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Original article

Effectiveness of chronic hepatitis C treatment with direct-acting antivirals in the Public Health System in Brazil

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ABSTRACT

Introduction: Chronic hepatitis C virus (HCV) infection is one of the major causes of cirrhosis, hepatocellular carcinoma and liver transplantation. Treatment using direct-acting antivirals (DAA) has revolutionized the treatment of HCV, increasing long-term prognosis after cure. The goal of the present study was to evaluate the effectiveness of DAA in HCV treatment in a Public Health System in southern Brazil.

Methods: A retrospective study evaluated all patients with chronic HCV infection who underwent treatment at one center of the Public Health Department of the State of Rio Grande do Sul – Brazil, according to the Brazilian Clinical Protocol and Therapeutic Guidelines. The effectiveness was assessed in terms sustained virological response (SVR) 12 weeks after the end of treatment.

Results: A total of 1002 patients who were treated for chronic HCV infection were evaluated. The mean age was 58.6 years, 557 patients (55.6%) were male and 550 (54.9%) were cirrhotic. Overall SVR was observed in 936 (93.4%) patients. There was a difference in SVR rate varied according to sex, 91.6% in men and 95.7% in women ($p = 0.009$), length of treatment in genotype 1, 92.7% with 12 weeks and 99.1 with 24 weeks ($p = 0.040$), and genotype, 94.7% in genotype 1, 91.7% in genotype 2, and 91.4% in genotype 3 ($p = 0.047$).

Conclusion: The treatment of chronic HCV infection for genotypes 1, 2 or 3 with the therapeutic regimens established by the Brazilian guidelines showed high rates of SVR, even in cirrhotic patients.

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Introduction

Approximately 1.6% of the world population is infected with hepatitis C virus (HCV), which corresponds to about 80 million individuals worldwide[1] and around two million chronically infected in Brazil.[2] HCV represents 70% of the causes of chronic hepatitis in the world, being considered a major public health issue globally.[3]

A population survey conducted by the Brazilian Ministry of Health analyzed 20,000 individuals, showing anti-HCV prevalence of 1.38%.[4] In parallel with this prevalence, the prognosis of the disease is frightful to patients, considering the possibility of progression to cirrhosis, hepatocellular carcinoma and death.[5]

The main goal of chronic hepatitis C (CHC) treatment is to eradicate the virus, characterized by sustained virological response (SVR), with subsequent reduction of liver damage and HCV transmission.[6]

Interferon-based treatment outcomes were unsatisfactory, with cure rates below 60%.[7,8] The use of the direct-acting antivirals (DAA) represents a major advance in CHC therapy, including advances in patients who are refractory and/or intolerant to interferon (IFN). The association of DAA showed SVR rates between 80 and 100% depending on the presence of cirrhosis, genotype, and previous treatment of CHC.[9–16]

However, it is necessary to consider that such results may reflect the conditions of clinical research and may not fully correspond to the results in medical practice. Therefore, it is essential to assess the results under real-life clinical conditions.

The Clinical Protocol and Therapeutic Guidelines (CPTG) for Hepatitis C of the Brazilian Ministry of Health, published in 2015,[17] aimed to provide a cost-effective strategy for the treatment of CHC within the public health system, offering new therapeutic options with lower rates of significant adverse events, higher effectiveness, flexibility of access, and greater expectation of cure. Among the new antiviral drugs for treating hepatitis C that were incorporated into the CPTG are Sofosbuvir (SOF), a nucleotide analogue inhibitor of HCV polymerase, Simeprevir (SIM), a protease inhibitor, and Daclatasvir (DAC), a NS5A inhibitor.[17]

Given that the incorporation of the new treatment for CHC in the public health system took place in 2015,[17] published data on the effectiveness of these therapeutic regimens in Brazil is scarce[18,19] and compiled partially outside national government guidelines.

Thus, the present study aimed to evaluate the effectiveness of the new therapeutic regimens for treating CHC in patients who underwent treatment under the national program of the Ministry of Health of Brazil.

Material and methods

This was a retrospective study, performed by data collection and review of medical records of patients with CHC who underwent treatment with DAA from December 2015 to December 2016.

The treatment of patients receiving care at a public health center in the State of Rio Grande do Sul, Brazil – Hospital Sanatório Partenon – was analyzed. The patients' clinical, laboratory and demographic data were abstracted from medical records.

The variables studied were age, sex, viral load, rate of liver fibrosis (as determined by liver biopsy, elastography, fibrotest, APRI or FIB4 scores), HCV genotype, treatment status (naïve or experienced), therapeutic regimen, treatment length and response to treatment.

Response to treatment was assessed by viral load analysis (quantitative HCV-RNA). Those whose HCV-RNA was undetectable at the end of treatment, but detectable three months thereafter were considered relapsing patients. Non-responders were those who had positive HCV-RNA at the end of treatment.

The data was analyzed using the statistical software SPSS (Statistical Package for Social Science) version 22.0. The quantitative variables are presented as means and standard deviations or medians and variations when they were not normally distributed, and analyzed by Student t test. Qualitative variables are presented as frequencies and percentages, analyzed by Pearson Chi Square test (χ^2). Means were compared using the Student's t test and frequencies using the chi-square test. To evaluate the association between the variables under scrutiny and SVR, logistic regression models were used to generate OR estimates with its respective 95% confidence intervals (95% CI). Variables associated in univariate analysis with a $p < 0.20$ were included in a multivariate logistic regression, obtaining the adjusted OR estimates. The assumed level of significance was 5%. The present study was approved by the Research Ethics Committee of the Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA) and was endorsed by the Ethics Committee of the Escola de Saúde Pública of the Public Health Department of Rio Grande do Sul.

Results

A total of 1431 records of CHC treatment were recorded during the studied period; 773 (54.0%) patients had cirrhosis. Twelve (0.8%) patients died during treatment and three (0.2%) interrupted treatment due to unrecorded causes. Quantitative PCR tests were available after 12 weeks or more after the end of treatment (SVR) for 1002 patients, who constitute the study population.

Of the 1002 treated patients, 557 (55.6%) were men, mean age of 58.6 ± 9.9 years (Table 1); 447 patients (44.6%) were over 60 years of age, 517 (51.6%) were between 41 and 60 years, and only 38 (3.8%) patients were less than 40 years of age.

Pre-treatment viral load (PTVL) was available for 945 patients; 416 patients (43.2%) had PTVL below 600,000 IU/mL and 529 patients (56.8%) had PTVL equal to or above 600,000 IU/mL (Table 1).

Regarding genotype, 606 (60.5%) patients had genotype 1, 60 (6.0%) had genotype 2, and 336 (33.5%) had genotype 3 (Table 1).

A total of 550 (54.9%) patients had cirrhosis, 229 (22.8%) stage 3 fibrosis, and 127 (12.7%) had stage 2 fibrosis for longer than three years (Table 1).

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