Lymphocyte Subtype and Immunglobulins Levels in HCV Positive Hemodialysis Pateints

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ABSTRACT

Epidemiological studies indicate that in chronic HD patients, bacterial and viral infection rank second place in mortality and morbidity, behind cardiovascular disease. Chronic hepatitis C virus (HCV) is very prevalent in some Hemodialysis (HD) centers. We have investigated lymphocyte subtype count and immunoglobulin levels in hemodialyzed patient with HCV. We studied 55 patients with end stage renal disease (ESRD) on chronic HD and 21 healty subjects. Patients group included 34 female and 21 male with mean age 46.5±16.1(18-77) years. Serum concentrations of IgG, IgM, IgA, CD4, CD8, CD19, CD16-56 lymphocytes were measured. Kt/V values were calculated according to DOQI guideline. Lymphocyte and lymphocyte subgroups values of HD patients were significant lower than healty persons. IgG, IgM and ALT levels of HCV positive HD patients compared with significant higher than HCV negative HD patients. CD4/CD8 ratios within groups were no differences. Lymphocyte subtype count of between HCV positive and HCV negative HD patients was no differences. IgG and IgM levels of HCV positive HD patients were higher than HCV negative HD patients. High Ig levels were also associated with ALT levels

Key words: HCV, hemodialysis, lymphocyte subtype, immunoglobulins

HCV Pozitif Hemodiyaliz Hastalarında Lenfosit Subtipleri ve İmmunglobulin Düzeyleri. HCV, Hemodiyaliz, Lenfosit ve İmmunglobulinler

ÖZET

Epidemiyolojik çalışmalar kronik hemodiyaliz (HD) hastalarında bakteriyel ve viral enfeksiyonların mortalite ve morbiditede kardiyovasküler hastalıklardan sonra ikinci sırada yer aldığını göstermiştir. Kronik hepatit C virus enfeksiyonu bazı HD merkezlerinde çok yaygındır. Çalışmamızda, HCV?li HD hastalarında lenfosit subtiplerini ve immunoglobulin seviyelerini araştırdık. 55 HD teadvisi alan son dönem böbrek yetmezlikli hasta ve 21 sağlıklı gönüllü çalışmamıza aldık. Hasta grubuna ort yaş 46.5±16.1(18-77) olan 34 kadın ve 21 erkek dahil edildi. IgG, IgM, IgA serum konsantrasyonları ve CD4, CD8, CD19, CD16-56 lenfosit sayıları ölçüldü. Kt/V değerleri DOQI klavuzuna göre hesaplandı. Lenfosit ve lenfosit subgrup sayıları HD hastalarında kontrol grubuna göre anlamlı olarak düşük bulundu. IgG ve IgM değerleri HCV?li HD hastalarında HCV negatif HD hastalarına göre anlamlı olarak daha yüksekti. CD4/CD8 oranı açısında gruplar arasında fark yoktu. HCV negatif ve pozitif HD hastalarının lenfosit subtipleri sayıları arasında fark yoktu. HCV pozitif HD hastalarının IgG ve IgM seviyeleri HCV negatif HD hastalarından daha yüksekti. Yüksek Ig düzeyleri ALT seviyeleri ile ilgili olabilir.

Anahtar kelimeler: *HCV, hemodiyaliz, lenfosit subtipleri, immunglobulinler*

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INTRODUCTION

Hepatitis C virus (HCV) infection is one of the major health problems of the world. Approximately 200 million people worldwide are known to be infected with HCV. 80% of infected individuals' progress to chronic disease is an important cause of morbidity and mortality. In our country, the prevalence of HCV is highest in the group, hemodialysis and renal transplant patients. Duration of hemodialysis, nosocomial infection, blood and blood product transfusions are the most important risk factors (1,2).

Spontaneous clearance of HCV-specific CD4 and CD8 T-cell response in peripheral blood virus shown to be continuous and strong. In patients with chronic infection, these cell functions are insufficient (3) . Chronic HCV infection is partly a result of infected immune cells or their functions are inadequate because of changes in CD4, CD8 response. The progressive deterioration of renal function in CRF, leads to a complex immune deficiency syndrom with an increased morbidity and mortality. There is a defect in the immune response to viral infections (4).

HBV carriers are around 30% of these patients. If you need to emphasize an important point, hemodialysis treatment cannot improve immune deficiency syndrome especially caused by uremia. Therefore, in patients undergoing hemodialysis treatment, lacks of humoral and cellular immune response cause an inadequate response and anerjik skin tests in bacterial, viral and mycobacterial infections.

In various studies, HCV-induced liver disease in patients receiving hemodialysis treatment was determined. Mild or moderate disease activity has been reported in many series. The majority of patients, ALT levels were normal and there was less severe fibrosis and cirrhosis. 5-32 % rate of hepatic fibrosis or cirrhosis observed in these studies (5,6).

Uremia leads to defect in cellular immunity. On the other hand, the frequency is higher than the normal population of HCV patients on hemodialysis. Recent studies show that HCV has different effects on immune system. According to recent human studies, HCV replication stimulates secretion of endogenous type 1 IFN γ levels although it is not enough to inhibit HCV. Immunosuppressive effect of HCV at the same time, are discussed. In light of this study, we investigated the effect of HCV on lymphocyte subtypes and on Ig levels, in hemodialysis patients.

MATERIAL AND METHODS

55 patients undergoing hemodialysis were recruited. 34 patients were female and 21 were male. The mean age was 46.5±16.1 (18-77) years, mean duration of hemodialysis time 3.5±2.9 (1-15) years. The patient group, those with DM or any disease affecting the immune system, active infection, inflammatory disease, those who planned the treatment for HCV, HIV and HBsAg positivity and those who use drugs that affect the immune system were excluded. As a healthy control group including 10 men and 11 women mean age 40.5±13.3 (18-61) of the 21 volunteers enrolled in the study. In the control group, there was not any active infection, diabetes mellitus or other systemic disease affecting the immune system, and anti-HCV positivity. In all the patients enrolled to the study CRP levels were below 5 mg/L. Lymphocytes (CD3, CD3-CD16+ CD56+, CD19, CD4, CD8) were counted with Flowcytometry method (Beckam Coulter). Immunoglobulin levels were measured by nephelometric method. Kt/V values were calculated according to DOQI guideline.

Annova test was used to compare the data. $p< 0.05$ was considered significant values.

RESULTS

Demographic data are shown in Table 1. HCV positive and HCV-negative HD patients and healthy control groups comparison of AST and ALT levels, lymphocyte sub-groups and the immunoglobulins Table 2. Examines the demographic characteristics of the patients, HCV + patients were significantly longer duration of stay in the treatment of dialysis.

Demographic characteristics in terms of duration of hemodialysis was significantly longer in patients with HCV-positive HD. HD patients with HCV-positive and negative, there is no significant difference between lymphocyte counts, and lymphocyte subsets. All three groups were when compared with each other, lymphocyte and lymphocyte subsets were significantly lower in all HD patients. Between the groups of HD patients compared with HCV-positive and negative IgG, IgM, and ALT levels were significantly lower in HCV-negative group. CD4/ CD8 levels were not different in the three groups.

***Table 1**. Demographic characteristics of the patients and the healthy control group*

	HCV(+)	HCV (-)	Healthy volunter	p value
n	25	30	21	
Male/female	13/12	21/9	10/11	0.22
Mean age, years	42.3±15.8 (18-74)	49.9±15.8	40.5±13.3	0.06
Hemodialysis duration, years	5.4± 3.2 (1-15)	2±1.2 (1-5)		0.00
.Kt/V	1.12±0.17	1.07± 0.09		0.17

DISCUSSION

The prevalence of HCV is approximately 9% in chronic hemodialysis patients. This ratio can reach up to 40% in some hemodialysis centers . Taking necessary measures for infection control, reduction of HCV incidence and prevalence have been identified. HD patients, the CRF and HD procedure varies depending on the cellular immunity, this is probably connected to the HCV infection itself . Impairment of Th1 response is available in HD patients. Th2 response is not affected.

Chronic HCV infection plays a critical role in the development of CD4 and CD8 T-cell response, T cell response to HCV in chronic HCV significantly inadequate, this may explain viral persistence. T-cell function is impaired in HD patients, the response may be affected by HCV. Many studies demonstrated that in HCV patients after kidney transplantation major problems may occur more frequently. Some of them are life-threatening infections, CMV, pneumocistis Carini infection, acute vascular rejection, the emergence of new glomerulopathy. The appearance of these findings, the effect of HCV on the immune response by changing the levels of lymphocytes (TB and NK cells) granulocytes and monocytes or not is unknown . In another study, in hemodialysis patients with HCV-specific CD4 + cell response was limited.

In our study, no statistically significant difference has been detected between the lymphocyte, lymphocyte subgroup and neutrophil counts in HCV postive and negative HD patients. Compared to the healthy control group, lymphocyte and lymphocyte subgroup counts in both HCV positive and HCV negative HD patients were low. CD4/CD8 ratio was the unchanged.

In a study performed by Rostiang et al., no difference was detected between the lymphocyte subgroups and the cytokine levels generated in HCV positive and HCV negative HD patients. Both B and T lymphocyte activities were similar. However, lymphocyte count was detected to be low, compared to the healthy control group. When compared to HCV negative HD patients, Th1 cytokine production in HCV positive patients was not detected to be insufficient. These findings support the data in our study. In a study performed by Sester et al., it is observed that there is a distinctive decrease in the activations of T cells in HD patients .

***Table 2**. HCV positive and HCV-negative HD patients and healthy control groups comparison of AST and ALT levels, lymphocyte sub-groups and the immunoglobulins (Annova).*

	HCV (+)	HCV(-)	Healthy volunter	p value
N	25	30	21	
Lymphocyte count (/mm3)	1353±313	1439 ±546	2555±663	0.00
CD3	902±328	991±472	1792±684	0.00
CD16-56	143±69	162±137	334±134	0.00
CD19	118±50	109±69	233±218	0.03
CD4	572±170	641±294	1106±290	0.00
CD8	326±128	353±178	718±330	0.00
CD4/CD8	1.94±0.82	1.97±0.64	1.7±0.6	0.41
IgA (g/l)	2.18±0.74	2.19±1.02	2.9±1.1	0.07
IgG (g/l)	14.5±5.1	11.8±3.1	14±2.2	0.033
IgM (g/l)	1.3±0.7	0.9±0.4	1.3±0.6	0.020
ALT(mg/dl)	29±23	15±9	24±13	0.005
AST (mg/dl)	23±15	16±10	23±7	0.04

When all three groups in our study are compared, the IgG and IgM levels of HCV negative patients have been detected to be significantly lower than the HCV positive and healthy patients.

The reason why IgG and IgM levels were detected to be higher in the positive group compared to the HCV negative group could be associated with chronic HCV infection. Recent studies shown that immunoglobulins directly stimulated fibrogenesis. In their study, Watt et al., have detected a strong correlation between the hepatic fibrosis and immunglobulin levels in HCV positive patients, but they were unable to explain the physiopathology of this finding .

In the study performed by Wang et al., high levels of Ig and low levels of C3 were shown to be correlated with the liver damage. High Ig levels were also associated with ALT levels . There are no biopsy findings from our patients. The high Ig levels in our patients could be due to the chronic inflamation in our HCV positive patients.

As a result of our study, no clear effect of the existance of HCV on lymphocyte and lymphocyte subgroups has been detected. IgG and IgM levels were found to be low in HCV negative patients, and similar in HCV positive and healthy patients. The clinical importance of this finding is unknown.

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