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Serum cytokine contents in schizophrenia patient with metabolic syndrome and their correlation with nerve electrophysiology

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ABSTRACT

Objective: To analyze serum cytokine contents in schizophrenia patient with metabolic syndrome (MS) and their correlation with nerve electrophysiology. **Methods:** A total of 90 chizophrenia patient with MS, including 41 cases with simple schizophrenia and 39 cases with simple metabolic syndrome were included for study. The values of nerve electrophysiology indexes and serum illness-related indexes were compared among included patients, and the correlation between the two was further analyzed. **Results:** Compared with simple schizophrenia group and simple MS group, P300 latency of schizophrenia with MS group was longer, and the amplitude was shorter; N2-P3 latency and amplitude were shorter (P<0.05); serum SOD, S100b, BDNF, ABAb, PAI-1, α-HBDH, AST, cystatin c, TG, FBG and 2hPG values of schizophrenia with MS group were higher, IGF1, HMW-APN and HDL-C levels were lower, and compared with simple schizophrenia group and simple MS group, differences were significant (P<0.05); P300 latency, P300 amplitude, N2-P3 latency and N2-P3 amplitude of schizophrenia with MS group were directly correlated with serum cytokine contents (P<0.05). **Conclusions:** There are significantly abnormal serum cytokines and nerve electrophysiology indexes in schizophrenia patient with MS, and nerve electrophysiology detection can be used as the means to judge disease and guide treatment.

1. Introduction

Schizophrenia is very common in clinical practice, and taking antipsychotic drugs may have certain impact on patients' levels of humoral parameters. Metabolic syndrome (MS) means that there are blood lipid and blood glucose abnormality, hypertension, etc. in same individual, and humoral parameters are in serious state of disorder[1,2]. The occurrence of MS has many precipitating factor, and taking antipsychotic drugs is one of important ones. In patients with schizophrenia, the probability of metabolic syndrome is not low, and efficient and sensitive technique is needed for early diagnosis and timely treatment. In the research, serum cytokine contents in schizophrenia patient with metabolic syndrome (MS) and their correlation with nerve electrophysiology were mainly analyzed, hereby reported as follows.

2. Materials and methods

2.1. General information

A total of 90 schizophrenia patient with MS were included for

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study, and the information of hospitalization and test results from September 2011 to August 2014 was obtained. A total of 41 cases with simple schizophrenia and 39 cases with simple metabolic syndrome who received treatment in our hospital during the same period were selected as research subjects. Schizophrenia with MS group included 47 male cases and 43 female cases, they were 21-67 years old, and the average was (45.92±4.76) years; simple schizophrenia group included 20 male cases and 21 female cases, they were 19-69 years old, and the average was (46.76±4.09) years; simple metabolic syndrome group included 19 male cases and 20 female cases, they were 20-65 years old, and the average was (45.98±4.71) years. Differences in baseline information were not significant among three groups (P>0.05) and they were comparable.

2.2. Serum obtaining and nerve electrophysiology detection

Under the premise of awaking and relaxing all muscles, patients stayed focused. Bravo brain evoked potentiometer was used, recording electrodes were placed on the forehead area, central region and the top area, and eye movement electrodes were placed in 2 cm of upper margin of left eye and right margin of right eye respectively. Impedance between electrodes was lower than 5 k , the sensitivity was 5 uV, and two sets of triggering and stimulating systems were used for completely independent P300 tests. Detection frequency was set to 1/s, stimulus duration was 20 ms, non-target stimulus accounted for (80%), the intensity was 8 585 dB and the frequency was 100 Hz. Key-pressing actions to target stimulation of the subjects were recorded into the computer through software, and after removing eye movement and other interference factors, the levels of target indexes were analyzed.

2.3. Observation indexes

Nerve electrophysiology indexes: P300 and N2-P3 latency and amplitude. Serum superoxide dismutase (SOD), S100b protein, anti-brain antibody (ABAb), brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1 (IGF1), plasminogen activity inhibitor-1 (PAI-1), high molecular weight-adiponectin (HMW-APN), α -hydroxybutyrate acid dehydrogenase (α -HBDH), aspartate aminotransferase (AST), and cystatin c levels. Serum metabolism-related indexes: triglyceride (TG), high density lipoprotein cholesterol (HDL-C), fasting plasma glucose (FPG) and 2-hour postprandial blood glucose (2hPG).

2.4. Statistical methods

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

3. Results

3.1.Nerve electrophysiology indexes

P300 and N2-P3 latency and amplitude were statistically significant different among three groups (P<0.05), P300 latency of schizophrenia with MS group was longer, and the amplitude was shorter; N2-P3 latency and amplitude were shorter, and compared with simple schizophrenia group and simple MS group, there were significant differences (P<0.05), shown in Table 1.

3.2.Levels of SOD, S100b, BDNF and so on

Serum SOD, S100b, BDNF, ABAb, IGF1 and PAI-1 levels of three groups were statistically significant different (P<0.05), serum SOD, S100b, BDNF, ABAb and PAI-1values of schizophrenia with MS group were higher than those of simple schizophrenia group and simple MS group, and IGF1 level was lower than that of simple schizophrenia group and simple MS group (P<0.05), shown in Table 2.

3.3. HMW-APN, α -HBDH, AST and cystatin c levels

Serum HMW-APN, α -HBDH, AST and cystatin c levels of three groups were statistically significant different (P<0.05), serum α -HBDH, AST and cystatin c values of schizophrenia with MS group were higher than those of simple schizophrenia group and simple MS group, and HMW-APN level was lower than that of simple schizophrenia group and simple MS group (P<0.05), shown in Table 3.

3.4. Metabolism-related indexes

Serum TG, HDL-C, FBG and 2hPG levels of three groups were statistically significant different (P<0.05), serum TG, FBG and 2hPG values of schizophrenia with MS group were higher than those of simple schizophrenia group and simple MS group, and HDL-C level was lower than that of simple schizophrenia group and simple MS group (P<0.05), shown in Table 4.

3.5. Correlation between electrophysiology indexes and serum indexes

P300 latency was inversely proportional to S100b, IGF1, HMW-APN and HDL-C levels, and directly proportional to SOD, BDNF, PAI-1, α -HBDH, AST, cystatin c, TG, FPG and 2hPG; P300 amplitude, N2-P3 latency and N2-P3 amplitude were inversely proportional to SOD, BDNF, PAI-1, α -HBDH, cystatin c, TG, FPG and 2hPG levels, and directly proportional to S100b, ABAb, IGF1, HMW-APN, AST and HDL-C (P<0.05).

Table 1

Nerve electrophysiology index values of three groups.

Groups	P300		N2-P3	
	Latency	Amplitude	Latency	Amplitude
Simple schizophrenia group	345.77±32.62	5.27±0.49	83.28±7.43	7.53±7.94
Simple MS group	302.18±24.95	9.32±0.85	87.11±8.09	8.16±0.79
Schizophrenia with MS group	361.65±32.41	4.39±0.37	79.34±7.66	7.04±0.69
F	8.293	6.384	8.293	7.823
P	<0.05	<0.05	<0.05	<0.05

Table 2

Comparison of SOD, S100b, BDNF and other indexes among three groups.

Groups	SOD (ng/mL)	S100b (μg/L)	BDNF (μg/L)	ABAb (mg/mL)	IGF1 (μg/L)	PAI-1 (ng/mL)
Simple schizophrenia group	782.16±70.95	0.98±0.08	8.48±0.83	6.48±0.69	134.28±12.93	14.38±1.34
Simple MS group	593.82±54.61	0.067±0.005	5.03±0.46	1.27±0.18	113.93±10.76	35.27±3.09
Schizophrenia with MS group	1253.82±109.86	1.72±0.13	11.67±1.34	9.34±0.83	89.73±7.65	68.11±5.97
F	12.398	5.384	8.342	7.324	11.093	8.293
P	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 3

Comparison of serum HMW-APN, α -HBDH, AST and cystatin c levels among three groups.

Groups	HMW-APN (mg/L)	α -HBDH (IU/L)	AST	cystatin c
Simple schizophrenia group	2.84±0.23	128.95±12.34	23.47±2.41	0.86±0.07
Simple MS group	1.19±0.11	115.38±11.29	17.29±1.45	0.73±0.06
Schizophrenia with MS group	0.76±0.06	157.39±14.36	29.83±2.76	0.97±0.09
F	5.384	8.293	7.273	5.182
P	<0.05	<0.05	<0.05	<0.05

Table 4

Comparison of serum metabolism-related indexes among three groups (mmol/L).

Groups	TG	HDL-C	FBG	2Hpg
Simple schizophrenia group	1.07±0.12	1.36±0.14	5.27±0.51	6.59±0.61
Simple MS group	1.79±0.16	1.17±0.12	6.21±0.59	7.89±0.72
Schizophrenia with MS group	2.18±0.22	0.98±0.08	7.27±0.69	8.16±0.78
F	5.382	5.984	6.182	7.283
P	<0.05	<0.05	<0.05	<0.05

Table 5

Correlation between electrophysiology indexes and serum indexes.

Indexes	P300 latency		P300 amplitude		N2-P3 latency		N2-P3 amplitude	
	Determination coefficient *r*	*P*	Determination coefficient *r*	*P*	Determination coefficient *r*	*P*	Determination coefficient *r*	*P*
SOD	0.783	<0.05	-0.694	<0.05	-0.643	<0.05	-0.645	<0.05
S100b	-0.694	<0.05	0.732	<0.05	0.719	<0.05	0.832	<0.05
BDNF	0.784	<0.05	-0.783	<0.05	-0.776	<0.05	-0.746	<0.05
ABAb	0.832	<0.05	0.803	<0.05	0.834	<0.05	0.794	<0.05
IGF1	-0.809	<0.05	0.837	<0.05	0.698	<0.05	0.684	<0.05
PAI-1	0.763	<0.05	-0.738	<0.05	-0.754	<0.05	-0.755	<0.05
HMW-APN	-0.774	<0.05	0.763	<0.05	0.675	<0.05	0.781	<0.05
α -HBDH	0.683	<0.05	-0.672	<0.05	-0.764	<0.05	-0.894	<0.05
AST	0.703	<0.05	0.774	<0.05	0.688	<0.05	0.756	<0.05
cystatin c	0.783	<0.05	-0.817	<0.05	-0.856	<0.05	-0.864	<0.05
TG	0.834	<0.05	-0.835	<0.05	-0.734	<0.05	-0.823	<0.05
HDL-C	-0.748	<0.05	0.721	<0.05	0.698	<0.05	0.787	<0.05
FPG	0.849	<0.05	-0.684	<0.05	-0.563	<0.05	-0.824	<0.05
2hPG	0.784	<0.05	-0.721	<0.05	-0.673	<0.05	-0.765	<0.05

4. Discussion

Schizophrenia belongs to common mental illnesses, which poses more serious injuries to both patients and society. MS refers to the phenomenon that obesity, hypertension and abnormal glucose metabolism, dyslipidemia and other cardiovascular disease risk factors gather in the same individual[3]. Studies have pointed out that the probability of schizophrenia patients with MS is significantly higher than that of normal people, and believed that it may be because that antipsychotic drugs blocking of 5-HT, H1 and M1 receptors leads to increased appetite, resulting in obesity, insulin resistance and decreased islet β cell response to blood glucose level. The occurrence of MS not only exacerbates internal environment

disorder in patients, but can also reduce the sensitivity of patients to psychiatric drugs, increasing the difficulty of the treatment of schizophrenia. At the same time, the MS symptoms in schizophrenia patients are more severe, blood fat and blood glucose disorder is not easy to control, and thus it indicates that MS easily occurs in patients with schizophrenia, and the interaction can lead to the aggravation of both diseases, forming a vicious cycle[4,5].

In order to early and accurately diagnose schizophrenia with MS, serum cytokine levels and neural electrophysiological characteristics in such patients were studied the research, hoping to find reliable means to diagnose disease and determine its severity[6]. Schizophrenia patients have abnormal neural electrophysiological examination indexes, P300 is the most important part in ERP studies, and many studies have confirmed that P300 amplitude is reduced and the latency is delayed patients with schizophrenia. P300 can be used as an endogenous brain electrical sign of genetic predisposition to schizophrenia, and it has the positive significance in disease diagnosis and severity judgment. ERP N2-P3 peak amplitude and latency can be used as the nerve electrophysiology index for brain information acquisition, storage and cognitive process[7,8]. Above research results showed that P300 latency of schizophrenia with MS group was longer, and the amplitude was shorter; N2-P3 latency and amplitude were shorter, indicating that complication of MS could make the abnormality of brain electrical sign more significant in schizophrenia patients.

Schizophrenia patients with MS also have many changes in serological factor expression, and the dopamine hyperfunction causes excessive generation of oxygen free radicals in the brain and induces the production of large amounts of SOD. S100b protein is mainly distributed in the astrocytes of central nervous system and participates in the central nerve regeneration and repair, and in cases of brain tissue damage, S100b can be released into the cerebrospinal fluid and enter into the blood through the damaged blood brain barrier[9]. There is anti-brain antibody (ABAb) positive in more than 50% of patients with schizophrenia, it may be because brain tissue antigens enter blood circulation and stimulate the system, the antibody can increase the permeability of blood brain barrier, and therefore, ABAb can be detected in blood circulation. BDNF can accelerate the striatum dopamine metabolism and increase the number and the kindling speed of active substantia nigra neurons, indicating that BDNF can be as a neurobiological marker of schizophrenia, and participate in the disease process at the same time. Insulin resistance exists in a variety of diseases, IGF1 has insulin-like metabolic effect, and research[10] shows that IGF1 can improve the sensitivity of insulin and insulin receptor. There is high IGF1 level in patients with MS, IGF1 level in normal patients is the same or even declines, and it becomes a specific indicator of schizophrenia patients with MS. PAI-1 activity is decided by the fibrinolytic activity, there are increased levels of PAI-1 and fibrinolytic abnormality in patients with diabetes, there is also PAI-1 levels rise in patients with MS, and so when the schizophrenia patients have abnormal levels of PAI-1, the complication of MS should be highly suspected after diabetes is excluded[11]. Above research results showed that serum SOD, S100b, BDNF, ABAb and PAI-1values of schizophrenia with metabolic syndrome group were higher, and IGF1 value was lower, indicating that the occurrence of the two diseases at the same time could mutually increase the conditions and treatment difficulty.

Study has shown that HMW-APN level is closely related to MS, and with the decrease of HMW-APN level, the incidence of MS increases. α-HBDH is similar to lactate isozyme and can reflect the body's myocardial damage, and the increase of its activity is common in acute myocardial infarction and skeletal muscle damage, *etc*[12]. There may be a certain degree of α-HBDH level rise in MS patients, and when they are complicated with schizophrenia and take antipsychotic medications, the rise of α-HBDH level is more significant. AST can be used as a sensitive indicator of the impact of psychiatric drug on cardiac function, indicating that the rise of myocardial enzyme levels in patients is caused by antipsychotic drug application. Cystatin C is a kind of cysteine proteinase inhibitor, widely exists in various body fluids, is an endogenous marker for glomerular filtration rate, and can indirectly reflect the damage of antipsychotic drugs to patients' renal tissues. Patients with metabolic syndrome are associated with blood glucose, blood lipids and other metabolic abnormalities, including TG, HDL-C, FPG and 2hPG, *etc*, simple MS patients are with increased TG, FPG and 2hPG levels and decreased HDL-C level, and when they are complicated with schizophrenia, the effect of antipsychotic drugs can further aggravate the blood lipid and glucose metabolism disorder, and intensify the changes of above indicators[13,14]. The research results showed that α-HBDH, AST, cystatin c, TG, FBG and 2hPG values were higher while HMW-APN and HDL-C levels were lower in schizophrenia patients with metabolic syndrome, indicating that there was serious disorder of body fluids cytokine levels in schizophrenia patients with metabolic syndrome, the companion of the two diseases increased the abnormal changes of above factor levels, and this was also the internal reason of poor clinical effect for such patients by treatment of schizophrenia alone or metabolic syndrome alone. A study shows that for schizophrenia patients with metabolic syndrome, the effect of treating the two diseases at the same time is greater than that of treating a single disease, and the idea needs to be verified by further research.

Because there are numerous detectable serum indexes for schizophrenia and metabolic syndrome, a single serological indicator lacks directivity to the disease, combined detection of many indicators is mostly needed in order to improve the detection rate and accuracy, but repeated serum index detection increases the pain of the patients, and long waiting time for the inspection results

may also delay patients' conditions[15]. Nerve electrophysiology detection is noninvasive, convenient, efficient, and so on, there are specific nerve electrophysiology detection results in schizophrenia patients, and when they are associated with metabolic syndrome, it was further studied in the research whether the changes of nerve electrophysiology indexes are consistent with the change trend of serological indexes. Correlation analysis between the values of nerve electrophysiology indexes and the levels of serological factors showed that P300 latency, P300 amplitude, N2-P3 latency and N2-P3 amplitude were directly correlated with the values of serological indexes, and nerve electrophysiology detection could quantitatively judge the disease severity and concomitant disease.

To sum up, it is concluded as follows: there are significantly abnormal serum cytokines and nerve electrophysiology indexes in schizophrenia patient with MS, and nerve electrophysiology detection can be used as the means to judge disease and guide treatment and is worth popularization in clinical practice in the future.

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