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Seroprevalence of Cytomegalovirus Antibodies in Haemodialysis Patients

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Background: Although symptoms of infection caused by cytomegalovirus (CMV) in healthy adults are generally mild, the virus is known to produce severe symptoms most often in immunocompromised patients. Patients with chronic renal failure are prone to CMV infection. CMV, as a nosocomial infection in immunocompromised patients, is a problem for clinicians.

Aim: We aimed to investigate the seroprevalence of CMV infection among the haemodialysis (HD) patients in our region.

Patients and Methods: Serum samples were taken from 255 patients who received treatment in 3 different HD clinics and a control group of 70 healthy persons. Enzyme-linked immunosorbent assay (ELISA) was used to investigate anti-CMV IgG and IgM antibodies.

Results: Positivity for anti-CMV IgG was found in 254 (99.6%) of the 255 HD patients and 58 (82.9%) of the 70 controls. The difference between the 2 groups was statistically significant ($P < 0.05$). Positivity for anti-CMV IgM antibody was noted in 1 (0.4%) of the 255 HD patients.

Conclusions: The prevalence of CMV infection among HD patients in our region was quite high. Because patients receiving HD treatment can be exposed to CMV infection, we recommend that HD patients who are susceptible to CMV infection should be identified with anti-CMV IgG and IgM specific serological tests.

Key Words: Haemodialysis, CMV, seroprevalence

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Hemodiyaliz Hastalarında Sitomegalovirus Antikor Seroprevalansı

Giriş: Sağlıklı yetişkinlerde CMV'nin neden olduğu enfeksiyonlar genellikle ılımlı olmasına rağmen, bu enfeksiyonlar immun zorluklularda çoğunlukla ciddi semptomlar oluşturmaktadır. Kronik böbrek hastalığı olan hastalar CMV enfeksiyonuna yatkındır. İmmun zorluklu hastalarda CMV nozokomiyal enfeksiyonları klinisyenler için önemli bir problemdir.

Hastalar ve Yöntem: Üç hemodiyaliz merkezinde tedavi edilen 255 hastadan ve kontrol grubu için 70 sağlıklı kişiden serum örnekleri alındı. Anti-CMV IgG ve IgM antikorlarını araştırmak için enzim bağlı immunosorbent testi kullanıldı.

Bulgular: Toplam 255 hemodiyaliz hastasının 254 (% 99.6)'ünde ve kontrol grubundaki 70 kişinin 58 (%82.9)'inde anti-CMV IgG pozitivitesi tespit edildi. İki grup arasındaki fark istatiksel olarak anlamlı bulundu ($P<0.05$). Hemodiyalizdeki 255 hastanın 1 (% 0.4)'inde anti-CMV IgM antikor pozitivitesi tespit edildi.

Sonuç: Sonuç olarak, bölgemizdeki hemodiyaliz hastaları arasında CMV prevalansı oldukça yüksek bulunmuştur. Hemodiyaliz tedavisi alan hastalar CMV enfeksiyonuna maruz kalabileceğinden, CMV enfeksiyonuna duyarlı hemodiyaliz hastalarının anti-CMV IgG ve IgM spesifik serolojik testleriyle taranmasını önermekteyiz.

Anahtar Sözcükler: Hemodiyaliz, CMV, seroprevalans

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Introduction

Cytomegalovirus (CMV) is found throughout the world among all socio-economic groups and infects between 50% and 85% of adults by the age of 40 years. CMV infection is more widespread in developing countries and in areas of low socio-economic conditions. Once a person becomes infected, the virus remains alive, but usually dormant, within that person's body for the duration of their lifespan. It rarely causes recurrent disease unless the person's immune system becomes suppressed due to therapeutic drugs or disease. Therefore, for the vast majority of people, CMV infection is not a serious problem (1,2).

It has been well studied and documented that uraemic patients, as well as patients on haemodialysis (HD), have impaired immune responses, which result in higher prevalence rates of morbidity and mortality as a result of viral bacterial, or parasitic infections, or from malignant maladies (3,4).

With regard to viral infections, in chronic patients on HD, the association of both hepatitis B and hepatitis C virus has been extensively investigated worldwide. Investigations concerning commonly encountered viral infections in HD patients have been quite limited, except for studies of CMV (5).

CMV infection can occur at any time during the lifespan of humans; it can even be acquired in utero. The incidence of seropositivity increases with age. Among HD patients, 60%-90% are seropositive, depending on age and socio-economic circumstance (6).

While initial CMV infection can cause serious disease in immunocompromised patients, a more common problem is reactivation of the dormant virus. Infections caused by CMV are a major cause of disease and death in immunocompromised patients, which include organ transplant recipients, patients undergoing HD, cancer patients, patients receiving immunosuppressive drugs, and HIV-infected patients (5,6).

The aim of this study was to investigate the seroprevalence of anti-CMV IgG and IgM in patients on HD in 3 different HD clinics in our region.

Materials and Methods

This study was carried out in Antakya, Turkey, between March 2004 and June 2004 and included 255 HD patients between the ages of 14 and 91 years who were selected from 3 Antakya area HD clinics (Haemodialysis Centre of Antakya State Hospital, Antakya Haemodialysis Centre, Emir Haemodialysis Centre). The control group included 70 healthy volunteers who were between 12 and 65 years old.

To determine the seroprevalence of CMV infections, blood samples were collected from the 255 HD patients and the 70 healthy persons for antibody testing, and centrifuged at 1500 rpm for 5 min to obtain serum samples, which were then stored at -20 °C until tested. The length of the time on HD and the weekly number of HD treatments of each HD patient was recorded.

Enzyme-linked immunosorbent assay (ELISA) (Abbott kits, Abbott Laboratories, USA) was used to test for the presence of anti-CMV IgG and IgM antibodies according to the manufacturer's instructions.

Statistical analysis

The statistical analysis was performed using chi-square test and Statistical Package for the Social Sciences (SPSS) software. P values less than 0.05 were considered statistically significant.

Results

The mean age of the 255 HD patients was 53.94 ± 17.3 years (mean ± SD). The gender distribution of the patients was 175 (68.6%) males and 80 (31.4%) females. The mean age of the healthy control group was 47.21 ± 18.6 years (mean ± SD) and included 33 (47.1%) males and 37 (52.9%) females. Positivity for anti-CMV IgG was determined in 254 (99.6%) of the 255 HD patients and 58 (82.9%) of the 70 controls. The difference between the 2 groups was statistically significant ($P < 0.05$) (Figure 1).

Although all of the subjects in the control group were seronegative for anti-CMV IgM, 1 (0.4%) of the HD patients was seropositive for anti-CMV IgM. The difference between the 2 groups was not statistically significant ($P > 0.05$).

The length of the time on HD was 35.1 ± 32.7 months (mean ± SD) in patients with anti-CMV IgG seropositivity. A significant correlation was not found between the length of the time on HD and anti-CMV IgG seropositivity ($P > 0.05$).

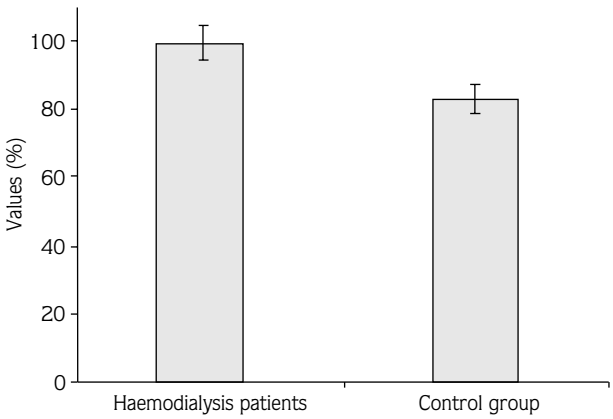

Figure 1. The ratio of CMV IgG antibodies in haemodialysis patients compared to healthy control group.

Discussion

CMV is the prototype member of the Betaherpesvirinae. As with all members of the Herpesviridae, CMV has the ability to persist in the host in a dormant state following primary infection. More than 80% of healthy adults are seropositive, indicating previous exposure (7). CMV infections are ubiquitous throughout the world, infecting between 40% and 100% of the entire human population (2,3).

Seroprevalence rates of CMV vary geographically. de Ory Manchon et al. (8) found that seroprevalence for anti-CMV IgG in the general population in Madrid was 62.8%, ranging from 58.4% in men to 66.7% in women (8). In another study, carried out in Tunisia, anti-CMV IgG antibodies were detected in 98.57% of women and 95.71% of men (9). Studies of pregnant women in France and Saudi Arabia reported CMV seroprevalences of 51.5% and 92.1%, respectively (10,11). In a study of the general population in Turkey, an 87.5% seropositivity rate for anti-CMV IgG was found (12), which is similar to the 82.9% rate of the present study's control group, but lower than the rate in our HD patients (99.6%).

Infectious disease is the most serious complication in immunosuppressed patients and is the major cause of death in renal transplant recipients. Bacterial, fungal, and protozoan infections, and viruses of the human herpes group (herpes simplex virus, varicella-zoster virus, Epstein-Barr virus, and CMV) are known to be of major importance. The most common and clinically relevant virus of this group is CMV (13). While CMV infection proceeds asymptotically in the majority of immunocompetent persons, it can lead to serious complications in immunosuppressed patients (2,3).

It is well known that patients on regular HD treatment are in an immunodeficient state (14). Patients on HD suffer from general immune incompetence, resulting in a high incidence of infectious complications. Various abnormalities in T cell function of HD patients have been described (15). It has been suggested that changes in immune response to infectious agents in patients on HD might be due to impaired monocyte function; uraemic and HD patients overproduce proinflammatory cytokines, such as interleukin-1 beta, tumour necrosis factor-alpha, and interleukin-6 (16). Yalinay et al. (17) investigated the presence of CMV in immunosuppressive patients and positivity for CMV-DNA was 31.7% in HD patients (17). The rate of positivity for anti-CMV IgM was 13.7% (116/846) in a kidney transplantation series by Moray et al. (18). In the present study, none of the 70 healthy controls tested positive for anti-CMV IgM antibody, but 1 HD patient (0.4%; 1/255) was positive for anti-CMV IgM. These data suggest that patients with chronic renal failure and immunosuppression are at risk for CMV infection. In the immunocompetent individual, the virus and host exist in a symbiotic equilibrium and disease manifestations are rarely encountered. However, when the host immune system is compromised, the virus is able to exert its full pathogenic potential (19,20). Bacterial and viral infections represent the most frequent complications in patients with chronic renal failure, due to changes in immunological status (21).

Very few studies have been conducted to determine seroprevalence of CMV infection in HD patients in Turkey. In the present study, while the rate of anti-CMV IgG seropositivity in HD patients was 99.6%, this rate was 82.9% in the control group. The difference between the 2 groups was statistically significant ($P < 0.05$), which may have been due to transmission of CMV during the HD procedure.

With regard to studies from other countries on the seroprevalence of anti-CMV antibodies in HD patients, Konstantopoulou et al. (22) investigated the distribution of anti-CMV IgG and IgM in 173 HD patients. While positivity for anti-CMV IgG was found in 85 (85%) of 100 healthy controls, 161 (93%) of the 173 HD patients were seropositive for anti-CMV IgG antibodies (22). In a study conducted by Korcakova et al. (23) positivity for anti-CMV IgG was found in 80% of HD patients and in 62% of healthy blood donors, whereas positivity for anti-CMV IgM was found in only one of the 30 dialysed patients. Compared to healthy blood donors, a higher percentage of CD 8 lymphocytes and natural killer activity was impaired in all chronic patients in the HD programme (23). The results of this study were similar to our results, though the reported seropositivity for anti-CMV IgG among HD patients was lower than the 99.6% found in the present study.

In a study of infectious complications in 453 renal transplant recipients, CMV infection was the most frequent opportunistic pathogen occurring in renal

transplants (24). The data support that patients with chronic renal failure have a risk of CMV infection. As a result, although CMV is not an important micro-organism in immunocompetent persons, it is a serious pathogen in immunosuppressed people, like HD patients.

Abbas et al. (25) reported that anti-CMV antibodies in patients with chronic renal failure undergoing HD were correlated to the number of the dialysis sessions (20). In the current study, a significant correlation was not found between the length of the time on HD treatment and anti-CMV IgG positivity ($P > 0.05$).

In conclusion, the results of the present study confirm a high prevalence of CMV infection among HD patients in the Antakya region. Patients on HD can be exposed to CMV infection. For this reason, we recommend that HD patients who are susceptible to CMV infection be identified by anti-CMV IgG- and IgM-specific serological tests.

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