REVISTA DE GASTROENTEROLOGÍA DE MÉXICO
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LETTERS TO THE EDITOR

Optimizing the treatment strategy to achieve hepatitis C virus elimination in Mexico☆

Optimización de la estrategia terapéutica para lograr la eliminación del virus de la hepatitis C en México

Some points in the Mexican Consensus on the Treatment of Hepatitis C,[1] should be carefully considered. For example, for genotype 2, the treatments recommended in the Consensus were sofosbuvir + daclatasvir ± ribavirin for 12 weeks or sofosbuvir + velpatasvir for 12 weeks. In their study, Zhou et al.[2] reported the worldwide prevalence of the L31 M polymorphism at 52, 41, and 86% in the United States, Europe, and Asia, respectively. The importance of that polymorphism lies in the fact that it confers up to 100-fold resistance to daclatasvir. There are no data in Mexico, but prevalence can be expected to be similar to that in the United States, in other words, 50%, which would be the cause of (and explanation for) the therapeutic failure of the combination with daclatasvir in some of those patients. Those results were confirmed in a prospective, real-life study on a French cohort that evaluated sofosbuvir + daclatasvir ± ribavirin, in which the sustained virologic response 12 weeks after treatment (SVR12) was 88% (n = 244/278).[3] In contrast, in clinical trials and real-world studies, the sofosbuvir/velpatasvir and glecaprevir/pibrentasvir combinations showed that the polymorphism had no impact on the SVR12.[4]

The World Health Organization proposed the goal of hepatitis C virus (HCV) elimination by 2030, but very few countries have been able to implement an adequate strategy for achieving that objective. Resources must be optimized in Mexico, given that it is a country that faces many difficulties, such as not having access to all treatments (the pan-genotype glecaprevir/pibrentasvir combination), the impossibility of treating all patients (especially after a therapeutic failure), and the lack of resistance tests, whose importance has been demonstrated in the treatments in which the resistance-associated substitutions (RASs), such as first-generation antivirals, have had an impact. Currently, there are 2 new pan-genotype treatments that have shown their efficacy in clinical trials and in real-world studies. The SVR12 was reported at over 95%, there were no severe side effects, tolerance was good in all the patient groups, and retreatment was efficacious in patients with first treatment failure, as well as in patients that were considered difficult-to-treat. Both the treatment and the tests needed before, during, and after treatment are simplified with those combinations.

Based on the data described above, a simplified treatment with 2 pan-genotype combinations appears to be more appropriate as a national strategy. France and England are leaders in eradication strategy, and they have adopted that treatment route, and those combinations have been recommended in the recently published European guidelines, as well.[5] In addition, treatment simplification will make it possible to concentrate efforts on early detection in patients, a crucial stage for achieving elimination. An expert consensus can be used to recommend public health strategies to the government and to work with the pharmaceutical industries to facilitate said public health policies. The elimination of HCV is in everyone's best interest.

Financial disclosure

Isaac Ruiz received predoctoral fellowship grants from the National Agency for Research on AIDS and Viral Hepatitis (ANRS) and the *Consejo Nacional de Ciencia y Tecnología de México* (*CONACYT*).

Conflict of interest

Isaac Ruiz has served as an advisor for Abbvie.

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☆ Please cite this article as: Ruiz I. Optimización de la estrategia terapéutica para lograr la eliminación del virus de la hepatitis C en México. Revista de Gastroenterología de México. 2019;84:267–268.

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Response to Dr. Isaac Ruiz from Dr. Francisco Javier Bosques Padilla, on behalf of the consensus group of the Mexican Consensus on the Treatment of Hepatitis C☆

Respuesta al Dr. Isaac Ruiz del Dr. Francisco Javier Bosques Padilla en nombre del grupo del Consenso Mexicano para el Tratamiento de la Hepatitis C

We appreciate the opportune comments of Dr. Isaac Ruiz regarding the Mexican Consensus on the Treatment of Hepatitis C,[1] and our response follows below.

As Dr. Ruiz correctly points out, there is a growing concern worldwide about the appearance of resistance to the direct-acting antiviral drugs that aim to cure hepatitis C. Recent studies underline the fact that the frequency of the resistance-associated substitutions (RASs) has increased dramatically. Such is the case in China, where rates of 18% reported in 2008 rose to 42% in 2016, specifically for the NS5A nonstructural protein of the genotype 1B virus at position Y93H, conferring a medium-to-high resistance level on inhibitors, such as daclatasvir,[2] which we cited as a management option. There are no data in Mexico with respect to that, but as Dr. Ruiz stated, we can suppose that the situation is similar the information reported worldwide.

The suggestion made by Dr. Ruiz, and supported by European countries, to simplify treatment through the use of pan-genotype regimens as an appropriate strategy in a country with limited resources, such as Mexico, is appealing. We should clarify that at the date in which the consensus document was written and submitted for publication (August 2017), the sofosbuvir/velpatasvir regimen was not yet available, being approved in Mexico in November 2017, nor was the glecaprevir/pibrentasvir regimen available, as it was not on the market until October 2018.

As Dr. Ruiz proposes, we would focus on detecting the patients infected with the C virus, and as is the duty of the professional body we belong to, advise the proper authorities to comply with the recommendation of the World Health Organization, which seeks to eliminate the C virus by the year 2030.[3] However, it should be emphasized that such an ambitious goal is very complex and goes beyond recommending a specific regimen(s). To be achieved in Mexico, or in other countries, several coordinated actions must be integrated,[4] and they include the following:

- *Awareness and prevention:* achieving this though a multimedia campaign to raise social awareness about the HCV problem.
- *Testing and diagnosis:* a key factor in achieving elimination is increasing the case detection rate.
- *Linkage to care:* emphasizes the importance of regional healthcare networks made up of the numerous members connected to the theme (hepatitis team) that seek to monitor and protect local identification and link the patients with HCV from the different risk groups to clinical care.
- *Access to medications and qualified health services:* making it possible for virtually all patients to have access to care and treatment with direct-acting antivirals.
- *Monitoring and evaluation:* guaranteeing that all patients are registered and monitored at each step of the HCV healthcare cascade, which is essential for achieving its elimination.

Financial disclosure

No financial support was received in relation to this study/article.

Conflict of interest

Dr. Francisco J. Bosques Padilla has been a speaker for Takeda, Abbvie, and MSD.

DOI of refers to article: https://doi.org/10.1016/j.rgmxen.2018.07.005
☆ Please cite this article as: Bosques-Padilla FJ. Respuesta al Dr. Isaac Ruiz del Dr. Francisco Javier Bosques Padilla en nombre del grupo del Consenso Mexicano para el Tratamiento de la Hepatitis C. Revista de Gastroenterología de México. 2019;84:268–269.