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ORIGINAL PAPER

The Influence of Hemodialysis Duration on the Concentration of Inflammatory Agents in Chronic Hemodialysis Patients

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Goal: The goal of this study is to determine the effect of the hemodialysis durations on the concentration of inflammatory agents C-reactive protein concentration, fibrinogen and ferritin in hemodialysis patients. There is not enough reliable research data about the primary causes of the increase of these agents levels in the serum. The role of inflammatory agents in the development of primary renal disease, pathogenesis and morphogenesis and in particular the development of complications and comorbidities is unclear. **Patients and methods:** The study included 114 chronic hemodialysis patients who were on dialysis three times a week for 4 hours, according to the regular protocol of hemodialysis at the Cantonal Hospital Zenica, Department for hemodialysis. **Results and discussion:** Patients were analyzed according to the hemodialysis duration (years) and on the basis of duration of hemodialysis are divided into 3 groups: According to the average values of fibrinogen in all three groups was $p<0.05$ which is not statistically significant difference according to the hemodialysis duration. Average values of ferritin in group 1 (patients less than 1 year on hemodialysis) was 612±543 in group 2 (patients with hemodialysis duration between 1-10 years) was 1056±852, and in group 3 (patients with hemodialysis duration over 10 years) was 610±700. According to the average values of ferritin in all three groups we see that $p<0.05$. In the second group ferritin concentrations were highest. In the third group of patients the results were the same as in the first group. **Conclusion:** It was found that the duration and type of hemodialysis does not affect the concentration of inflammatory agents in the blood. Key words: duration of hemodialisis, inflammatory agens.

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1. INTRODUCTION

Inflammation/infection is an independent risk factor for the development of a number of complications during hemodialysis especially cardiovascular (1). Parameters: C-reactive protein, ferritin and fibrinogen are the most important parameters monitored in inflammatory reactions of various degrees and the genesis of the chronic kidney insuffitiency (2). Inflammation is present in 30-50% of patients treated with regular hemodialysis (3). In this regard, in hemodialysis patients with inflammatory mediators most often are followed C-reactive protein, fibrinogen and ferritin.

C-reactive protein is known in laboratory diagnosis as the most studied plasma protein that is used as an inflammatory marker, which is an important indicator of inflammation, tissue necrosis or trauma. In addition to the discovery of the acute inflammatory response, C-reactive protein is useful in assessing disease progression and therapeutic efficacy. It has high sensitivity and low specificity. In contemporary literature, a strong emphasis is placed on an elevated C-reactive protein levels as a risk factor for morbidity and mortality in patients on hemodialysis. In addition, there is a relationship between elevated levels of C-reactive protein, atherosclerotic plaque and malnutrition (MIA syndrome). It is a major cause of hospitalization for hemodialysis patients. If C-reactive protein is >10 mg/L, clinical experience and literature data indicate that it is a case of an acute or chronic inflammatory process and a smaller percentage indicate the existence of malignancy, vasculitis and symptomatic disease in the form of thrombosis or resorptive result after surgery (4).

Fibrinogen may be increased in any form of inflammation, as it is acute phase protein. Fibrinogen level always reflects activity of emergent, recurrent or chronic primary process with or without activation signs. It is also believed that many of the above processes in a dynamic relationship with the level of fibrinogen are sometimes reversible and recurrent (5).

Ferritin as a marker of acute inflammation, it may also be of the chronic one. The increase of ferritin level in serum is a strong predictor of hospitalization in patients on hemodialysis. It is believed that serum albumin is a strong

long-term indicator of mortality in patients undergoing hemodialysis. It is also considered that the increase in serum ferritin represents reliable indicator of short-term mortality for the period of 12 months in patients on hemodialysis. Therefore, in case of stable concentration of iron, high levels of ferritin in serum may be a morbidity risk factor. Also, the recent increase in serum ferritin can carry an increased risk of mortality in these patients (6).

2. PATIENTS AND METHODS

The study included 114 chronic hemodialysis patients who are on dialysis three times a week for 4 hours, according to the regular protocol of hemodialysis at the Cantonal Hospital Zenica, Department for hemodialysis. Hemodialysis is performed on machines Fresenius MC 4008, Fresenius 5008, Braun Dialog. All patients had a diagnosis of end-stage renal disease on the basis of official criteria and diagnostic parameters which are recorded in their medical records and recorded in their dialysis notebooks. Patients in the study were registered until the 2010. Monitoring of dialysis patients is performed, besides periodic laboratory tests, also by examinations of specialists according to official recommendations and guides for hemodialysis (7). The research was conducted in the Cantonal Hospital Zenica at the Department for hemodialysis. Blood samples were collected before hemodialysis venous puncture. Outcomes were measured by inflammatory parameters and years on hemodialysis.

To test the statistical significance of differences between the samples were used parametric and non-parametric tests (Chi-square test, Student's t-test and Mann-Whitney test), as well as the linear correlation. Statistical hypotheses were tested at a significance level of a=0.05. The difference between samples was considered significant if the p<0.05.

3. RESULTS

The study included 114 patients, with mean age 55 (45-67) years, 56 men (49%), 48 women (51%). The parameters of inflammation in groups according to the duration of peritoneal hemodialysis treatment are shown in Table 1.

The parameters of inflammation	Group 1 N=37 (32%)	Group 2 N=64 (56%)	Group 3 N=13 (12%)	p
C-reactive protein	5.1 (3.2-13.5)	3.7 (3.2-8)	4.8 (3.2-6.9)	>0.05
Fibrinogen	3.3 ± 1.8	3.7 ± 1.2	3.3 ± 1.2	>0.05
Ferritin	612 ± 543	1056 ± 852	610 ± 700	<0.05

Table 1. The parameters of inflammation in groups according to the length of dialysis service
Legend: N-number of respondents

The table shows the parameters of inflammation in groups according to the duration of hemodialysis. In group 1 (patients less than 1 year on hemodialysis), the average value of C-reactive protein was 5.1 mg/L. In group 2 (patients with hemodialysis duration between 1-10 years) the average value of C-reactive protein was 3.7. In group 3 (patients with hemodialysis duration over 10 years) the average value of C-reactive protein was 4.8.

By average C-reactive protein values there was no significant differences between the three groups of patients and the difference between groups was not statistically significant (p>0.05). Average values of fibrinogen in group 1 (patients less than 1 year on hemodialysis) was 3.3±1.8 in group 2 (patients with hemodialysis duration between 1-10 years) was 3.7±1.2, and in group 3 (patients with hemodialysis duration over 10 years) was 3.3±1.2 g/L.

According to the average values of fibrinogen in all three groups was p<0.05 which is not statistically significant difference according to the hemodialysis duration.

Average values of ferritin in group 1 (patients less than 1 year on hemodialysis) was 612±543 in group 2 (patients with hemodialysis duration between 1-10 years) was 1056±852, and in group 3 (patients with hemodialysis duration over 10 years) was 610±700. According to the average values of ferritin in all three groups we see that p<0.05. In the second group ferritin concentrations were highest. In the third group of patients the results were the same as in the first group. We believe that a possible reason for this was the insufficient number of patients in the third group, or only 12%.

It is known that the increased concentration of ferritin is associated with inflammation and in particular receiving iron during hemodialysis treatment.

4. DISCUSSION

In this study elevation of inflammatory parameters in relation to the duration of the hemodialysis service was not shown. In this study (Table 1) by the duration of hemodialysis treatment average C-reactive protein values was 5.1, which is a significant increase compared to baseline (3.2). However, the highest concentration was 13.5 which is a big range. The first group had the shortest duration hemodialysis, up to one year. We believe that these are patients who are just starting hemodialysis treatment in the stabilization phase of the organism and there are impacts of disease and comorbidity. In the second and third groups according to the duration of hemodialysis treatment was recorded lower average levels of inflammatory agents. Results are consistent with earlier studies which presented that duration of hemodialysis treatment affects the increase in inflammatory agents levels, particularly C-reactive protein (8). Many studies and surveys show that there is elevation of C-reactive protein in patients on dialysis. A prospective multicenter study was made on the influence of hemodialysis treatment on the C-reactive protein values (9, 10). Increased levels of C-reactive protein were recorded in 25% of patients during dialysis treatment. In addition, regardless of the level of predialysis C-reactive protein, changes in the level of C-reactive protein during hemodialysis treatment was associated with an increased risk of mortality, or an increase of 1 mg/L in C-reactive protein levels is associated with a 9% increase in mortality. This means that patients with increased levels of C-reactive protein for more than 3 mg/L during hemodialysis treatment will have an increased risk of death for about 30% (9, 10).

Patients who are for many years on hemodialysis have elevated fibrinogen levels (11). High levels of fibrinogen in the plasma can cause thrombi

in arteriovenous fistulas. It is known that many factors influence the level of fibrinogen in the plasma, including diet, medications, age, smoking, alcohol, body mass, gender, exercise and race (11).

All researchers agree that there are numerous variations in the concentration of ferritin and that they are the reflection of many processes which is particularly associated with administration of iron and erythropoietin preparations (12). These results agree with studies by other authors (6) in which ferritin is elevated in most patients undergoing hemodialysis. According to the duration of hemodialysis there is a significant increase in serum concentrations of ferritin in patients who are longer in treatment.

5. CONCLUSION

The reason why it was not shown the elevation of inflammatory parameters can be in good dialysis which patients undergo, the quality of care, but also advanced technology, better appliances and filters in the last decade compared to the previous period, which effectively removes inflammation mediators. Examples of such technologies include high flow hemodialysis and online hemodiafiltration, which effectively removes medium to large molecules, while inflammatory mediators fall into that category.

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