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Original Article

Correlation between serum cystatin C level and elderly hypertensive patients combined coronary heart disease

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Abstract: Objectives: To explore the correlation between serum cystatin C level and elderly hypertension with coronary heart disease patients. Methods: 500 hypertensive patients combined coronary heart disease were selected by coronary angiography. 321 of them were elderly patients with hypertension (male 204, female 117), and 400 of them were elderly patients with coronary heart disease (male 257, female 143), The serum cystatin C level of all patients were detected by immunoturbidimetry, and analyzed the correlation between the serum cystatin C level and different degree of blood pressure and the degree of coronary artery stenosis in elderly patients. Results: The serum cystatin C level was closely related with the blood pressure and the degree of the coronary artery stenosis. The higher the blood pressure level and the more serious the coronary artery stenosis, the higher the serum cystatin C level; The serum cystatin C level of hypertensive patients with coronary heart disease patients (Group D) were markedly higher than the level of the patients without hypertension and coronary heart disease patients (Group A), and the level of the patients with coronary heart disease (Group B) and the hypertension group (Group C) ($P < 0.05$). Conclusion: The serum cystatin C level of elderly patients with hypertension and coronary heart disease were closely related with the degree of blood pressure and coronary arteries stenosis. The serum cystatin C maybe a predictor of disease severity in elderly hypertensive patients with coronary heart disease.

Keywords: Cystatin C, elderly patients, hypertension, coronary artery disease, correlation

Introduction

Coronary heart disease (CHD) is one of the serious cardiovascular diseases, especially in the elderly, it has become the important disease that threaten the health of the elderly and the quality of life. Clinical studies have found that early diagnosis and treatment of CHD was very important to improve the prognosis and the life quality for the elderly patients. Koenig [1] have shown that serum cystatin C level were strong correlation with cardiovascular events independently. Mendiluce [2] reported that serum cystatin C level was increased significantly in children than in adults, after 60 years old, the serum cystatin C level was increased with age because of renal insufficiency or degeneration. This study detected the serum cystatin C level of elderly patients with hypertension, and to investigate the relationship between the serum cystatin C level and degree of coronary artery lesions in elderly hypertensive patients with coronary heart disease.

Materials and methods

Materials

500 hypertensive patients combined coronary heart disease were diagnosed by coronary angiography, range from November 2011~May 2014 in the nuclear industry 215 hospital and first affiliated hospital of Xi an jiaotong university. There were 321 senile patients with hypertension (male 204, female 117), the average age (68.04 ± 5.9 years), and there were 179 cases without hypertension (male 179, female 60), mean age (68.16 ± 6.01 years). Consent of all patients, their history, physical examination, X-ray examination, electrocardiogram, echocardiogram and related laboratory tests were recorded. Excluded all infections, autoimmune

Table 1. CHD group (Group B) and hypertension with CHD group (Group D) basic data comparison ($\bar{x} \pm s$)

Parameter	B group	D group	t	P
Case	130 (male 86/female 44)	270 (male 171/female 99)		
TBIL	14.48 ± 6.86	13.46 ± 6.28	1.485	0.138
DBIL	6.2 ± 3.21	5.69 ± 2.6	1.717	0.087
IBIL	8.22 ± 4.59	7.81 ± 4.17	0.888	0.375
TG	1.57 ± 1.04	1.61 ± 0.9	-0.424	0.672
CHOL	3.94 ± 1.02	4.11 ± 0.98	-1.619	0.106
HDL	1.1 ± 0.3	1.12 ± 0.31	-0.786	0.432
LDL	2.28 ± 0.81	2.38 ± 0.84	-1.128	0.260
LPA	0.24 ± 0.2	0.28 ± 0.26	-1.604	0.109
APO-A1	1.16 ± 0.29	1.19 ± 0.26	-0.755	0.451
APOB	0.92 ± 0.26	0.93 ± 0.26	-0.480	0.631
UA	289.73 ± 90.54	299.49 ± 92.15	-0.998	0.319
BUN	5.12 ± 1.93	5.23 ± 1.81	-0.515	0.607
CRE	72.66 ± 18.02	74.47 ± 18.55	-0.923	0.357
hs-CRP	9.22 ± 22.05	7.27 ± 14.93	0.919	0.359

disease, metabolic disease (not including diabetes) and severe chronic diseases (such as cirrhosis, thyroid disease and chronic renal insufficiency).

Grouped data

(1) The patients were divided into the following categories as per hypertension with or without CHD: Neither hypertension nor CHD (Group A), CHD group (Group B), hypertension group (Group C), hypertension combined CHD (Group D). Group A had 49 cases (male 33, female 16), average age (66.53 ± 6.34 years); Group B had 130 cases (male 130, female 44), average age (68.77 ± 5.78 years); Group C had 51 cases (male 33, female 18), average age (67.98 ± 5.41 years); Group D had 270 cases (male 171, female 99), the average age (68.05 ± 6.00 years).

(2) The patients were divided into the following categories as per degree of blood pressure: No hypertension group had 179 cases (male 119, female 60), mean age (68.16 ± 6.01 years); Stage 1 hypertension group had 123 cases (male 80, female 43), mean age (68.49 ± 6.18 years); Stage 2 hypertension group had 131 cases (male 86 female 45), mean age (67.42 ± 5.49 years); Stage 3 hypertension group had 67 cases (male 45, female 22), mean age (68.21 ± 5.09 years).

(3) The patients were divided into the following categories as per degree of coronary artery lesions: No lesion group (no narrow or stenosis < 30% in any of coronary artery) had 100 cases (male 66, female 34), average age (67.27 ± 5.9 years old); Single lesion group (stenosis ≥ 50% in 1 vessel) had 150 cases (male 91, female 69), the average age (67.99 ± 5.88 years old); Double branch lesion group (stenosis ≥ 50% in any 2 vessels) had 117 cases (male 64, female 53), average age (67.47 ± 5.07 years old); Triple vessel group (stenosis ≥ 50% in any 3 vessels) had 133 cases (male 73, female 60), average age (68.26 ± 5.78 years old).

Methods

(1) Determination of cystatin C: Each patient was collected elbow venous blood 5 ml in the morning after 12 hours empty stomach and saved them in -80°C refrigerator for test. The serum cystatin C levels were detected by immunoturbidimetry (according to the test instructions).

(2) Coronary angiography: According to the guidelines for coronary angiography of ACC/AHA, the coronary angiography was performed for each patient and coronary artery narrow degree was judged.

Statistical analysis

All Statistical analyses were performed with SPSS11.0/PC Package, and all values were expressed as mean ± standard deviation ($\bar{x} \pm s$). The comparisons of the levels of serum cystatin C were made by using Student's T-test, and the criteria for significance difference was $P < 0.05$.

Results

Comparison of the basic data of CHD group (group B) and hypertension combined CHD group (group D).

The basic data showed that there were not difference between Group B and Group D on age, gender, total bilirubin (TBIL), direct bilirubin (DBIL) and indirect bilirubin (IBIL), serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low density lipoprotein (LDL-C), lipoprotein A (LPA), apolipoprotein A1 (APO A1), apolipoprotein B (APOB), uric acid (UA), blood urea nitrogen (BUN), creatinine (CR) and high-sensitivity C-reactive protein (hs-CRP) (**Table 1**).

Serum cystatin C level of different stage of blood pressure

The serum cystatin C level of either stage hypertension was significantly higher than that of no hypertension group ($P < 0.01$), the serum cystatin C level of stage 3 hypertension group was significantly higher than that of stage 1 or stage 2 hypertension group ($P < 0.05$). There was no significant difference ($P > 0.05$) between stage 1 and grade 2 hypertension group.

Serum cystatin C level of different degree of coronary artery lesions

The serum cystatin C level of patients with single coronary artery lesions was significantly higher than that of the patients without coronary lesion group ($P < 0.01$), the serum cystatin C levels of patients with double or three branch coronary lesions were significantly higher than that of the patient with 1 lesion ($P < 0.05$), while the serum cystatin C level of patients with double branch was no significant difference compare with that of the patients with 3 lesions ($P > 0.05$).

Serum cystatin C level of different groups patients

The serum cystatin C levels of Group D were significantly higher than that of the Group B, Group C and Group A ($P < 0.05$).

Correlation analysis

Multiple stepwise regression analysis was used to further understand the factors that influence cystatin C, and the analysis results showed: the influence factors were age, CR, UA, HDL, APOA1, diabetes history, history of hypertension and coronary artery lesion counts. APOA1 level was negatively related to the level of serum cystatin C, the others were positively correlated to the level of cystatin C. CR was the biggest influence ($P < 0.001$, 95% CI 0.003~0.006), followed by coronary lesion counts ($P < 0.001$, 95% CI 0.048 to 0.094), a history of high blood pressure ($P < 0.001$, 95% CI 0.045~0.092), age ($P = 0.006$, 95% CI 0.002~0.010) and a history of diabetes ($P = 0.008$, 95% CI 0.021~0.139).

Discussion

Cystatin C is one of the members of cysteine protease inhibitors family, expressed in all mononuclear cells, widely exists in animals, plants and the parasite cysteine protease inhibitors, participate in the cells inside and outside protease hydrolysis [3]. All nucleated cells of body are producing cystatin C in constantly, and it is also regulating the protein hydrolysis inside and outside of cells, and protecting cells from inadequate endogenous or exogenous protease hydrolysis. In physiological conditions, it was found that the main physiological function of cystatin C was to inhibit the activity of endogenous cysteine protease, neutrophil migration and participate in the inflammatory process [4, 5]. Recent studies [6, 7] found that cystatin C involved in the pathological and physiological processes of cardiovascular system, cystatin C was closely related with the occurrence of atherosclerosis disease such as CHD, peripheral arterial sclerosis. It has become one of the potential important prognosis factors for diagnosis and treatment of cardiovascular disease.

This study shows that the serum cystatin C level of either stage hypertension was significantly higher than that of no hypertension group ($P < 0.01$), the serum cystatin C level of stage 3 hypertension group was significantly higher than that of stage 1 or stage 2 hypertension group ($P < 0.05$). There was no significant difference ($P > 0.05$) between stage 1 and grade 2 hypertension group. The results were as same as Kestenbaum's reports [8, 9], and showed that people with high cystatin C level had higher clinical risk of high blood pressure occurrence.

Cystatin C was used as a sensitive factor of early renal damage, but the risk can not be predicted by routine clinical renal function, and speculated that cystatin C improve the occur-

rence of cardiovascular events through other ways [10, 11]. It may be that cystatin C inhibits some cysteine protease, the balance is damaging of protease and its inhibitors when the content of protease is reducing, and resulting in pathological damage. This study found that the levels of cystatin C were significant differences between patients with different coronary artery lesions. The serum cystatin C level of patients with single coronary artery lesions was significantly higher than that of the patients without coronary lesion group ($P < 0.01$), the serum cystatin C levels of patients with double or three branch coronary lesions were significantly higher than that of the patient with 1 lesion ($P < 0.05$), while the serum cystatin C level of patients with double branch was no significant difference compare with that of the patients with 3 lesions ($P > 0.05$). Koenig [12] prospective study found that cystatin C was associated with the risk of cardiovascular events, it might be an independent prognosis factor for CHD.

This study also found the influence factors of cystatin C as follows: age, CR, UA, HDL, APOA1, diabetes history, history of hypertension, coronary artery lesion counts. APOA1 level was negatively related to the level of cystatin C, the lower APOA1 level, the higher cystatin C level. The others were positively correlated to the level of cystatin C, CR was the biggest influence. This result was as same as Li Weicong's reports [13] that reduced levels of APOA1 were associated with elevated risk of coronary heart disease (CHD).

With the development of Chinese basic medical, cystatin C testing is more and more widely used in clinic, and it is one of the independent impact factors in CHD [6], it will be very significant for elderly hypertensive patients with CHD. Because of the limited materials, it is unclear that cystatin C involved in the occurrence and development of atherosclerosis, especially with the correlation of hypertension and CHD, and need more basic and clinical researches to confirm it.

Disclosure of conflict of interest

None.

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