

Effect of anti-HCV positivity on response to hepatitis B virus vaccine in haemodialysis patients

Hemodiyaliz hastalarında anti-HCV pozitifliğinin hepatit B aşısına cevap üzerindeki etkisi

Ali KOŞAR MD, Mahmut DALMAZ MD, Şerife SAĞMANLIGİL MD, Mehdi YEKSAN MD, Süleyman TÜRK MD

Selçuk University, Faculty of Medicine, I. Department of Internal Medicine, Konya

SUMMARY: There are different factors that affect the response of recombinant hepatitis B vaccine in hemodialysis patients. A total of 36 patients on a hemodialysis program (HD) were included in this study; 17 of patients were anti-HCV-positive and 19 were anti-HCV-negative. All serological markers of anti-HBs, HBs, anti-HBc IgM and anti-HBc total were negative in all patients. A 20 µg dose of vaccine (Genhevac B Pasteur Merieux, France) was given intramuscularly at 0, 1 and 6 months. Anti-HBs levels were measured at 1, 2, 7 and 16 months and an anti-HBs titer >10 IU/mL was accepted as a protective level against hepatitis B virus infection. At 1, 2 and 7 months there was no statistically significant difference between these groups according to anti-HBs levels. However, anti-HBs levels were lower in anti-HCV-positive group at the 16th month ($p<0.05$).

Anti-HCV positivity in HD patients has a negative effect on the antibody response to hepatitis B virus vaccine. This can be a result of the hepatitis or of the effect on the immune system which is caused by HCV. This negative effect could not be explained in this study and we believe more studies should be carried out in selected patients and larger series.

Key words: Hemodialysis patients, anti-HCV, hepatitis B vaccine

ÖZET: Hemodiyaliz hastalarında rekombinant hepatit B aşısına antikor cevabını değişik faktörler etkilemektedir. Bu çalışmaya 17 anti-HCV-pozitif ve 19 anti-HCV-negatif hemodiyaliz hastası dahil edildi. Anti-HBs, HBs, anti-HBc IgM, ve anti-HBc total tüm hastalarda negatifti. Rekombinant hepatit B aşısı (Genhevac B Pasteur Merieux, France) 0, 1 ve 6 aylarda 20 µg intramuskuler olarak yapıldı. Anti-HBs düzeyi 1, 2, 7 ve 16 aylarda ölçüldü. Anti-HBs >10 IU/mL düzeyi hepatit B enfeksiyonuna karşı koruyucu düzey olarak kabul edildi. İki grup arasında 1, 2 ve 7 aylarda istatistiksel olarak anlamlı bir fark yoktu. Fakat 16. ayda anti-HBs düzeyleri açısından iki grup arasında istatistiksel olarak anlamlı bir fark saptandı ($p<0.05$).

Hemodiyaliz hastalarında anti-HCV pozitifliğinin hepatit B aşısına antikor cevabını olumsuz yönde etkilediği düşünülmektedir. Bu durum HCV enfeksiyonunun neden olduğu hepatitten veya immun sistemin baskılanmış olmasından kaynaklanabilir. Fakat, bu çalışmada bu konuya tam olarak açıklık getirilememiştir. Daha geniş ve daha selektif gruplar üzerinde daha uzun süreli çalışmaların yapılmasının uygun olacağı kanaatindeyiz.

Anahtar sözcükler: Hemodiyaliz hastası, anti-HCV, hepatit B aşısı

Hepatitis B is an important problem in hemodialysis (HD) units and response to hepatitis B virus (HBV) vaccine is lower in HD patients than the normal population (1, 2). There are different factors that affect the response to the recombinant hepatitis B vaccine in HD patients. The patient's age, gender, times of dialysis, dialysis age, use of drugs and use of erythropoietin could influence the response to the recombinant HBV vaccine (3,

4). The response rates to HBV vaccine in HD patients have been reported as 50-80%. Anti-HBs levels were decreased rapidly in HD patients (5, 6). This was reported to be related to the immune status of the patients. In spite of these, there are some reports that HCV infection affected the immune status of these patients (7, 8). The prevalence rate of anti-HCV is about 48% in our country and our hemodialysis center (9). In this study, we

Table 1. Anti-HBs response to HBV vaccine in anti-HCV-positive and -negative groups

Variable	n	Age	Male/female	Anti-HBs level (IU/mL)				Protection (%)			
				1	2	7	16	1	2	7	16
Anti-HCV-positive	17	35 ± 14	11/6	31 ± 7.5	51 ± 6.5	87 ± 10	66 ± 8.7	64	66	70	57
Anti-HCV-negative	19	34 ± 14	12/7	34 ± 6.8	55 ± 9.1	94 ± 9.7	59 ± 8.9	52	64	72	82
p	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	<0.05

NS: Not significant

aimed to investigate the effect of anti-HCV positivity on response to HBV vaccine.

MATERIALS AND METHODS

Anti-HCV-positive (n=17) and -negative (n=18) HD patients were included to study. There were no statistically significant differences in sex, age and dialysis age between two groups. All patients had 4 hours of hemodialysis treatment with polysulfone membrane twice or three times a week. In addition, they were given 0.25 mg of calcitriol and 2 g of calcium per day and other conservative medications when required. Levels of anti-HBs and anti-HCV were measured by ELISA (second generation test, Hepanostica C, Organon Technique B.V. Boxtel, Holland). Anti-HBs, HBs, anti-HBc IgM and anti-HBc total levels were negative in all patients before HBV vaccination. Liver biopsies were performed in seven patients found as HCV-RNA-positive on polymerase chain reaction (PCR) (PCR study was performed at Istanbul University, Faculty of Medicine). Liver biopsy was not performed in HCV-negative patients. A 20 mg dose of vaccine (Genhevac B Pasteur Merieux, France) was given intramuscularly at 0, 1 and 6 months. Anti-HBs levels were measured at 1, 2, 7 and 16 months and an anti-HBs titer >10 IU/mL was accepted as a protective level against HBV infection.

The results were statistically analyzed by a computer program (Minitab), and data were analyzed with correlation test and Student's t-test.

RESULTS

There were 17 anti-HCV-positive (11 male, 6 female, mean age 35 ± 14 ys) and 19 -negative (12 male, 7 female and mean age 34 ± 14 ys) HD patients. All results have been given at Table 1. At 1, 2 and 7 months, there was no statistically sig-

nificant difference between anti-HBs levels of two groups while the levels were lower in anti-HCV-positive group at the 16th month (p<0.05). Anti-HCV positivity had no effect on the response to HBV vaccine at 1, 2 and 7 months except the 16th month. Anti-HBs levels were lower in HCV RNA-positive group compared to HCV RNA-negative group, but the difference was not statistically significant. Liver biopsy results revealed fatty liver in 1 case, chronic persistent hepatitis in 4 cases and active hepatitis in 2 cases.

DISCUSSION

It is very well known that HD patients are one of the higher risk groups for HBV and HCV exposition (9-11). Because of the frequency of and effective route of exposures on the basis of these patients' immunodeficient status, HD patients commonly become chronic carriers of HBV and HCV. It has been shown at controlled studies that hepatitis B vaccines are highly effective in providing protection against HBV infection (12, 13). However, the rate of antibody response in these patients is low compared to healthy adults. Currently available data indicate that vaccine-induced antibody levels significantly decrease over the years (6). Vaccination studies carried out among healthy adults demonstrated that 10-15% of the responders had undetectable anti-HBs levels after 5 years follow-up (6). Hemodialysed patients not only have lower rates of response to hepatitis B vaccination than healthy adults, but also their responses are frequently transitory (6-9). This was reported to be related to the immune status of the patients. HCV infection is common in our country and our hemodialysis center (9). The infection of HCV can range from asymptomatic carrier stage to acute hepatitis, chronic hepatitis, cirrhosis of liver and hepatocellular carcinoma (14). Cellular immune responses, particularly those

mediated by CD8, may be important pathogenetic factor and control hepatitis C virus infection (15-17). We previously showed the increase of CD8 lymphocyte count in HD patients (15), suggesting the probable immunosuppressive role in these patients (15-18).

Currently, it is being observed that the response to HBV vaccine is modulated by a number of viral infections such as HCV and human T-cell lymphotropic type II/lymphadenopathy-associated virus (19). Our results showed that 70% (6 of 17 cases) of HCV-positive patients and 72% (13 of 19 cases) of HCV-negative patients responded to vaccination after 7 months of follow-up. However, only 23% of HCV-positive patients had detectable

levels at the 16th month. This fact suggests the cellular immunosuppression of humoral immunity due to increased count and activity of CD8 cells. Navarro et al. also reported only 3 out of the 13 HCV-infected patients having good response to HBV vaccination. Our preliminary results suggest that HCV infection could modify the effectiveness of hepatitis B vaccine.

Our result shows that HCV infection may affect the antibody production and reduce the effectiveness of hepatitis B vaccine in HD patients. But, further studies are necessary to clarify the possible influence of HCV infection on the vaccination response in nonuremic subjects.

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