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Hepatology highlights

Saad S. Alkhowaiter,* John C.T. Wong,* Eric M. Yoshida

From the Division of Gastroenterology, University of British Columbia, Canada. * Co-primary authors of equal significance.

Patient adherence to antiviral treatment for chronic hepatitis B and C: a systematic review

Lieveld F, *et al.* Chronic hepatitis B and C are a common medical problem. For chronic hepatitis B patients with an indication for treatment, they will need to take antiviral agents for a long period of time if not life long. However, chronic hepatitis C patients have a finite course of treatment that currently ranges from 24 to 48 weeks. Compliance is an important aspect for the success of viral suppression/eradication and preventing progressive disease. Virologic breakthrough has been observed in up to 30% of patients on treatment for chronic hepatitis B, and it was related to medication noncompliance in clinical trials.[1]

The systemic review of Lieveld, et al. evaluated compliance with treatment in patients with chronic hepatitis B and C. It was noted that the mean adherence compliance for chronic hepatitis C patients varied from 27 to 97%, compared to the mean adherence reported in chronic hepatitis B studies that ranged from 81 to 99%. For both HCV and HBV studies, the highest adherence rates were reported in studies using self-reporting whereas lower adherence rates were reported in studies using pharmacy claims.

Clearly, the finding of better adherence to therapy with chronic hepatitis B is most likely because of a better side effect profile. Although these results are encouraging, adequate counseling at the time of treatment start plays a crucial role. Counseling about the negative consequences of non-compliance should include the risk of developing anti-viral resistance and the risk of disease flare and progression.[1] Additionally, patient should be counseled about expected side effects as well as the long-term benefits such as preventing disease progression and decreasing the risk of hepatocellular carcinoma, which is a major problem with advanced liver disease.[2-6] Patient's awareness of the positive and negative impacts of compliance will certainly increase compliance rate.

Impact of sustained virologic response on quality of life in chronic HCV carriers

Morais-de-Jesus M, *et al.* Chronic hepatitis C is one of the common referrals in a hepatologist's daily life. Many patients with chronic hepatitis C will progress to liver cirrhosis and eventually will have a decompensating disease, which will affect their life quality significantly.[7] There has been great deal of effort in improving the likelihood of eradicating chronic hepatitis C. The goal of therapy is to prevent complications of chronic hepatitis C. In a patient who has compensated liver cirrhosis, the achievement of sustained viral response (SVR) will prevent the development of esophageal varices.[8] SVR is also associated with the prevention of progression to liver failure, which will definitely reflect on patient's life quality.[5,9]

The study of Morais-de-Jesus, *et al.* evaluates health-related quality of life (HRQOL) in patients with chronic hepatitis C. Eleven studies were included in the systematic review and four in the meta-

Correspondence and reprint request: Eric M. Yoshida MD, MHSc, FRCP(C), FACP, FACG, FCAHS
Professor of Medicine, Head, Division of Gastroenterology, University of British Columbia, Canada
Vancouver General Hospital, Diamond Health Care Centre 5153-2775 Laurel Street, Vancouver, BC, V5Z 1M9, Canada.
Tel.: 604-875-5371, Fax: 604-875-5447.
E-mail: eric.yoshida@vch.ca

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analysis. Of these, nine studies showed more favorable outcomes for responders, and they had a better outcome even in studies that evaluated only cirrhotic patients, previous non-responders, relapsers, patients in first treatment and patients unaware of treatment response. Moreover, the meta-analysis showed that the general health and vitality domains had statistically significant mean change difference between responders and non-responders, presenting a summary effect of 6.3 (CI 95% 2.5-10.0) and 7.8 (CI 95% 3.4-12.1) respectively.

In patients with compensated cirrhosis or extrahepatic manifestations treatment is clearly indicated. Identifying patients with chronic hepatitis C who are likely to progress to cirrhosis is more challenging but reasonable as a systematic review showed that 4-24% of HCV-infected patients progress to cirrhosis after 20 years of infection.[7] There is, however, significant variability for disease progression between person-to-person and selecting patients for treatment on this basis alone become a challenge and may exclude many patients who may benefit from virus eradication. The study of Morais-de-Jesus, however supports the belief that patients should be encouraged to have treatment to improve quality of life.

Transjugular intrahepatic portosystemic shunt is associated with significant changes in mitral inflow parameters

Pudil R, *et al.* Indications for transjugular intrahepatic portosystemic shunts (TIPS) include control of acute bleeding from esophageal and gastric varices refractory to pharmacological and endoscopic therapy, and management of refractory cirrhotic portal hypertensive ascites.[10] By decompressing the portal venous system, however, the increased preload may result in decompensation of a compromised cardiovascular system. Pre-existing cardiopulmonary disease in these patients can be related to cirrhotic cardiomyopathy, characterized by systolic/diastolic dysfunction and electrophysiological changes in the absence of other independent cardiac diseases.[11] Diastolic dysfunction specifically results from increased left ventricular thickness, fibrosis and subendocardial edema, which results in impaired relaxation, and inability to accommodate the increased preload after TIPS, leading to heart failure.[12,13] The 2009 AASLD Practice Guidelines on the role of TIPS in management of portal hypertension recommends pre-TIPS cardiac evaluation in individuals with symptoms or history of cardiovascular disease.[1] Methods to characterize diastolic function pre and post TIPS may improve patient selection for the procedure, and better predict its cardiovascular effects post procedure, respectively.

The study by Pudil et al included 55 cirrhotic patients undergoing TIPS, and evaluated their diastolic function by measuring the transmitral flow by echocardiography at various timepoints (pre-procedure, 24 h, 7, 30 and 180 days after TIPS). Specifically, the left ventricle end-diastolic diameter increased progressively from pre-procedure to 6 months followup, with changes seen as early as 7 days post TIPS. Both the peak early filling velocity (E) and the peak late atrial filling velocity (A) changed significantly, with increases as early as 24 h. Overall, the E/A ratio increased post procedure.

This study reported the use of echocardiography to document hemodynamic changes in a cohort of cirrhotic patients who underwent TIPS. While changes were noted post TIPS, it would be interesting to correlate them to clinical outcomes such as incidence of decompensated heart failure, effect on clearance of ascites, related hospitalizations and overall mortality. Rabie, *et al.* noted their post TIPS patients with an E/A ratio of ≤ 1 had less ascites clearance and increased mortality compared to patients with an E/A of > 1.[14] With further characterization, the E/A ratio may play a future role in monitoring hemodynamic changes in cirrhotics, and those undergoing TIPS.

Poor response to hepatitis C treatment in elderly patients

Silva I, *et al.* Predictors of poor response to hepatitis C (HCV) treatment include patient related factors: age > 40, male gender, African ethnicity, body weight > 75 kg, insulin resistance, and presence of steatosis/fibrosis/cirrhosis, and viral factors: Non genotypes 2 and 3 and high baseline viral load.[15] Understanding such predictors in an elderly population is particularly important, in light of the recent Centers for Diseases Control and Prevention recommendation to universally screen individuals born between 1945 and 1965 for HCV.[16] Such predictors

could help better select patients for treatment, and optimize reversible factors to improve sustained virological response (SVR).

This study by Silva, *et al*., included 231 patients with genotype 1 HCV undergoing PEG-IFN and ribavirin treatment. Dichotomizing them into patients < and ≥ 60 years of age, their SVRs were compared, and predictors of poor response in the elderly group were determined. SVR for the < 60 years group was 46% compared to 25% in the ≥ 60 years group, with higher hemoglobin and lower glucose correlating with higher SVR.

The reported SVR was similar to the study of Giannini, *et al*.,[17] who reported 24% SVR among 25 HCV genotypes 1 and 4 in patients > 65 years of age treated with PEG-IFN and ribavirin. In contrast, the study of Hu, *et al*.[18] found no age dependant SVR differences among genotype 1 HCV although they did find that younger age did predict for higher SVR among non genotypes. The finding of a higher hemoglobin being a positive predictor for SVR was not unexpected given anemia, need for supportive treatment such as erythropoietin, and need for ribavarin dose reduction are more common among the elderly.[19] Although SVR in genotype 1 HCV elderly patients was low, this study identified a reversible risk factor to optimize it, which may help to overcome existing physician reluctance to treat this population, as highlighted by Tsui, *et al.'s* study,[20] where only 25% of 364 HCV patients > 60 years of age were considered for treatment, with only 10% actually starting on it. Whether age specific differences in treatment response will persist in the era of direct acting antiviral therapy remains to be studied.

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