The blood pressure does not affect the heart fatty acid binding protein in the blood of patients on hemodialysis

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Abstract

Objectives: We hypothesized that serum heart fatty acid binding protein (HFABP) levels could be affected by hypertension in addition to renal impairment in patients on hemodialysis. The aim was to find out possible association between serum HFABP and hypertension in patients treated by hemodialysis.

Methods: The cross-sectional study included 72 patients, both gender, age 18-78 years who were recruited from Clinic for Hemodialysis, University Clinical Center Sarajevo. According to Kidney Disease Outcomes Quality Initiative criteria for hypertension, patients were distributed into 2 groups: normotensive (HD-N) and hypertensive (HD-H) group. The cardiac biomarker HFABP was measured using ELISA kit Human FABP3 (Elabscience Biotechnology Co., Ltd, on immunoanalyzer STAT FAX 2100, USA. The kidney functional biomarkers were measured spectrophotometrically using automated analyzer.

Results: Serum HFABP level was lower in HD-H group (3.02(1.96-4.13) ng/mL) compared to serum HFABP in HD-N group (3.38(1.98-5.37) ng/mL) (p=0.359). Patients in HD-N group were older and treated by hemodialysis for a longer time than those in HD-H group (p<0.001 and p=0.029, respectively).

Conclusion: Serum HFABP level in normotensive patients on hemodialysis is not significantly different compared to hypertensive patients suggesting that heart type fatty acid binding protein might not be significantly affected by hypertension in hemodialysis patients.

Keywords: HFABP, hemodialysis, blood pressure, cardiovascular risk

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Introduction

Heart fatty acid binding protein (HFABP) is a small molecular size protein representing the isoform of the fatty acid binding proteins family. It has been expressed mainly in cardiac and skeletal muscles but to a lesser extent in the tissues such as brain, lung, stomach and kidney [1]. As a small cytosolic protein, HFABP has been proposed as an early marker of cardiac damage in acute myocardial infarction [2]. Clinical conditions such as cardiomyopathies, myocarditis, pericardial disease, aortic dissections and aneurisms and heart failure are positively associated with HFABP [3]. An elevated HFABP levels measured in patients treated with hemodialysis is the result of renal failure, as it is known that renal clearance is one of the most important determinant affecting HFABP levels. Elevated levels of HFABP are also consequence of ongoing myocardial injury due to uremic cardiomyopathy in those patients [4]. It is known that gender, age, obesity, creatinine clearance and blood pressure affect blood values of HFABP in general population. According to Otaki et al. [5], hypertension together with other risk cardiovascular factors was related to higher levels of HFABP and study results pointed that HFABP could be an useful indicator for identification of high risk individuals in general population. The hypertension is considered the risk factor for developing the cardiovascular disease as the main cause of mortality and morbidity in patients treated with hemodialysis. So, we hypothesized that HFABP levels could be affected by hypertension in addition to renal failure.

The study aim was to find out possible association between serum HFABP and hypertension in patients treated by hemodialysis.
Subjects and Methods

Subjects

The cross-sectional study included seventy two patients (n=72), both gender, age 18-78 years. Patients treated by hemodialysis were recruited from Clinic for Hemodialysis, Clinical Center, University of Sarajevo. According to Kidney Disease Outcomes Quality Initiative (KDIGO) [6], criteria for diagnosing of hypertension was met if blood pressure value was higher than 140/80 mmHg in pre-HD and 130/80 mmHg in post-HD patients or if patients were taking antihypertensive medications. We measured blood pressure in pre-HD treatment patients. Two groups of patients were defined following that criterion such as normotensive group of patients (HD-N) and hypertensive group (HD-H). The study was approved by Ethic Committee Faculty of Medicine University of Sarajevo and participants gave informed consent for the study. Investigations were carried out in accordance with the Declaration of Helsinki as revised in 2000.

Methods

Serum samples were collected and blood urea and creatinine were measured spectrophotometrically using routine laboratory methods on analyzer Architect ci8200. The blood pressure (BP) was measured with mercury sphygmomanometer after 15 minutes of rest. The cardiac biomarker HFABP was quantified using ELISA kit Human FABP3 (Fatty Acid Binding Protein 3, Muscle and Heart; Elabscience Biotechnology Co., Ltd; Catalog No: E-EL-H1431 96T) at the Laboratory for Molecular Medicine, Center for Genetics, Faculty of Medicine University of Sarajevo. Reading was performed using the immunoanalyzer STAT FAX 2100, USA. The detection range of the used sandwich-ELISA method for human FABP3 was 0.156-10 ng/mL with the minimum detectable dose of 0.094 ng/mL.

Statistical analysis

Normality of data distribution was tested by Shapiro-Wilk test. Frequency was used to present the categorical variables. The data were reported as median with 25th-75th percentile or range of minimal and maximal values. The categorical variables are presented as total and percent of total number in the group or total number of the study population. The difference in frequency among groups is tested by Chi square test.

Results

Baseline characteristics of patients are shown in Table 1. The median age of the 72 patients enrolled in the study and treated by hemodialysis was 56.5 (18.0-78.0) years, 57% were males (Table 2). The mean age of patients at the time of HD initiation was 48 (11-75 years; and median hemodialysis vintage was 50.0 (12.0-295.0) months.

Discussion

Arterial hypertension is frequent complication in patients treated with hemodialysis and small number of them controls blood pressure adequately [7]. Prevalence of hypertension varies between 70 and 100% depending on the study population. As risk factor, hypertension is associated with development of cardiovascular disease, heart failure and cerebrovascular disease in the general population, but in hemodialysis patients that...
relationship is not clear due to numerous comorbid conditions. The left ventricular hypertrophy is commonly found in hemodialysis patients as consequence of poorly controlled hypertension [8]. Pathological substrate considered as the cause of hypertension is an excessive amount of the circulating fluid in the body [9,10]. The prevalence of hypertension in hemodialysis patients ranges from 73-86% [9]. Regarding different comorbidities in the hemodialysis patients, influence of renal clearance and ongoing myocardial injury due to uremic cardiomyopathy, the present study investigated the possible role of HFABP levels in serum in detection of hypertension as an additional factor contributing to ongoing myocardial damage in those patients. Previous study reported that HFABP serum values are elevated in chronic renal failure in patients on hemodialysis treatment [10-13]. High levels HFABP and liver type fatty acid binding protein (LFABP) can be used as a prognostic marker in the initial hemodialysis [14]. It is widely known that an increase in the levels of HFABP and other cardiac biomarkers as a result of renal failures due to decreased clearance (HFABP) is a molecular weight below 25 kDa, have a relatively free passage through the glomerular filtration membrane, increased production due to the cardio-renal syndrome and uremic cardiotoxins [10]. Uremic cardiomyopathy is a recognized complication of chronic kidney disease and it may be possible that some of the leakage of HFABP could reflect sub-clinical myocardial injury [11]. The study of Karbek et al. [15] found a positive association between carotid artery intima-media thickness and serum HFABP and pointed at need to investigate the relationship between HFABP levels and long-term development of cardiac injury and atherosclerosis. Despite our expectation, the study results showed that the values of HFABP in normotensive patients were significantly higher than in those who are hypertensive. Normotensive patients were significantly older and hemodialysis vintage was almost twice compared to those with hypertension. Contrary to general population, the systolic blood pressure in elderly HD patients decreases with age due to possible arterial stiffening that occurs at younger age and the elderly HD patients are being at increased risk for cardiomyopathy. Normal blood pressure in those patients is considered as a sign of malnutrition and poor cardiac function [16]. In the study of Glatz et al. [17] investigating the plasma reference value of HFABP it has been found that HFABP in plasma increases with age and values are higher in men than in woman. In the present study, males were predominant (57%). It is known that men have higher serum HFABP than women due to their higher muscle mass. Considering that fact, the HD-H group included more male than female patients but the sex distribution among groups was insignificantly different what could not be considered as additional factor affecting values of serum HFABP. It is known that the HFABP is affected by glomerular filtration rate and the additional factors contributing the serum HFABP such as age and HD vintage could be taken into account. Considering

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HD-N (n=32)</th>
<th>HD-H (n=32)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61 (18-78)</td>
<td>53.5 (23-65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>The age of HD initiation (years)</td>
<td>50(11-75)</td>
<td>46.5(18-62)</td>
<td>0.074</td>
</tr>
<tr>
<td>Hemodialysis vintage (months)</td>
<td>82(12-295)</td>
<td>40 (13-149)</td>
<td>0.029</td>
</tr>
<tr>
<td>Blood urea (mmol/L)</td>
<td>22.40(19.45-28.30)</td>
<td>24.40(20.42-28.0)</td>
<td>0.444</td>
</tr>
<tr>
<td>Serum creatinine (μmol/L)</td>
<td>940.50(864.50-1043.250)</td>
<td>984.0(828.50-1232.50)</td>
<td>0.207</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>110(100-120)</td>
<td>150(140-160)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>70(60-80)</td>
<td>80(80-900)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Demographic data given in table are presented as median with minimum-maximum values. Clinical characteristics are given as median with 25th-75th percentile. The difference in variables between two groups is tested by Mann-Whitney test. HD-N-normotensive patients on hemodialysis treatment; HD-H-hypertensive patients on hemodialysis treatment; SBP-systolic blood pressure; DBP-diastolic blood pressure.
the process of aging itself, it can induces the increase of serum HFABP as a sign of the subclinical cardiac diseases such as heart failure and renal dysfunction supported by higher abnormal electrocardiogram score and lower creatinine clearance. In addition, aging is associated with production of a diffuse loss of ventricular myocytes causing the burden of the remaining myocytes with stress and hypertrophy. Weak association between blood pressure and HFABP in a general Japanese population was found in the study of Niizeki et al. [18]. The positive association of serum HFABP levels with systolic and diastolic blood pressure in a general population may suggest that blood pressure affects serum HFABP levels but in the presented study we could not prove the association in the hemodialysis patients. That may suggest that hypertension is one of the causes of sustained ongoing myocardial damage but not only one causing the clear discrimination of hypertensive and normotensive patients treated with hemodialysis.

Our study has some limitations. This study is a cross-sectional design, which does not prove causal relations. A longitudinal study and interventional study are needed to clarify what underlies the relationship between HFABP, renal failures and hypertension. The subjects of our study were only from one dialysis center, relative small number of participants, and it is unclear whether the present findings can be generalized.

**Conclusion**

The study has shown that the serum HFABP level in normotensive patients on hemodialysis is not significantly different compared to hypertensive patients suggesting that heart type fatty acid binding protein might not be significantly affected by hypertension in hemodialysis patients.

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**Declaration of Interest**

Authors declare no conflict of interest.
References


