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Hepatitis C Virus Infection Complicated by Kidney Disease

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Dear Editor,

We read with interest the editorial by Dr. Alavian recently published in Nephro-Urology Monthly (1). We agree that control of the components of metabolic syndrome can influence the development of chronic kidney disease (CKD) and further progression to end stage kidney disease (ESKD). Furthermore, early intervention of these risk factors can mitigate cardiovascular morbidity and mortality associated with kidney disease and following renal transplantation. There are 3 distinct patient populations of interest in regard to hepatitis C virus (HCV) infection that should be more fully appreciated including: 1) patients with CKD not yet on dialysis, 2) patients receiving renal replacement therapies, and 3) transplant recipients.

Chronic HCV infection is most commonly associated with cryoglobulinemic glomerulonephritis renal injury, implicating it as both a cause and complication of CKD (2). Prompt recognition and treatment are key to improving renal outcomes and limiting extra-renal manifestations. The primary goal of antiviral therapy in CKD is to eradicate the virus. Secondary aims are focused on preventing the progression to ESKD, liver cirrhosis and hepatocellular carcinoma via sustained viral suppression. Although we agree utilization of antiviral therapy in this population is an important consideration, its use is dependent on the severity of kidney disease and is complicated by the identification of viral genotype, treatment risks, tolerance to therapy, and the presence of other comorbidities that may affect outcome (3). It is well established that combination antiviral treatment with interferon-based therapy and ribavirin in patients with estimated glomerular filtration rate (GFR) ≥60 mL/min/1.73 m^2 is recommended (4).

In patients with GFR <50 mL/min/1.73 m2 or in those receiving renal replacement therapy, the use of interferon-based monotherapy is recommended (4). The use of ribavirin in combination with interferon-based therapy in these patients is not recommended by the American Gastroenterological Association (AGA) due to increased risk of hemolytic anemia (5). In light of the impact of chronic HCV infection on outcomes, and new evidence, the use of ribavirin in combination therapy may be considered with extreme caution in well-monitored settings, at low doses, with weekly monitoring of hemoglobin, and administration of high doses of erythropoietin (4, 6).

Although renal transplantation had been associated with improved long-term survival compared to remaining on dialysis in early studies (7), more recent data has

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failed to confirm this benefit. The impact of HCV infection on dialysis patient mortality has been demonstrated to be statistically significant (hazard ratio 1.25; 95%CI 1.07-1.46); however, patient mortality following renal transplantation is both statistically and clinically meaningful (hazard ratio 2.38; 95%CI 1.69-3.37) (8). Compared to HCV negative renal transplant patients, HCV positive recipients were more likely to die from hepatic failure (hazard ratio 22.1; 95%CI 3.99-121.84), cardiovascular disease (hazard ratio 2.74; 95%CI 1.61-4.65), and malignancy (hazard ratio 2.52; 95%CI 1.08-5.89) (8). This observed increase in death due to hepatic failure may be partially explained firstly by inadequate screening to identify candidates with the highest likelihood for success following transplantation and secondly in the resistance to treat active HCV infection in the post-transplant period due to its association with increased risk of chronic allograft nephropathy and graft loss (4). Other considerations in the clinical management in these patients include complications related to immunosuppressive agents, leading to a more aggressive infection as well as extra-hepatic post-transplant complications, such as new onset diabetes, post-transplant glomerulonephritis, and sepsis (4). Nevertheless, renal transplantation should remain a viable option in those HCV positive patients that undergo extensive pre-transplant evaluation. Preventative cardiovascular risk reduction strategies including control of pre-existing or new onset diabetes, hypertension, dyslipidemia, obesity, and smoking cessation, and immunsuppression tapering where indicated, should also be implemented.

Author's Reply: Hepatitis C Infection and Diabetes Mellitus; It is just a Beginning

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Dear Editor,

I read with interest the letter to editor by Salinitri *et al.* (9), as they mentioned that the Mixed Cryoglobulinemia (MC) is most commonly and strictly associated with hepatitis C virus (HCV) infection (10). Under ideal circumstances, the MC treatment aims to eradicate the HCV infection, but unfortunately interferon (IFN) therapy is not associated with a promising response (10). However, the HCV infection is the main cause for chronic liver disease in hemodialysis patients and control of this infection is very critical in this high risk group. HCV treatment has been recommended for all infected patients regardless of the HCV genotype (11, 12). Using ribavirin in hemodialysis patients is still under debate (13). I agree that using interferon or pegylated interferon along with ribavirin can cause higher sustained viral response rate in hemodialysis patients, however administration of ribavirin needs close monitoring of CBC and serum ribavirin concentration.(13). And finally I would like to mention that all the questions regarding the HCV Infection in renal transplant recipients have not been answered yet (14). It seems that the renal transplantation in HCV infected patients can improve survival rate in comparison with hemodialysis (15), however, I strongly suggest that all infected patients receive interferon therapy with consideration to the their compliance and comorbidity.

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