Comparison of Serum Levels of IL-35, MyD88, hsCRP and NO between Patients with Premature Ventricular Contraction and Healthy Subjects

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Abstract: Objective: To observe the effect of serum levels of IL-35, MyD88, hsCRP and NO in patients with premature ventricular contractions with Qi and Yin deficiency and healthy subjects. Methods: From August 2020 to August 2021, 40 patients with premature ventricular contractions with Qi and Yin deficiency admitted to the outpatient department and inpatient department were divided into the observation group, and 40 healthy people admitted to the treatment center were divided into the control group. The serum levels of IL-35, MyD88, hsCRP and NO in the two groups were observed. Results: The serum levels of IL-35 and NO in the observation group were significantly lower than those in the control group, and the differences were statistically significant (P < 0.05). The serum levels of MyD88 and hsCRP in the observation group were significantly higher than those in the control group, and the differences were statistically significant (P < 0.05). Conclusions: Compared with healthy people, the serum levels of MyD88 and hsCRP in patients with Qi-Yin deficiency are significantly increased, while the levels of IL-35 and NO are significantly decreased, indicating that there is a relationship between the relevant factors in patients with premature ventricular contraction, which provides experimental theoretical basis for the study of the mechanism of premature ventricular contraction.

1. Introduction

Premature ventricular contractions are common complications of coronary heart disease and one of the high risk factors for death caused by adverse cardiovascular events. Premature ventricular contractions, also known as precontractions, refer to precontractions caused by premature depolarization of ectopic excitatory foci of ventricular muscles below his bundle and its branches [1]. Individuals with normal heart structure can also develop PVCs, and the incidence of PVCs is higher in patients with structural heart diseases such as coronary heart disease, cardiomyopathy, and valvular heart disease. The incidence of PVCs increases with age, but it is also common in children and adolescents [2-3]. Excessive drinking, smoking, mental strain, overwork...
and so on are the factors that induce VT. At present, various antiarrhythmic drugs and catheter ablation are mainly used in clinical treatment rooms.

2. Relationship between IL-35, MyD88, hsCRP, NO and PVCS

The pathogenesis of premature ventricular contractions is related to inflammatory reaction, apoptosis, energy failure and ion accumulation [4]. In recent years, inflammatory reaction has been proved to be an important link in functional ventricular prephase contraction [5]. IL-35 is mainly secreted by regulatory T cells and has certain anti-inflammatory activity, which can inhibit the activity of Th17 cells and reduce the level of IL-17. It can also rapidly induce Th1 cells to secrete interferon (IFN)-γ and other anti-inflammatory factors to clear infection and reduce the inflammatory state of the body [6]. Inflammatory response plays an important role in the pathogenesis of ventricular premature contractions. Toll-like receptor 4/ myeloid differentiation factor 88/ nuclear factor-κB (TLR4/MyD88/NF-κB) signaling pathway is the main pathway mediating inflammatory response [7]. Patients with arrhythmia often produce a large amount of high-sensitivity C-reactive protein (hsCRP) and other inflammatory factors, which can induce cardiomyocyte hypertrophy and apoptosis, accelerate the formation of thrombosis, and increase the probability of acute cardiovascular events [8]. Nitric oxide (NO), as an important vasoactive substance, can relax endothelial cells and increase the ability of vascular expansion. In this study, the levels of IL-35, MyD88, hsCRP and NO in serum of healthy people and patients with ventricular premature contraction were observed, and the mechanism of action was discussed from the aspects of anti-inflammatory and antioxidant damage, so as to provide scientific basis for clinical use.

3. Data and methods

3.1. Source of cases

From August 2020 to August 2021, 40 patients with coronal ventricular premature contractions with Qi and Yin deficiency admitted to the cardiovascular Clinic of Xi’an Hospital of Traditional Chinese Medicine and 40 healthy people admitted to the physical examination center were selected. Patients with premature ventricular contractions were included in the observation group. Healthy people were selected as the control group, 40 cases in each group. The average age of the observation group was 55.2±7.7 years old (36-69 years old), and the average age of the control group was 41.8±6.7 years old (28-57 years old). There was no significant difference in the general data between the two groups (P>0.05).

3.2. Diagnostic criteria

The diagnostic criteria of Western medicine refer to the diagnostic criteria of "premature ventricular contractions" in the journal of Practical Internal Medicine edited by Chen Haozhu [9]: ① There is no P wave or no related P wave in the QRS-T wave front in advance; ② The time limit of QRS is usually more than 0.12s, and the direction of T wave is mostly opposite to the direction of QRS main wave. ③ It is often complete compensatory intermittence. The diagnosis criteria of TCM refer to "Guiding Principles for Clinical Research of New Chinese Medicine" [10]. Patients with central palpitations are characterized by deficiency of both Qi and Yin, characterized by palpitations, dead air, hot nerves, shortness of breath, weakness, dizziness, dry mouth, insomnia and dreams, red tongue, little moss, and fine pulse.
3.3. Inclusion criteria

Observation group: ① Patients who met the diagnostic criteria of traditional Chinese and western medicine for palpitation and syndrome differentiation were Qi and Yin deficiency; ② It met the diagnostic criteria of Western medicine for premature ventricular contractions, and the Lown classification was ii-ivα[11]; ③ Age ≥30 years and ≤75 years, both sexes; ④ Did not receive relevant treatment within 3 months before enrollment; ⑤ Patients gave informed consent to the study and signed informed consent.

Control group: patients who underwent physical examination in our hospital were excluded from organic heart disease, hypertension, diabetes and other diseases by medical history, physical examination, electrocardiogram, chest X-ray, echocardiogram, three major routine and blood biochemical tests.

3.4. Exclusion criteria

1) Acute heart failure, III degree atrioventricular block and other serious cardiovascular diseases; 2) Complicated with intracerebral hemorrhage, cerebral infarction and other acute cardiovascular and cerebrovascular diseases; 3) Severe liver, lung and renal dysfunction; 4) Combined with immune diseases, hematopoietic system diseases and malignant tumors; 5) Complicated with cognitive impairment, mental disease or other reasons.

3.5. Observation index and content

Blood index: 5ml peripheral venous blood was collected from patients and healthy people in the morning. After serum separation, the levels of human interleukin-35 (IL-35), human myeloid differentiation factor 88 (MyD88), high sensitivity C-reactive protein (hsCRP) and nitric oxide (NO) were measured by double-antibody sandwich. The above operations are performed by fixed inspectors in strict accordance with the kit instructions.

Safety indicators: blood routine examination, urine routine examination, liver and renal function examination, electrocardiogram before enrollment.

3.6. A statistical approach

SPSS 22.0 statistical software was used for processing, count data were expressed as (%), and X2 test was used. Measurement data conforming to normal distribution were expressed as mean ± standard deviation (x±s), and comparison between two groups was performed by paired sample t test. P < 0.05 indicates statistical significance.

4. Result

1) In the observation group and the control group without treatment, the serum level of IL-35 in the control group was higher than that in the observation group, while the serum level of MyD88 was lower than that in the observation group, and the difference was statistically significant (P < 0.05). The results are shown in Table 1.
Table 1: Comparison of serum levels of IL-35 and MyD88 between the observation group and the control group

|                         | number of cases | IL-35       | MyD88        |
|-------------------------|-----------------|-------------|--------------|
| observation group       | 40              | 39.6±10.14  | 13.11±2.17   |
| control groups          | 40              | 44.52±10    | 11.88±2.88   |
| t-value                 |                 | 2.184       | 2.162        |
| p value                 |                 | 0.032       | 0.034        |

2) In the observation group and the control group without treatment, the serum level of NO in the control group was higher than that in the observation group, while the serum level of hsCRP was lower than that in the observation group, and the difference was statistically significant (P < 0.05). The results are shown in Table 2.

Table 2: Comparison of serum levels of IL-35 and MyD88 between the observation group and the control group

|                         | number of cases | NO           | hsCRP        |
|-------------------------|-----------------|--------------|--------------|
| observation group       | 40              | 39.54±37.3   | 170.15±81.54 |
| control groups          | 40              | 61.21±31.47  | 136.45±39.71 |
| t-value                 |                 | 2.547        | 2.134        |
| p value                 |                 | 0.013        | 0.038        |

5. Discuss

Western medicine believes that ventricular premature beats are ectopic pacing point in advance before the normal pacing point, resulting in ventricular depolarization, clinical symptoms mainly manifested as palpitations, chest tightness, heart arrest sense, serious can lead to systemic effective blood volume perfusion caused dizziness, amaurosis and angina attack, even cause sudden death. Is no arrhythmia in traditional Chinese medicine, according to its symptom and clinical manifestation belongs in the category of "heart palpitations and other secondary", its etiology and pathogenesis of qi and blood, Yin and Yang deficiency, phlegm turbidity, water to drink one spirit as the standard, the proof of the palpitation is a virtual to real, arrhythmia is the main pathological changes of heart palpitations, can be caused by organic disease, see more at functional lesion. Through the experiment, the serum levels of MyD88 and hsCRP in patients with ventricular premature contractions with Qi and Yin deficiency were higher than those in the healthy group, while the levels of NO and IL-35 were lower than those in the healthy group, and the differences were statistically significant. Nitric oxide is a protective factor secreted by endothelial cells, which plays a key role in relaxing blood vessels and maintaining the healthy flow of blood in various organs of the body. In patients with premature ventricular contractions, endothelial cell injury is often accompanied by a corresponding decrease in NO secretion. IL-35 can inhibit inflammatory response and is closely related to the progression and instability of atherosclerotic plaques. The study of Hu Ruilan et al.\(^{[12]}\) also confirmed the correlation between IL-35 and the development of coronary heart disease. This study also further demonstrated the reduction of serum IL-35 in patients with premature ventricular contractions. MyD88 signaling pathway can regulate the secretion of IL-6, which is one of the proinflammatory factors and can accelerate the synthesis of inflammatory response proteins\(^{[13]}\). The results of this study showed that the proinflammatory level of patients with Qi-Yin deficiency type PVCS was high, the content of MyD88 and hsCRP was high, and the levels of NO and IL-35 were low, indicating that there was a relationship between protective factors and proinflammatory seal in patients with PVCS, suggesting that traditional Chinese medicine could play an important role in anti-inflammatory and endothelial cell protection.
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References

[1] Cao K J, Chen K P, Chen M L, et al. 2020 Chinese expert consensus on ventricular arrhythmia (2016 updated version) [J]. Chin J Cardiac Pacing & Electrophysiology, 2020, 03: 189-253.
[2] Cohen M I. Frequent premature ventricular beats in healthy children: when to ignore and when to treat? [J]. Current Opinion in Cardiology, 2018, 34(1): 1.
[3] Drago F, Leoni L, Bronzetti G, et al. Premature ventricular complexes in children with structurally normal hearts: Clinical review and recommendations for diagnosis and treatment [J]. Minerva Pediatrica, 2017, 69(5): 427-433.
[4] Zhang Tao, Wang Yunlong, Liang Zuo, Han Zhihong, Zhao Hua, Ren Xuejun. Effect of radiofrequency ablation of idiopathic right ventricular outflow tract preventricular contraction using inverted U method combined with ordinary bending method under zero radiation [J]. Chin J Interventional Cardiology, 2019, 04: 193-198.
[5] Huang Y, Wang J Y. The relationship between QT interval shortening and ventricular arrhythmias in patients with variant angina pectoris by 24h holter detection [J]. Electrocardiogram and circulation, 2019, 02: 124-127.
[6] Fang Dihai, LAN Zhimei. Serum IL-17 levels in patients with heart failure and arrhythmia after myocardial infarction [J]. Modern Medicine, 2017, 03: 381-384.
[7] Chen Jinsong, Liu Yunyang, Zeng Gaofeng, Liu Xinyao, Huang Bing, Yuan Huiying. Relationship between Toll-like receptor 4 signaling pathway and the severity and prognosis of chronic heart failure [J]. South Central Journal of Medical Science, 2016, 06: 653-656+714.
[8] Fu Shengdi, Xie Hui. Clinical efficacy and safety of carvedilol combined with amiodarone in the treatment of arrhythmia [J]. Chin J Clinical Pharmacology, 2016, 07: 579-581.
[9] Chen Haozhu. [M]. 3 Ed. Beijing: People's Medical Publishing House, 2009: 1398-1399.
[10] Ministry of Health of the People's Republic of China. Guiding Principles for clinical research of New Chinese Medicine [M]. Beijing: Ministry of Health of the People's Republic of China, 1995: 91-94.
[11] Chen Q. The differentiation of Lown classification of premature ventricular contractions [J]. Journal of Clinical Electrocardiology, 2005, 01: 3-4.
[12] Hu Ruilan, Ren Jun, Zhang Dongfeng. Plasma IL-35 level in coronary heart disease and its correlation with Gensini score and LYEF [J]. Marker immunoassay and clinic, 2017, 04: 408-410.
[13] Hao Jian, Xu Liping, Lu Tiegang. Effects of preparation of Rhubarb-ligusticum Chuanxiong on the apoptosis of renal tubular epithelial cells and renal inflammatory cytokines IL-6 and IL-1β induced by contrast agent in rats through TLR4/Myd88/NF-κB signal [J]. Chinese Journal of Gerontology, 2018, 23: 5772-5775.