LONG-TERM RESULTS OF INTERFERON TREATMENT IN HEMODIALYSIS PATIENTS WITH CHRONIC C HEPATITIS


ABSTRACT

The prevalence of anti-HCV among patients on dialysis is consistently higher than those in the non-uremic population. In these patients different treatment regimens are being applied. Although results are better than non-uremic patients they are still not satisfactory. In this study we evaluated the effectiveness of interferon treatment (3 MU three times a week for 12 months, subcutaneously) in a long-term. With this aim, we included 33 (25 men and 8 women, mean age 37.3±10.4 years) anti-HCV and HCV-RNA-positive patients who were on maintenance hemodialysis. None of the patients had side effect that cause to withdraw from the trial. Mean follow up time after the end of the treatment was 12±0 months. Sustained eradication of HCV was achieved in 12 (%36) patients. Number of virological relapsers after the cessation of interferon at 12th month was eight (24%). Interferon is well tolerated and appears to be effective in hemodialysis patients as in non-uremic patients in HCV infection and in hemodialysis patients 12 months interferon treatment probably lowers the relapsing rate.

Key words: Hemodialysis, HCV infection, interferon.

ÖZET

Kronik Hepatit C İnfeksiyonlu Hemodiyaliz Hastalarında Interferon Tedavisinin Uzun Dönemde Etkinliği.


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INTRODUCTION

In our country hemodialysis patients comprise the group with highest incidence of HCV (Hepatitis C Virus) infection. Among the normal population the prevalence of anti-HCV is between 0.3 and 1.8 %. However, the prevalence of anti-HCV among hemodialysis and renal recipient patients is approximately 50 % (1-3) . HCV infection in hemodialysis patients is mainly post-transfusional and correlated with the number of blood transfusions; transmission is nosocomial in about 10% of cases, possibly by hand carriage from one patient to another (4-6). Also HCV infection incidence is correlated with the duration of hemodialysis program (3). The mortality and morbidity of liver disease in hemodialysis patients increase following kidney transplantation but short-term data to date have not shown detrimental effects on overall allograft and/or patient survival (7-9).

It is thought that the use of immunosuppressive treatment after transplantation pave the way for the progression of chronic hepatitis C (10,11). Because interferon is known to cause significant impairment in the function of the allograft kidney, it is advised to perform the interferon treatment during the dialysis period(12-13). In this study we examined the efficacy and tolerability of interferon α-2b used for one year on HCV infection in hemodialysis patients. Also long-term (one year after the treatment) effect was evaluated.

PATIENTS AND METHODS

With this aim, we included 33 (25 men and 8 women, mean age 37.3±10.4 years) anti-HCV and HCV-RNA-positive patients on maintenance hemodialysis. Mean duration of hemodialysis was 4.6±1.9 years. Before and during the interferon α-2b therapy (every four weeks) hemogram, serum transaminases, alkaline phosphatase (ALP), -glutamyl transpeptidase (GGTP), bilirubine, albumine were monitored. Before the onset of therapy, liver ultrasonography was performed and α feto protein level was checked. All patients had elevated serum transaminase levels. Liver biopsy was not done, because of its high incidence of mortality in hemodialysis patients. None of the patients was seropositive for HBsAg or anti-HIV. All patients received recombinant interferon α-2b subcutaneously at a dose of 3 MU three times weekly (tiw) for six months. Administration of interferon α-2b at the same dose was extended to 12 months in patients who were HCV-RNA-negative at 6th month of the treatment. At the end of 12 months HCV-RNA was detected at every three months interval for one year. Blood transfusions were applied if the haemoglobin level was under 8g/dl and patients developed symptoms of anemia despite an increase of erythropoietin dosage.

Anti-HCV was tested by second-generation enzyme immunoassay (EIA II) and qualitative polymerase chain reaction (PCR) assay was used for HCV-RNA detection.

RESULTS

None of the patients had any side effects that caused to withdraw from the trial. All patients had flu-like symptoms especially on the first two months. Four patients (12%) required blood transfusions.
haemoglobin before treatment was 11.5 ±2.7 g/dl. At the end of the 6th month 13 (40%) patients were positive for HCV-RNA (non-responders) and 20 (60%) patients were negative for HCV-RNA (responder). Number of virological relapsers after the cessation of interferon at 12th month was eight (24%). Six (75%) of them were positive for HCV-RNA three months and two of them six months after the cessation of interferon therapy. The number of sustained responders was 12 (36%). Mean follow up time after the end of the treatment was 12±0 months. The number of biochemical responders was 22 (67%) (Table 1). In the non-responder and relaper groups serum transaminase levels were persistently normal in 10 (48%) patients.

**Table 1: Results of our patients.**

<table>
<thead>
<tr>
<th>Sustained response</th>
<th>Relapses</th>
<th>Biochemical response</th>
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<td>12 (%36)</td>
<td>8 (%24)</td>
<td>22 (%67)</td>
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**DISCUSSION**

While the systemic side-effects of interferon are usually transient in non-uremic patients, hemodialysis patients are less tolerant to these side-effects (14). Nearly in all patients on interferon treatment flu-like symptoms can be seen. In 10-40% of patients side effects cause dosage lowering and in 5-15% of patients stopping the interferon treatment. In patients on hemodialysis malnutrition, depression, exacerbation of anemia and resistance to erythropoietin are the most important side-effects of interferon (15). The last two side effects may relate to the induction of erythroid progenitor apoptosis by interferon (16). In our study, incidence of required blood transfusions is lower than other studies (17). This may be attributed to higher values of hemoglobin before treatment.

Our study showed that recombinant interferon α 2b therapy in hemodialysis patients with HCV infection is well tolerated and has the same effectiveness that was observed in non-uremic patients (17-20). In non-uremic patients with HCV infection interferon α 2b therapy causes 25% long-term response, 25% relapses and 50% non-response (17-22). Response rate depends on virological and host factors( 3,23). Type 1b genotype, present in the majority of patients with post-transfusional hepatitis as in hemodialysis patients, is associated with poor long-term responsiveness, ranging from 10-15 % (24). This could be partly attributable to the higher level of viraemia in type 1b infection (25). Although genotype was not evaluated in our study, most of HCV infections in Turkey show the genotype 1b (26). Increased hepatic iron and/or serum ferritin have been associated with poor response to interferon therapy (27,28). Patients on hemodialysis may have iron overload due to repeated transfusions. But in our study the rate of responders was the same as in the non-uremic group. Hence host factors may be more effective on the outcome of the interferon treatment in our study. In the study of our department; it was shown that in patients who were positive for HLA DRB1*13 the effect of interferon α 2b on HCV infection was less in comparison to the negative group (29). Also hemodialysis patients have low replication of HCV (23). These low viraemic values may reflect a replication with other viruses, such as hepatitis G in particular. Such a low viral replication may also be linked to hemodialysis itself, which reduces the viral load by one log (30). Our results may also reflect an increased effectiveness of interferon, because its pharmacokinetics appear to be modified by hemodialysis, and accumulation of the drug has also been described so ophthalmological events were reported in the course of treatment (31). In our study all relapses were seen in the first six months as in the literature (17). The relapsing rate of our patient group is lower than some six months
of interferon treatment studies (17, 23). Expanding the interferon treatment to 12 months in the responder group may be the cause of the low relapsing incidence.

In conclusion, interferon is well tolerated and appears to be effective in hemodialysis patients as in non-uremic patients with HCV infection and in hemodialysis patients, interferon treatment lasting for 12 months probably lowers the relapsing rate.

LITERATURES

18. Davis GL, Balart LA, Schiff ER, Lindsay K, Bodenheimer HC Jr, Perillo RP and the Hepatitis Interventional therapy group. Treatment of chronic hepatitis C with recombinant interferon alpha. A


