Successful treatment of chronic hepatitis C in a kidney transplant patient with only 2 weeks of direct-acting antiviral therapy

Eficacia del tiempo de tratamiento ultracorto con terapia antiviral de acción directa para la hepatitis C crónica en un paciente con trasplante de riñón: reporte de un caso

Dear Editor:

Hepatitis C is an important health care problem, affecting 200 million people all over the world. About 1.8–8% of renal transplant patients are estimated to be infected with hepatitis C virus in developed countries.[1] With the advent of direct-acting antivirals (DAAs) HCV treatment has evolved, allowing treatment with less systemic toxicity. As they were only recently approved for clinical use (in 2013), a lot of unanswered questions remain regarding their optimal clinical use, such as the minimum treatment duration. Their long-term effects are still unknown and the experience with these regimens on kidney transplant patients is still scarce[2].

FS is a 44-year-old white male with a kidney transplant since January 2016. His maintenance immunosuppression was tacrolimus, mycophenolate mophetil and prednisolone. He developed stable chronic transplant dysfunction, with serum creatinine (sCr) of 1.8 mg/dl one month after transplant. In his period on hemodialysis, from 2009 to 2015, he always showed negative serologic tests for hepatitis B, C and HIV. In August 2015 hepatitis C antibodies were detected during routine screening. Following the detection of hepatitis C infection, he was referred to the Hepatology Department. At the time of his first appointment, in November 2015, genotype 1b was identified and the viral load of HCV RNA was 1.6 log IU/ml. He missed subsequent appointments and did not comply with the scheduled exams. He got a kidney transplant in February 2016. In August he returned to his Hepatology department to complete investigation. The viral load was at this time 6.1 log copy/ml. In January 2017 he began his treatment of eight weeks with ledispavir (90 mg per day) plus sofosbuvir (400 mg per day). Transient hepatic elastography revealed the value of 6.5 kPa and he maintained normal asparate aminotransferase (21 U/L) and alanine aminotransferase (19 U/L). Tacrolimus trough level was around 5–5.5 ng/mL.

On a routine blood scan 14 days later, acute kidney dysfunction was diagnosed – sCr 2.2 mg/dl – and a low through level of tacrolimus was noted (3.8 ng/ml). Consensus between Hepatology and Nephrology departments was to withhold treatment with DAAs. He was admitted to Nephrology ward and, as kidney dysfunction persisted, a kidney biopsy was performed on January 30th. The histopathology showed acute cellular rejection stage IA Banff with negative C4d. DSA (donor specific anti-HLA antibodies) were negative. He was treated with intravenous methylprednisolone bolus and antithymocyte globulin infusion, but maintained a stable sCr of 2.2 mg/dl at the time of discharge. In his last kidney transplant routine appointment, sCr was 2.3 mg/dl and tacrolimus trough levels were 6.7 ng/ml.

HCV viral load determinations at 3 weeks after the beginning of treatment and sustained viral response at 24 weeks were negative. Hence, cure for hepatitis C was assumed with an ultra-short treatment time of 14 days. SVR is associated with greater survival and less likelihood of developing hepatic disease. Smith Palmer et al.[3] in a systematic review report a cure rate of 98–99% four years after achieving SVR. Meanwhile, information over identical follow up in kidney transplant (KT) patients is still scarce. Fernandez et al.[4] in 2016, reported one of the largest retrospective series (103 patients) on kidney transplant patients treated with DAAs. Treatment with sofosbuvir and ledispavir or sofosbuvir and daclatasvir in KT patients achieved a 98% rate of SVR. Although immunosuppression levels needed adjustment in 55% of patients there were only three acute rejection episodes that quickly resolved with therapy. Levels of sCr, glomerular filtration rate and proteinuria did not differ significantly from baseline.

In the immediate post-transplant period, the risk of acute rejection of the kidney transplant is not despisable. Post-KT population has an elevated risk of infectious, immunologic and neoplastic complications as well. KT patients represent a high level of financial investment and therefore require a larger effort in the management of their comorbidities.

Our case report shows cure of HCV infection only with 14 days of treatment. It seems to us to be the shortest treatment time with efficacy ever reported with ledispavir and sofosbuvir for treatment of HCV infection in a KT patient[5,6]. Short treatment times were also reported by Lau G et al.,[7] in a phase 2 study on a Chinese population without cirrhosis, but we stress that a triple (not double) regimen was used, for 3 weeks. Sawinski et al.[5] report a patient, black race, who achieved negative viral load after 29 days of treatment of ledispavir and sofosbuvir. This is, to date, the shortest response ever reported with these two agents. Meissner et al.[8] report a case of successful treatment with sofosbuvir and ribavirin for 27 days. More experience is needed on the treatment of chronic hepatitis C in

kidney transplant patients. The opportunity of using shorter treatment times, in an effective and more tolerable way, will be a great driver for investment and research in this area.

Conflicts of interest

None.

BIBLIOGRAFÍA

1. Lin MV, Sise ME, Pavlakis M, Amundsen BM, Chute D, Rutherford AE, et al. Efficacy and safety of direct acting antivirals in kidney transplant recipients with chronic hepatitis C virus infection. PLOS ONE. 2016;11, e0158431.
2. Jakobsen JC, Nielsen EE, Feinberg J, Katakam KK, Fobian K, Hauser G, et al. Direct acting antivirals for chronic hepatitis C. Cochrane Database Syst Rev. 2017;9:CD012143.
3. Smith Palmer J, Cerri K, Valentine W. Achieving sustained virological response in hepatitis C: a systematic review of the clinical, economic and quality of life benefits. BMC Infect Dis. 2015;15:19.
4. Fernández I, Muñoz-Gómez R, Pascasio JM, Baliellas C, Polanco N, Esforzado N, et al. Efficacy and tolerability of interferon-free antiviral therapy in kidney transplant recipients with chronic hepatitis C. J Hepatol. 2017;66:718–23.
5. Sawinski D, Kaur N, Ajeti A, et al. Successful treatment of hepatitis C in renal transplant recipients with direct-acting antiviral agents. Am J Transplant. 2016;16:1588–95.
6. Kamar N, Marion O, Rostaing L, Cointault O, Ribes D, Lavayssière L, et al. Efficacy and safety of sofosbuvir-based antiviral therapy to treat hepatitis C virus infection after kidney transplantation. Am J Transplant. 2016;16:1474–9.
7. Sawinski D, Kaur N, Ajeti A, trofe-Clark J, Lim M, Bleicher M, et al. Efficacy and safety of 3-week response-guided triple direct acting antiviral therapy for chronic hepatitis C infection: a phase 2, open-label, proof-of-concept study. Lancet Gastroenterol Hepatol. 2016;1:97–104.
8. Meissner EG, Nelson A, Marti M, Masur H, Osinusi A, Kottilil SAT Sustained virologic response for chronic hepatitis C infection after 27 days of treatment with sofosbuvir and ribavirin. Open Forum Infect Dis. 2014;1:013.

Sofia de Sá Guimarães Cerqueira[a,*], Mónica Dinis Mesquita[b], Rui Arlindo Castro[a], Paulo Carrola[b], Teresa Margarida Pinto Ribeiro Morgado[a], Paula Marques[b]

[a] *Nephrology Department, Centro Hospitalar Trás Montes e Alto Douro, Vila Real, Portugal*
[b] *Internal Medicine Department, Centro Hospitalar Trás Montes e Alto Douro, Vila Real, Portugal*

[*] *Corresponding author.*
E-mail address: ssacerqueira@gmail.com (S. de Sá Guimarães Cerqueira).

https://doi.org/10.1016/j.nefro.2018.03.002

Trasplantar receptores hepatitis C negativos con riñones de donantes seropositivos. ¿Por qué no?

Transplantation of hepatitis C infected kidneys into uninfected recipients. Why not?

Sr. Director:

El enemigo a batir es el virus de la hepatitis C (VHC), un virus RNA de 30 a 38 nm de tamaño con envoltura icosaédrica, del género *Hepacivirus*, familia *Flaviviridae*, que presenta 7 genotipos[1]. Su transmisión es parenteral y por ello su contagio a través de órganos sólidos trasplantados ha sido bien documentado y causa de hepatitis aguda y crónica[2]. Este hecho ha sido clave para que el trasplante procedente de donantes portadores de anticuerpos frente al VHC haya estado totalmente contraindicado para receptores no infectados, por lo que se estima que más de 500 injertos renales de alta calidad se descartan anualmente en EE.UU. por esta causa[3]. En nuestro medio un total de 15 riñones no fueron implantados únicamente por este motivo en el 2016[4]. En un primer momento, parte de estos órganos pudieron ser trasplantados a receptores ya infectados por el VHC[5], pero la universalización y eficacia de los antivirales de acción directa eliminó esta población de las listas de espera[6] y con ello la posibilidad del uso de estos órganos, en una sociedad claramente deficitaria de ellos[4].

En la actualidad disponemos de herramientas para cambiar este panorama que han sido claramente enunciadas en la Conferencia de Consenso sobre la Hepatitis C de la American Society of Transplant[7].

Por un lado, la delimitación del riesgo de trasmisión del VHC, con la distinción entre donante portador de anticuerpos,