

RESPONSE LETTER

Reviewer's code: 00004594

- This is an interesting manuscript. I have some comments which need to be addressed: a) other drugs than NSAIDS and PPI are able to induce microscopic colitis such as: veinotonics, serotonin reuptake inhibitors, antiplatelets – b) there are other causes of increase of intra-epithelial lymphocytes such as Whipple, SIBO, auto-immune enteropathy, non celiac gluten sensitivity – c) for those patients who did not have colonoscopy, a rectosigmoidoscopy could have been performed which is generally sufficient to make the diagnosis of microscopic colitis.

Answers:

- **We thank the reviewer for the flattering assessment of our article and for the comments that allow us to improve it.**
 - a) **No patient was taking venotonics. Patients who took serotonin reuptake inhibitors or antiplatelets were excluded from the analysis.**
 - b) **The auto-immune enteropathy has been considered: “Among patients without MC The diagnosis was in in the last one (4.3%) autoimmune enteritis.”**

No signs of Whipple disease were reported in duodenal biopsies. Moreover, patients affected by small bowel bacterial overgrowth were excluded from the analysis.

Regarding gluten sensitivity, fourteen (56%) patients undertook a gluten-free diet for at least 1 month with a clinical improvement in 3/14 (21.4%). It is possible that these 3 patients in which the symptoms have improved, after the gluten-free diet, were affected by the non celiac gluten sensitivity; however the sample size is too small to establish a correlation between the non celiac gluten sensitivity and the lymphocytic enterocolitis.

- c) **To make the diagnosis of microscopic colitis we followed the AGA 2016 guidelines (Gastroenterology 2016;150:242-246): “Because microscopic colitis**

occurs in 7.5% of patients undergoing evaluation for chronic diarrhea, it would be prudent when assessing these patients with endoscopy to perform colonoscopy with biopsies of multiple segments of the colon. If for any reason flexible sigmoidoscopy is performed instead of colonoscopy, it is important to obtain biopsy specimens from the descending colon in addition to those from the rectosigmoid colon because biopsy specimens from the latter may not reveal the disease in some cases". We could find the microscopic colitis from biopsy specimens from the sigmoid colon but if the results had been negative we could not exclude that biopsy specimens from the right colon would have been positive and so we choose to use more stringent criteria.