



UNIVERSITÀ DEGLI STUDI DI SALERNO
FACOLTÀ DI MEDICINA E CHIRURGIA

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To the Editor-in-Chief

World Journal of Gastroenterology

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name wjg-2014-9470 Review.doc).

Title: Bloating and Functional Gastro-Intestinal Disorders: where are we and where are we going?.

Author: Paola Iovino, Cristina Bucci, Fabrizio Tremolaterra, Antonella Santonicola, Giuseppe Chiarioni

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9470

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

Reviewer 1

This is a well-written comprehensive review article that covers all recent literature on the subject. One minor suggestion: would the authors want to add a few lines on the antiflatulents (simethicone, polysiloxone) and prokinetics (domperidone, itopride) that are commonly used by practitioners?

We thank the Reviewer for the useful comments and we added and referenced the use of those drugs in bloating or IBS (page 24, line 22: page 23, line 19 and page 24 line 5)

Reviewer 2



Major 1. The authors review about bloating in detail. However, some parts in this article are redundant and each conclusion is a little incomprehensible. The authors should make the point at issue clear by using tables in at least pathophysiology part.

We are grateful to the Reviewer for the comments and added figure 1 to better summarize pathophysiology theories beyond bloating.

2. The abstract was described in only the part of background. The authors should add the parts of pathophysiology and treatment, and should do the whole sentence briefly.

The abstract has been changed according to Reviewer's suggestions (page 4, line 16)

Reviewer 3

The manuscript by Iovino et al. reviews the state of the art in the field of bloating. It is very well written in general, in an orderly and succinct manner and as far as science goes it has been a pleasure to read/review. I have a few comments as follows.

1. There is some contradiction regarding the definition of bloating, which is actually features in Rome III but the abstract and core tip state that it has no clear diagnosis.

The Reviewer is correct. We modified the core tip and the abstract adding a citation of the Rome III criteria for functional bloating (page 3, lines 3 and page 4 line 8).

2. I found useful the mention of translations of 'bloating', because these may be very meaningful given the diffuse nature of the condition. In fact I would even go for a recompilation of translations to get their approximate meaning. For instance, in Spanish I don't think there is one single translation, 'hinchazón' comes to mind and it corresponds to 'fulness', a feeling of pressure from the stomach.

We show appreciation to the Reviewer for the comment. We fully agree with the complexity of bloating definition that lead to so many different meanings.

3. Please clarify postprandial distress syndrome - I assume is a subclassification of dyspepsia but this is not evident from the text. The same with the last sentence of that paragraph regarding aerophagia.



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We changed the definition of postprandial distress syndrome and removed the sentence on aereophagia that is beyond the scope of this review. The manuscript has been changed accordingly (page 6, line 4).

4. In P11 the controlled bed rest results are somewhat confusing. First, the authors should explain why this leads to constipation. Then how feces accumulation in the rectum produces constipation.

The manuscript has been adjusted taking into account the underlying mechanism that lead to constipation in bed rest (page 12, line 1).

5. Regarding the use of myorelaxants in IBS, what about Aliment Pharmacol Ther. 2001 Mar;15(3):355-61? Also it should be indicated that the three drugs mentioned are antimuscarinic.

We added this reference n 130 that clarified the role of those drugs in IBS and clarified the drug class (page 24, line 13)

6. I think it is quite exaggerated to speak of neostigmine as of a 'potent prokinetic'. I would tone it down since many authors would even contest the very concept.

The definition has been changed.

Minor comments

1. No page numbers.

2. P2, L2: also by patients. L18: while there is ... L19: (22), only

3. P6, L6: to some extent. At the end: 'incriminating time after time'?

4. P6-P7, list: avoid the 'an' OK

5. P7, first paragraph under 'Gas' - I don't understand it. First sentence after that is superfluous. Later: 'alkali in the upper gut), and'

6. Microbiota rather than flora.

7. P9: the sentence 'Everything adjusts...', please rephrase.

8. What is the Barcelona team?

9. P10: 'might be relevant etiology as well', please rephrase.

10. P10: experimentally induced rectal distension

11. P12: 'being an excessive weight', please rephrase. After that: However, the relationship...



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12. P13, please rephrase the sentence 'Preliminary data...'

13. P14: 'retained in their gut, not their stomach'?

The review is correct, it has not been tested in the stomach.

14. P14: 'independently of the mechanism (i.e. barrier obstructing flow or an impaired propulsion)'

15. P14, L20: eliminate 'due'? OK

16. P15, L5: brackets before reference

17. P15, L16: but to gas displacement?

18. P16: 'express a similar posture dependent on coordination' - that doesn't sound quite right. Also explain 'cephalic expansion'.

19. P19, L3: increasing means accelerating? L10: gastroenterologist. L15: passage of gas? More importantly: in the exclusion group?

20. P22, L8: although maintenance. L23: among the other items? L28: HC? L30: neostigmine.

We do appreciate the attention of the Reviewer that significantly improved our work. Most of the changes have been made. Regrettably, we weren't able to find some of his suggestions due to pages and lines shift during revision.

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

Sincerely yours,

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