups were analyzed by t test, chi-square test, and Fisher's exact test. P<0.05 was considered as significantly different.

Results

Serum irisin expression level in sleep apnea syndrome (SAS) group was significantly lower than that in healthy control (P<0.05) (**Table 1**).

Serum irisin analysis showed that its level decreased following the increase of the severity of SAS (P<0.05), suggesting that irisin level reduced following the aggravation of the disease (**Table 2**).

The value of serum irisin in OSAHS diagnosis

According to Anastasilakis AD *et al.* result, serum irisin level was related to multiple factors including age, gender, body mass index, and movement [10]. So it is unable to define the normal level in the crowd. In this study, we took the average value of healthy control as critical point, and defined positive as less than such value. **Table 3** showed that serum irisin level in severe group was obviously lower than in moderate and mild group (P<0.05), while it was slightly lower in moderate group than that in mild group (P<0.05).

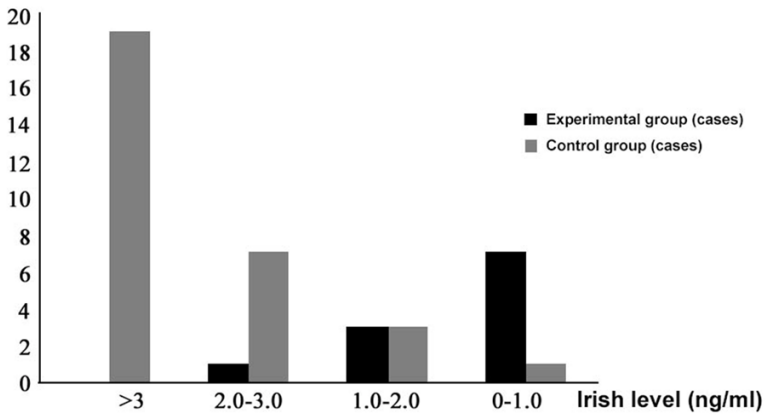

Figure 1. Serum irisin level value distribution in SAS.

Serum irisin level value distribution in SAS

Serum irisin expression in healthy control was high, whereas it was lower in SAS group. Further analysis showed that serum irisin level in most SAS patients was between 0 and 1 ng/ml, while it was generally more than 3 ng/ml in healthy control (**Figure 1**).

Discussion

Following the improvement of quality of life and eating habits changes, obese or overweight could be seen widespread. Its combination with other pathogenic factors is the main mechanism of cardiovascular disease, metabolic disease, and many other diseases [11-15]. SAS is a type of disease that seriously affect human health which can directly or indirectly caused cerebral infarction, coronary atherosclerosis, heart disease, hypertension, sudden cardiac death, and arrhythmia. While these diseases can further worsen SAS and form a vicious circle, leading to the morbidity and mortality of SAS increased year by year. OSAHS is the most common type that accounts for 90.0%. Obesity is one of the key controllable factors affected the condition except age and respiratory tract abnormal anatomy. The incidence of OSAHS in obese people is obviously higher than in normal population. A study reported that visceral fat content was positive correlated with AHI, while pulmonary capacity and pulmonary compliance decrease in obese patients lead to apnea in the night and even severe hypoxemia [16, 17]. OSAHS causes patients sleepiness in the daytime and exercise capacity decreased obviously, and it leads to blood glucose elevation and fat formation. Therefore, they form a vicious cycle, and eventually deteriorate both obesity and apnea. Obesity controlling is the key for these patients.

Irisin is a new kind of factor found by Bostrm in 2012, whose expression is affected by peroxisome proliferators-activated receptorγ synergy stimulating factor 1α (PGC1α) and exercise [18-20]. It was reported that it can act on white fat cells in vivo and in vitro to stimulate UCP1 expression and regulate related factors, and eventually become brown fat changes. This transformation process with the increase of the heat production can enhance insulin sensitivity, reduce weight, and improve the glucose tolerance [21, 22]. Recent clinical studies have shown that irisin level was correlated with its precursor FNDC5 and PGC1α mRNA level, and more and more researches also confirmed that fat cells can release irisin [23-25]. One of the main predisposing factors of OSAHS is obesity, and irisin has similar function with leptin that expressed highly in healthy people. Irisin level is closely associated with numerous diseases [26]. Thus, our study evaluated serum irisin level in OSAHA patients to investigate their relationship.

We first detected irisin level in both OSAHA group and healthy control, and the results showed that OSAHS group was significantly lower than healthy control. At the same time, it presented the decrease trend following the increase apnea degree. Serum irisin level in severe group was obviously lower than in moderate and mild group, while it was slightly lower in moderate group than that in mild group. Serum irisin level in most SAS patients was between 0 and 1 ng/ml, while it was generally more than 3 ng/ml in healthy control.

To sum up, we believed that serum irisin level was related to SAS, and its level can provide basis for SAS diagnosis and severity evaluation.

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Disclosure of conflict of interest

None.

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