Rescue use of Pegylated Interferon in Dialysis Patient who Failed to Respond Sofosbuvir

Sir,

Up to 20% of patients on maintenance hemodialysis (MHD) have evidence of hepatitis C virus (HCV) infection.[1] HCV treatment in people on MHD is challenging. The renal safe direct-acting antiviral (DAA) approved in eGFR <30 ml/min is not available in India. Sofosbuvir use for the MHD population was approved in November 2019. We report a HCV viremic MHD patient who relapsed after two courses of sofosbuvir containing regimens and achieved sustained virological response (SVR12) with sofosbuvir/velpatasvir/pegylated-interferon combination.

A 53-year-old male on MHD had acute HCV infection as suggested by recent (<6 months) seroconversion, >10-fold elevation in alanine aminotransferase (ALT) from 12 to 165 IU/mL, and absence of other cause for liver injury. He had no features of cirrhosis on clinical examination, laboratory investigations, ultrasound abdomen, or endoscopic examination. Molecular tests identified genotype 3a and viral load of 4,395,561 IU/ml. At the time of the first course of DAA in October 2017, sofosbuvir was not approved for those on dialysis. However, we treated our patient with 8 weeks of sofosbuvir 200 mg/daclatasvir 60 mg. After achieving undetectable RNA after 4 weeks of treatment (RVR4), he was dialyzed on HCV negative machine. The viremia reappeared after 4 weeks of stopping the treatment (SVR4) which was not accompanied by ALT or aspartate aminotransferase (AST) elevation. For the first retreatment in February 2018, we again discussed with the patient about the off-label use of sofosbuvir and mutually decided to prolong the treatment duration instead of using sofosbuvir in full-dose. The patient was retreated for 24 weeks with sofosbuvir 200 mg/daclatasvir 60 mg. He was not treated with sofosbuvir/velpatasvir combination to avoid exposure to full-dose sofosbuvir. RVR4 was achieved but SVR4 detected viremia with normal ALT/AST. On the second relapse in April 2019, the data on the safety of full-dose sofosbuvir in the dialysis population was communicated to the patients and mutually decided for a 12-week treatment with sofosbuvir/velpatasvir/pegylated interferon α 2b combination. He achieved SVR12 and underwent renal transplantation in December 2019. The transplanted organ is functioning normally, and HCV RNA remained undetectable till May 2021. All SVR4 and SVR12 results were reconfirmed in fresh specimen with COBAS AmpliPrep/COBAS TaqMan HCV quantitative Test, v2.0 (Roche, Branchburg, NJ, USA), with the lower limit of detection of 15 IU/mL. The details of the anti-HCV treatment and virological response are summarized in Table 1.

HCV is treated with sofosbuvir-containing regimens, which are safe, effective, require negligible monitoring, and have minimal adverse effects. Sofosbuvir is metabolized in the liver to produce its predominant metabolite GS-331007, which is excreted through the kidneys. In patients with eGFR <30 ml/min, the serum level of sofosbuvir and GS-331007 metabolites are elevated manyfold as compared to those with normal renal function.[2] Concerns about the toxic effect of accumulated metabolites had restricted sofosbuvir use in the dialysis population till November 2019.

The renal safe DAAs, such as glecaprevir/pibrentasvir or grazoprevir/elbasvir, approved for the MHD population are not available in India. In absence of access to abovementioned renal safe DAAs, people have used sofosbuvir in its full dose, that is, 400 mg once daily for those with eGFR below 30 ml/min. Previously, we treated dialysis-dependent HCV-infected patients with low-dose pegylated-interferon/low-dose ribavirin[3] and low-dose sofosbuvir.[4] Half-dose sofosbuvir/daclatasvir combination is effective against all the genotypes in MHD patients with chronic[4] or acute[5] HCV infection. Several reports support the use of full-dose sofosbuvir in people on MHD.[6-9]

There was no guideline for HCV retreatment, in particular for those on MHD. The data on HCV retreatment in the dialysis population are further limited. At all the three courses of DAA, we took an informed decision about the choice of drug and dose for treatment/retreatment after discussion about the following aspect of various available treatment (i) risk of exposure to the high concentration of GS-331007 metabolite on use of full-dose sofosbuvir (ii) prolonged use of half-dose sofosbuvir/daclatasvir combination (iii) safety, efficacy, and adverse effects on addition of ribavirin or pegylated interferon (iv) experimental treatment with a combination of them. The treating physician and the patient unanimously decided the retreatment with 24 weeks of daclatasvir plus a half-daily dose of sofosbuvir on the first relapse followed by sofosbuvir/velpatasvir and pegylated interferon combination on the second relapse.

Pegylated-interferon/ribavirin combination in HCV-infected dialysis patients showed 33%–74% SVR12. Their use had several limitations such as suboptimal success, high rate of

Table 1: Laboratory investigations, treatment details, and virological response with HCV treatment

	1st treatment Acute HCV	2nd treatment Chronic HCV	3rd treatment HCV relapse
Time period	October 2017-December 2017	February 2018–July 2018	April 2019–June 2019
Platelet (×1000)/mm^3	242	273	243
Total bilirubin (mg/dL)	1.6	0.6	0.2
ALT (IU/L)	165	7	14
AST (IU/L)	133	17	28
Albumin (g/dL)	4.4	4.1	4.0
INR	1.02	1.03	1.06
Serum creatinine (mg/dL)	7.4	8.7	5.1
Liver stiffness (kPa)	11.6	Not tested	5.1
APRI	1.4	0.2	0.3
FIB-4	2.3	1.3	1.6
Treatment regimen	Sofosbuvir 200 mg/d Daclatasvir 60 mg/d	Sofosbuvir 200 mg/d Daclatasvir 60 mg/d	Sofosbuvir 400 mg/d Velpatasvir 100 mg/d Pegylated interferon α-2b 50 mic.gm/weekly
Treatment duration	8 weeks	24 weeks	12 weeks
HCV RNA (IU/mL)	4,395,561	4,142,467	180,429
HCV Genotype	3a	Not tested	3a
RVR4	Undetectable	Undetectable	Undetectable
ETR	Undetectable	Undetectable	Undetectable
SVR4	4,142,467 IU/mL	180,429 IU/ml	Undetectable
SVR12	Not tested	Not tested	Undetectable

ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; APRI, AST platelet ratio index; RVR4, rapid virological response; ETR, end of treatment response; SVR4, sustained virological response after 4 weeks of stopping treatment; SVR12, sustained virological response after 4 weeks of stopping treatment

adverse effect, drug discontinuation, high cost, and need for intense monitoring during treatment. The availability of DAAs has pushed the pegylated-interferon on a backbench. At present, sofosbuvir can be given in full dose in those on MHD. In uncommon situations of HCV-infected non-cirrhotic MHD patients who have failed to respond with full-dose sofosbuvir containing regimen and have no access to renal-safe DAAs, pegylated-interferon could be pondered as an alternative for retreatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Goel A, Seguy N, Aggarwal R. Burden of hepatitis C virus infection in India: A systematic review and meta-analysis. J Gastroenterol Hepatol 2019;34:321-9.
2. Gane EJ, Robson RA, Bonacini M, Maliakkal B, Liu L, Sajwani K, *et al*. Anti-viral efficacy and pharmacokinetics (PK) of Sofosbuvir (SOF) in patients with severe renal impairment. Hepatology 2014;60:667A.
3. Goel A, Bhadauria DS, Kaul A, Prasad N, Gupta A, Sharma RK, *et al*. Safety and effectiveness of response-guided therapy using pegylated interferon and ribavirin for chronic hepatitis C virus infection in patients on maintenance dialysis. Nephrology (Carlton) 2017;22:706-11.
4. Goel A, Bhadauria DS, Kaul A, Verma P, Mehrotra M, Gupta A, *et al*. Daclatasvir and reduced-dose sofosbuvir: An effective and pangenotypic treatment for hepatitis C in patients with estimated glomerular filtration rate<30 mL/min. Nephrology (Carlton) 2019;24:316-21.

5. Goel A, Bhadauria DS, Kaul A, Verma A, Tiwari P, Rungta S, *et al*. Acute hepatitis C treatment in advanced renal failure using 8 weeks of pan-genotypic daclatasvir and reduced-dose sofosbuvir. Nephrol Dial Transplant 2021;36:1867-71.
6. Arora A, Kumar A, Prasad N, Duseja A, Acharya SK, Agarwal SK, *et al*. INASL-ISN joint position statements on management of patients with simultaneous liver and kidney disease. J Clin Exp Hepatol 2021;11:354-86.
7. Gaur N, Malhotra V, Agrawal D, Singh SK, Beniwal P, Sharma S, *et al*. Sofosbuvir-velpatasvir fixed drug combination for the treatment of chronic hepatitis C infection in patients with end-stage renal disease and kidney transplantation. J Clin Exp Hepatol 2020;10:189-93.
8. Poustchi H, Majd Jabbari S, Merat S, Sharifi AH, Shayesteh AA, Shayesteh E, *et al*. The combination of sofosbuvir and daclatasvir is effective and safe in treating patients with hepatitis C and severe renal impairment. J Gastroenterol Hepatol 2020;35:1590-94.
9. Li M, Chen J, Fang Z, Li Y, Lin Q. Sofosbuvir-based regimen is safe and effective for hepatitis C infected patients with stage 4-5 chronic kidney disease: A systematic review and meta-analysis. Virol J 2019;16:34.

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