CORRELATION OF PLASMA ADIPONECTIN AND AB DEPOSITION-RELATED INDEXES WITH VEGF, FOL, AND VITB12 IN PATIENTS WITH ALZHEIMER'S DISEASE

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ABSTRACT

Objective*: This study investigates the correlation between plasma adiponectin and β-amyloid deposition-related indexes and the vascular endothelial growth factor, folic acid and vitamin B12 in patients with Alzheimer's disease (AD).*

Methods: *Sixty (60) patients with AD admitted to the hospital from July 2018 to July 2019 were recruited as the study group and divided into mild (n=21), moderate (n=20) and severe (n=19) groups. Also, 30 healthy people who received examinations at the hospital during the same period were randomly enrolled in the control group. The serum adiponectin (APN), β-amyloid (Aβ) 1-40, Aβ1-42, vascular endothelial growth factor (VEGF), folic acid (FOL) and B12 (VitB12) levels of patients in each group were detected through an enzyme-linked immunosorbent assay. The serum levels of each group were compared and the correlations of serum APN, Aβ1-40 and Aβ1-42 and FOL, VEGF and VitB12 in AD patients were studied.*

Results: *The serum Aβ1-40 and Aβ1-42 levels of AD patients in the mild group were significantly higher than those in the control group. The Aβ1-40 and Aβ1-42 levels of AD patients in the mild group were significantly higher than those in the mild group and the control group, as well as those in the mild to moderate group and the control group, and the differences were statistically significant (P<0.01). The level of serum APN in patients with mild AD was significantly lower than that in the control group. The level of APN in patients with AD in the mild group was significantly lower than that in the mild group and the control group, and the differences were statistically significant (P<0.01). The levels of serum FOL, VEGF and VitB12 in patients with mild AD were significantly lower than those in the control group. The levels of FOL, VEGF and VitB12 in patients with AD in the mild group were significantly lower than those in the mild group and the control group. The levels of FOL, VEGF and VitB12 in patients with severe AD were significantly lower than those in the mild to moderate group and the control group, and the differences were statistically significant (P<0.01). Regarding the correlations with FOL, VEGF and VitB12, APN was positively correlated (r were 0.361, 0.426 and 0.436, P<0.05), Aβ1-40 was negatively correlated (r were -0.261, -0.124 and -0.412, P<0.05) and Aβ1-42 was also negatively correlated (r were -0.325, -0.479 and -0.384, P<0.05).*

Conclusion: *The level of APN in AD patients is decreased and positively correlated with FOL, VEGF and VitB12, and the levels of β-amyloid deposition-related indexes are increased and negatively correlated with FOL, VEGF and VitB12. The changes of APN and β-amyloid deposition-related indexes in AD patients may be related to the structure and functional damage of blood vessels.*

Keywords: *Alzheimer's disease, plasma adiponectin, Aβ deposition-related indicators, VEGF, FOL, VitB12, correlation.*

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Introduction

Alzheimer's disease (AD) is a neurological degenerative disease with progressive development[1]. Clinical manifestations include generalized dementia symptoms such as memory impairment, cognitive decline, executive dysfunction, decreased daily living ability, impaired visual space skills, and personality and behaviour changes[2]. Familial inheritance, being female, head trauma, thyroid disease, viral infections, low education levels and epilepsy may all contribute to the onset of AD[3]. Over the years, the population has gradually aged and the incidence of AD has begun to occur more frequently in younger people. Also, because of the hidden onset of AD, it seriously endangers people's health[4].

APN is an endogenous biologically active peptide. Studies have shown that serum APN levels have

a relationship with AD, delaying its progression[5]. Aβ is a peptide produced by the proteolytic action of β-amyloid precursor protein and γ-secretase, which release from cells to the blood, cerebrospinal fluid and interstitial fluid. After precipitation and accumulation, it has a strong neurotoxic effect[6]. This study investigates the correlations between plasma APN, Aβ1-40 and Aβ1-42 and FOL, VEGF and VitB12 in AD patients.

Information and methods

General information

AD patients admitted to the hospital from July 2018 to July 2019 were recruited for the study group. To be included in the study, all patients had to meet the American College of Neurology, Speech Disorders and Stroke-Alzheimer's Disease Diagnostic criteria for AD. Also, all participants had not used cholinesterase inhibitors or other Chinese and Western medicines that can improve cognitive function for one month before the study. Further, all patients were found to have an Hachinski ischemic index score ≤ 4 points and were judged to have AD using a simple intelligent mental state scale.

Finally, participants and their families were informed and required to sign a consent form. Patients were excluded from the study if they had other neurological diseases affecting cognitive function, a recent history of severe infections, severe heart disease such as myocardial infarction, the presence of traumatic brain injury, brain tumours or brain surgery, severe liver or kidney dysfunction, autoimmune diseases or malignant tumours. Finally, those who had taken drugs containing FOL or VitB12 within the previous six months before the study were also excluded, leaving 60 patients in the study group.

The patients were divided into mild, moderate or severe groups according to the simple intelligent mental state scale (mild: score ≥ 21 points; moderate: 10≥ points ≥20 points; severe: score <10 points). There were 21 patients in the mild group, consisting of 9 males and 12 females, with an average age of 72.16±6.98 years and an average BMI of 20.13±1.10 Kg/m2. For education, five patients had a primary school diploma, nine had a junior high school diploma, and seven had middle school diplomas or higher. There were 20 patients in the syndrome group, including 10 males and 10 females, with an average age of 71.98±6.49 years and an average BMI value of 20.16±1.09 Kg/m^2. Of these patients, five had a primary school diploma, nine had a junior high school diploma, and six had a middle school diploma or higher. There were 19 patients in the severe group, including 9 males and 10 females, with an average age of 72.16±6.43 years and an average BMI value of 20.14±1.06 Kg/m^2. For education, five patients had a primary school diploma, eight had a junior high school diploma, and six had a middle school diploma or higher. Meanwhile, the healthy people who received examinations at the hospital were selected as the control group. Participants in the control group had no signs of dementia.

The control group consisted of 30 patients, including 14 males and 16 females, with an average age of 72.13±7.19 years and an average BMI value of 20.12±1.11 Kg/m^2. Of the control group, 6 patients had a primary school diploma, 15 had a junior high school diploma, and 9 had a middle school diploma or higher. There were no significant differences in the age, gender and BMI of the subjects in each group (P>0.05), as shown in Table 1.

Group	Age (years)	Gender (cases)		BMI value (kg/m^2)	Average education (case)		
		Male	Female		Primary school	Junior	Middle school and higher
The control group (n=30)	72.13± 7.19	14	16	20.12± 1.11	6	15	9
The mild group (n=21)	72.16± 6.98	9	12	20.13± 1.10	5	9	7
The moderate group (n=20)	71.98± 6.49	10	10	20.16± 1.09	5	9	6
The severe group (n=19)	72.16± 6.43	9	10	20.14± 1.06	5	8	6
F/χ^2	0.000	0.216		0.010	0.510		
P	0.999	0.975		0.999	0.998		

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

Observation indexes

First, 5 ml of fasting venous blood was collected from all subjects in each group in the morning and centrifuged at 3,000 r/min for 15 min at room temperature. Then, the serum was carefully separated and stored in the -80 °C refrigerator for testing to avoid repeated freeze-thaw. The levels of APN, Aβ1-40, Aβ1-42, FOL, VEGF and VitB12 in each group were detected via an enzyme-linked immunosorbent assay and compared.

Statistical methods

The data in this study were analysed using the SPSS20.0 software package. All measurement data comparisons were expressed as ($\bar{x}\pm s$) and the comparison between groups was tested using an F-test.

The enumeration data were expressed as percentages and the comparison between groups was tested by χ^2.

The ranked data comparison was performed using the Ridit test. The correlations between APN, Aβ1-40 and Aβ1-42 and FOL, VEGF and VitB12 levels were determined through a Pearson linear analysis. Results were considered statistically significant at P<0.05.

Results

Comparison of APN, Aβ1-40 and Aβ1-42 levels of subjects in each group

As shown in Table 2, the levels of serum Aβ1-40 and Aβ1-42 in patients with mild AD were significantly higher than those in the control group, and the levels of Aβ1-40 and Aβ1-42 in patients with AD in the mild group were significantly higher than those in the mild group and the control group. Also, the levels of Aβ1-41 and Aβ1-42 were significantly higher than those of the mild to moderate group and the control group, and the difference was statistically significant (P<0.01). The level of serum APN in patients with mild AD was significantly lower than that in the control group.

The level of APN in patients with AD in the mild group was significantly lower than that in the mild group and the control group (P<0.01). The level of APN in patients with severe AD was significantly lower than that in the mild to moderate group and the control group, and the difference was statistically significant (P<0.01).

Group	APN (μg/L)	Aβ1-40 (pg/mL)	Aβ1-42 (pg/mL)
The control group (n=30)	8.14±1.26	5.49±3.15	4.16±2.01
The mild group (n=21)	6.49±1.19[a]	13.19±4.16[a]	17.42±2.43[a]
The moderate group (n=20)	5.18±1.12[ab]	29.16±5.22[ab]	32.18±2.78[ab]
The severe group (n=19)	3.46±0.86[abc]	50.18±6.13[abc]	61.18±3.42[abc]
F	71.310	406.500	2070.660
P	<0.001	<0.001	<0.001

Table 2: Comparison of APN, Aβ1-40 and Aβ1-42 levels of subjects in each group ($\bar{x}\pm s$).
Note: The superscript a represents P<0.05 compared with the control group, b represents P<0.05 compared with the mild group, and c represents P<0.05 compared with the neutral group.

Comparison of FOL, VEGF and VitB 12 of subjects in each group

As shown in Table 3, the levels of serum FOL, VEGF and VitB12 in patients with mild AD were significantly lower than those in the control group. The levels of FOL, VEGF and VitB12 in patients with AD in the mild group were significantly lower than those in the mild group and the control group. The levels of FOL, VEGF and VitB12 in patients with severe AD were significantly lower than those in the mild to moderate group and the control group, and the differences were statistically significant (P<0.01).

Group	FOL (mmol/L)	VEGF (ng/L)	VitB12 (pmol/L)
The control group (n=30)	12.51±2.61	203.12±33.15	436.18±112.58
The mild group (n=21)	11.92±1.89[a]	169.42±32.16[a]	381.43±71.43[a]
The moderate group (n=20)	8.46±1.56[ab]	139.15±26.13[ab]	339.15±61.52[ab]
The severe group (n=19)	6.15±1.26[abc]	112.18±23.43[abc]	267.18±43.16[abc]
F	49.520	41.620	17.980
P	<0.001	<0.001	<0.001

Table 3: Comparison of FOL, VEGF and VitB 12 of subjects in each group ($\bar{x}\pm s$).
Note: The superscript a represents P<0.05 compared with the control group, b represents P<0.05 compared with the mild group, and c represents P<0.05 compared with the neutral group.

Correlation analysis of APN, Aβ1-40 and Aβ1-42 levels with FOL, VEGF and VitB12 levels

As shown in Table 4, the Pearson linear analysis indicated the following correlations with FOL, VEGF and VitB12: APN was positively correlated (r were 0.361, 0.426 and 0.436, P<0.05), Aβ1-40 was negatively correlated (r were -0.261, -0.124 and -0.412, P<0.05) and Aβ1-42 was also negatively correlated (r were -0.325, -0.479 and -0.384, P<0.05).

Indexes	FOL		VEGF		VitB12	
	r	*P*	*r*	*P*	*r*	*P*
APN	0.361	0.016	0.426	0.012	0.436	0.034
Aβ1-40	-0.261	0.023	-0.124	0.043	-0.412	0.036
Aβ1-42	-0.325	0.049	-0.479	0.017	-0.384	0.015

Table 4: Correlation analysis of APN, Aβ1-40 and Aβ1-42 levels with FOL, VEGF and VitB12 levels.

Discussion

AD is the most common type of dementia, accounting for about 60-80% of senile dementia[7]. In recent years, the incidence of AD has increased, bringing a heavy economic burden and grief to numerous families. APN is an insulin-sensitizing hormone, which is mainly secreted by the adipocytes but can also be secreted by skeletal muscle and en-

dothelial cells[8]. APN can promote the acidification of fat and the absorption of sugar and reduce atherosclerotic lesions. Studies have shown that APN can improve insulin resistance and atherosclerosis in mice[9], regulate the vascular endothelial secretory function by reducing the adhesion of monocytes, reduce the production and release of the tumour necrosis factor TNF, inhibit the release of inflammatory factors such as IL-1 and IL-6, and inhibit the inflammatory response. Changes in TNF, IL-1 and IL-6 levels are closely related to the condition of AD[10].

Aβ has strong neurotoxicity. Studies have shown that when Aβ is injected into the cerebral cortex of rats, symptoms such as tissue necrosis, peripheral neuron loss and neurokeratosis will appear in the injection site of rats, and their severity is significantly correlated with the dosage[11]. After a large amount of precipitation and accumulation of the cell matrix, the vascular wall is amyloidized, resulting in poor vascular elasticity, and it may even rupture or result in thrombosis. It also induces neurons to undergo early apoptosis, neurite atrophy and neuron degeneration, which leads to AD[12]. In this study, the serum APN level of AD patients was significantly lower than that of healthy people, the APN level of AD patients gradually decreased with the worsening of the disease, and the difference was statistically significant ($P<0.01$). The serum levels of Aβ1-40 and Aβ1-42 in AD patients were significantly higher than those in healthy people, the levels of Aβ1-40 and Aβ1-42 in AD patients gradually increased with the worsening of the disease, and the difference was statistically different ($P<0.01$), showing that APN is a protective factor of AD and that Aβ1-40 and Aβ1-42 may promote the development of AD.

VEGF is a highly specific vascular endothelial cell growth factor that can increase vascular permeability, promote degeneration of the extracellular matrix, and accelerate the migration and proliferation of vascular endothelial cells and angiogenesis. Studies have shown that VEGF can also protect nerves, promote nerve regeneration and repair nerves[13]. FOL is a pteridine derivative isolated from the liver that can promote protein synthesis and cell division, as well as the formation of normal red blood cells. The absence of FOL causes megaloblastic anaemia and neural tube defects[14]. VitB12 is the only vitamin containing metal elements, and it is involved in the production of bone marrow red blood cells and prevents malignant anaemia. It is also indispensable for the function of the nervous system, is involved in the formation of lipoproteins in neural tissues, and can prevent cerebral nerves from being damaged[15]. In this study, serum levels of FOL, VEGF and VitB12 in AD patients were significantly lower than those in the control group, the levels of FOL, VEGF and VitB12 in AD patients had gradually decreased with the progression of the disease, and the differences were statistically significant ($P<0.01$), suggesting that the decrease of serum FOL, VEGF and VitB12 levels in AD patients is related to the destruction of blood vessels, a decrease in the ability to self-repair blood vessels, and the decline of the blood vessel function. In addition, regarding the correlations with FOL, VEGF and VitB12, APN was positively correlated and Aβ1-40 and Aβ1-42 were both negatively correlated, suggesting that changes in the APN levels and Aβ1-40 and Aβ1-42 levels in AD patients, damage to the structure and function of blood vessels, and the aggravation of AD are related to changes in FOL, VEGF and VitB12 levels.

In conclusion, the level of APN in AD patients is decreased and is positively correlated with FOL, VEGF and VitB12, the level of Aβ1-40 and Aβ1-42 is increased and is negatively correlated with FOL, VEGF and VitB12, and the changes in Aβ1-40 and Aβ1-42 in AD patients may be related to the structure and functional damage of blood vessels to a certain extent.

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