

July 5, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 18803-review.doc).

Title:

Author: Massimo Bellini, Dario Gambaccini, Paolo Usai-Satta, Nicola De Bortoli, Lorenzo Bertani, Santino Marchi, Cristina Stasi

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 18803

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

11 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

- (1) This is an interesting non-systematic review paper regarding chronic functional constipation. I enjoyed reading it, and basically agree to your opinions. I should be grateful if you could answer my comments shown below. Comments: 1. The title should be changed to "Chronic constipation: Fact and Fiction", because IBS-C is just a part of chronic constipation, which is also pointed out by yourselves stating "many gastroenterologists have serious doubts about clearly separating these two disorders." on page 3. The separation of IBS-C from chronic constipation is proposed only by Rome criteria, and is quite artificial.

- We are conscious that "many gastroenterologists have serious doubts about clearly separating" IBS-C and CC, as we state on page 3, but we would prefer to keep the title as it is because up until now the Rome criteria have maintained the separation between

IBS-C and chronic constipation. However, we are happy to accept the Editor's final decision.

- (2) Regarding the importance of digital rectal examination (DRE) on page 11, it is also important to examine if there is any fecal impaction in the rectum from the view point of chronic constipation management.

-We agree with the referee's opinion and we have stressed the importance of DRE in detecting fecal impaction.

- (3) As for the appropriate usage of laxatives on page 15, lubiprostone should be mentioned and added to "a second line treatment" because it is one of the important non-stimulant laxatives with different mechanisms of action.

- We agree: lubiprostone has been mentioned as a second line treatment.

- (4) With regard to the risks by laxatives on page 16, I do not think that "melanosis coli" is the result of "direct mucosal damage". It is just pigmentation of the wall of the colon with lipofuscin, not melanin, in macrophages and has no significant correlation with disease. This is why "pseudo-melanosis coli" is more accurate and appropriate term. I agree with you that "osmotic laxatives are better than stimulant agents", and stimulant laxatives such as senna which causes pseudo-melanosis coli should be used only on a need to use basis as a rescue. In this sense, the pseudo-melanosis coli should be avoided, but it does not necessarily mean that the pseudo-melanosis coli itself is harmful or pathogenic. If you would like to claim that "melanosis coli" is equivalent with "direct mucosal damage", some evidence should be presented.

- We completely agree with the referee and we modified the paragraph.

- (5) The Figure 2 regarding the management of chronic constipation should be reformed, emphasizing the importance of differentiation between slow transit constipation (STC) and defecation disorder (DD), because the management between them is basically totally different. For example, "Pelvic floor rehabilitation" is useful for functional DD, but not for STC, and

“Colectomy” could be effective for severe STC but is a contraindication for DD.

- Figure and legend have been modified according to the referee's suggestions.

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

Sincerely yours,

Massimo Bellini
Dario Gambaccini
Paolo Usai-Satta
Nicola De Bortoli
Lorenzo Bertani
Santino Marchi
Cristina Stasi