ANSWERING REVIEWERS

April 5, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2206-review.doc).

Title: *Helicobacter pylori* infection as a cause of iron deficiency anaemia of unknown origin.

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

Rev 00183471:

1. Histology and 13C-urea breath test (UBT) are diagnostic tests with high accuracy for diagnosing H pylori infection. The positive predictive value of a positive histology is of 100% (Ou et al. BMC Gastroenterology 2013;13:7; Monteiro L et al. Am J Gastroenterol 2001; 96:353-8; Sudraba A et al. J Gastrointestin Liver Dis 2011; 20:349-354), and of UBT is 95-100% (same references). On the other hand, the specificity of H&E staining on histological samples is of 100% (Hartman DJ et al. Am J Clin Pathol 2012; 137:255-260). Thus, on the basis of present acknowledge and evidence-based data, we have used very high accurate standard methods to diagnose Hpylori infection.
The studies on Pseudomonas sp in gastric biopsies are very intriguing but until now there is no enough scientific evidence about a possible role in pathology or about the possibility of being the cause of false positives in standard tests for diagnosing Hpylori infection. Finally, the triple standard omeprazole, clarytromicine and amoxicillin therapy for H pylori infection has no effect on Pseudomonas sp.

2. Speculations about the pathogenesis of IDA are mentioned in the references in the introduction section. We have added a sentence in this sense (page 4, 2nd paragraph).

3. We agree with the referee about the too much repetition of 'final diagnosis', and we have changed this term by 'Hp as the aetiology of IDA'. We think that this suggestion improve the reading of the paper.

Rev 00503418:

1. All patients had either iron refractoriness or iron dependency. This was an inclusion criteria to the study. Now this is also clearly stated on page 5, 4th paragraph, before the definitions of both conditions.

2. All patients included in the study had H pylori infection. This was an inclusion criteria in the study as was stated in page 5, 2nd paragraph. In the results section it is stated the number of patients in whom the anaemia disappeared after Hp eradication without relapse after a long-term follow-up. In all these 32 patients (38.1%) it was considered that Hpylori was the aetiology of iron-deficient anaemia.

This was described in page 9, 3rd paragraph. We have changed the term 'final diagnosis' by 'Hpylori as the aetiology of IDA' to make more understandable this paragraph.

3. In patients in whom Hpylori infection was considered to be the cause of the anaemia, there was no relapse of anaemia after a mean follow-up of 21 months (see page 9, 3rd paragraph). We have not performed studies to assess if there was re-infection or new infection with Hpylori but we had no clinical data to suggest that, and in our country re-infection is a very rare situation (less than 1% yearly) (Gisbert JP et al. Am J Gastroenterol 2012; 107:1197-1204). A sentence commenting re-infection rates has been added in the discussion section (page 8, 2nd paragraph).

4. Patients with a positive celiac predisposition genetic study (HLA-DQ2 and/or HLA-DQ8) in whom anaemia persisted after H pylori eradication, and in whom a lymphocytic duodenosis was present, were offered a gluten-free diet. None of them had normal duodenal histology (Marsh 0). A gluten-free diet was offered to 13 patients in whom IDA persisted after Hp eradication, and only in 4 of them a gluten-sensitive enteropathy was diagnosed. This has now been clearly stated (page 7, 4th paragraph).

References and typesetting were corrected

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

Sincerely yours,

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