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Case Report

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Pegylated interferon alpha-2a monotherapy in a peritoneal dialysis patient with chronic hepatitis C

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Abstract

Background: Although pegylated interferon (PEG-IFN) is now the standard treatment for chronic hepatitis C, there are few reports targeting dialysis patients and treatment protocol for hepatitis C virus (HCV) infection has not been determined, particularly in patients on peritoneal dialysis.

Case: A 34-year-old woman with chronic hepatitis C started peritoneal dialysis because of progressive renal disease 2 years after peripheral blood stem cell transplantation for aplastic anaemia. The regimen was a single 6-h dwell of 2L glucose dialysate. Considering that her HCV genotype was 2a and that she was a candidate for cadaveric kidney transplant, we decided to treat her with PEG-IFN alpha-2a monotherapy 1 year after the beginning of peritoneal dialysis. We adopted a dose escalation strategy to minimize the total amount of PEG-IFN administration, thereby reducing the risk of adverse effects. Her HCV-RNA disappeared at the 17th week and sustained virus response was achieved thereafter. Only minor side effects were observed including flu-like symptoms and mild anaemia, and residual renal function remained stable during the treatment of 48 weeks (renal Kt/V; from 1.28 to 1.26).

Conclusion: PEG-IFN monotherapy with dose modification may be a safe and effective treatment for HCV infection in patients undergoing peritoneal dialysis.

Keywords: HCV; interferon; peritoneal dialysis; transplantation

Introduction

Chronic hepatitis C virus (HCV) infection is common in dialysis patients, causing an increased morbidity and mortality. Interferon (IFN) has been widely used to treat chronic hepatitis C, and recently pegylated (PEG)-IFN with or without ribavirin has been reported to be the most efficient treatment for HCV infection in the general population and also in haemodialysis (HD) patients [1,2]. However, few case reports are available regarding the treatment of HCV infection in peritoneal dialysis (PD) patients, and moreover treatment protocol for PEG-IFN including the dose and timing of administration during PD has not been determined. In addition, adverse events after PEG-IFN therapy are shown to be more common and severe in dialysis patients, probably due to an enhanced half-life caused by renal dysfunction [3]. Thus, it is crucial to know the treatment protocol for HCV infection observed in PD patients that may provide a maximal therapeutic effect with minimal adverse events and also may not affect residual renal function.

Here we report the case of a PD patient with chronic hepatitis C who was successfully treated by PEG-IFN monotherapy without deteriorating renal function. This is, as far as we know, the first case report of HCV genotype 2a treated by PEG-IFN during PD, providing a promising treatment strategy for the selected group of end-stage renal disease (ESRD) patients.

Case report

A 35-year-old female with ESRD was admitted to our hospital 2 years ago. She had a history of aplastic anaemia since she was 11 years old and was complicated by chronic hepatitis C probably due to frequent blood transfusion. She underwent peripheral blood stem cell transplantation at the age of 32. Her renal function deteriorated rapidly after the treatment. She started PD with the regimen of a single 6-h dwell of 2 L glucose dialysate. Considering that her genotype of HCV was 2a, which is known to be more susceptible to IFN therapy than genotype 1, and that she was a candidate for cadaveric kidney transplant, we decided to treat her with PEG-IFN alpha-2a (Pegasys&#61650, Hoffmann-LaRoche, Basel, Switzerland) monotherapy 1 year after the beginning of PD.

Laboratory results before introduction of PEG-IFN were as follows: white blood cell count, 7000/μL; neutrophil count, 56%; haemoglobin, 9.9 g/dL; platelet count, 261 000/μL; serum albumin, 3.9 g/dL; aspartate

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transferase, 13 IU/L; alanine transferase, 16 IU/L and HCV-RNA, 3600 KIU/ml. Because IFN may adversely affect residual renal function, we adopted a dose escalation strategy in order to minimize the total dose of PEG-IFN. Thus, the treatment was initiated at a dose of 30 μg subcutaneously once a week for the first 6 weeks, being escalated to a maximum dose of 90 μg over the next 4 weeks and continued for subsequent 38 weeks. The plasma HCV-RNA levels decreased to be undetectable at the 17th week and constantly negative thereafter. During the PEG-IFN therapy, flu-like symptoms and progression of anaemia were observed, which were treated by a transient cessation of PEG-IFN therapy for a couple of weeks and an increase in the dose of erythropoietin, respectively. The residual renal function remained stable during the course of 48 weeks (renal Kt/V; from 1.28 to 1.26). Six months after the end of the treatment, sustained virological response (SVR) was achieved.

Discussion

Although there have been several studies for the treatment of HCV infection targeting HD patients, this may be, as far as we know, the first case report that clearly documented successful treatment of HCV genotype 2a infection by PEG-IFN alpha-2a monotherapy during PD. In addition, we adopted a dose-escalation strategy for PEG-IFN, which may contribute to a favourable outcome and possibly preserving renal function.

Bruchfeld *et al*. reported a pilot study investigating the effect of combination of PEG-IFN and ribavirin in five HD and one PD patients, in which the PD patient showed a relapse during the treatment [4]. More recently, Chan *et al*. treated five HD and one PD patients [5], but the PD patient did not complete the 48 weeks of treatment course because the patient decided to withdraw from the study.

PEG-IFN has a prolonged half-life compared to conventional interferon. Indeed, PEG-IFN alpha-2a is a conjugate of a 40-kDa branched PEG polymer with lysine residues of interferon, which is metabolized in the liver, in contrast to PEG-IFN alpha-2b which is cleared in the kidney. Thus, PEG-IFN alpha-2b is associated with a rapid onset of side effects, whereas those of PEG-IFN alpha-2a gradually increase during the first several weeks of treatment. However, the pharmacokinetic study showed that clearance of PEG-IFN alpha-2a decreased from 94 ml/h in controls to 63 ml/h in dialysis patients, resulting in a longer half-life from 52 to 58 h [6]. Thus, the standard protocol for haemodialysis patients is suggested to be weekly administration of 135 μg PEG-INF alpha-2a at the end of haemodialysis session, which is <180 μg in patients without renal failure. Because pharmacokinetics of PEG-IFN alpha-2a and the standard protocol of administration for PD patients are not known, we adopted a dose escalation strategy expecting to minimize the total amount of PEG-IFN, thereby reducing the risk of adverse events with a maximal therapeutic effect. In a cohort study for dialysis patients, more than half of the subjects with chronic hepatitis C were forced to discontinue the interferon treatment due to several side effects [7]. Thus, we began PEG-IFN by subcutaneous administration of 30 μg per week and increased stepwise up to 90 μg per week, at which dose the HCV titre started to decrease and finally became negative.

It is well known that the HCV genotype is a good predictor of treatment response of PEG-IFN monotherapy for patients with normal renal function. It was reported that only 12% of patients achieved SVR after 48 weeks of PEG-IFN monotherapy in genotype 1, whereas HCV was eradicated in 51% of those with genotypes other than 1 [8]. Other factors that may contribute to better outcome in the PEG-IFN monotherapy are higher alanine transferase, low viral load, small body-surface area, less advanced liver disease and younger age. In this patient, young age, mild liver disease and genotype 2a possibly contributed to SVR. The combination of PEG-IFN and ribavirin is widely used as a standard regimen for patients with normal renal function, which achieves 41% of SVR even in patients with HCV genotype 1 [8]. Although ribavirin has been regarded as a contraindication for dialysis patients because of the risk of severe haemolytic anaemia, recent reports evaluating combined standard IFN alpha plus low-dose ribavirin showed the SVR rates of 50% after 24–48 weeks of treatment [9]. Thus, the combination therapy with low-dose ribavirin might be considered in dialysis patients with HCV genotype 1 infection.

Lastly, it is reported that patients with chronic HCV infection before renal transplantation have a fivefold increased risk of post-transplant exacerbation of hepatitis because of the use of immunosuppressant, which can be fatal in the form of cholestatic hepatitis [10]. Moreover, graft survival was reported to be higher in the HCV-negative renal recipient group than in the HCV-positive group (93.2% versus 81.4%) at 1 year [11]. Thus, anti-viral treatments to eradicate HCV infection should rather be performed, if possible, before renal transplantation. It is suggested that renal transplant candidates undergoing PD with chronic hepatitis C may be a relative indication for PEG-INF therapy.

Conclusion

The PEG-IFN monotherapy with dose modification may be safe and effective, providing a new treatment strategy for HCV infection in PD patients.

Conflict of interest statement. None declared.

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