

## ANSWERS TO REVIEWERS



October 24, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Pozzetto et al.\_revised version.doc) together with a version enlightening in yellow the main corrections that were performed.

**Title:** Health care-associated hepatitis C virus infection

**Authors:** Bruno Pozzetto, Meriam Memmi, Olivier Garraud, Xavier Roblin, Philippe Berthelot

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 13006

Please find enclosed a revised version of the above manuscript. The manuscript was edited according to the remarks of the reviewers, as detailed below.

### **Reviewer 00181536**

*"This review article summarized the health care-associated hepatitis C infection. They summarized the content according to the transmission pattern. The contents are interesting, however, they are some to add as followings."*

OK.

*"Comments 1. Page 8. In the chapter of transmission of HCV in hemodialysis units, trying interferon for hemodialysis patients to reduce patients' risk to progress to cirrhosis or hepatocellular carcinoma must be mentioned. Although the sustained viral response is difficult to achieve in hemodialysis patients as ribavirin is contraindicated for these patients, continuous pegylated interferon could reduce viral load and might reduce the both patients disease progression risk and the healthcare workers HCV transmission risk."*

According to the comment of the reviewer, we added a paragraph at the bottom of page 8 concerning the possible treatment of patients with pegylated interferon monotherapy. Two references were also added (n°27 & 28) to sustain this attitude.

*"2. An additional chapter explaining how to erase HCV from environment i.e. the methods of disinfection or sterilization should be added. This information may be included in standard precautions, however, better to write or add an additional table."*

As suggested, we added a new paragraph entitled "Methods of disinfection and sterilization" that was placed after the chapter dedicated to standard precautions (page 15 of the new manuscript).

*"Minor comments 1. Page 4, line 22; ribavirine must be ribavin. 2. Page 7, Line 9; major factor risk must be major risk factor."*

The change was done in pages 4 and 7 of the new manuscript, respectively.

*"3. Page 13, line 4; Additional references explaining the reduction of HBV infection in healthcare workers are needed to add."*

As required, two references were added (N° 72 & 73) to document the reduction of HBV infection in HCWs.

#### **Reviewer 00004847**

*"The aim of the review by Pozzetto et al. was to summarize the major epidemiological conditions that could lead to the transmission of HCV in various medical settings. Overall the paper is well-written but it refreshes the information well-known by at least 20 years ago and reported in many position papers of all the specific scientific society. They are no new informations and, I believe that all the measures reported in the text are currently wide used in the majority of Countries. Otherwise, the authors should underline the necessity to renew such informations."*

I agree with the referee that most of the data summarized in this review paper are already known. However, I am not sure that the measures described there are fully applied through the world, as exemplified by the cases of HCV infection that raised in different places in USA a few years ago (referenced in 39 & 40) or by the nosocomial transmission of other viruses such as SRAS-CoV in Toronto in 2003 or Ebola virus in Texas or Spain recently.

*"The recommendations for post-exposure management are insufficient. The timing of HCV RNA testing should be reported (e.g. 1 and 3 months) and if PCR is positive a discussion of the opportunity to offer antiviral therapy should be done. In particular, as reported by many authors, peg-interferon should be utilized based on the evidence of its efficacy in acute hepatitis."*

As proposed by the reviewer, details were given regarding the biological follow-up of HCWs exposed to blood infected by HCV (8 first lines of page 16 in the new manuscript). Concerning the therapy by peg-interferon in contaminated HCWs, this point was fully discussed in the original manuscript (page 17, second paragraph).

*"In the introduction, the authors enunciated that in "the last part of the review will discuss a few research directions that need to be explored in order to reduce the risk of HCV transmission in care settings". This part of the paper could be the new and interesting section, but it is completely absent. I suggest to review in a short paragraph the current status and on the opportunity to have a vaccine to prevent HCV infection; in addition, to discuss the possible future role of new DAA in the post-exposure to HCV in preventing the development of disease."*

As suggested by the reviewer, a new paragraph was added at the end of the paper about the need for an HCV vaccine in the context of HCW protection (p18-19 of the new manuscript). In addition, we extended the discussion relative to new treatments based on DAAs (bottom of page 17 and top of page 18 of the new manuscript). However, it is difficult to say more about the use of DAA in acute hepatitis C since no trial has already been conducted with these drugs by now.

#### **Reviewer 02462664**

*"This review article entitled "Health care-associated hepatitis C virus infection" described the details of health care-associated HCV transmission. The authors also described about the prevention and treatment of HCV transmitted in such situation. Although this review article would be helpful for the countermeasure of HCV transmission-associated with health care workers, more details about countermeasure of HCV transmission will be*

*needed. The special comments were shown below. Minor 1) Many reports pointed that HCV-RNA is elevated prior to HCV-Ab in the window period, indicated that monitoring of HCV-RNA will be useful for identification of HCV-contaminated individuals. The authors should describe about how to identify the HCV-contaminated persons (both patients and HCWs) who had the incidence to contaminate HCV."*

As proposed by the reviewer, more data were added about the diagnosis of HCV infection in HCWs after an exposure to contaminated blood (bottom of page 16 and top of page 17 of the new manuscript). More details were also given about the necessity to confirm a positive result in subjects found positive for HCV (first four lines of the second paragraph of page 17).

*"2) The authors described the potential of DAA for the treatment of health care associated HCV. Recent works documented the details of DAAs against HCV infected patients. Recent studies also revealed that about 20% of HCV-infected patients had the DAA-resistant mutation of HCV before initiating DAA treatment. Although 85% of HCV patients treated with DAAs (daclastavir and asunaprevir) could eliminate HCV, the response rate was decreased below 50%. These results would indicate the limitation of DAA therapy for the treatment of health care associated HCV. The authors should describe more details about the potential and limitation of DAA therapy and may indicate the strategy of the treatment in such patients in the text and the new schema in the basis of the recent knowledge."*

This comment regarding DAA is similar to the one of the previous referee. As required, a few comments were added on this topic (bottom of page 17 and top of page 18 in the new manuscript). However, as mentioned above, it is difficult to anticipate the results that will be obtained with new treatments since no clinical trial has already been conducted in subjects with acute hepatitis C. To prevent the emergence of resistance, it is currently recommended to use combined therapies (see top of page 18). As also explained, the present cost of DAAs constitutes a strong limitation to the use of these drugs in acute infection.

*"3. Tables 1 and 2 may be summarized more".*

It was a lot of work to build these two tables. It seems difficult to summarize more the data compelled in the tables. The objective of Table 1 is to show that health care-associated HCV is still a huge problem of Public Health in many parts of the world (the name of the Journal is World Journal of Gastroenterology). Concerning Table 2, the data reported herein are not available under this form in any of the previous papers cited in this review. If the Editor thinks that one or the two Tables are not useful, they can be erased...

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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