

Original Article

Serum somatostatin and neuron-specific enolase might be biochemical markers of vascular dementia in the early stage

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Abstract: Objectives: To estimate whether serum somatostatin (SS) and neuron-specific enolase (NSE), the representative neuropeptide relative to learning and memory, to be biochemical markers of the vascular dementia (VaD) in the early stage. Methods: 42 patients with VaD were randomized in the VaD group and 38 stroke patients without dementia was in the control group. Radioimmunoassay was used to detect SS in the serum and CSF, and Enzyme linked immunosorbent assay to detect NSE in the serum and CSF. SS and NSE in CSF were compared 3 days after stroke. SS and NSE contents in serum were compared 3 days, 3 months and 6 months poststroke. Results: CSF and serum SS contents in VaD group were lower than that in the control group ($P < 0.05$). SS in the frontal cortex, hippocampus and the temporal lobe, thalamus were lower than that in the occipital lobe ($P < 0.05$); Serum NSE contents in VaD group were significantly higher than that of control group 3 days after stroke, 3 months and 6 months ($P < 0.01$, respectively), and has a tendency to increase ($P < 0.05$); SS contents significantly lower than that in the control group with the trend to decrease ($P < 0.05$). Conclusions: NSE increased and SS decreased with the lower content in the frontal cortex, hippocampus and the temporal lobe which has close relationship with learning and memory, thus Serum NSE and SS might be the biochemical markers of VaD in the early stage.

Keywords: Vascular dementia, cerebral infarction, cerebrospinal fluid, serum somatostatin, neuron-specific enolase

Introduction

As population compositions tending to aging in China, the burdens of cognitive dysfunction are increasingly prominent. The prevalence rate of vascular dementia (VaD) is 1.1%~3%, in the population of more than 65-year-old in China, and vascular dementia in the elderly city citizen is higher than that in the rural areas [1]. VaD is the only dementia could be cured and prevented now, this means early treatment can reverse this cognitive disorders [2]. Some neuropeptides or neurotransmitters are associated with learning and memory. As we already known that the typical neuropeptides regulating learning and memory are somatostatin (SS) and Neuron-specific enolase (NSE). So it is reasonable to infer that SS and NSE may be relative with VaD.

Many possible biochemical markers associated with VaD have been reported such as interleukin 6, tumor necrosis factor- α , interleukin-1,

interleukin-10, sE-selectin, vascular endothelial cell adhesion factor-1, nerve microfilament proteins, α -synuclein, γ -synuclein. In recent years, NSE has been reported negatively correlated with neuron damage, and might be correlated with the degree of VaD [3]. But the representative neuropeptides such as SS and NSE have not been widely accepted as the biochemical markers of VaD. Therefore this study was to estimate whether serum SS and NSE related to vascular dementia and to be biochemical markers of VaD in the early stage.

Patients and methods

Patients and group

VaD group

42 in-patients with VaD were chose between January 2012 and December 2014, at Department of Neurology, Ningxia People's Hospital,

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Table 1. Comparisons of SS, NSE contents in CSF between two groups ($\bar{x}\pm s$, ng/L, ng/mL)

Group	n	SS (ng/L)	NSE (ng/mL)
VaD group	42	821.50±107.30*	30.52±7.62*
Control group	38	1100.20±141.40	25.17±8.15

Compared with control group, *P<0.05.

Table 2. Locations of brain infarction and SS content in CSF ($\bar{x}\pm s$, ng/L)

Location	VaD group n (%)	Control group n (%)	SS (ng/L)
Occipital lobe	2 (66.7)	1 (33.3)	1340.4±241.6
Frontal lobe	8 (66.6)	4 (33.3)	822.5±112.3
Temporal lobe	13 (65.0)	7 (35.0)	810.2±108.7
Thalamus	6 (54.6)	5 (45.4)	984.1±201.4
Basal ganglia	25 (64.1)	14 (38.9)	913.7±156.3
Cerebellum	3 (60.0)	2 (40.0)	1279.3±194.2
Parietal lobe	1 (50.0)	1 (50.0)	1380.0±308.1

including 30 cases of male, 12 cases of female; aged 52 to 86 years; the average years of age: 68.2±6.4 years; the average period of the education: 8.62±1.62 years.

Including: Based on Chinese medical standards for the diagnosis of vascular dementia by Chinese Medical Association Branch of Neurology in 2002 version [4]. (1) More than one brain infarction in brain MRI; (2) Dementia occurred 3 months after stroke; (3) Hachinski ischemia index scale (IHS) score was larger than 7.

Excluding: (1) Serious language disorders or sensorimotor impaired. (2) Other type of dementia.

Distribution of brain infarctions: Brain MRI: 25 cases of brain infarction located in the basal ganglia regions mono-laterally or bilaterally, 6 cases in the hypothalamus, 1 case in the parietal lobe, 13 cases in the temporal lobe, 2 cases in the occipital lobe, 8 cases in the frontal lobe, 3 cases in the cerebellum.

Control group

At the same period 38 patients with brain infarction were chosen at Department of Neurology in the same hospital, 20 cases were male, 18 cases were female; aged 50 to 83 years, and the average years of age: 65.2±7.1 years; the average period of the education: 7.83±1.81 years.

Including: (1) The diagnosis of cerebrovascular disease was based on the National Standards of Chinese Medical Association. (2) The brain MRI showed more than one brain infarction. (3) The stroke without dementia occurred more than 3 months. (4) MMSE score showed no dementia.

Excluding: (1) Disturbance of consciousness. (2) Serious language disorders or sensorimotor impaired.

Distribution of brain infarctions: Brain MRI: 14 cases of brain infarction located in the basal ganglia regions mono-laterally or bilaterally; 5 cases in the hypothalamus; 1 case in the parietal lobe; 7 cases in the temporal lobe; 1 case in the occipital lobe; 4 cases in the frontal lobe; 2 cases in the cerebellum.

SS content and NSE content detections

SS content detection

3 days after admitted to hospital, 3 mL CSF and 3 mL venous blood (fasted) were obtained. SS content was detected by Radiation immunity analysis (RIA) (Beijing Equation Biological Technology Co., Ltd, Beijing, China).

NSE content detection

3 mL venous blood (fasted) were obtained at admission, 3 months, and 6 months poststroke. 10 min centrifugal at 3000 r/min, then the supernatant was persevered at -70°C. NSE content in the serum and CSF was detected using double antibody sandwich enzyme-linked immunosorbent (ALISEI automatic enzyme standard instrument, Radim Company, Italy; antibody, Endogen Company, USA).

Statistical analysis

SPSS11.0 statistical software was used. Analysis of variance between two groups was used; Pearson correlation analysis was used for correlation analysis.

Results

Comparison of general data

There was no statistically difference between the gender, age, education and other general information using different statistical methods according the characteristics of the numerical data or non-numerical data (P>0.05, respectively). This result suggested that the gender, age, education and other general information

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Table 3. Comparison of serum SS contents between two groups ($\bar{x} \pm s$, ng/L)

Group	n	3 days poststroke	3 months poststroke	6 months poststroke
VaD group	42	726.24±136.78*	616.14±138.28*	427.86±156.98 ^{a,c}
Control group	38	1021.20±135.30	825.33±164.67	685.89±143.21 ^b
t		3.903	4.031	4.875
P		<0.01	<0.01	<0.01

Note: *P<0.05, compared with control group. ^aP<0.05, Pearson correlation analysis in VaD group; ^bP<0.05, Pearson correlation analysis in the control group; ^cP<0.05, Pearson correlation analysis in VaD group compared with the control group.

Table 4. Comparison of serum NSE contents between two groups ($\bar{x} \pm s$, ng/L)

Group	n	3 days post-stroke	3 months poststroke	6 months poststroke
VaD group	42	26.28±6.42*	29.52±4.21*	33.72±4.12 ^{a,c}
Control group	38	22.77±6.95	25.17±4.60	29.18±3.45 ^b
t		4.03	3.19	4.75
P		<0.01	<0.01	<0.01

Note: *P<0.05, compared with control group. ^aP<0.05, Pearson correlation analysis in VaD group; ^bP<0.05, Pearson correlation analysis in the control group; ^cP<0.05, Pearson correlation analysis in VaD group compared with the control group.

were comparable between VaD group and the control group.

Comparisons of SS, NSE contents in CSF between two groups within 3 days of admitted to hospital

As shown in **Table 1**, SS decreased while NSE increased significantly in VaD group compared with control group (P<0.05, respectively).

Distribution of SS in patients with VaD

As shown in **Table 2**, SS content in different cerebral infarction areas were different; the highest concentration was in the parietal lobe infarction, and the lowest was at the temporal lobe infarction. Different cerebral infarction locations were compared with occipital and showed that cerebral infarction located in the frontal lobe, the temporal lobe, thalamus and the basal ganglia were lower than that in the occipital lobes significantly (P<0.05, respectively); There was no statistically difference between brain infarcts in the parietal lobe, the cerebellum and the occipital lobe (P>0.05, respectively).

This result suggested that SS content in CSF in patients with cerebral infarction in the frontal

cortex, hippocampus, the temporal lobe, thalamus, and the striatum were decreased following cerebral infarction.

Serum SS decreased following brain infarction and vascular dementia

CSF was more difficult to obtain than the venous blood, and clinically difficult to dynamic monitor, so the serum SS content were dynamic compared

according to the result of CSF after patients admitted to hospital for two groups of stroke patients with or without dementia. The serum SS contents were lower than that in the control group 3 days after stroke, 3 months and 6 months poststroke (P<0.01, respectively); Pearson correlation analysis showed a tendency to decrease gradually (P<0.05), **Table 3**.

Serum NSE increased following brain infarction and vascular dementia

Serum NSE contents were higher than that in the control group 3 days poststroke, 3 months poststroke and 6 months post stroke as shown in **Table 4** (P<0.01, respectively); Pearson correlation analysis showed a tendency to decrease gradually (P<0.01).

Theses results suggested that the degree of ischemic injury was severe in VaD group. With the gradually recovery of neural function, the brain infarction degree was reduced gradually.

Discussions

Neuropeptide is associated with learning and memory, and the representatives of neuropeptides in cerebral ischemic injury are somatostatin and neuron-specific enolase [5, 6]. This study showed that SS in CSF of VaD was lower than that in the control group, NSE was higher than that in the control group; there is a similar pattern in serum 3 months and 6 months after cerebral infarction. SS had different distribution the lower content in the frontal cortex, hippocampus and the temporal lobe which has close relationship with learning and memory in patients with VaD, therefore SS and NSE in serum might be used as biochemical markers of VaD in the early stage.

Somatostatin is a 14-amino peptide, and widely distributed in the nervous system. As a neu-

rotransmitter or modulator it is involved in physiological regulation of cognitive function, motor, sensory. Studies have shown that serum SS levels significantly reduced in patients with VaD [7], and the possible explanation is that the SS interneurons in the brain might be highly vulnerable to ischemic injury. In the hippocampus, SS mRNA expression decreased following cerebral ischemia [8]. SS microinjected into the rat brain would be helpful for learning and memory restore [9]. The present study showed that SS content in CSF in patients with VaD was significantly lower than that in the control group. This implied that SS synthesis and release decreased in the ischemic neurons. SS can inhibit alpha and beta adrenergic receptors indirectly to dilate blood vessels, thus decreased SS can cause disturbance of cerebrovascular distillations resulting in aggravating the cerebral ischemia. SS as modulators may regulate a variety of neurotransmitters involved in the pathogenesis of dementia through the adjustment and the interaction between the networks of CNS. SS content decreased in patients with VaD suggested that SS was closely related with the development of VaD.

Physiological study [10] showed higher SS content in the cerebral cortex, hippocampus, the basal ganglia and the hypothalamus. The numbers and the volume of cerebral infarction lesions have close related to the severity of dementia. The present study showed lower SS contents in the frontal cortex, hippocampus and the temporal lobe cortex, the thalamus, the striatum in patients with VaD. Our results coincide with the literature. This study suggested that SS in CSF could be used as the indicators of early estimate of brain dysfunction such as VaD.

NSE is an enzyme of biological glycolysis metabolism in the brain, thus has a vital catalytic role in producing intermediate phosphate embolization pyruvate. Physiologically NSE is located within the neurons, but "leak-out" of the cell when ischemia, hypoxia and other injury, enter the intercellular space of the central nervous system, pass-out through the blood-brain barrier into the peripheral circulation. Therefore NSE is regarded as one of the most sensitive indicators of the brain injury, and increased NSE is associated with severity of ischemia [11, 12].

CSF and serum NSE expression is closely related to the onset and development of VaD, and detect the expression of NSE are very important to the diagnosis of VaD. The present study investigated the pattern of serum NSE 3, 6 months after cerebral infarction and VaD. Serum NSE increased in patients with early VaD.

This study was a small sized observational assessment of VaD in the early stage; further larger sample research is needed.

Disclosure of conflict of interest

None.

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