Safety and efficacy of Sofosbuvir in end stage kidney disease patient: Case report.

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ABSTRACT

Objectives: The existing standard of care for chronic hepatitis C virus (HCV) infection includes the use of pegylated interferon and ribavirin as primary components of treatment, with the addition of a direct-acting antiviral therapy. Sofosbuvir, an oral nucleotide inhibitor of the HCV nonstructural protein 5B RNA dependent RNA polymerase enzyme, was recently approved for use in combination with ribavirin and/or pegylated interferon for chronic HCV infection, depending on the genotype. Sofosbuvir is orally administered, and peak plasma concentrations are not affected by food. The drug is renally eliminated and does not require adjustment in mild to moderate renal insufficiency or in any degree of hepatic impairment. **Case Report**: A 62 year-old lady, presented to our center in view of accidentally discovered high serum creatinine. Diagnosis of end stage renal disease was established by both laboratory and radiological finding. Unfortunately she had hepatitis C virus infection during hemodialysis. She received Sofosbuvir with both early and sustained viral response. **Conclusion**: We try to use Sofosbuvir in a well educated renal failure patient but we cannot grantee its effect on others. Sofosbuvir is a promising drug, need more researches and randomized controlled trials among end stage renal disease patients.

INTRODUCTION:

The general idea behind modern antiviral drug design is to identify viral proteins, or parts of proteins, that can be disabled. These "targets" should generally be as unlike any proteins or parts of proteins in humans as possible, to reduce the likelihood of side effects. The targets should also be common across many strains of a virus, or even among different species of virus in the same family, so a single drug will have broad effectiveness. For example, a researcher might target a critical enzyme synthesized by the virus, but not the patient, that is common across strains, and see what can be done to interfere with its operation **[1].**

The goal of treatment is to eradicate hepatitis C virus RNA, which is predicted by the achievement of a sustained virological response (SVR), defined by the absence of HCV RNA by polymerase chain reaction six months after stopping treatment. An SVR is associated with a 99 percent chance of being HCV RNA negative during long-term follow-up. Achievement of an SVR has also been associated with improved clinical outcomes **[1].**

MONITORING VIRAL LOAD DURING THERAPY:

Once therapy has been started, the likelihood that a patient will fail to achieve a sustained virologic response (SVR) can be predicted by the virologic response at 12 weeks of therapy and probably even earlier, a rapid virologic response is the strongest on-treatment predictor of achieving an SVR. Some but not all data suggest that shorter courses of therapy (eg, 24 weeks) may not adversely affect patients who achieve a rapid virologic response (negative HCV RNA after four weeks of treatment).

An early virologic response (EVR) is defined as at least a 2 log10 reduction in HCV RNA or HCV RNA negativity by week 12. A patient with a "complete EVR" has attained complete viral suppression by week 12; a patient with a "partial EVR" has achieved greater than a 2 log10 decline in viremia but continues to have detectable HCV RNA. An SVR is unlikely in patients who lack an EVR, and it is generally recommended that treatment be stopped in patients who fail to achieve an EVR. Patients who are "partial responders" have lower overall SVR rates compared with complete responders (ie, no detectable viremia at 12 weeks). Studies are ongoing to determine if there are patients (such as patients who have a slow decline in HCV RNA) who would benefit from extended courses of therapy. **[2]**

Sofosbuvir (Sovaldi, Gilead Sciences) is an uredines nucleotide analogue that inhibits hepatitis C virus (HCV) polymerase, preventing viral replication. The recommended dose is 1daily 400 mg tablet, taken orally. It should be used in combination with peg interferon alfa and ribavirin, or ribavirin only, as stated in the summary of product characteristics. Monotherapy with sofosbuvir is not recommended.

Sofosbuvir is not metabolized by cytochrome P450 isoenzymes, nor does it induce or inhibit the metabolism of agents that are substrates of these enzymes. Sofosbuvir demonstrates a high barrier to resistance and was well tolerated by patients in clinical trials. Overall efficacy rates vary between 70% and 90%.

CASE SCENARIO:

62 year old female patient, she suffered from fatigue and mild bilateral lower limb edema since September 2014. She thought medical advice and discovered high serum creatinine, microcytic hypochromic anemia and small sized both kidneys by sonographic assessment, serum Creatinine was increased in follow up visits from 3 up to 7mg/dl. She was admitted to our ICU in October 2014 with pulmonary edema and start 1st hemodialysis session in November 2014. During routine laboratory investigations incidentally discovered HCVAb +ve and liver enzymes and serum albumin within normal range. In April 2015 HCVPCR was 2400000 IU/ml with serum albumin 4gm/dl, serum bilirubin 0.4mg/ml alanine aminotransferase and aspartate aminotransferase were 18 U/L, 21 U/L respectively. She was treatment with Sofosbuvir (Sovaldi) mono-therapy. After

60 days PCR was carried out and became negative in June 2015, HCV PCR was repeated again and was negative. Stop Sovaldi after 6 months. Liver function tests during the whole course were normal and maintained a sustained virology response.

Discussion:

Sofosbuvir is the newest antiviral agent to be approved by the FDA and represents the first in a novel class of agents, an NS5B polymerase inhibitor, indicated in the treatment of chronic HCV infection in combination with RBV and with/ without peg interferon. Infection with genotypes 1 and 4 can be treated with SOF/RBV/interferon for 12 weeks in treatment- naive/treatment-experienced/cirrhotic **[3].**

Our patient was a sixty two year old lady. She had hepatitis C viral infection during hemodialysis. Actually there is no data available about use of Sofosbuvir in end-stage renal disease patients and no one can deny that it is an adventure to use new drug with no experience in immunocompromized patient but actually our patient is a well educated mother with medical background and knew the risk and independently take a decision to receive Sofosbuvir in spite of vague effect. Laboratory Follow up was carried out every two weeks and HCV-RNA-PCR was done repeatedly and revealed sustained virology response.Other alternatives like ribavirin and interferon need special medical fitness and normal hemoglobin level. Unfortunately our patient had anemia of chronic illness and this made her unsuitable for ribavirin or interferon **[3].**

CONCLUSION:

We try to use Sofosbuvir in a well-educated renal failure patient but we cannot grantee its effect on others. Sofosbuvir is a promising drug, need more researches and randomized controlled trials among end stage renal disease patients.

REFERENCE:

1- Swain MG, Lai MY, Shiffman ML, et al. A sustained virologic response is durable in patients with chronic hepatitis C treated with peginterferon alfa-2a and ribavirin. Gastroenterology 2010; 139:1593.
2- Ghany MG, Strader DB, Thomas DL, et al. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology 2009; 49:1335.
3- George M. Abraham and Linda M. Spooner: Sofosbuvir in the Treatment of ChronicHepatitis C:New Dog, New Tricks Clinical Infectious Diseases 2014; 59 (3): 411–5