Assessment of MR-ProADM and N-Terminal B-Type Natriuretic Peptide of Serum Levels in Patients with Heart Failure.

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Abstract

Background: Heart failure timely and effective diagnosis and treatment directly affects the prognosis of patients, so early diagnosis of heart failure treatment is very important. The current diagnosis of heart failure has yet to be further improved. To investigate the relationship between plasma levels of MR-ProADM and NT-proBNP in cardiac structure and function in patients with heart failure (HF) and the early detection of failure. **Methods**: Patients were recruited from the coronary care unit (CCU) of Al-Yarmouk Teaching Hospital and were admitted and verified as cases of HF by specialist cardiologists. Between the 1st of November 2017 and the 1st of April 2018; 48 patients (29 males and 19 females), were diagnosed to have HF and were included in the study. The total number of HF patients admitted to the CCU of the hospital during the study period was 100 patients but 52 patients were ruled out according to the exclusion criteria of the study such as Acute Myocardial Infarction, active myocarditis, Drug abuse or an alcohol drinker, renal failure .Apparently healthy subjects were recruited from the staff of Al-Mustanseryeah Medicine College. They comprised (40) subjects (30 males and 10 females). Each subject who was recruited in the control group has underwent a full history and physical examination with a recording of : age, gender, smoking, chronic diseases and medications.

Any subject in control group in this study must be fasting for 8-14 hours at the time of drawing of blood specimen. Consent was taken from all subjects in the control group after being told about the aim of the study. The plasma MR-ProADM and NT-proBNP levels were compared between the two groups to observe the value of plasma MR-ProADM combined with NT-proBNP in the diagnosis of heart failure. **Results:** the levels of plasma MR-ProADM and NT-proBNP were significantly higher in patients with heart failure Compared with the healthy control group. The levels of plasma MR-ProADM and NT-proBNP increased significantly ($P < 0.01$). The area under the ROC curve for the combined detection of plasma MR-ProADM and NT-proBNP was greater than the area under the three alone tests. **Conclusion**: The combined detection of MR-ProADM and NT-proBNP has high sensitivity and specificity in the diagnosis of heart failure and can be used as a new detection mode.

Keywords *: MR-ProADM = mid-regional prohormone adrenomedullin, N-Terminal B-Type Natriuretic Peptide, Heart Failure .*

Introduction

Heart failure is a clinical syndrome that results when the heart is unable to provide sufficient blood flow to meet metabolic requirements or accommodate systemic venous return its timely and effective diagnosis and treatment directly affects the prognosis of patients [(1)], so early diagnosis of heart failure treatment is very important. This study was to investigate the relationship between plasma levels of MR-ProADM and NT-proBNP in cardiac structure and function in patients with heart failure (HF) early detection of failure . The clinical data

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of 48 patients with heart failure and normal healthy people 40 subjects. The purpose of this study was to analyze the clinical significance of combined detection of plasma MR-ProADM and N-terminal B-type natriuretic peptide in the diagnosis of heart failure value. The study found that inflammation can aggravate myocardial injury, thereby worsening cardiac function, plays a very important role in ventricular remodeling [(2)]. Most of the inflammatory cytokines have a negative inotropic effect, thereby reducing myocardial contractility and cardiac output, worsening cardiac function [)3( )4(].

MR-ProADM is secreted in various tissues, including the heart, lungs, central nervous system, kidneys and gastrointestinal organs; it is also expressed in endothelial cells, vascular smooth muscle cells, fibroblasts and adipocytes. MR-ProADM has a hypotensive effect: it stimulates diuresis and natriuresis and also causes vasodilation, lowering blood pressure. In HF, as a consequence of pressure/volume overload and ventricular wall stretching, the MR-ProADM gene is upregulated in cardiac myocytes. The resulting high MR-ProADM levels appear to have a protective effect in the myocardium, as they lead to a decrease in preload and afterload. Some studies suggest that MR-ProADM additionally inhibits cell growth and hypertrophy; it has also been associated with reductions in remodeling and fibrosis[)5(].

One of the first responses to cardiac dysfunction is the activation of the sympathetic nervous system. Mid-regional proadrenomedullin (MR-proADM) is a precursor to a potent vasodilator with inotropic properties, adrenomedullin, originally isolated from pheochromocytoma cells. MR-proADM is elevated in patients with acute and chronic HF and is a strong predictor of clinical outcomes such as mortality and HF hospitalization, even when added to BNP or NT-proBNP.

Materials and Method

Research Objects and Groups

The study was carried out at the department of Chemistry and Biochemistry -College of Medicine- Al Mustansiry University. Patients were recruited from the coronary care unit (CCU) of Al-Yarmouk Teaching Hospital and were admitted and verified as cases of HF by specialist cardiologists. Between the 1st of November 2017 and the 1st of April 2018; (29 males and 19 females), aged ≥ 30 years, and we selected 48 patients were diagnosed to have HF. Diagnostic criteria for HF had based on the manifestation of three or four findings including: **EF in Echocardiogram** ,**Clinical presentation, ECG changes**, **and troponin positivity. The diagnosis is sometimes aided by the results of cardiac enzymes levels.** Blood was collected on admission to the CCU for the qualitative troponin-I testing. It is a device rapid test using cassette method as well as measuring complementary cardiac enzymes (GPT). Also the qualitative troponin-I testing by cassette method was repeated for double checking in the blood sample taken on the next morning for analysis of baseline laboratory tests and the study parameters. ECG changes were detected by electrocardiography done by expert nursing staff using under supervisor and specialist cardiologist electrocardiogram–recording apparatus (BIOMED Company, USA).

Any subject enrolled in control group must be fasting for more than 8 hours at the time of drawing of blood specimen.

Patients were interviewed using a questionnaire that included:

- Time of admission to CCU after chest pain.
- Past medical history , history of DM, current alcohol consumption.

Patients with Heart failure but have the following conditions were excluded in this study :

1. Acute Myocardial Infarction
2. Active myocarditis.
3. Strok , skeletal muscle injury, or trauma.
4. Age is <30 years.
5. Had abdominal enlargement for any reason other than central obesity.
6. Valvular heart disease

Apparently healthy subjects were recruited from the staff of Al-Mustansiryah Medicine College. They comprised (40) subjects (30 males and 10 females).

Each subject who was recruited in the control group has underwent a full history and physical examination with a recording of : age, gender, smoking state , chronic diseases and medications. They have no symptoms or history of coronary heart disease. They were age and sex-matched to study patients (41.55±7) and also comply to the criteria of exclusion in patients group. In addition, they underwent electrocardiographic screening to check for any ECG changes which might exist in spite of no clinical features of HF so as to be excluded from the study.

Method

Blood collection was performed at 8.00 – 9.00 a.m. in the fasting state,

Collected blood was transferred into the tube while ensuring flowing down the wall of the tube, then serum was obtained and divided into aliquots in eppendorf tubes and stored at -20˚C until analysis.

Determination of serum NT-proBNP level by AFIAS ,is a fluorescence Immunoassay (FIA) for the quantitative determination of NT-proBNP in human serum, Boditech .While Determination of human MR-proADM concentration by enzyme linked immune sorbent assay kit (MyBioSource /USA) Application of it is measured according to kit instructions for testing .

Statistical Methods

SPSS 22.0 software was used for statistical analysis. The t test was used to measure the data between the two groups. Chi-square test was used to count data. Logistic regression was used to analyze the risk factors for screening heart failure. The test level was 0.05. When $P < 0.05$, has statistical significane. The working curve (ROC curve) of subjects tested separately and jointly with MR-proADM and NT-proBNP was established to calculate their specificity and sensitivity.

Results

comparison between Heart Failure Group and Control Group in Plasma Levels of MR-proADM and NT-proBNP.

Heart failure group increased significantly compared with the control group, the difference was statistically significant ($P < 0.01$, Table 1). Plasma levels of MR-proADM and NT-proBNP in HF group were significantly higher than those in control group ($P < 0.01$, Table 1) .

Table 1: Heart failure group and control group heart function and plasma levels of MR-proADM and NT-proBNP.

	Heart failure N= 48	**Healthy controls N= 40**	P value
MR-Pro ADM (pg/ml) mid-regional prohormone adrenomedullin	23.88±21.67 (0.591-80.0)	4.20±3.94 (0.891-25.21)	0.0001*
NT-proBNP (ng/ml) N-terminal pro b-type Natriuretic Peptide	763.1855±298.94661 (22.1-2131.22)	134.54±48.59 (59.30-232.10)	0.0001*
- Data were presented as Mean±SD (Range)			
*Significant difference between two independent means using Students-t-test at 0.05 level.			

Table 2. The Best Discriminative Area Under the Curve MR-Pro ADM and NT-proBNP Parameters that Best in HF.

Test Result Variable(s)	Cut-off value	Sensitivity	specificity	Area	P value
MR-Pro ADM (pg/ml)	7.22050	75.0	97.5	0.869	0.0001*
NT-proBNP (ng/ml)	195.40000	83.3	85	0.847	0.0001*

Table 3: correlation of plasma levels of MR-Pro ADM and NT-proBNP in HF group .

Correlations			
		MR-Pro ADM	NT-proBNP
	N	48	48
NT-proBNP	r	0.028	1
	p	0.852	
	N	48	48
**. Correlation is significant at the 0.01 level (2-tailed).			
*. Correlation is significant at the 0.05 level (2-tailed).			

Discussion

In clinical work, the diagnosis and differential diagnosis of heart failure is still a major problem, easily lead to missed diagnosis. Rapid progress of heart failure, once the condition deteriorated, often endanger the lives of patients. heart failure with poor prognosis)3(.

In recent years, NT-ProBNP has become hot spots in the early diagnosis of heart failure)6-10(. This study aimed to explore the value of MR-Pro ADM and N-terminal B-type natriuretic peptide in the diagnosis of heart failure.

This study aimed to explore the value of MR-Pro ADM and N-terminal B-type natriuretic peptide in the diagnosis of the heart failure. A large number of studies have shown that BNP can better reflect the function of the heart [1], making it widely used in the diagnosis of heart failure. BNP is a chemical that is pulled in the ventricular wall and released into the blood by cardiomyocytes [9] [10]. BNP is also present in normal tissues and is present in very low plasma concentrations. Cardiomyocytes release BNP while also releasing equimolar NT-ProBNP into the bloodstream. Compared with BNP, NT-ProBNP has higher stability in blood plasma, longer half-life and is less affected by other substances. As the heart expands, the hemodynamics and neuroendocrine activities in the heart cavity change. The higher the pressure in the ventricle, the stronger the ventricular wall is pulled and the higher the level of NT-ProBNP secreted by cardiomyocytes [11]. In the present study, the level of NT-proBNP was significantly higher than that of the control group, confirming that NT-proBNP has a very important clinical value in the diagnosis of heart failure. Nomura et al. [12] showed that serum NT-proBNP were elevated in heart failure and that agree with this study.

Conclusion

In this study, our results showed that plasma levels of MR-Pro ADM and NT-proBNP in patients with heart failure were significantly higher than those in healthy controls, both of which could be used as indicators of heart failure. There was no significant difference in the levels of MR-Pro ADM and NT-proBNP between the

heart failure group.

ROC curve results show that the detection of MR-Pro ADM and NT-proBNP alone in the diagnosis of acute heart failure has a good sensitivity and specificity.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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