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Research progress about effects of myocardial enzyme and troponin on uremia with acute left ventricular failure

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Abstract. – OBJECTIVE: We studied the diagnostic value of CK-MB and troponin (cTnI) in uremia with acute left ventricular failure patients.

PATIENTS AND METHODS: We enrolled 130 uremia patients with maintenance hemodialysis (MHD) and divided them into two groups: (i) the observation group with patients suffering from acute left ventricular failure (n=30) and (ii) the control group which contained cases without acute left ventricular failure (n=100). We verified CK-MB, cTnI, serum creatinine, blood urea nitrogen, pro-BNP and LVEF levels at 6 h, 12 h, 24 h, 48 h, 72 h, 7 d and 14 d after the attack and carried out 1-year follow-up to compare total mortality and cardiogenic mortality.

RESULTS: Our results showed that CK-MB and cTnI levels in the observation group were significantly higher than those in the control group ($p<0.05$). CK-MB and cTnI in the observation group increased into platform stage slowly with no peak or downtrend. They were in a linear pattern in the control group. Comparison of SCr and BUN in two groups at different time points produced no statistically significant differences ($p>0.05$). Pro-BNP levels in the hospital as well as 1 month, 6 months and 12 months follow-ups were higher than those in the control group, and differences were of statistical significant ($p<0.05$). While in hospital LVEF level in the observation group was higher than that in the other group, differences regarding 1 month, 6 months and 12 months follow-up between two groups had no statistical significance ($p>0.05$). Total mortality and cardiogenic mortality in the observation group were higher than those in the control group, and differences were statistically significant ($p<0.05$).

CONCLUSIONS: CK-MB, cTnI, SCr, BUN, pro-BNP and LVEF were independent risk factors for total mortality while CK-MB, cTnI and pro-BNP were independent risk factors for cardiogenic mortality.

Key Words:
CK-MB, Troponin, Uremia, Acute left ventricular failure.

Introduction

MHD treatment on uremia significantly improves the survival period as well as the prognosis. Uremia combined with heart failure is a severe complication and the main cause of mortality in patients (60%)[1]. Main causes of uremia with heart failure are hypertension, anemia, uremia cardiomyopathy, water-sodium retention, uremia pericarditis, hyperlipidaemia, increased parathyroid hormone, electrolyte disturbance, acid-base disturbance and arrhythmia[2]. The occurence rate of myocardial infarction caused by uremia is about 1 to 5% while the abnormal increasing rate for uremia with CK-MB and (or) troponin (cTnI) is as high as 20 to 40%. It is indicated that uremia cardiac muscle injury is more common[3]. Few studies on biochemical markers of uremia cardiac muscle injury are available, and the diagnostic value of predicting clinical results is still unclear.

Patients and Methods

Patients

From January 2014 to January 2015, 130 uremia cases treated by MHD in our hospital were enrolled in this study. We divided them into two groups: (i) the observation group with patients suffering from acute left ventricular failure (n=30) and (ii) the control group which contained cases without acute left ventricular failure (n=100). We included patients: (i) who were treated with MHD for at least 3 months, 3 to 4 times each week, 4 h each time and had a positive outcome from their MHD treatment; (ii) with stable condition for at least 3 months who had no primary heart diseases such as coronary heart disease, cardiomyopathy, valvular heart disease and myocarditis; (iii) who

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were under treatment for primary uremia diseases such as chronic glomerulonephritis, diabetic nephropathy and nephrotic syndrome; (iv) with good compliance and complete clinical profiles. Exclusion criteria: (i) patients with severe condition and the predicted survival time of fewer than 12 months; (ii) patients who participated in other studies at the same time; (iii) patients who quitted the study or didn't participate in follow-up visits. This research was approved by Ethics Committee in our hospital and received informed consent forms from patients and their family members.

In the observation group, there were 18 males and 12 females with ages ranging from 56 to 72 years (average=65.4±12.3 year). MHD time was 1 to 6 months (average=3.4±1.3 months). In the control group, there were 58 males and 42 females between 53 to 75 years old (average=64.7±15.4 years). MHD time was 1.5 to 7 months (average=3.3±1.4 months). Differences between two groups regarding gender, age and dialysis time were not statistically significant ($p>0.05$). Dialysis-related acute left ventricular failure event is defined as events during dialysis period that are in accordance with clinical symptoms and diagnosis of acute left ventricular failure (mainly abnormal increase in pro-BNP level and abnormal reduction in LVEF level).

Research Methods

CK-MB, cTnI, serum creatinine (SCr), blood urea nitrogen (BUN), pro-BNP and LVEF levels at 6 h, 12 h, 24 h, 48 h, 72 h, 7 d and 14 d after attack were determined during 1 year and total mortality rate and rate of mortality related to cardiogenic events were compared. 5 to 8 ml peripheral venous blood was collect and coagulated for 30min at room temperature. It was then centrifuged at 3000 rpm for 5 min, and then the upper serum was collected. Hitachi 7600 fully automatic biochemical analyzer and kits from Shanghai Shenneng Reagent Company were used for measuring CK-MB, SCr, and BUN. CK-MB values greater than 24 U/L were considered as diagnosis value while reference range of SCr was 53 to 140 μmol/L and the range for BUN was 3.2 to 7.1 mmol/L. The level of cTnI was measured using microparticle enzyme immunoassay; Ci8200 fully automatic biochemical analyzer and kits from Abbott Laboratories Ltd (Abbott Park, IL, USA) were used and the reference range was <0.4 ng/mL. pro-BNP was measured using electrochemiluminescence and kits from Roche Diagnostics GmbH (Penzberg, Germany), the reference range was <300 pg/mL.

Color ultrasonic apparatus was used in LVEF, and the transducer frequency was 3.0 MHz. It was used to perform M type sampling in mitral chordae section of left ventricular short axis beside sternum guided by two-dimensional echocardiogram, and the sampling line was kept vertical with paris posterior of the interventricular septum. We measure left ventricular end diastolic diameter and end systolic diameter and output LVEF automatically based on Teichholtz correction formula. Total mortality was defined as all death events caused by any reasons during follow-up visit period, and cardiogenic mortality was defined as death caused by sudden cardiac attacks such as heart failure, arrhythmia, and shock.

Statistical Analysis

SPSS 19.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for inputting and analysis. Quantitative data were presented by mean value±standard deviation; comparison between groups was done using *t*-test; comparison within group at different time points was tested by repeated measurement data. Qualitative data were shown in case or percentage (%), and comparison between groups was done through χ^2 testing. A logistic model was used in multi-factor regression analysis and $p<0.05$ referred to statistically significant differences.

Results

Comparison of CK-MB and cTnI at Different Time Points

CK-MB and cTnI levels in the observation group were higher than those measured in the control group at different time points, and differences were statistically significant ($p<0.05$). CK-MB and cTnI in the observation group increased into platform stage slowly with no peak or downtrend and in the control group, they were a linear pattern (Figures 1 and 2).

Comparison of SCr and BUN at Different Time Points

Comparison of SCr and BUN in two groups at difference time points produced no statistically significant differences ($p>0.05$) (Figures 3 and 4).

Comparison of pro-BNP and LVEF in two Groups

Pro-BNP levels in the hospital, 1 month, 6 months and 12 months follow-up were considerably higher in the observation group compared

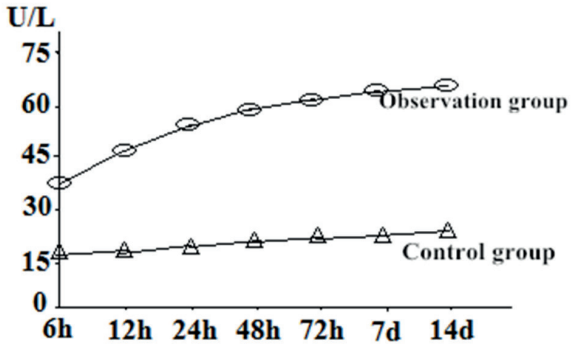

Figure 1. Change trend of CK-MB at different time points.

with those in the control groups and differences were statistically significant (p<0.05). LVEF level in the hospital was significantly higher in the observation group, while differences regarding 1 month, 6 months and 12 months LVEF levels showed no statistically significant differences (p>0.05) (Table I).

Mortality in two Groups and Multi-Factor Regression Analysis

For the observation group, there were 18 death cases, in which 14 were considered cardiogenic deaths. In control group, there was a total of 30 deaths, and 14 cases were considered cardiogenic deaths. Total mortality and cardiogenic mortality rates in the observation group were higher than those in the control group, and differences were statistically significant (60.0% vs. 30.0%, χ^2=8.918, p=0.003: 77.8% vs. 46.7%, χ^2=4.480, p=0.034). Taking age, gender, dialysis time, CK-MB, cTnI, SCr, BUN, pro-BNP and LVEF at different time points as independent variables and total mortality and cardiogenic mortality as dependent variables, it was concluded through Logistic model that CK-MB, cTnI, SCr, BUN, pro-BNP and LVEF were independent risk factors for total mortality while CK-MB, cTnI and pro-BNP were independent risk factors for cardiogenic mortality (Tables II and III).

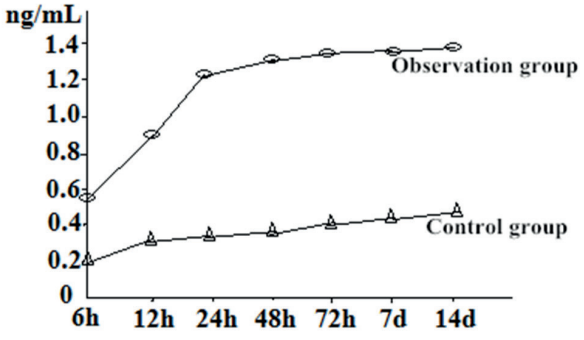

Figure 2. Change trend of cTnI at different time points.

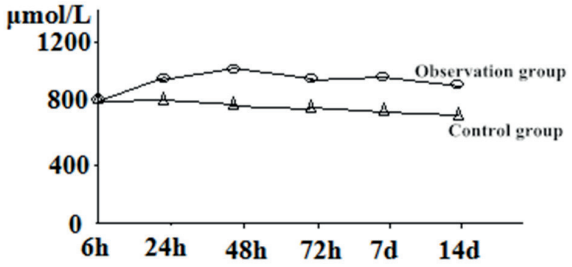

Figure 3. Change trend of Scr at different time points.

Discussion

Main cardiac changes in uremia patients are left ventricular hypertrophy, coronary vascular sclerosis, increasing heart volume and myocardial dysfunction. Increasing burden on the heart caused by any reasons will result in heart failure or even sudden death. Myocardial enzyme and troponin have higher sensibility and specificity in terms of primary myocardial infarction lesions, and it is because that myocardial cells are lacking blood and oxygen in such a short time and initiate the apoptosis and autophagy processes[4]. Mechanisms such as oxidative stress and Ca^{2+} overloading mediate cell remodeling may also be triggered[5]. CK-MB only exists in cardiac muscle, and it accounts for 15 to 25% of total cardiac muscle amount[6]. As one of three subunits of cardiac muscle troponin, cTnI can release a large amount of in-flowing blood when there is reversible or irreversible ischemic injury of cardiac muscle. Therefore, it has higher diagnostic sensitivity in slight cardiac muscle injuries[7].

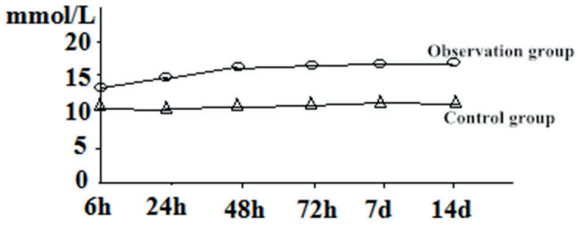

Figure 4. Change trend of BUN at different time points.

Table I. Comparison of pro-BNP and LVEF in two groups.

	pro-BNP (pg/mL)				LVEF (%)			
Group	In hospital	1 month follow-up	6 months follow-up	12 months follow-up	In hospital follow-up	1 month follow-up	6 months follow-up	12 months follow-up
Observation group	725.6±62.5	563.7±54.3	458.2±42.6	421.3±35.9	32.4±2.3	34.8±2.4	35.3±2.3	33.2±2.2
Control group	152.3±32.5	142.0±36.3	135.7±32.4	138.2±30.7	35.3±2.5	35.4±2.4	35.2±2.6	35.3±2.5
t	12.624	10.527	8.623	7.524	5.627	0.632	0.427	0.325
p	<0.001	<0.001	<0.001	<0.001	0.028	0.968	0.758	0.626

Table II. Regression analysis of total mortality.

Factors	β	Wald	*p*	OR	95% CI
CK-MB	0.023	8.627	<0.001	3.524	2.301-4.102
cTnI	0.114	8.458	<0.001	3.316	2.034-4.523
Scr	0.236	5.324	0.021	1.428	1.035-3.629
BUN	0.315	4.639	0.026	1.132	0.637-2.564
pro-BNP	0.108	6.203	<0.001	2.867	1.624-3.302
LVEF	0.227	5.756	0.017	2.130	1.224-3.645

Our results revealed that CK-MB and cTnI levels in the observation group were meaningfully higher than those in the control group at different time points. CK-MB and cTnI in the observation group rose into platform stage slowly with no peak or downtrend while the control group demonstrated a linear pattern. It was indicated that acute left ventricular failure caused by uremia might be different from the pathological process of primary myocardial infarction[8]. Cardiac muscle injury might get more and more severe with no peak, increasing or downtrend.

Also, differences concerning the comparison of SCr and BUN in two groups at different time points showed no statistical significance. It was indicated that acute left ventricular failure caused by uremia might not increase renal damage, which is usually related to the treatment of MHD[9]. In general, residual renal function during uremia period is low and MHD plays an important role in maintaining renal function and reducing renal complications. It was discovered that MHD might increase cardiac muscle injury in some degree[10], which may be the reason why changes of SCr and BUN were not consistent with CK-MB and cTnI. In our observation group, pro-BNP levels in hospital, 1 month, 6 months and 12 months follow-up were significantly higher than those in the control group. Differences regarding 1 month, 6 months and 12 months LVEF levels showed no significant differences. As a sensitive index for heart failure diagnosis and prognosis prediction, pro-BNP is closely related to changes of CK-MB and cTnI not only in the development of heart failure after acute myocardial infarction but also in heart failure cases caused by uremia[11]. Although pro-BNP level decreased gradually after the treatment, it was still higher than that in the control group. LVEF lacked a stable sensibility; it was probably related to slight changes of cardiac mechanical structure and poor improvement of heart function[12].

The innovative part of this study was comparing and analyzing biochemical indexes of uremia with acute left ventricular failure patients at different time points. We did a complete follow-up on significant objective indexes in the prognosis of heart failure such as pro-BNP and LVEF. We also conducted statistical analysis on total mortality and cardiogenic mortality rates. It was found out that the rate in the observation group was significantly higher than that in the control group. We, through multi-factor regression analysis, observed that CK-MB, cTnI, Scr, BUN, pro-BNP and LVEF were independent risk factors for total mortality while CK-MB, cTnI and pro-BNP were independent risk factors for cardiogenic mortality.

Conclusions

This study demonstrated the diagnostic value of CK-MB and cTnI in uremia with acute left ventricular failure patients, which provided references for clinical diagnosis, treatment, and evaluation of prognosis.

Table III. Cardiogenic mortality regression analysis.

Factors	β	Wald	*p*	OR	95% CI
CK-MB	0.105	9.635	<0.001	4.628	3.625-5.302
cTnI	0.135	9.237	<0.001	4.421	3.327-5.521
pro-BNP	0.221	7.658	<0.001	3.209	2.528-4.414

Conflict of interest

The authors declare no conflicts of interest.

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