

Clinical research of homocysteine, high-sensitive C-reactive protein and D-Dimer in patients with vascular dementia

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Abstract: Aim of the present research work was to study the relationship between the degree of dementia and the serum levels of homocysteine(Hcy), high-sensitive C-reactive protein(hs-CRP), D-Dimer and vascular dementia(VaD) of patients, and to investigate the mechanism of Hcy, hs-CRP and D-Dimer in the vascular dementia. Subjects were divided into normal group and VaD group. CRP and D-Dimer protein of each sample were detected by nephelometry method, and the serum Hcy level was detected by Fluorescent labeling immunoassay method. Compared with the normal control group, Hcy, hs-CRP and D-Dimer in VaD group were significantly higher than that of control group, and the difference was statistically significant. Linear correlation analysis showed a negative association between Hs-CRP, Hcy and MMSE score. There was no correlation between the levels of D-Dimer and the MMSE score. Hcy, hs-CRP and D-Dimer are involved in the pathogenesis of vascular dementia (VAD), There is a significant correlation between the severity of vascular dementia and Hcy and Hs-CRP.

Keywords: Vascular dementia, homocysteine, D-Dimer, high-sensitive C-reactive protein (hs-CRP)

INTRODUCTION

Recent study results show that the increase of HCY levels are an independent risk factor for atherosclerosis and thrombosis (Hassan *et al*, 2004). Hs-CRP plays a key role in the formation and development of atherosclerosis, and also one of the important inflammatory marker (Heringa *et al*, 2014). D-dimer level is a specific marker of hyperfibrinolysis and hypercoagulation status, which improvement means the increase of fibrinolytic activity. D-dimer is not only involved in the occurrence and development of acute cerebral infarction (ACI), but also plays a very important role in the initiation and development of atherosclerosis. Atherosclerosis is closely related to the occurrence, development and prognosis of cerebral vascular disease. Vascular dementia (VaD), as an acquired disturbance of intelligence caused by cerebrovascular disease, the risk factors of cerebrovascular disease are also involved in its pathogenesis. Therefore, this study detected the serum level of HCY, hs-CRP, D-dimer to explore their effect on the pathogenesis in VaD patients, contributing to the prevention and prognosis. The ethical approval was taken from Ethics Committee of the First Affiliated Hospital of Zhengzhou University has approved this research.

MATERIALS AND METHODS

Object of study

60 cases (30 male cases, 30 female cases) of VaD patients from February 2013 to October 2015 in our hospital were selected for the study. Among which, 28 cases were mild

dementia, and another 32 cases were severe dementia. 60 cases (30 male cases, 30 female cases) of healthy people in the same period were selected as the control group, which average age were 66.5±7.6 years old.

Inclusion criteria of VaD patients: According to the ICD-10 of WHO, the diagnostic criteria for vascular dementia needs to meet the following requirements: (1) Mini-mental state examination (MMSE) score: In the patients with dementia, 13-23 indicatess mild dementia, 5-12 moderate dementia, and below 5 severe dementia. (2) The score of modified hachinski ischemic score is more than 4 points. (3) Meeting the VD standards of IV - DSM developed by the American Psychiatric Association (Fratiglioni *et al*, 1992). (4) Having a history of cerebrovascular disease or evidence of previous cerebral vascular disease showed through MRI examination.

Exclusion criteria: (1) AD and mental illness patients; (2) Having taking drugs that affect HCY levels in the past 1 months, such as contraceptive drugs, antiepileptic drugs, dopamine, folic acid or VitB12; (3) Nutritional and metabolic diseases existed, such as thyroid disease, severe anemia and malnutrition, folic acid and VitB12 deficiency, severe liver, kidney and other organ diseases.

Methods

The fasting blood was taken from cubital vein in the morning from VaD patients so as to detect HCY, hs-CRP and D-dimer. After 1-2h placing in room temperature, to centrifuge them for 15 minutes in 2000r/min and then about 200ul serum was extracted to preserve them in –

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Table 1: Comparison of the serum levels of Hcy, hs-CRP and D-Dimer between the two groups.

Testing index	Control Group	VaD Group	T value	P
Hcy (mmol/L)	13.27±4.68	29.35±8.27	4.796	0.009
Hs-CRP (mmol/L)	3.53±2.96	8.36±3.57	2.827	0.006
D-dimer (mg/L)	0.58±0.32	1.85±0.75	2.365	0.004

Table 2: Comparison of the serum levels of Hcy, hs-CRP and D-Dimer in patients with different degree of dementia

Testing index	Mild	Moderate and severe	F value	P
Hcy (mmol/L)	22.45±9.68	34.67±19.35	22.47	<0.01
Hs-CRP (mmol/L)	6.27±3.26	10.98±5.65	9.36	<0.01
D-dimer (mg/L)	1.83±0.75	1.89±1.24	1.507	>0.05

70°C refrigerator. The experiment was divided into 2 groups: normal control group and VaD group. The content of c-reactive protein and D-dimer were detected by nephelometry method and HCY level was detected by fluorescent labeling immunoassay method.

STATISTICAL ANALYSIS

SPSS20.0 software was used for analysis, and the measurement data were expressed by $\bar{x} \pm s$; T test was used in the analysis of the difference between groups. Correlation analysis were analyzed by Pearson. The inspection level was $\alpha=0.05$.

RESULTS

Research results showed that the value of Hcy, hs-CRP and D-Dimer in VaD group was obviously higher than that of control group ($P<0.01$), with statistical significance. As shown in table 1.

Linear correlation analysis showed that the value of Hs-CRP, Hcy ($r=-0.461$, -0.625 $P<0.01$) and MMSE score were negatively correlated. With the increase of MMSE score in VaD patients, the severity of dementia decreased, the plasma Hs-CRP and Hcy levels decreased. There was no correlation between the level of D-dimer and the MMSE score ($r=-0.216$ $p=0.325$).

The Hcy and Hs-CRP value in mild dementia patients was obviously lower than that in the moderate and severe dementia patients, with statistical significance. There was no significant difference in the D-dimer value. As shown in table 2.

DISCUSSION

As the population ages, dementia has become an important issue in the world today. Cerebral vascular diseases directly lead to cognitive dysfunction, and its risk factors is directly involved in the pathophysiological mechanism of VaD. Atherosclerosis, diabetes,

hypertension, high HCY hyperlipidemia and other vascular risk factors may be the direct cause of vascular dementia. As the intermediate metabolite of methionine, Hcy is a sulfur-containing amino acid. It can promote the formation of oxygenized low density lipoprotein (oxLDL), causing vascular endothelial damage and platelet aggregation. So it is an independent risk factor for cardiovascular and cerebrovascular diseases. CRP is a marker of inflammatory response, which can produce anti-inflammatory effects through the immune response (Juma *et al*, 2011). The inflammation in atherosclerotic plaque is related to the improvement of serum inflammatory factors level, and the increase degree of CRP is closely related to the degree of cerebral arteriosclerosis (Kettunen *et al*, 2011; Nordestgaard and Zacho, 2009; Alizadeh Dehnavi *et al*, 2008). Research shows that inflammatory factor, especially the increase of CPR can predict the decline of the cognitive function (Singh-Manoux *et al*, 2014; Silverman *et al*, 2012). D-dimer level is a specific marker of hyperfibrinolysis and hypercoagulative state, whose improvement shows the fibrinolytic activity increased. D-dimer level is significantly increased in the acute phase of ischemic stroke, and decreased during the recovery period. D-dimer participates in the occurrence and development of acute cerebral infarction. It plays a very important role in the initiation and development of atherosclerosis. Its plasma levels are inversely proportional to the thickness of the plaque fibrous cap. Therefore, abnormally elevated fibrinogen may lead to plaque rupture and thrombosis (Heijboer *et al*, 1992; Kario *et al*, 1992). 128 patients with vascular dementia studied by Carcaillon have shown that the increase in D-dimer is significantly increased the incidence rate of vascular dementia (Carcaillon *et al*, 2009).

CONCLUSION

The results of this experiment showed that: the Hcy, Hs-CRP and D-dimer level in VaD group were significantly higher than that in the control group, with statistical significance, which mean that the Hcy, Hs-CRP and D-dimer were involved in the pathogenetic process of VaD.

The results were in consistent with previous research findings (Liu *et al*, 2015; Krarup *et al*, 2011; Kong and Chua, 2009; Barber *et al*, 2006). The results of this study also showed that the Hcy, Hs-CRP in VaD group were negatively correlated with MMSE scores. There was no statistical significance in the D-dimer between mild dementia and moderate-severe dementia, indicating that D-dimer may be involved in the pathogenetic process of VaD, but do not related to the progression of vascular dementia. All in all, Hcy, Hs-CRP and D-dimer may be closely related to the occurrence and development of vascular dementia and intervention on Hcy, Hs-CRP and D-dimer may have an effect on the occurrence and progression of vascular dementia, which provides a useful index of evaluation of thinking for the secondary prevention of cerebrovascular disease.

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