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Effect of Inflammatory Factors on β 2-Microglobulin in Hemodialysis Patients.

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Abstract:

Introduction: Systemic inflammation is a common complication in patients with chronic renal dysfunction including hemodialysis patients. The aim of this study is evaluating association of inflammatory factors on β 2-microglobulin (β 2-m) in hemodialysis patients

Materials and Methods: This is a single-center prospective study conducted on 39 hemodialysis patients in Sina hospital in 2009. All cases had well-functioning arteriovenous (AV) access or permanent venous catheter and were dialyzed thrice weekly. All patients were hemodialyzed using low flux membranes and Ferzinuce system. Blood samples were taken from the arterial line for the following assessments: Hct, hemoglobin, WBC, platelets, erythrocyte sedimentation rate (ESR), blood urea and serum creatinine, HDL cholesterol (HDL-C), total protein, albumin, CRP, and β 2- microglobulin. The statistical analyses were performed using Chi-square test for relationships. All tests were two-tailed and with $P < 0.05$ were considered significant.

Results: The cases included 28 females (71.8%) and 11 males (28.2%) with the mean age of 60.61 ± 15.25 yrs. There was no significant relationship between CRP, HDL-C, Albumin and β 2-microglobulin ($P \geq 0.05$).

Conclusion: Although the rise of inflammatory factors may increase β 2-microglobulin levels, we found no significant relationship between inflammatory factors and β 2-microglobulin when low-flux biocompatible membranes are used.

Keywords: Hemodialysis, β 2-microglobulin, CRP, HDL cholesterol, Albumin.

Introduction:

Long term hemodialysis may lead to amyloidosis in which β 2-microglobulin (β 2-m) is the main component of amyloid fibrils.⁽¹⁾ B2-microglobulin plasma levels may increase as much as 5–10 times in chronic hemodialysis (CHD) patients.⁽²⁾ All nucleated cells of the body such as defensive cells create and discharge β 2-m. Infections are the most common conditions in hemodialysis. Inflammatory conditions can increase the secretion rate and the serum levels of β 2-m by activating defensive cells.⁽³⁾ Several human body cells can discharge C - reactive protein (CRP) as a specific inflammatory factor for CHD and other inflammatory markers.^(4,5) Inflammation in hemodialysis patients has a considerable role in developing cardiovascular diseases, malnutrition, erythropoietin resistance, anemia, osteopathic diseases, becoming prone to developing infections and cancers as well as reducing the remaining renal performance.⁽⁶⁻⁸⁾ Thus, reducing inflammation in hemodialysis patients can play an important role in preventing the mentioned complications.

The aim of this study is evaluating the role of inflammatory factors on β 2-microglobulin in hemodialysis patients

Materials & Method:

Patients: Hemodialysis

The cases were included 39 hemodialysis patients in this study. All cases had been conventional dialyses for more than 3 months via arteriovenous (AV) fistulla or venous catheter. The duration of each dialysis session was four hours. All patients were hemodialyzed using low flux membranes and Ferzinuce system.

The cases had no infection sign or symptoms (including fever $>38^{\circ}\text{C}$, WBC \geq

10000/mm³, and other clinical signs of infection). All cases had eKt/V ≥ 1 .

Laboratory Investigation

Blood samples were taken before hemodialysis and midsession in same laboratory. The samples were for the following assessments: Hct, hemoglobin, WBC, platelets, erythrocyte sedimentation rate (ESR), blood urea and serum creatinine, HDL cholesterol, total protein, albumin, CRP, and β 2- microglobulin.

B2-microglobulin was measured through immunoenzymometric assay with a normal range of 0.75-12 mg/L; Albumin and HDL cholesterol were biochemically measured. The normal range for serum albumin was 3.5-5 g/dl and for HDL cholesterol, it was 30-70 mg/dl. CRP was measured with high sensitive ELIZA method and the normal range was ≤ 10 mg/L.

The tests were conducted in one laboratory using a single system.

Statistical Analysis

The statistical analyses were performed using Chi-square test for relationships. All tests were two-tailed with $P < 0.05$ considered significant. Results are expressed as mean (standard deviation) for normally distributed continuous variables and as frequency (%) for categorical variables.

Results:

There were 39 cases including 28 females (71.8%) and 11 males (28.2%). The mean age of the cases was 60.61 ± 15.25 years. The mean duration of the disease was 48.15 ± 40.53 days.

Underlying renal diseases were diabetes mellitus (DM), hypertension, and obstructive disorders in 51.3%, 30.8% and 5.1% of patients respectively.

Baseline plasma CRP levels were over the upper normal limit of 10 mg/L in 64.3% of the population. β -m levels were upper in patients with CRP \geq 10 mg/L (mean difference:1.96). There was no significant relationship between CRP and β -microglobulin (P value: 0.71.95% confidence interval (CI): -13.03, 9.11.power:6%).

At baseline, 69.2% of HDL-cholesterol concentrations were greater than 30 mg/dl in patients. β -microglobulin levels were upper in patients with HDL \leq 30 mg/L (mean difference:5.37). There was no significant difference between HDL-C and β -microglobulin (P.value:0.24. 95% CI: -14.55, 3.8. power:23%).

Serum albumin levels in 92.3% of the patients were over the upper normal limit of 3.5 g/dl; β -m levels were upper in patients with Albumin \geq 3.5 mg/L (mean difference: 8.96). And there was no significant relationship between Albumin and β -m (P:0.26, 95%CI: -24.9,6.9. Power: 73%).

There was no significant relationship between disease duration and β -m (P.value:0.42).

Discussion:

Hemodialysis is a process that removes uremic toxins, one of which is β -2 microglobulin of the middle molecules that is normally discharged or metabolized through the kidneys. Middle molecules are removed by high flux membrane that plays an important role in developing amyloidosis in hemodialysis patients.⁽¹¹⁾

The rate of CRP, an inflammatory marker, and interleukin-6 is high in hemodialysis patients due to the inflammatory state of the disease. The multifactorial nature of the process of hemodi-

alysis causes inflammation; inflammation stimulates the secretion of cytokines, interleukin I and the others as well as TNF α and finally, β -2 microglobulin synthesis is stimulated.⁽¹²⁾

In this prospective study, we found no significant relationship between inflammatory factors such as CRP and β -m. Perhaps it was because of high β -m levels in all studied patients. The results of our study were similar to Hakim's study performed in 1996.⁽⁹⁾

CRP levels were greater than the normal range in 63.4% of the cases. CRP rises in inflammatory conditions in chronic hemodialysis patients, it could be caused by membrane bioincompatible and or catheters. In a study performed on 76 hemodialysis patients by Kalocheritis in 2008, similar to our study, they used low flux membranes and found no relations between CRP and β -microglobulin, but they found a significant relationship between β -m and procalcitonin which is an inflammatory factor; however it is more an infectious marker.⁽³⁾

In the study of Asim et al, β -2 microglobulin levels were high in hemodialysis patients undergoing low flux hemodialysis.⁽¹¹⁾ In the study of Raymond, et al also reported β -2 microglobulin hi levels in all patient using biocompatible and bioincompatible low flux membrane; the only difference was observed in the manner of β -2 microglobulin increase.⁽¹⁵⁾ According to the report of Furuya et al, the application of ultra pure dialysis reduces β -2 microglobulin levels.⁽¹⁷⁾ β -2-microglobulin removal is higher in patients undergoing high-flux hemodialysis⁽¹⁰⁾ and biocompatible membrane reported the same result.

In our study, there was no significant relationship between serum albumin levels and β 2-m. Although albumin is a negative inflammatory factor, it is known as a well nutrition factor in hemodialysis patients. In the study of Entezari et al, there was no relationship between CRP, the inflammatory marker, and albumin, the nutritional marker, in chronic hemodialysis patients.

Conclusions:

Although the rise of inflammatory factors may increase β 2-microglobulin levels, we found no significant relationship between inflammatory factors and β 2-microglobulin when low-flux biocompatible membranes are used.

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