

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9470

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

Reviewer code: 00049578

Science editor: Ya-Juan Ma

Date sent for review: 2014-02-13 15:08

Date reviewed: 2014-02-18 22:50

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|--|-------------------------------------|--|
| <input checked="" type="checkbox"/> Grade A (Excellent) | <input checked="" type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good) | <input type="checkbox"/> Grade C: a great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D (Fair) | <input type="checkbox"/> Grade D: rejected | <input type="checkbox"/> Existed | <input checked="" type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E (Poor) | | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision |

COMMENTS TO AUTHORS

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. 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 recopilation 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. 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. 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. 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. 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. 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' 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



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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... 12. P13, please rephrase the sentence 'Preliminary data...'. 13. P14: 'retained in their gut, not their stomach'? 14. P14: 'independently of the mechanism (i.e. barrier obstructing flow or an impaired propulsion)' 15. P14, L20: eliminate 'due'? 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.

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9470

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

Reviewer code: 00503417

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| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|--|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent) | <input type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good) | <input type="checkbox"/> Grade C: a great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D (Fair) | <input type="checkbox"/> Grade D: rejected | <input type="checkbox"/> Existed | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E (Poor) | | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision |

COMMENTS TO AUTHORS

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 antifatulents (simethicone, polysiloxone) and prokinetics (domperidone, itopride) that are commonly used by practitioners?

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

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

Reviewer code: 00044509

Science editor: Ya-Juan Ma

Date sent for review: 2014-02-13 15:08

Date reviewed: 2014-02-23 15:16

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent) | <input checked="" type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good) | <input type="checkbox"/> Grade C: a great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D (Fair) | | BPG Search: | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade E (Poor) | <input type="checkbox"/> Grade D: rejected | <input type="checkbox"/> Existed | <input checked="" type="checkbox"/> Minor revision |
| | | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision |

COMMENTS TO AUTHORS

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. 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.

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9470

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

Reviewer code: 71456

Science editor: Ya-Juan Ma

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| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent) | <input checked="" type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good) | <input type="checkbox"/> Grade C: a great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D (Fair) | <input type="checkbox"/> Grade D: rejected | <input type="checkbox"/> Existed | <input checked="" type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E (Poor) | | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision |

COMMENTS TO AUTHORS

To the Authors

The Authors performed a review from the literature of the pathophysiologic mechanisms and treatments for abdominal bloating of functional origin. The work is appreciable, but there are some lacunae in pathophysiology and treatment.

PATHOPHYSIOLOGY

1) The Authors did not consider the mechanisms of the functional bloating that starts immediately after meals, increases during the morning and disappears during the night (Chang L. Am J Gastroenterol 2001;96:3341, Lewis MJ. 2001;48:216). The early onset of distension after meals excludes the origin from colonic fermentation and suggests a postprandial marked loss of tonic motor activity of the intestinal musculature of neuro-humoral reflex origin, that determines an increase of the capacitance of the loops, subsequently filled by gas coming from blood, where it has a pressure higher than that of intestinal lumen (Bortolotti M. Scand J Gastro 2009;44:383).

2) Another pathophysiologic topic that should be further developed is the increased perception of intestinal stimuli. The Authors completely ignored that the visceral hypersensitivity, considered greatly important in the pathogenesis of IBS (ref. 12) and of bloating (ref. 10), is due to an increased expression of the capsaicin sensitive fibres TRPV1 that play a pivotal role in the genesis and maintenance of colonic hypersensitivity in IBS patients (Holzer P. Eur J Pharmacol 2004;500:231) with particular reference to abdominal bloating (Quigley EM. Gut 2003;52:1659).

In fact a desensitization of these fibres decreased significantly the symptoms of bloating as well as that of pain (Bortolotti M. Dig Dis Sci 2011;56:3288)

TREATMENT

1) The treatment with prokinetics is scarcely developed. Some studies were not referred, as that with neostigmine (Caldarella MP. *Gastroenterology* 2002;122:1748), pyridostigmine (Accarino A. *Am J Gastroenterol* 2008;103:2036), octreotide (Lyford G. *Curr Treat Options Gastroenterol*. 2004;7:317) and erythromycin (Sarna SK. *Gastroenterology*. 1991;101:1488). These drugs are useful for stimulating intestinal transit.

2) With regard to trimebutine, the authors should remember that, besides an antispasmodic effect on colonic musculature, it also possesses a prokinetic effect on gastric and small intestinal musculature inducing phases III of the migrating motor complex through a stimulation of peripheral K opioid receptors in man, with acceleration of small intestinal transit (Grandjouan S. *Aliment Pharmacol Ther* 1989;3:387; Bueno L. *Gastroenterol Clin Biol* 1987;11:97B; Chaussade S. *Eur J Clin Pharmacol* 1987;32:615).

3) Finally, the effect on bloating of the treatment based on desensitization of fibres TRPV1 is completely ignored, although a controlled study has been published recently (Bortolotti M. *Dig Dis Sci* 2011;56:3288) and should be mentioned in the review.

References 73, 119 and 105 do not correspond to the text.