The efficacy of antiviral therapy after renal transplant in a HCV-positive recipient from a HCV-positive donor

La eficacia de la terapia antiviral después del trasplante renal en un receptor con HCV positivo de un donante con HCV positivo

Dear Editor:

In the general population, the Hepatitis C virus (HCV) infection is a leading public health problem worldwide; in patients on long-term hemodialysis the prognosis of HCV-infected patients is significantly worse than in patients without HCV infection; in renal transplant recipients this infection is responsible for both hepatic (mainly hepatocellular carcinoma and chronic hepatitis) and extra-hepatic complications (transplant glomerulopathy, HCV-related glomerular disease, acute rejection, new onset diabetes after transplant, cardiovascular disease, infections).[1] HCV-positive patients with kidney transplant have increased risk of graft loss, increased morbidity and mortality rate compared to HCV-negative recipients. The interferon and ribavirin treatment for HCV infection in kidney transplant recipients is limited, because of the risk for allograft rejection and poor tolerability. In 2011 the U.S. Food and Drug Administration approved the introduction of direct-acting antiviral agents (DAAs) for the treatment of chronic HCV infection. Since 2014, in the European Union, Sofosbuvir (SOF) 400 mg/Ledipasvir (LDV) 90 mg (Harvoni®) is licensed for chronic HCV infection therapy. According to the EASL Guidelines, no dose adjustment of SOF/LDV is required for patients with mild or moderate renal impairment (estimated glomerular filtration rate [eGFR] >30 ml/min/1.73 m^2) and a full-dose SOF is recommended in patients with stage 5 chronic kidney disease (CKD) on dialysis; however, the safety has not been assessed in patients with stage 4 or 5 CKD not on dialysis.[2] In the experience of Saxena et al., a progressive deterioration of renal function and renal symptoms was reported in patients with eGFR ≤45 ml/min/1.73 m^2 receiving an SOF-based regimen, although efficacy was comparable to that observed in patients without renal impairment.[3] The experience of DAA therapy for HCV in the post kidney transplant setting is poor and limited than in liver transplant recipients.[4] There has been a concern that HCV-positive recipients of HCV-positive kidneys have worse clinical outcomes compared to HCV-positive recipients of HCV-negative grafts.[5] Here we report our experience. In September 2015 a 54-year-old female, suffering from ADPKD, on long-term hemodialysis, became HCV-positive (genotype 1b, viral load 1,260,000 UI/ml), without abnormal liver laboratory investigations. In November 2015 she successfully received a renal transplant from HCV-positive (genotype 1b, viral load 960,000 UI/ml) deceased donor, with early functioning graft (creatinine 0.66 mg/dl). From March to May 2016 she received anti-HCV therapy. She was taking prednisone, everolimus and tacrolimus. She was treated with SOF/LDV 1 tablet/day for 12 weeks. At the baseline (January 2016), the viral load was 18,770,000 UI/ml. The patient had a Sustained Virological Response at 12 and 24 weeks after treatment. In this period, she did not suffer from any of the most common adverse events of SOF/LDV treatment (fatigue, headache, anemia requiring blood transfusion, nausea), and we did not observe any abnormalities of the common laboratory parameters. At follow-up (February 2018), the HCV-RNA detection was negative.

Our experience confirms the positive results by Gallegos-Orozco JF et al.,[5] We highlight the efficacy of antiviral therapy in a HCV-positive (with active HCV-RNA replication) renal transplant recipient from HCV-positive donor, without severe adverse events or drug–drug interactions with her immunosuppressive therapy.

DOI of original article:
https://doi.org/10.1016/j.nefro.2018.07.003.

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https://doi.org/10.1016/j.nefroe.2018.11.015

Chemotherapy and dialysis: A challenge☆

Quimioterapia y diálisis: un reto

Dear Editor,

With a population of more than 4 million patients, Spain is one of the European countries with the highest prevalence of chronic kidney disease. Of that population, 31,735 are on renal replacement therapy, either on kidney transplant programmes, peritoneal dialysis or haemodialysis (HD); 23,709 are in the HD group, and more males are affected than females.[1] The causes of end-stage renal disease (ESRD) are multiple (diabetes, glomerulopathies, vascular diseases, etc.); in these patients, replacement therapy has shown benefits and increased life expectancy.[2]

Cancer is one of the main causes of morbidity and mortality in Spain. It is predicted that 315,413 new cases will be diagnosed by 2035.[3] Chemotherapy is a standard systemic treatment for cancer, the efficacy of which has been reported in randomised studies, where an improvement in patients' disease-free time and survival has been demonstrated. However, the majority of clinical trials demonstrating the efficacy of chemotherapy include populations with normal renal function.[4]

In this context, it is now more common to find patients with kidney disease who develop cancer and vice versa.[4] This has led to the importance of involving Nephrology and Oncology being assessed in recent years.[2]

There is a higher incidence of cancer in HD patients compared to controls[2] and urogenital cancers have been found to be the most prevalent in this population.[4,5] A recent epidemiological study examined the causes of death in patients on renal replacement therapy and found cancer to be the third leading cause, at 20%, after cardiovascular events and infections.[2,5] Carcinogenesis in patients with HD could be explained by the increase in chronic oxidative stress, which damages cell structures, the alteration of the cellular immune system, exposure to viral infections and the medications administered in these patients.[6,7] Alternatively, the increased incidence of cancer may be related to screening in kidney transplant programmes.[2]

Chemotherapy is not contraindicated in patients with ESRD on replacement therapy. However, as described by Funakoshi et al. in a retrospective study of 675 patients,[4] these patients are reported to have a high mortality rate due to causes other than cancer compared to non-dialysed patients. The CANDY (CANcer and DialYsis) multicentre study studied anti-cancer treatment in patients on long-term HD. This study reported that 88% of the patients required specific management of the cytotoxic drug, 44% developed iatrogenic toxicity in relation to inappropriate dose adjustment due to the lack of management recommendations in this specific group of patients, and overdose of chemotherapy drugs was more often associated with haematological, gastric and neurological side effects.[2] As renal excretion plays an important role in the elimination of anti-cancer agents, renal failure can lead to accumulation of the drug, which increases toxicity.[8] In contrast, some reports point to a reduction in neurotoxicity in patients with non-Hodgkin's lymphoma on chemotherapy and renal failure requiring HD.[9]

The current challenge is to establish the role of the nephrologist when our patients on HD or with acute kidney injury are indicated chemotherapy. First of all, it must be borne in mind that each patient has a unique context: type of cancer; clinical stage; performance status; and a type of drug indicated with established doses and specific pre- or post-HD administration time.

In day-to-day practice, the clinical course of these patients is complex in view of the lack of evidence in the literature on the management of cytotoxic drugs in patients with ESRD on HD; the optimal time for administration, dose adjustments depending on the size of the molecule and pharmacokinetic behaviour are poorly understood. There are a few case series and scarce expert opinions that fail to reach a consensus on this subject and this is reflected in the small number

DOI of original article:
https://doi.org/10.1016/j.nefro.2018.10.003.
☆ Please cite this article as: Arana Aliaga C, Luna-Abanto J. Quimioterapia y diálisis: un reto. Nefrologia. 2019;39:314–315.