Depression, Anxiety, and Quality of Life in Hepatitis C Patients Treated with Direct-Acting Antiviral Agents

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Dear Editor,

We read with great interest a published article by Kesen et al[1] in which the authors evaluated depression, anxiety, and quality of life in patients with chronic hepatitis C infection before and after treatment with direct-acting antiviral agents (DAAA). The authors reported significant improvements in depression and anxiety after treatment in the study patients. However, comparing men and women, it was shown that a significant difference was only noted in women.

Although this study has some clinical merits, we want to highlight some concerns about it. First, the inclusion criteria are not clearly described. In the method section, it was mentioned that only patients who received DAAAs were enrolled in the study. However, based on the results, 64.4% of patients were treated with interferon (IFN) and ribavirin and 11.0% with IFN, ribavirin, and telaprevir/boceprevir (that are DAAA). If these patients have experienced treatment failure, it seems that more details regarding the time span from the previous treatments needed to be mentioned for clarifying the study patients, especially for those who were treated with IFN which might have affected the symptoms such as depression. It seems that the administration of DAAAs can preclude the effects of IFN as a risk factor for depression. However, as DAAAs are newer agents compared to IFN in clinical practice, currently, the extent of associated neuropsychiatric side effects is not completely clear, and data in this regard are emerging.[2]

Moreover, the included patients in this study were infected with various genotypes of the hepatitis C virus (1a, 1b, 3, and 4). Thus, it can be anticipated that they were treated with different regimens.[3] Even if a pan-genotypic regimen were prescribed to all patients, it is very informative if the treatment protocols and medication regimens for the treatment of naïve patients as well as the cases of treatment failure in the study were pointed out in the article. Since the adverse effect cannot always be generalized to all regimens and although it was not the primary aim of the research, through these studies evidences regarding the potential differences in the adverse effects may become evident.

In the study, patients who received treatment for major depression and those with suicide ideation were excluded. However, patients receiving antidepressants for the treatment of other psychiatric conditions such as anxiety as well as other mood disorders were not excluded. It is anticipated that antidepressants dose, initiation, interruption, or continuity of treatment might probably affect the results. Moreover, it seems that the medication-induced psychiatric disorders were not evaluated through the study. For example, 6 patients with solid organ transplantation were among the study patients. These patients were probably treated with corticosteroids or cyclosporine as a part of their immunosuppressive regimen, which can cause psychiatric side effects and may confound the results. Additionally, other comorbidities that may present with symptoms similar to psychiatric disorders such as anemia or thyroid disorders were better to be documented.

In addition, we want to address several points regarding the result section. It is generally known that the more inferences are made, the more likely the erroneous inferences may occur.[4] In this study, the researchers performed almost 50 *t*-tests using 73 samples. In these circumstances, type 1 error is very high and its value does not remain at a level of 0.05. If the researchers were

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interested in studying the effects of gender or cirrhosis, it was more appropriate to use general linear model models instead. Additionally, the data presented in table 3 arise many doubts. First, in the statistical analysis section, it was mentioned that the chi-square test was used to compare categorical data. However, using the usual chi-square test for dependent tables is not suitable. Indeed, McNemar's test can be used for the assessment of the difference between paired proportions.[5] Second, in the depression scores section of the mentioned table, the *P* value reported was .075. While the frequencies of patients before and after treatment were exactly the same, which leads to a *P* value equals to 1. Moreover, in the anxiety score section, using the frequencies in the table and manual calculations for the chi-square test, the *P* value is assumed to be .092. However, it was reported to be .0001.

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