CORRESPONDENCE

Functional Bowel Disorders in Adults

by PD Dr. med. Winfried Häuser, Prof. Dr. med. Peter Layer, Prof. Dr. med. Peter Henningsen, Prof. Dr. med. Wolfgang Kruis in volume 5/2012

Diamine Oxidase Deficiency

In *Box 5*, which lists special diagnostic tests depending on the lead symptoms, I miss under the main symptom “diarrhea” any mention of diamine oxidase deficiency, which in my opinion is an important cause of histamine intolerance. Maintz, Bieber, and Novak described this in an issue of *Deutsches Ärzteblatt* in 2006. Schleips and Lübke describe further literature on histamine intolerance and how to live with it (3, 4).

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Conflict of interest statement

The author declares that no conflict of interest exists.

Uncritical Assessment

I am missing critical commentaries with regard to several of the listed medical therapeutic options, some of which are rather questionable, even though it is obvious that extensive discussion of the literature is not possible in the confines of a review article. To give but one example: rifaximine is listed as an option with evidence level A. The cited TARGET study, which this assertion is based on, was funded by the manufacturers and reported improved symptoms in only 10% of patients compared with placebo. In terms of clinical relevance this is clearly on the borderline. Even if one “believes” the results, they hardly justify treatment with an expensive substance (therapy/patient >400€, without effect in 90%) whose long-term side effects, such as the destruction of the gut flora, are entirely unknown. I refer readers to the assessment in the *Arzneimittelbrief* (2011, 45, 14a).

Listing bulking agents, and “phytotherapeutic agents” in particular, as therapeutic options is too undifferentiated. Ford et al found in a meta-analysis of randomized controlled trials (BMJ 2008, 337, a2313) a positive effect for plantago (NNT 11), but not wheat bran. Peppermint oil has been found effective as a phytotherapeutic agent (NNT 2.5).

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The author declares that no conflict of interest exists.

Thinking Outside the Box

For many years, I have taken an interest in stool diagnostics and diagnosis of chronic gastrointestinal symptoms—the so called irritable bowel syndrome. It is amazing in how many patients in whom traditional medicine has not found any pathological indicators, stool diagnostics shows up the cause for their symptoms. In this scenario, nothing pathological means laboratory testing according to the recommended diagnostic strategy will find only normal serum values, and an absence of pathological bowel bacteria and normal calprotectin in stools. However, the range of diagnostic tools one could deploy is vast. Especially food intolerances and allergies are of importance in this setting. According to the article, 50–70% of patients with the so called irritable bowel syndrome have food intolerances. The fact that these can be confirmed as the trigger of the symptoms, and that adequate therapy can alleviate the symptoms, is being ignored and diagnostic testing is explicitly advised against. Histaminosis, which is extremely common and needs to be distinguished from genuine histamine intolerance, is not mentioned at all. The therapeutic recommendations merely aim at the symptoms, although very good causal therapeutic options are available for certain findings. In my opinion, great relief could be offered to many patients by looking at the bigger picture and uses adequate and appropriate stool diagnostics, even if only as the second step.

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The author declares that no conflict of interest exists.

In Reply:

We thank your correspondents for the interesting comments, which we understand as an expression of the importance of the topic and unanswered questions.

Buchheim misses any mention of histamine intolerance as the cause of diarrhea in *Box 5* and cites the article by Maintz et al (1). We focused on the main symptoms and the recommendation that specialized diagnostic evaluation should be carried out depending on the initial findings. In the article by Maintz et al, diarrhea is mentioned as one of many symptoms, without any indication of its prevalence. Furthermore, the authors said: “The diagnosis of histamine intolerance is made in the presence of at least two typical symptoms.” The approach if diarrhea is the lead symptom therefore differs from that for the symptoms of histamine intolerance that typically affect different organ systems.

Lache criticizes our mentioning rifaximine treatment. Our cautious assessment was phrased as follows: “Another therapeutic approach is to treat the enteric flora ... with ... rifaximine.” A controlled study which included a large number of cases has been published (2), which represents evidence of a quality that is not available for many commonly used treatments. We wish to correct the proportion of patients in whom therapy was successful: this was not 10% but 40.8%.

We mentioned plantago several times (see reference e25 and *eTable 2*) and mentioned wheat bran in the context of constipation only once. Peppermint oil is effective but has known side effects (a burning sensation in the esophagus and the anus), which impose limitations on its usefulness (3).

Rosler criticizes the lack of recommendations of adequate and appropriate stool diagnostics to confirm

food intolerance and allergies. We have to confess that we were not aware of existing scientific studies of the topic.

With regard to histamine intolerance, we refer readers to our response to Buchheim.

In addition to these letters to the editor we have also received a considerable amount of direct feedback, which was targeted at one or several “controversial” questions. Our article was based as far as possible on the available scientific evidence. Undoubtedly this is limited, and many efforts will have to be made into find satisfactory answers to questions arising from clinical practice.

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Conflict of interest statement

Professor Kruis acts as an adviser to Ardeypharm and Shire. He has received honoraria from Ardeypharm and Shire for preparing further educational scientific events. He has received honoraria from both companies for conducting commissioned clinical studies, as well as funding for a research project he himself initiated.