Dilemmas in Clinical Practice. Combined Use of Interferon and Ribavirin in Haemodialysis Patient with Established Cirrhosis

S. Spaia, N. Askepidis, M. Pazarloglou, M. Tersi, V. Iliadi and K. Baltatzi

Dialysis Unit, 2nd Hospital of IKA-ETAM, Thessaloniki, Greece

Abstract

We describe a dialysis patient with HCV infection and cirrhosis, non responding to INF monotherapy, in spite of his non type 1 genotype. Application of long term combined interferon and ribavirin treatment in this patient was individualized. The case was followed up for 9 years with repeated liver biopsies. We had to employ lower doses of interferon, because of side effects, mainly of hematological origin. On the other hand duration of treatment far exceeded the usually recommended period of 48 weeks in non-responders, and lasted 3 years, and one year being with negative HCV RNA titer. Our experience suggests that treating hemodialysis patients is individualized and effective even in difficult cases, in spite of the severity of liver lesions.

Key words: HCV infection, cirrhosis, interferon, ribavirin

Introduction

Virus of hepatitis C has caused many problems in dialysis units all over the world over the last decades. Early recognition, avoidance of blood transfusions in epoetin era and appropriate treatment led to a substantial reduction of the frequency of HCV infection. Recent reports deal with the limitations of the use of both pegylated interferon-alpha-2b and ribavirin in dialysis patients infected with hepatitis C virus. (1,2). While dialysis patients in Greece respond well to interferon treatment, as we have already reported (3), there are also cases difficult to manage, which cause difficulties in therapeutic approach.

Case report

We present a male patient, 72 years old, 60 kg of Body Weight, who was on dialysis since 1997. At dialysis onset, he was anti-HCV negative but we observed seroconversion along with transaminasemia 4 months later. Blood transfusions because of very low hct (16%) at the commencement of dialysis were considered to be the source of infection. He had PCR HCV RNA in serum of $4.63X10^6$ copies/ml and his liver biopsy showed moderate to severe chronic active hepatitis with fibrosis leading to cirrhosis, findings compatible with HCV infection. HCV genotype was 4a. Laboratory values, other than ALT and AST were within normal range. Cryoglobulins were negative. Initially, he was treated with interferon- alpha2b (INF-a) 3,000,000IU after each dialysis session for six months according to our standard protocol. Response was inadequate, as levels of PCR HCV RNA of $3.3X10^5$ copies/ml evidenced it. A second cycle of INF-a at the same dose was administered, but we had to reduce it to 1,500,000IU/session, 3 months later, due to neutropenia, anemia and thrombocytopenia. However, 10 months later, PCR HCV RNA increased to $2X10^6$ and ascetic fluid became apparent. Ribavirin was added at a dose of 400mg/day, according to data in available studies (4,5). Two months later ribavirin was withdrawn (along with INF-a) due to severe haemolysis (Hct 30%...21%). Liver biopsy was repeated 3 months after discontinuation of the treatment. It showed findings of overt cirrhosis. Esophageal varices were also present in endoscopy. PCR HCV RNA revealed $5.5X10^6$ copies/ml and we had to perform frequent draining of the ascetic fluid. Finally, we chose to combine a low dose of both INF-a and ribavirin (1,500,000IU and 200mg/session respectively). This resulted in a substantial clinical improvement and initial reduction of HCV RNA by PCR to $3,5X10^5$ at 12 mo, $1,5X10^4$ at 24mo, until complete eradication at 36 mo. Ascitic fluid didn't recur and a new liver biopsy showed lesions of chronic hepatitis with scarce localized activity with fibrosis (Hepatic Activity Index 6: fibrosis 3, portal inflammation 2, intralobular necrosis 1). Treatment was discontinued after one year with negative HCV RNA by PCR. However, four months later and while the patient remained in satisfactory clinical condition, HCV RNA relapsed to $7X10^5$ copies/ml.

Once more combined treatment with ribavirin 200mg/session and this time pegylated interferon-alpha-2b at a dose of 50mcg/week (0.8/kgBW) was initiated. The latter was shortly reduced to 50mcg every other week due to neutropenia. HCV RNA in serum decreased to $7X10^4$copies/ml at 3 months, to $7X10^3$copies/ml at 6 months and the patient remains well with no side effects, still on treatment.

Patient is being dialyzed via the original vascular access, is maintained on bicarbonate dialysis and attention is steadily given to the dialysis adequacy (kt/v was kept >1,4). He suffers from adynamic bone disease but otherwise he is doing well and copes with daily demands. His current medications are phosphate binders and iron, folate and vitamin supplements.

Discussion

We describe a patient, non responder to INF monotherapy, in spite of his non type 1 genotype. Application of combined treatment in this patient was individualized based on an intention to treat. Actually, we had to employ lower doses, because of side effects, mainly of hematological origin. On the other hand duration of treatment far exceeded the usually

Correspondence to: Sophia Spaia, 21 Anapafseos str, Hortiatis 57010, Thessaloniki, Greece; E-mail:sspaia@otenet.gr

recommended period of 48 weeks in non-responders, and lasted 3 years and more than one year with a negative HCV RNA titer. Treatment is still ongoing. Dilemmas on how long should we treat were answered by patients clinical status. It's noteworthy that this particular patient's liver function appeared to deteriorate with the interruption of therapy. Available data are limited and prolongation of treatment in cirrhotic, even non-renal patients is debated on cost basis and incidence of toxicity (6). However the fact that this patient- otherwise ill-fated- did extremely well with the above mentioned non aggressive approach points to the need of a sustained treatment. Lowering the doses up to the point of optimum tolerance is of a critical importance. Contributing to the discussion taking place and until strong evidence becomes available our experience suggests that treating dialysis patients is individualized and effective even in difficult cases and in spite of the severity of liver lesions.

References

1. Russo MW, Ghalib R, Sigal S, Joshi V. Randomized trial of pegylated interferon alpha-2b monotherapy in haemodialysis patients with chronic hepatitis C. *Nephrol Dial Transplant*. 2006; 21 (2): 437-43
2. Bruchfeld A, Lindahl K, Reichard O, Carlsson T, Schvarcz R Pegylated interferon and ribavirin in haemodialysis patients. *Nephrol Dial Transplant.* 2006; 21(5): 1444-5; author reply 1445-6
3. Raptopoulou-Gigi M, Spaia S, Garifallos A et al: Interferon-a2b treatment of chronic hepatitis C in hemodialysis patients. *Nephrol Dial Transplant* 1995, 10: 1834-1837
4. Glue P. The clinical pharmacology of ribavirin. *Semin Liver Dis* 1999; Suppl 1: 17-24
5. Bruchfeld A, Stahle L, Andersson J, Schvarcz R. Ribavirin treatment in dialysis patients with chronic hepatitis C virus infection--a pilot study. *J Viral Hepat*. 2001 Jul; 8 (4): 287-92
6. Bonis AP, Chopra S. Administration of combined interfernalfa-2b and ribavirin in the treatment of hepatitis C virus infection. Up to Date 2006