Case Series

Chronic Hepatitis C Virus treatment in Post Renal Transplant patients - case series

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ABSTRACT

Hepatitis C virus (HCV) infection is an important considerationin kidney transplantation candidates andgraft recipients. Mortality rates are higher amongHCV-infected dialysis patients than among HCV-negative patients. Evaluation of patients with chronic HCV infection is warranted todetermine stage of disease and the need for HCV therapy. Two new oral antiviral agents, simeprevir and sofosbuvir, have already been approved and are now available for treatment of patients with chronic HCV. It is now possible to cure chronic HCV in the vast majority of patients with chronic HCV and in many patients without interferon. We illustrate three cases of treating Chronic HCV in post renal transplant patients and brief review of literature on therapeutic approach.

Introduction :

Liver disease secondary to Chronic Hepatitis C virus (HCV) infection is an important cause of morbidity and mortality in kidney transplant recipients[1]. A major concern in these transplant recipients is the onset of an aggressive and rapid course of HCV-related infection and liver disease, facilitated by ongoing immunosuppression to prevent graft rejection[2,3]. The conventional treatment of interferon (IFN) injection with ribavirin carries the risk of allograft rejection. The availability of second generation oral anti-viral drugs has opened new avenues for HCV treatment[4]. We are sharing our experience of treating Chronic HCV in post renal transplant patients successfully through this case series.

Case 1 :

43 yrs. male with Chronic HCV infection, underwent live related transplant on 21/02/15. Donor being spouse with 1 haplotype match. Pretransplant USG and upper GI scopy showed normal liver echotexture and no varices respectively. Induction therapy included Basiliximab 2 doses (20 mg each), an IL2 Receptor antagonist followed by triple drug immuno-suppression (prednisolone, cyclosporine, mycophenolate mofetil [MMF]). He received 1 unit of leucodepleted blood transfusion in post operative period. His post transplant haemoglobin remained 6.5 to 7 gm/dl. His post transplant HCV viral load on 22/04/15 was 290 IU/ml with Genotype 1. Treatment with Sofosbuvir and RIbavarin initiated. After 3 and half months of treatment his haemoglobin dropped so Ribavarin was stopped. His haemoglobin improved after omitting Septran and Ribavarin. On 10/10/2015 during the 6 month of oral antiviral treatment, his HCV viral load was <34 IU/ml. He continues to do well till date after stopping anti HCV treatment on 23/10/2015.

Case 2 :

34 yrs. male with Chronic HCV infection underwent live related transplant on 19/04/2009. Donor being fatherwith 1haplotype match. Pretransplant USG and upper GI scopy showed normal liver echotexture and no varices respectively. Pre-transplant Liver biopsy showed no evidence of acute hepatitis or cirrhosis. Induction therapy included triple drug immuno-suppression (prednisolone, cyclosporine, mycophenolate mofetil [MMF]). In view of raised SGPT level opinion with Gastroenterologist was taken. His post transplant HCV viral load on 17/04/15 was 8320525 IU/ml with Genotype 3 (11/06/2015). Treatment with Sofosbuvir and Ribavarin initiated. On 18/12/2015

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and 19/04/2016 his HCV viral load were<1240 IU/ml and undetectable respectively. He continues to do well till date after stopping anti HCV treatment.

Case 3 :

64 yrs. male with Chronic HCV infection underwent live, emotionally related transplantion on 31/03/15. Pretransplant USG and upper GI scopy showed Liver parenchymal disease with no portal hypertension and oesophageal candidiasis respectively. Pretransplant liver biopsy done on 14/02/2015 showed chronic hepatitis (Gr. 4-5/18) with mild portal fibrosis (stage 1-2/6) with secondary hemosiderosis. ARFI for liver showed 2.80 m/sec suggestive of cirrhosis of liver. Induction therapy included Basiliximab 2 doses (20 mg each) on Day 0 and Day 4 alongwith triple drug immuno-suppression (Prednisolone, Cyclosporine, Mycophenolate mofetil [MMF]). His post transplant HCV viral load on 23/01/16 was 206000 IU/ml with Genotype 1. Treatment with Sofosbuvir and Ribavarin initiated. On 07/04/2016 his HCV viral load was <34 IU/ml. He continues to do well till date after stopping anti HCV treatment.

Discussion :

All 3 patients were not treated for HCV in view of non availability of oral antiviral easily. Patients treated with Pegylated IFN and ribavirin achieve SVR rates of approximately 55%.SVR, defined by an undetectable HCV RNA (<50 U/ml) in serum at least 6 months after stopping treatment1. They were explained about the availability of Pegylated interferon and cost of therapy. Early case reports of use of nonpegylated IFN in kidney transplant recipients showed deterioration in renal function in approximately 40% of cases[5,6]. However, these reports are largely from uncontrolled studies, and the findings were likely influenced by the type of maintenance immunosuppression regimen used, timing of treatment in relation to transplantation, and the interpretation of histologic changes in the kidney in the presence of IFN. Although treatment of kidney transplant recipients who havehepatitis C is not routinely recommended because of the potential risk for precipitating rejection, some clinical presentations warrant consideration of IFN-based therapy. The mostpressing reasons to consider HCV therapy are recurrent and progressive HCV-associated glomerulopathy in the transplanted kidney, severe cholestatic hepatitis, and advanced histologic stages of liver disease[7]. Ribavirin dosages must be adjusted on the basis of renal function to minimize the complications of anemia.

In 2011, the first two protease inhibitors, telaprevir and boceprevir, were approved to be utilized with peginterferon (PEGINF) and ribavirin (RBV) to treat chronic HCV genotype 1[8-12]. It showed increased sustained virologic response (SVR) in the treatment-naive population with HCV genotype 1 from about 40% to 70-75%. The main limitation of these first-generation protease inhibitors was side-effects, particularly anemia[14]. Many of whom had previously failed PEGINF and RBV, nearly half of all patients treated with either telaprevir or boceprevir developed serious adverse events, 25% discontinued treatment, over half developed severe anemia and required a hematopoetic growth factor and 12% died as a result of hepatic decompensation[13].

In late 2013, another protease inhibitor simeprevir and the first polymerase inhibitor, sofosbuvir, were approved for HCV treatment. Sofosbuvir is effective against all genotypes and when utilized with RBV represents the first interferonfree treatment for chronic HCV[14]. Treatment of patients with HCV genotype 1 includes SPV, peginterferon (PEGINF) andribavirin (RBV) for 24-48 weeks, SOF, PEGINF and RBV for 12 weeks, SOF plus RBV for 24 weeks or SOF and SPV for 12 weeks. The treatment of patients with HCV genotype 2 is SOF plus RBV for 12 weeks. The treatment of patients withHCV genotype 3 is SOF plus RBV for 24 weeks[14].

The combination of Sofosbuvir and RBV represents the first interferon free regimen approved for use to treat patients with chronic HCV. This combination was initially studied and is approved for use in patients with HCV genotypes 2 and 3[15-16]. In treatment naive patients, 12 weeks of sofosbuvir and RBV achieved SVR rates of 91 and 98% in patients with and without cirrhosis respectively. In patients

who had previously failed PEGINF and RBV SVR rates of 96 and 60% were observed with 12 weeks of treatment. Extending the duration of treatment from 12 to 16 weeks did increase the SVR in this subgroup of patients to 78%[14].

In patients with genotype 3, treatment with sofosbuvir and RBV for 12 weeks yielded an SVR rate of only 61% in patients without cirrhosis and 34% in patients with cirrhosis[15-16]. Extending the duration of sofosbuvir and RBV to 16 and 24 weeks increased the SVR rate in all patients with genotype 3 to about 62 and 84%, respectively[16-18].

Sofosbuvir and RBV were also studied in patients with genotypes 1, 2 and 3 who had coinfection with HIV[19]. The duration of treatment for patients with genotypes 1 and 3 was 24 and 12 weeks for patients with HCV genotype 2. SVR rates of 76, 92 and 88% were observed for patients with genotype 1, 2 and 3, respectively[14].

Sofosbuvir is a well tolerated antiviral agent with minimal side effects. In a study in which sofosbuvir and RBV were compared with placebo in patients who could not take PEGINF and RBV, the only side effectswith increased frequency above placebo were anemia and pruritus, both of which were attributed to RBV[16].

Conclusions :

Kidney transplant recipients who are positive for the HCV antibody have a reduced survival. Approximately 40% of transplant recipients will have progressive liver fibrosis within the first 5 yr, and those with advanced fibrosis are at risk forLiver related complications. It is now possible to cure HCV in the vast majority of patients with chronic HCV. SVR rates of 80-90% can be routinely achieved in patients with all HCV genotypes in as little as 12-24 weeks. Of the antiviral agents currently available, sofosbuvir appears to be the easiest to manage, the most efficacious and the antiviral agent with the broadest of indications[14]. Patients with genotype 1 who are unable to tolerate PEGINF and patients with HCV genotype 3 can be treated with sofosbuvir and Ribavarin for 24 weeks. SVR rates in these patients range from 75 to 83%. Patients with genotype 2 can be treated with sofosbuvir and RBV for 12 weeks with an SVR exceeding 90%[14]. In our cases, all the three patients as mentioned had good SVR with the oral antiviral treatment as described. This would certainly have a long term benefit as far as the progression of liver disease is concerned.

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