

April 5 2017

Dear Editor,

thank you for reviewing our Manuscript #33498: "Diet in IBS: what to recommend, not what to forbid to patients!". Your suggestions were very useful and we hope that we have improved our manuscript. On behalf of my group, I have the pleasure to present the revised version of the manuscript for your consideration. We appreciate all of the constructive criticisms, useful comments and thoughtful suggestions provided by both referees and Editor. All substantive points and suggestions arising from the referees have been carefully considered during revision of the original manuscript. In all cases, the suggested changes have been carefully considered and in most cases implemented in full.

All revisions made to the original paper have been highlighted in **red color** for Reviewer #00058573, in **green color** for Reviewer #00069819, and in **blue color** for Reviewer #00044509.

A detailed response to all comments from the reviewers and the editor is outlined in the accompanying response indicated by sentences starting with **Response:**. The original paper has been extensively revised in accordance with the comments and recommendations arising from the peer-review process, and as a result is much improved.

We hope that the revisions would allow the manuscript to be considered acceptable for publication.

With our best regards,

Prof. Dan Lucian Dumitraşcu, PhD

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 33498

Title: Diet in IBS: what to recommend, not what to forbid to patients!

Reviewer's code: 00058573

COMMENTS TO AUTHORS

Nicely written. Very detailed. It needs to be curtailed and references reduced. Its more of a Review article rather than an Editorial.

Response: We agree with this suggestion and according to this, we have attempted, as much as possible, to shorten the text and reduce the reference list. However, one other reviewer has requested additional explanations on several issues. Please see revisions highlighted in [red color](#) throughout the manuscript.

Reviewer's code: 00001787

COMMENTS TO AUTHORS

I read with interest the MS "Diet in IBS: what to recommend, not what to forbid to patients!" by Cozma-Petruț A et al. It is an innovative and well-designed review paper. I found deeply interesting the proposal of a diet advice pyramid to benefit IBS Tx. The Authors should be commended for providing such an innovative approach to deal with a relevant issue, thou commonly neglected.

Response: We acknowledge the reviewer for appreciation and positive comments.

Reviewer's code: 00069819

COMMENTS TO AUTHORS

This is an interesting and comprehensive review of dietary recommendations and lifestyle modifications for IBS patients. The manuscript is well written and informative. However, the manuscript type-Editorial-, as stated by the Authors, is inappropriate. I believe the article type is better be labeled as “review article”, as the present is in fact a narrative review of the topic. Furthermore, I wonder if the “IBS food pyramid” was developed “de novo” by the Authors or modified from previous works by others! In the former case, the Authors should state this clearly, by writing “we developed.....” and not “ it was developed” (second line of the first paragraph of the section “The IBS food pyramid). Overall, I believe that this review is useful for both patients and treating physicians, and therefore, it should attract a large number of readers.

Response: We agree with this comment and we have stated clearly in the text that we developed the “IBS Food Pyramid”. Please see revisions highlighted in green color throughout the manuscript. In particular, see the last sentence of the section “Introduction” and the first sentence of the section “The IBS Food Pyramid”.

Reviewer's code: 00044509

Response: Please see revisions highlighted in [blue color](#) throughout the manuscript.

COMMENTS TO AUTHORS

1. The pathology of IBS is composed of visceral hypersensitivity and abnormal bowel movement. The authors should discuss not only the effect of each food but also the relationship between disease condition, especially visceral hypersensitivity and diet.

Response: We agree with this comment and we have introduced some discussions on the relationship between diet and the pathophysiology of IBS. In particular we have added these paragraphs:

- “The pathophysiology of IBS is not completely understood, but several abnormalities appear to contribute to its pathogenesis, including disruption of the brain-gut axis, gut dysmotility, visceral hypersensitivity, low-grade mucosal inflammation, increased intestinal permeability, and altered microbiota^[4]. Moreover, a number of studies refer to the role of diet in IBS, which may be explained by atypical modulatory mechanisms of the gut in response to stimulation of gut receptors mediated by nutrients^[5]. Nutrients presence in the GI tract affects GI motility, sensitivity, barrier function, and gut microbiota^[5]. Likewise, food hypersensitivity and food intolerance have been targeted to underlie the pathogenesis of IBS, but there is a lack of quality evidence to support this mechanisms^[6]. Hypersensitivity to certain foods may play a role by causing low-grade intestinal inflammation, increased epithelial barrier permeability and visceral hypersensitivity^[5]. Bioactive chemicals in foods (e.g., salicylates) also may contribute and trigger GI symptoms in IBS, possibly by inducing visceral hypersensitivity following chronic exposure^[7]. Luminal distension is another mechanism by which food has been suggested to induce symptoms in IBS in that short-chain carbohydrates in the diet can increase luminal water retention and gas production, thereby leading to bloating, pain and increased visceral hypersensitivity^[6,7].”
- “Moreover, recent studies show that the by-products of the interaction between FODMAPs and gut microbiota act on intestinal stem cells, resulting in aberrant differentiation of these cells into endocrine cells and leading to an abnormal density of endocrine cells in the gut^[78]. GI endocrine cells regulate GI sensitivity, motility, secretion, absorption, local immune defense, and appetite^[47]. Therefore, abnormalities in the GI endocrine cells may play a major role in the development of visceral hypersensitivity, dysmotility, and abnormal intestinal secretion, all being features seen in patients with IBS^[47,78].”

We have added 4 references in the text and reference list:

1. **Hayes PA**, Fraher MH, Quigley EM. Irritable bowel syndrome: the role of food in pathogenesis and management. *Gastroenterol Hepatol (N Y)* 2014; **10**: 164-174 [PMID: 24829543] (reference 4)

2. **Oświęcimska J**, Szymbal A, Roczniak W, Girczys-Poędniok K, Kwiecień J. New insights into the pathogenesis and treatment of irritable bowel syndrome. *Adv Med Sci* 2017; **62**: 17-30 [PMID: 28135659 DOI: 10.1016/j.advms.2016.11.001] (reference 5)
3. **Gibson PR**. Food intolerance in functional bowel disorders. *J Gastroenterol Hepatol* 2011; **26**: 128-131 [PMID: 21443725 DOI: 10.1111/j.1440-1746.2011.06650.x] (reference 6)
4. **El-Salhy M**. Diet in the pathophysiology and management of irritable bowel syndrome. *Cleve Clin J Med* 2016; **83**: 663-664 [PMID: 27618354 DOI: 10.3949/ccjm.83a.16019] (reference 78)

Please see the section “Introduction”, the section “Second-line dietary approach in IBS: the low FODMAP diet”, and reference list.

2. Papers related to diet and IBS still have low levels of evidence and many conflicting results. IBS food pyramid figure is fine, but the authors should show how much the evidence level is.

Response: We agree with this suggestion and we have introduced the level of evidence for the recommendations included in the “IBS Food Pyramid”, as graded in the British Dietetic Association evidence-based practice guidelines for the dietary management of IBS in adults (the 2016 update). Within these guidelines, the evidence reviewed was graded using the Practice-based evidence in nutrition (PEN) grading criteria (level A, supported by good evidence to level D, evidence is limited).

Please see the section “The IBS Food Pyramid”, the Figure Legend and the Figure “IBS Food Pyramid”.

3. In this paper, the authors should explain why items of physical activity are necessary.

Response: We agree with this comment and we have added some information in the text to better explain the reason for including physical activity in a paper mainly focusing on dietary recommendations for IBS patients. In particular, we have added these paragraphs:

- “Current dietary guidelines for IBS management^[13,21] include recommendations on physical activity. This is due to the fact that physical activity serves as a basic complement to the diet^[61]. Regular exercise is beneficial to health in general and recent data highlights its positive effects also for IBS patients^[62,63].”
- “Mechanisms suggested to underlie the benefits of physical activity in IBS are decreased splanchnic blood flow, neuroimmuno-endocrine alternations, increased GI motility and mechanical bouncing during movement^[70]. The impact of exercise on psychological symptoms has also been postulated as a potential mechanism and studies have reported positive effects on quality of life, fatigue, anxiety, and depression after moderate increase in physical activity in patients with IBS^[67].”

We have added one reference in the text and reference list:

1. **Peters HP**, De Vries WR, Vanberge-Henegouwen GP, Akkermans LM. Potential benefits and hazards of physical activity and exercise on the gastrointestinal tract. *Gut* 2001; **48**: 435-439 [PMID: 11171839] (reference 70)

Please see the subsection “Physical activity” of the section “First-line dietary approach in IBS” and reference list.