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Chronic Hepatitis C Treatment with Direct-Acting Antiviral Agents in a Real-Life Setting

Ruby Ann Chirino-Sprung[1]*, Margarita Dehesa[2], Enrique Wolpert[3], Clara Corona-Lau[4], Ignacio García-Juarez[5], Juan Francisco Sánchez-Ávila[5], Carlos Moctezuma-Velázquez[5] and David Kershenobich[5]

[1]Hospital Ángeles Pedregal; [2]Fundación Mexicana para la Salud Hepática; [3]Clínica Lomas Altas; [4]Laboratorio Biomédica de Referencia; [5]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Mexico City, Mexico

ABSTRACT

Background: In clinical trials, new oral direct-acting antiviral agent therapies have demonstrated a high sustained virological response rate in patients with hepatitis C virus infection. We aimed to analyze the efficacy and safety data from direct-acting antiviral agent interferon-free therapy in hepatitis C virus infection in a study performed in five different clinical settings in Mexico City; four private practice sites and one academic medical center in a real-world scenario. **Methods**: Eighty-one patients were treated with seven different direct-acting antiviral agent regimens, in which the end of treatment, sustained virological response at 12 weeks post-treatment, and adverse effects were evaluated. At their discretion, attending physicians selected the treatment regimens and durations. **Results**: In total, 70.4% of the patients were female and the mean age was 60.7 years; 74.1% had blood transfusion as a risk factor. The most common genotype was 1b (70.4%). The fibrosis stage was F3 or F4 in 55.5% of patients; liver cirrhosis was present in 44%. The overall end of treatment response was 98.8%, and the rate of sustained virological response was 96%, independent of the regimen. Three patients did not achieve sustained virological response; they had cirrhosis and were treatment-experienced, and two had hepatocarcinoma. Non-significant adverse effects during treatment were documented. **Conclusions:** In this real-life setting in Mexico, a rate of 96% of sustained virological response to direct-acting antiviral agents was achieved in an older population of patients with advanced fibrosis. This study provides data that may be useful in guiding health professionals and authorities in the development of health policies. (REV INVES CLIN. 2016;68:201-9)

Key words: Chronic hepatitis C. DAA. Direct-acting antiviral agent. Epidemiology. Hepatitis in Latin America. SVR. Sustained virological response.

Corresponding author:
*Ruby Ann Chirino-Sprung
Hospital Ángeles Pedregal
Camino Sta. Teresa #1077, Consultorio 635 Torre A
Col. Héroes de Padierna, Magdalena Contreras
C.P. 01700, Ciudad de México, México
E-mail: r_chirino@yahoo.com

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INTRODUCTION

In the first decade of the 21st century, the treatment of chronic hepatitis C primarily relied on the administration of pegylated interferon plus ribavirin (PegIFN/RBV)[1-3]. Strategies were implemented around this treatment to increase the prediction of patient response to therapy, thereby increasing its effectiveness[4,5]; notably, the determination of interleukin 28[6] and the concept of rapid response at week 4 and early response at week 12[7] helped predict patient responses. Sustained virological response (SVR) was reported in approximately 50% of the patients with hepatitis C virus (HCV) genotype 1 and 70% of those with genotype 2. These data were obtained from clinical trials primarily performed in the USA, Europe, and Asia and included a significant number of patients[8,9].

The treatment in these studies was difficult, requiring weekly injections of PegIFN for 24-48 weeks, with frequent clinical and biochemical adverse effects that were primarily associated with anemia, leukopenia, and thrombocytopenia and required the use of hematopoietic growth factors. These results often indicated an important deterioration in patient quality of life[10].

With the advent of new oral direct-acting antiviral agents (DAA) as part of the therapeutic armamentarium for hepatitis C, a significant change has occurred in the past five years. There have been recent reports of SVR rates greater than 90% after 12 weeks of treatment for the most frequent genotypes[11], in addition to therapeutic drugs administered orally, free of interferon, that do not convey significant side effects[12]. However, the new DAAs are expensive, and this cost has become one of the most important constraints limiting the number of patients who have access to treatment.

Well-designed, individual and national epidemiological studies and cost-benefit analyses have been performed throughout Latin America, allowing comparisons with first-world countries[13-15]. However, these studies have not resulted in treatment opportunities. The region is remarkably similar in its strengths and vulnerabilities. Uncertainties in drug registration and economic and health policies are the main factors affecting access to new treatments.

There is a need to provide guidance to health professionals and patients through the dissemination of information. Consistent with this approach, the purpose of the present work was to analyze the real-life experience gained from the use of DAAs outside of controlled clinical trials in Mexico; this study focused on patients who have had access to DAAs either through their own resources or by being insured privately. We believe that by analyzing the data related to effectiveness, compliance, and side effects we can assist health professionals, health authorities, and the pharmaceutical industry with advancing the development of a public health policy regarding DAA use in hepatitis C patients.

The primary objective of this study was to evaluate the efficacy and safety data of the DAA interferon-free therapy in HCV infection in four private medical sites and one academic medical center, all in Mexico City, in a real-world scenario.

MATERIALS AND METHODS

Study design and patients

This multicenter, case series, retrospective study reviewed prospectively collected data concerning the efficacy and safety of DAAs, with or without RBV, in patients with chronic HCV infection. The study was conducted in five different clinical settings in Mexico City; four were private practice settings, and one was an academic, tertiary care referral center. The ethics and research committees of each institution approved this observational study. Patient demographics (age, gender, and risk factors), virological, and clinical data, including medication dosage, were collected through individual health record reviews. The clinical severity of liver disease was established at baseline. The fibrosis stage was determined by non-invasive tests, such as the FibroTest or elastography (MRI/FibroScan®), and/or liver biopsy.

The patients included in this study had HCV infection, and the study sample was composed of treatment-naive patients and patients who had been previously exposed to PegIFN and RBV. Patients were classified as relapsers, partial responders, non-responders, protease inhibitor failures (PegIFN/RBV/boceprevir or telaprevir), and liver transplant recipients. Relapsers were defined as patients who had an

undetectable viral load at the end of treatment (EOT), but who did not achieve SVR. Partial responders were defined as patients who achieved a 2 log10 drop in HCV RNA by week 12, but did not achieve an EOT response. Non-responders were patients who did not achieve a 1 log10 reduction in HCV RNA by week 4 or a 2 log10 drop in HCV RNA by week 12. They were included independently of their fibrosis stage and liver disease grade.

Laboratory procedures

All of the patients had serum anti-HCV antibodies, determined by using a commercial kit (Vitros® 5600; Ortho Clinical Diagnostics, Raritan, NJ, USA), with 100% sensitivity and 99.75% specificity. When the test was positive, serum HCV RNA levels were quantified using a commercial real-time RT-PCR (Abbott RealTi*m*e HCV, Abbott m2000rt; Abbott Molecular Inc., Des Plaines IL, USA), with a lower limit of quantification of 12 IU/ml. The HCV genotype and subtype were determined using a commercial kit (Abbott RealTi*m*e HCV Genotype II, Abbott m2000rt; Abbott Molecular Inc., Des Plaines IL, USA).

Laboratory tests, including liver function tests, red blood cell counts, white blood cell counts, and platelet counts, were monitored at baseline; at weeks 4, 12, and 24, as needed; and 12 weeks after the completion of treatment.

Study endpoints and treatment

The study endpoints were as follows: (i) the number of patients who achieved undetectable HCV RNA at the EOT, at 12 or 24 weeks; and (ii) the number of patients who achieved SVR 12 weeks after completing treatment (SVR12).

Treatment

The DAA treatment regimens and their durations (i.e. 12 or 24 weeks) were selected at the discretion of the treating physicians. Treatment regimens included combinations of sofosbuvir (SOF), ribavirin (RBV), simeprevir (SMV), ledipasvir (LDV), ombitasvir (OBV), paritaprevir (PTV), ritonavir (r), and dasabuvir (DSV). Seventy-three patients received 12 weeks of treatment; one patient with genotype GT2 received 16 weeks of SOF/RBV. Seven patients were treated with 24-week regimens: two patients with SOF/SMV, one with SOF/RBV, two with SOF/LDV, one with SOF/LDV/RBV, and one patient with OBV/PTV/r/DSV (Table 1).

Data on adverse side effects were collected for all patients during the entire treatment and follow-up periods. These data were reviewed to identify the causal relationship with the treatment regimens.

Statistical analysis

Continuous data are expressed by the mean values and standard deviation (SD); categorical variables are expressed as absolute and relative numbers and percentages. Categorical data were analyzed with the X^2 test, and an EPI value of ≤ 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

This study included 81 patients, 57 women (70.4%) and 24 men (29.6%). The age range was 41-81 years (mean age, 60.7 years). The most common risk factor was blood transfusion, reported in 60 patients (74.1%); three patients had a history of surgery without blood transfusion (3.7%); two were healthcare workers (2.5%), and one had a family member with hepatitis C (1.2%). In 15 patients (18.5%) we were unable to determine a risk factor. Co-morbidity was present in 32 patients (39.5%); diabetes mellitus and arterial hypertension were the most frequent (seven patients with each co-morbidity), followed by a history of cancer in five patients. Digestive, thyroid, and ocular diseases were present in three patients each, and dyslipidemia was present in two patients. Cardiovascular, rheumatologic, and cerebrovascular diseases were present in one patient each.

The most common HCV genotype was type 1, identified in 73 patients (90.1%); 16 patients (19.8%) had subtype 1a (GT1a), and 57 (70.4%) had subtype 1b (GT1b). Genotype 2 (GT2) was identified in seven patients (8.6%), and one patient (1.2%) had genotype 3 (GT3). In 71 patients (87.7%), the HCV RNA viral load was ≤ 6,000,000 IU/ml, and in 10 patients (12.3%) the viral load was > 6,000,000 IU/ml.

Table 1. Direct-acting antiviral regimens selected by the physicians to treat patients with chronic hepatitis C

DAA treatment regimens	Number of patients (n = 81)
SOF 400 mg QD/SMV 150 mg QD 12 weeks	11
SOF 400 mg QD/SMV 150 mg QD 24 weeks	2
SOF 400 mg QD/SMV 150 mg QD/RBV* 12 weeks	1
SOF 400 mg QD/RBV* 12 weeks	4
SOF 400 mg QD/RBV* 16 weeks	1
SOF 400 mg QD/RBV* 24 weeks	1
SOF 400 mg QD/LDV 90 mg QD 12 weeks	22
SOF 400 mg QD/LDV 90 mg QD 24 weeks	2
SOF 400 mg QD/LDV 90 mg QD/RBV* 12 weeks	6
SOF 400 mg QD/LDV 90 mg QD/RBV* 24 weeks	1
OBV/PTV/r (25/150/100 mg QD)/DSV (250 mg BID) 12 weeks	13
OBV/PTV/r (25/150/100 mg QD)/DSV (250 mg BID) 24 weeks	1
OBV/PTV/r (25/150/100 mg QD)/DSV (250 mg BID)/RBV* 12 weeks	16

*The ribavirin dose ranged between 800 and 1,200 mg.
BID: twice daily; DAA: direct-acting antiviral agent; DSV: dasabuvir; LDV: ledipasvir; OBV: ombitasvir; PTV: paritaprevir; QD: once daily; r: ritonavir; RBV: ribavirin; SMV: simeprevir; SOF: sofosbuvir.

Table 2. Baseline characteristics of patients with chronic hepatitis C

Patient characteristics	Number of patients (%) (n = 81)
Age (years)	
Mean age	60.77
Range	41-81
Gender	
Female	57 (70.4)
Male	24 (29.6)
HCV genotype	
1	2 (2.5)
1a	14 (17.3)
1b	57 (70.4)
2	7 (8.6)
3	1 (1.2)
Fibrosis stage	
F0	11 (13.6)
F1	17 (21.0)
F2	8 (9.9)
F3	9 (11.1)
F4	36 (44.4)
Child-Pugh class	
A	32 (88.8)
B	2 (5.6)
C	2 (5.6)
Treatment-naive	40 (49.4)
Treatment-experienced	41 (50.6)

HCV: hepatitis C virus.

Eleven patients (13.6%) underwent liver biopsy; five of them also had a non-invasive test done, and in all cases there was a correlation between both tests. In 86.4% of patients, fibrosis stage was determined by a non-invasive test: FibroScan in 12 patients; FibroTest in 13; magnetic resonance imaging in 16; abdominal ultrasound and clinical and laboratory findings in 42 patients. Regarding the fibrosis stage, the distribution in the study sample was as follows: F0 = 11 (13.6%), F1 = 17 (21%), F2 = 8 (9.9%), F3 = 9 (11.1%), and F4 = 36 (44.4%). Patients in stage F4 were further classified as Child A (88.8%), Child B (5.6%), or Child C (5.6%) (Table 2).

Of the 81 patients, 40 (49.4%) were treatment-naive, and 41 (50.6%) had been previously treated with PegIFN/RBV; five of these patients had also been treated with PegIFN/RBV/boceprevir; one patient had been treated with PegIFN/RBV/telaprevir, and one patient had received PegIFN/RBV/SMV. Of the previously treated patients, 18 (43.9%) were non-responders, 18 (43.9%) were relapsers, one (2.44%) had a partial response, and four patients (9.75%) had a history of discontinuing previous treatments because of adverse effects. Four patients (4.9%) had hepatocellular carcinoma (HCC), three had undergone liver transplantation (3.7%), and one patient (1.2%) had HIV.

Efficacy

An EOT response occurred in 80 of the 81 patients (98.8%), independent of the treatment regimen. So far, 75 patients have completed the time framework to evaluate response to treatment at 12 weeks after completing treatment (SVR12). The SVR12 rate was 96% (72/75 patients).

Table 3. Rates of sustained virological response at 12 weeks according to genotype, fibrosis stage, and prior treatment history

	EOT No. (%) (n = 81)	SVR12 No. (%) (n = 75)
	80/81 (98.8)	72/75 (96.0)
HCV genotype		
1a	15/16 (93.8)	14/16 (87.5)
1b	57/57 (100)	51/51 (100)
2	7/7 (100)	6/7 (85.7)
3	1/1 (100)	1/1 (100)
Fibrosis stage		
F0	11/11 (100)	11/11 (100)
F1	17/17 (100)	14/14 (100)
F2	8/8 (100)	7/7 (100)
F3	9/9 (100)	8/8 (100)
F4	35/36 (97.2)	32/35 (91.4)
Previous treatment	EOT 40/41 (97.5)	SVR12 35/38 (92.1)
Non-responders	17/18 (94.4)	17/18 (94.4)
Relapsers	18/18 (100)	13/15 (86.6)
Partial responders	1/1 (100)	1/1 (100)
IFN intolerant	4/4 (100)	4/4 (100)

EOT: end of treatment; IFN: interferon; SVR12: sustained virological response at week 12 of treatment.

According to genotype, the EOT response was 93.8% for GT1a, 100% for GT1b, 100% for GT2, and 100% for GT3. Considering the fibrosis stage, the EOT response was 100% in the F0, F1, F2, and F3 patients and 97.2% in the F4 patients.

The SVR12 rate was achieved in 87.5, 100, 85.7, and 100% of the patients with GT1a, GT1b, GT2, and GT3, respectively. The SVR12 rate was 100% in the patients with fibrosis stages F0, F1, F2, and F3. Patients in stage F4 achieved a lower SVR12 rate of 91.4%.

An EOT response was achieved in 97.5% of the patients previously exposed to PegIFN/RBV-based treatments. The response rate in the previous non-responders was 94.4%. In the relapsers, partial responders, and PegIFN/RBV intolerant patients the EOT responses were 100%. An SVR12 was achieved in 92.1% of the treatment-experienced patients. In the previous non-responders, the SVR12 rate was 94.4%; the rates were 86.6% in the previous relapsers and 100% in the partial responders and PegIFN/RBV intolerant patients (Table 3). The EOT response and SVR12 in naive patients were 100%.

According to the duration of therapies, the two patients that relapsed received 12-week regimens with SOF/SMV/RBV and SOF/RBV, and one non-responder patient was treated with OBV/PTV/r/DSV for 24 weeks.

Three patients (4%) did not achieve SVR12: one patient was a non-responder, and two patients relapsed (Table 4). The patient who failed to achieve an EOT response was a 70-year-old woman with cirrhosis, classified as Child A, who was a previous non-responder to PegIFN/RBV. The patient had GT1a and was treated with OBV/PTV/r/DSV, without RBV, for 24 weeks.

The two relapsers had cirrhosis, classified as Child A, and had relapsed from previous treatment, one from PegIFN/RBV and one from PegIFN/RBV/SMV; both patients had been diagnosed with liver cancer and were treated before receiving the DAA treatment. One patient was a 75-year-old woman with GT1a, with HCC classified as early stage (A) according to the Barcelona Clinic Liver Cancer (BCLC) staging system; she received radiofrequency ablation with no evidence of tumor during surveillance. She was treated with SOF/SMV/RBV for 12 weeks. The other patient was a 58-year-old man with GT2, who had HCC classified as BCLC intermediate stage (B), who had received transarterial chemoembolization and had no evidence of tumor when he was treated with SOF/RBV for 12 weeks. A total of four patients had a history of HCC: the two patients

Table 4. Rates of end of treatment and sustained virological response at week 12 of treatment according to direct-acting antiviral treatment regimens

	EOT (n = 81) No. (%)	SVR12 (n = 72) No. (%)	Non-responder (n = 1) No. (%)	Relapse (n = 2) No. (%)
SOF/SMV n = 13	13 (100)	13 (100)	0	0
SOF/SMV/RBV n = 1	1 (100)	0 (0)		1 (100)
SOF/RBV n = 6	6 (100)	5 (83.3)	0	1 (16.7)
SOF/LDV n = 24	24 (100)	22 (100)	0	0
SOF/LDV/RBV n = 7	7 (100)	7 (100)	0	0
OBV/PTV/r/DSV n = 14	13 (92.9)	11 (91.6)	1 (8.4)	0
OBV/PTV/r/DSV/RBV n = 16	16 (100)	14 (100)	0	0
Total n = 81	80 (98.8)	72 (96)	1 (1.4)	2 (2.6)

DAA: direct-acting antiviral; DSV: dasabuvir; EOT: end of treatment; LDV: ledipasvir; OBV: ombitasvir; PTV: paritaprevir; r: ritonavir; RBV; ribavirin; SMV: simeprevir; SOF: sofosbuvir; SVR: sustained virological response at week 12 of treatment.

referred to previously who did not achieve SVR12, and a 61-year-old woman, GT1b, naive to previous treatment, with F4 fibrosis stage and an HCC in early stage (A) who underwent surgical resection, with no evidence of tumor; she received SOF/SMV for 12 weeks and achieved SVR12. The other patient was a 62-year-old man, GT1b, naive to previous treatment, fibrosis stage F4, with HCC in early stage (A), who underwent radiofrequency ablation, with no evidence of tumor while being treated with SOF/SMV for 12 weeks, and who also achieved SVR12.

Three patients received treatment post-liver transplantation, all of whom achieved SVR12. Two of these patients (GT1b) received SOF/SMV for 12 weeks and SOF/LDV/RBV for 12 weeks, and one patient (GT2) was treated with SOF/RBV for 24 weeks.

Safety

Of the 81 patients, 35.8% experienced an adverse event. The events were minor in all of the patients, and none of them discontinued their treatment. The most common adverse events were asthenia in 12.3% of the patients, and headache in 6.2%, followed by pruritus, diarrhea, and malaise, which were each present in 3.7% of the patients. Less frequently occurring adverse events were rash, myalgia, and insomnia. Anemia occurred in six patients (8.6%), and it was the most common adverse event in patients receiving RBV. In two patients the RBV dose was modified but not suspended. No patient discontinued the treatment because of anemia or received erythropoietin or transfusion. According to the regimen received, the adverse effects occurred more frequently in patients treated with OBV/PTV/r/DSV or OBV/PTV/r/DSV/RBV at rates of 8.6 and 11.1%, respectively, followed by SOF/LDV or SOF/LDV/RBV, both at 3.7%. A total of 4.9% of the patients treated with SOF/SMV experienced adverse events; the adverse event rate was 2.4% for SOF/RBV, and no adverse events were reported in patients treated with SOF/SMV/RBV (Table 5).

Based on these results, we are proposing a decision-making algorithm for evaluation and treatment with DAA agents that can be applied independently of the selected treatment scheme (Fig. 1).

DISCUSSION

The effectiveness of DAAs as therapeutic agents for hepatitis C has been clearly demonstrated worldwide[16,17]. The present study aimed to evaluate the overall effect of DAAs on chronic hepatitis C and was

Table 5. Adverse events associated with direct acting antiviral treatment in patients with chronic hepatitis C

Adverse event	No. (%)
Any adverse event	29 (35.8)
Any adverse event leading to discontinuation	0
Any serious adverse event	0
Common adverse events	
Asthenia	10 (12.3)
Headache	5 (6.2)
Pruritus	3 (3.7)
Diarrhea	3 (3.7)
Malaise	2 (2.5)
Rash	2 (2.5)
Insomnia	2 (2.5)
Myalgia	1 (1.2)
Insomnia	1 (1.2)
Anemia	7 (8.6)
Thrombocytopenia	1 (1.2)
Leukopenia	1 (1.2)

not designed as a comparative study of different treatment regimens.

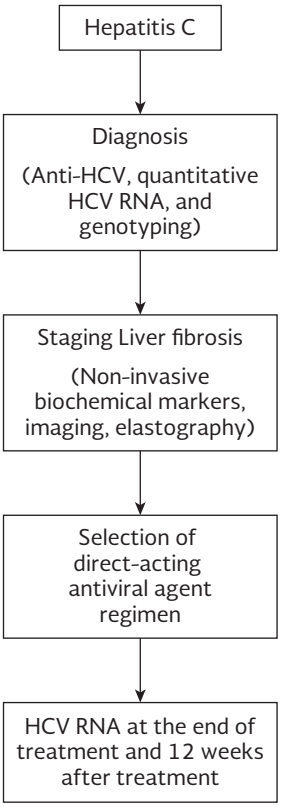
As the registration of DAAs in Mexico has become a reality[18], the only patients who have thus far benefited from these new forms of therapy are those with private insurance or the economic means to obtain the medication.

Herein, we analyzed the data obtained in this group of individuals with the purpose of contributing to the process of making these drugs available to the general public, who represent the vast majority of chronic HCV patients in the country, where only 0.44% of the population has private insurance[19]. Overall, this analysis may be helpful in determining soon who should be treated and when, in a scenario where prioritization is necessary.

This study represents real-life experiences and is not a large-scale HCV therapy controlled trial, which allows the identification of relevant issues that are specific to the region and that represent hurdles in accessing treatment.

Patients with genotypes 1, 2, or 3 were included, with GT1b being the most frequent. These results are similar to the findings previously reported in Mexico[20,21] and in other regions in Latin America[22,23]. Most novel DAAs are now recognized to induce a good response

Figure 1. Decision-making algorithm for hepatitis C evaluation and treatment with direct-acting antiviral agents.



in patients infected with GT1a and GT1b HCV, including those with compensated cirrhosis.

The mean age of the study population was 60.7 years. Among those patients who had received a transfusion, the length of exposure to the virus was 43.6 years. Not surprisingly, 55.5% of the patients had an F3 or F4 fibrosis stage, 36/81 (44.4%) had liver cirrhosis, three had undergone liver transplantation, and four had HCC. These data align with results from a previous report by our group using the FibroTest to identify the stage of liver fibrosis in 261 HCV-infected patients. In that study, stages F3 and F4 represented 55% of the sample[24].

In 1989, cirrhosis associated with hepatitis C accounted for only 5% of all cases in western countries; that rate increased to 10% in 1998 and 20% in 2006 as the age and duration of illness of those infected began to increase. The proportion of patients with cirrhosis was projected to reach 24.8% by 2010, 37.2% by 2020, and 44.9% by 2030[25]. Data from the present study indicate that the patients in our country are

late to receive the new DAA therapy. In addition, these patients are older, which validates the fact that fibrosis progression is in general inversely related to age, and explains why cirrhosis and its complications occur most commonly after 60 years of age.

Fibrosis staging has become a relevant issue in determining how to optimize hepatitis C treatment; clearly, the best strategy involves treating all patients (F0-F4), independently of the degree of fibrosis. Providing treatment at earlier stages will reduce the number of patients that develop more severe liver disease and will reduce the cost of care of the complications of advanced fibrosis and cirrhosis. However, giving treatment at stages F3-F4 implies treating those patients at a greater risk of developing complications in the near future, such as esophageal variceal bleeding, encephalopathy, and HCC. Furthermore, in F3-F4 patients achieving SVR, a significant decrease in morbidity and mortality related to liver disease has been demonstrated[26,27].

At present, no single policy regarding treatment for hepatitis C can be applied worldwide, and each region and country will need to adjust to their own situations. In particular in Latin America, funding and medical resources do not presently allow for a strategy in which all patients with hepatitis C can access DAA treatment. Interestingly, a recent report on how to optimize HCV treatment in resource-constrained countries (including Egypt, Thailand, and Ivory Coast) demonstrated that prioritizing treatment in patients in stages F3 and F4 is the most effective strategy in terms of life-years saved (i.e. 13.1-22.0% in the next 5-10 years)[28]. Any strategy is better than the alternative of continuing with the current treatment levels in which cases of advanced liver disease and liver-related deaths will continue to increase through 2030[29].

Treatment-experienced patients represented the most prevalent group (50.6%) in our study, including previous null responders, relapsers, partial responders, and patients who had interrupted previous IFN-based treatment because of significant side effects; the remaining 49.4% of participants were treatment-naive. The overall EOT response was 98.8%, and the SVR12 was 96%. Ten patients had a viral load > 6,000,000 UI/ml, all of whom responded to treatment independently of the regimen. This population represents 12% of our sample, which is greater than values previously reported in the literature[30] and may be related to the higher percentage of cirrhotic patients in our sample. Adverse events occurred in 35.8% of the patients; all the events were mild and did not affect their treatment compliance. These events occurred in 11.1% of patients receiving the OBV/PTV/r/DSV+RBV regimen and in 3.7% of patients receiving the SOF/LDV+RBV regimen.

The three patients who failed to achieve SVR had advanced fibrosis; two were older than 75 years, two had GT1a and one had GT2, and two had HCC. They were all experienced patients, including two relapsers and one non-responder.

The American Association for the Study of Liver Diseases (AASLD) 2015 guidelines recommend treatment in patients with HCC, regardless of whether they are candidates for liver transplantation. Our results show a low SVR12 in this group of patients because only 2/4 (50%) patients achieved SVR12, and none of those patients presented with decompensated liver function.

Based on these results, one can speculate that if the viremic population in Mexico is approximately 0.7%, there are about 355,000 patients in stages F3-F4 who would be candidates to receive DAAs in the public sector. This finding imposes an important health burden in terms of morbidity and mortality[31].

Contrary to the design of clinical trials, our real-life sample shows that 39.5% of the patients had an associated comorbidity, which may imply the need for additional medications independent of their health hazard risk. This finding becomes a relevant issue because one of the main factors that determine the percentage of SVR is the concomitant use of medications. These patients should be monitored at more frequent intervals than HCV patients without health conditions that promote liver injury[32]. If DAAs are to be approved for generalized use in the public and private sectors, the implementation of a solid system is necessary to identify and guide practitioners in the knowledge of drug-drug interactions to prevent adverse events and treatment failure[33].

Because most of the patients in Mexico and Latin America are as yet unaware of their disease[15] it is necessary to increase the level of education and awareness

among individuals at risk and in the medical community. There is a need to increase the diagnostic and service delivery capacities for HCV infection. Simultaneously, a new screening policy in addition to screening blood bank products must be implemented to allow earlier detection of patients and to identify the highest priority groups for prevention and treatment towards eradication. With such high SVR percentages, developed countries can voice concerns about eradication; however, eradication is not yet the case in the Latin American region where detection is still an important problem and testing policies are urgently needed. A significant caveat is that screening should be attached to access to treatment. Even in more advanced countries, no action has been taken in 30% of patients who tested positive for HCV[34], and only approximately 15% of the patients diagnosed with chronic HCV infection have actually received treatment[35].

Latin American countries must develop courageous, successful, and long-term planning policies that should lead to significant medical advances in the region, aligning them with the global preventive and therapeutic strategies being developed in other regions of the world. Real-world data can help guide health professionals and policy makers[36,37]. Undoubtedly, a national action plan accompanied by federal guidelines for the screening and treatment of hepatitis C should be advocated.

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