CASE REPORT

Rescue therapy with Sofosbuvir /Velpatasvir/ Voxilaprevir in a patient infected with Hepatitis C virus multidrug resistant variant—a much needed option for DAA-treatment failures in Pakistan? A case-report

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Abstract

Primary non-response to the currently available direct acting anti-viral (DAAs) in chronic hepatitis C virus (HCV) is rare and expected in approximately only 3-4% of the patients. Among the plausible explanations, HCV resistant variant may be one of the causes among the several other viral and host factors implicated in cases who do not achieve cure.

Ever since the approval of licensed DAAs in 2014, focus has been mainly on high cure rates. Hence, significantly less attention has been given to the few difficult to treat cases.

We present, herein, the case of a 50-year old male who had previously failed to respond to the currently available first and second-line DAA treatment and was then approved for a special treatment access programme. According to our knowledge this is the first case-report from Pakistan in favour of the physician's directive for special treatment access for HCV DAA-experienced patients.

Keywords: Hepatitis C virus, Direct acting anti-virals, Standard of care, Pakistan.

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Introduction

Pakistan has the highest prevalence of Hepatitis C virus (HCV)[1,2] globally. Lack of a prophylactic vaccine, has placed emphasis on the role of HCV testing and treatment.

Since the approval of licensed direct acting anti-virals (DAAs) in 2014, the focus of treatment has been mainly on virus clearance and documentation of high cure rates.

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National hepatitis C guidelines,[3] recommend direct acting anti-virals (DAA), Sofosbuvir and Daclatasvir[4] for 12 /24 weeks, based on APRI score. The second choice of treatment, Velpatasvir is reserved for those patients who do not clear the virus with standard of care (SOC) treatment. However, this treatment is almost three times more expensive and is currently the only licensed retreatment option available in Pakistan.

As of now, the third-line treatment (Sofosbuvir 400 mg, Velpatasvir 100 mg and Voxilaprevir 100 mg) is a pan-genotype combination, comprising a three-drug cocktail. This combination is used as a salvage therapy in many developed countries[5] for chronic HCV patients who have failed other therapies of DAA.

In Pakistan, the third-line treatment is not yet licensed. However, among the LMIC (low middle income countries), Pakistan has become the very first country for, "special access programme license".[6]

We present the case of a 50-year old male who had previously failed to respond to first and second line of treatments and was prescribed 12 weeks of third-line treatment through special access programme.

Case Report

A 50-year male presented to our private clinic in Karachi, in January 2017, with anti-HCV reactive report. Informed written consent was taken from the patient, at this time and documented. He was investigated further and was noted to have a detected HCV RNA. Since his APRI score was >1.5, he was treated for 24 weeks with first line treatment using Sofosbuvir and Daclatasvir. At 12 weeks post treatment, his SVR-12 showed the presence of the virus. Therein, after a gap of 16 weeks in 2018, he was given 12 weeks' treatment with the second line of treatment using Velpatasvir (Velpatasvir /Sofosbuvir). SVR at 12 weeks again showed persistence of virus ((viral load 121,0000 IU/ml) and, therefore, he was labelled as a non-responder to both treatment regimens. As we did not have any other registered regimen, only supportive treatment was given to the patient at that time.

In 2021, (Voxilaprevir/Velpatasvir/Sofosbuvir) was

approved by the drug regulatory authority of Pakistan to be used only through "special access programme license" and under specialist prescription. The patient was, therefore, started on this regimen for a duration of 12 weeks in 2022. His HCV RNA became negative at the end of the treatment (ETR) and also after 12 weeks of stopping treatment (SVR-12). During the treatment, his APRI score improved from 1.6 to 0.5 and has remained stable in the follow-up as well. The patient is coming for follow-up to assess his liver disease regression and or any signs of decompensation; so far he has completed further 12 weeks of follow-up. The medicine is very expensive, therefore, only a limited number of patients can afford it and that is why it has been prescribed to a limited number of cases on the special access programme but to the best of our knowledge this is the first case report of treatment from Karachi, Pakistan.

Discussion

Pakistan is facing an epidemic of chronic Hepatitis C virus.[7] CDA modelling depicts that out of nine million viraemic cases, only 30% have been diagnosed and 15% treated.[8,9] Majority still remain undiagnosed; hence, there is a need to identify patients with active infection who then can be treated and cured.[10]

Due to the limited choice of DAAs and their price, the national guidelines for the HCV testing and treatment[3] were developed to ensure maximum treatments with minimum investment. Patients who do not respond to the first line of treatment, are eligible to be treated with the second line therapy using Velpatasvir and further no other re-treatment option is available for non-responders. Though non-response to available DAAs is only about 3-4%, ideally these cases should be identified and treated to prevent chronic complications of the disease. If left untreated, this heterogeneous pool of HCV resistant cases can act as a nidus for perpetuation of the HCV infection.

Though a large majority of the infected population in Pakistan can be treated with the current first- and second-line treatment, large-scale diagnosis and treatment of HCV cases can help Pakistan achieve the WHO's hepatitis C elimination target by year 2030.

Conclusion

According to our knowledge this is the first case-report from Karachi, Pakistan, where third-line retreatment has been used as rescue therapy, for HCV-infected patients with previous treatment failures. However, further follow-up is needed to see the long-term benefits in similar cases and those experiencing decompensating events and/or cirrhosis.

Consent: Written consent was obtained from the patient for publishing his case.

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Authors' Contribution:
AA, HQ: Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.