Apelin and PDCD5 levels in patients with chronic heart failure

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Abstracts: Objective: To detect the plasma levels of apelin and Programed Cell Death 5(PDCD5) antibody in elderly patients with chronic heart failure. **Methods:** Forty patients with chronic heart failure were divided into 3 groups CHF according to NYHA class II~IV, and twenty normal volunteers were enrolled. Plasma levels of apelin and PDCD5 antibody were detected by enzyme-linked immunosorbent assay. **Results: (**1)The plasma levels of apelin in patients with heart failure(NYHA class Ⅱ~Ⅳ) were significantly lower than that in control group,and it was lower in NYHA class Ⅲ-Ⅳ groups than that in NYHA class Ⅱ group ($P < 0.05$); (2) The plasma levels of PDCD5 were increased in CHF patients($P < 0.05$). **Conclusion**: Detecting the plasma levels of apelin and PDCD5 antibody might be usful to evaluate the heart functon.
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Key words: heart failure；apelin；PDCD5

1. Introduction

Heart failure is frequently due to coronary heart disease and often leads to prolonged disability. Most patients admitted to hospital with heart failure are more than 65 years old and they have a very poor prognosis.Approximately 50% of patients with severe heart failure will die within 2 years.

Heart failure is associated with complex neurohormonal changes including activation of the RAS and the sympathetic nervous system.Apelin was consided as the most potent endogenous inotrope, which is the endogenous ligand for the orphaned G protein-coupled receptor APJ. The apelin gene are present in endothelial cells,vascular smooth muscle cells, and cardiomyocytes. In preclinical models, apelin signaling exerts major effects on both vascular tone and cardiac contractility. Apelin might be the most potent endogenous inotrope described so far, and it can cause vasorelaxation and cause a rapid fall in both arterial blood pressure and systemic venous tone with corresponding reduction in left ventricular afterload and preload.But there is no report about apelin changes in elderly patients with heart failure publicated so far, and the efficacy of apelin on heart function and cardiomycyte apoptosis have not been elucidated. We recently examined the levels of apelin and PDCD5 antibody in 40 elderly patients with chronic heart failure and 20 normal volenteers to determine the changes of apelin in heart failure and whether apelin could affect the heart function in elder subjects or not.

2. Material and Methods

Study population

Patients data: From July 2010 to December 2011, 40 elderly patients with heart failure (male 27 and femal 13, aged 70±10 years old). All patients had no diabetes mellittus, pumanary disease, carcinoma, blood disease, infectious disease, coronary heart disease or stroke by physical examnation, electrocardiography, routine biochemistry teting, x-ray, color echocardiography (UCG).

Control group: 20 healthy volunteers without any symptoms or illness were enrolled (male 8 and female 12，aged 65±8 years old). There was no difference of age, gender, height and weight between patient group and normal group.

Ethics approval

Ethics approval was obtained from the Ethics committee of the first affiliated hospital of Zhengzhou University，and all patients gave informed before participation in the study.

Assays

Apelin levels measurement

Blood samples were obtained from all patients within 24h of hospital admission. Blood samples (3mL) were drown into tubes containing EDTA and kept at -80℃ after centrafugation at 4℃. The plasma apelin-13 levels were measured with ELISA. Apelin kit was from R&D Co, USA. Tetrabenzidine(TMB）was used to colure, Optical density(ODvalue） were read at wave length of 450nm.

PDCD5 antibody levels measurement

Group	n	PDCD5 ug/ml
Normal	20	1.6±1.2
Class Ⅱ	21	2.2±0.5[1)]
Class Ⅲ	10	2.9±1.4[1)2)]
Class Ⅳ	9	3.3±1.0[1)2)3)]

PDCD5 kit was from R&D Co,USA. PDCD5 combined with PDCD5 antibody labbled with horseradish peroxidase(HRP） then appeared as blue and then yellow when acting with TMB. Optical density (OD value） were read at wavelength of 450nm.

Statistics

All values were expressed as mean ±SD($\bar{x}$±s)，The student's *t*- test was used to compared two groups. A value of $P<0.05$ was considered significant.

3. Results

Apelin levels in patients with heart failure and control group.

Apelin was 2.18±0.80 ng/ml in HF group and 4.29±0.77 ng/ml in control group（$P<0.05$）. Apelin levels in patients with NYHA class Ⅲ and Ⅳ were decreased compared with that in NYHA class Ⅱ group （$P<0.05$）, Table 1.

Table 1. Apelin levels in normal and heart failure patients.

Group	n	Apelin ng/ml
Normal	20	4.29±0.77
Class Ⅱ	21	2.90±0.65[1)]
Class Ⅲ	10	2.15±0.44[1) 2)]
Class Ⅳ	9	1.46±0.43[1) 2) 3)]

1）Compared with normal,2）compared with class Ⅱ，3）compared with class Ⅲ：$P<0.05$.

Plesma PDCD5 levels in HF and control group

PDCD5 antibody was higher in HF group than that in control group（$P<0.05$），PDCD5 in NYHA class Ⅳ was higher than that in class Ⅱ and class Ⅲ;and it was higher in class Ⅲ than that in class Ⅱ （$P<0.05$）, Table 2.

Table 2 . PDCD5 antibody levels in normal and HF patients

1） Compared with normal,2）compared with class Ⅱ，3）compared with class Ⅲ：$P<0.05$.

4. Discussion

Apelin is a recently isolated novel endogenous ligand for the angiolike 1 receptor（APJ）, it was consided as the most potent endogenous inotrop [1,2]. Rat heart apelin infusion could increase myocardial contrtility in vitro[3,4]. Ashley[5] reported that apelin administration for a long period could increase myocardial contractility, and decrease preload and afterload but no myocardial hypertrophy. This differed from the β_1 adrenalin action.

Apelin and APJ expression decreased[6] in rats myocardial ischemia model induced by isoproterenol. Apelin decreased in early AMI and lasted for 24 weeks[7]. Kuklinska[8] reported that apelin-36 concentrations are reduced in low risk first STEMI patients during the first days, regardless of the degree of LV dysfunction and prognosis.

Acute myocardial infarction(AMI) secondary to lethal ischemic-reperfusion contributes to much of the mortality and dysfunction from ischemic heart disease[9]. Apoptosis plays a major role in the myocardial ischemia-reperfusion injury[10~11]. Piot et al[12] reported that there are two forms of cell death during ischemic-reperfusion after AMI,including cell necrosis and apoptosis. In ischemia period cell necrosis occurred, and the cell apoptosis mainly occurred or obviously accelerated in reperfusion period, myocardial apoptosis induced by ischemic reperfusion injury is the main form of myocyte loss and the main reason for the expansion lesions and heart dysfunction[13].

Zhang[14] identified that apelin protected heart against ischemic cardiomyocyte apoptosis via activation of the PI3K/Akt pathway，and observed the endogenous apelin-APJ system was compensatorily up-regulated and ultimately down-regulated following sustained myocardial ischemia.Tao[15] reported administration of apelin at 1μg/kg not only completely abolished the activation of ER stress-induced apoptosis signaling pathways at 2h of reperfusion but also significantly attenuated time-related changes at 24h of reperfusion. Another study [16] found that apelin-13 administrated 5 minutes before reperfusion could decrease apoptosis during ischemic reperfusion.

Apelin is reduced in patients with heart failure and also of ischemic heart disease[17]. Using TUNEL method, Narula [18] analized the failure heart and found that the apoptotic index was 35.5%, which was more higher than that in normal group. Apelin could suppres Bax and Caspase-3 expression, and increase Bcl-2 expression and therefor suppress myocardial apoptosis.

We found that PDCD5 levels were higher in heart failure than that in normal group. PDCD5 increased significantly in heart failure induced by ischemic heart disease than that in dilated cardiomyopathy or rheumatic heart disease. PDCD5 is a gene regulating apoptosis. PDCD5 expression increased during apoptosis. This suggests that myocardial ischemia or heart failure could induce myocardial apoptosis, and detecting the PDCD5 levels might be useful in the evaluation of heart failure.

In conclusion, there were some significantly changes of apelin and PDCD5 levels in patients with chronic heart failure. Because fewer cases were analyzied in this article, detailed clinical investigation is now required to determine the changes of apelin and

myocardial apoptosis and the therapeutic efficacy of augmenting apelin–APJ activity in patients with heart failure.

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