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LETTERS TO THE EDITOR

Are the anti-CdtB and anti-vinculin antibodies really ready for use in patients with diarrhea in Mexico? Regarding microscopic colitis☆

¿Están realmente listos los anticuerpos anti-CdtB y anti-vinculina para emplearse en pacientes con diarrea en México? A propósito de la colitis microscópica

To the Editors:

I read the work by Dr. Schmulson et al.[1] with interest, in which they present their experience with the use of the anti-CdtB/anti-vinculin antibodies for confirming the presence of diarrhea-predominant irritable bowel syndrome (IBS-D) in a small group of patients presenting with pain, abdominal bloating, and diarrhea. The authors concluded that their results support the use of this test as a first-line diagnostic tool for confirming the presence of IBS-D (Rome III).[1] Obviously, this conclusion exceeds the scope of their study, given that this test has not been adequately validated in the broad clinical spectrum of patients with pain, bloating, and diarrhea, especially those with microscopic colitis (MC).

The correct validation of a diagnostic test demands specific characteristics. First, the test in question should be compared with an accepted or ''criterion standard'' diagnostic test. The problem is that no ''criterion standard'' has been defined in relation to IBS-D diagnosis, given that the Rome criteria have insufficient sensitivity and specificity, whereas colonoscopy with biopsies should be carried out in many of the patients with IBS-D.[2] In Mexico, 18% of the patients with IBS-D criteria systematically studied with colonoscopy and biopsies present with MC.[3] Second, validation must include a wide range of subjects with the clinical symptoms that characterize the disease. Even though in this study patients with tropical sprue, celiac disease, diverticular disease, and MC were included, the number was very small and other entities belonging to the scope of symptoms were not even considered (e.g., intestinal parasitosis, bile acid and carbohydrate malabsorption, exocrine pancreatic insufficiency, or neoplasias). Finally, bias must be prevented by having all the study subjects undergo the test being evaluated, as well as the ''criterion standard'', which clearly was not done in this study.

Even though anti-CdtB/anti-vinculin antibody determination has been validated in inflammatory bowel disease, the same has not occurred with MC. In fact, MC is characterized by overlapping with IBS-D, by having a good response to initial treatment with budesonide, high relapse rates, and an elevated response to retreatment.[4,5] Thus, the reappearance of pain, bloating, and diarrhea in a patient with MC that responded well to initial treatment should be considered disease relapse, and cannot be taken as evidence of IBS-D with overlapping MC. Relapse occurs in 60-82% of the cases of MC and is the main indication for giving prolonged maintenance treatment.[4,5] Studies published up to now that evaluate the use of these biomarkers have included a surprisingly low number of patients with MC, given the prevalence of this disease. The results of the study by Dr. Schmulson et al. reaffirm the need to correctly validate these tests in the wide range of patients with IBS-D criteria, including an adequate number of patients with MC and others with the symptomatic complex of pain, abdominal bloating, and diarrhea that have not yet been taken into account.

Conflict of interest

Ramón Carmona-Sánchez is a Member of the Advisory Board of Mayoly-Spindler, a Speaker for Mayoly-Spindler and Allegan, and participates in research protocols funded by Laboratorios Senosian and Asofarma.

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Answer to Carmona R.: Are the anti-CdtB and anti-vinculin antibodies really ready for use in patients with diarrhea in Mexico? Regarding microscopic colitis☆

Respuesta a Carmona R.: ¿Están realmente listos los anticuerpos anti-CdtB y antivinculina para emplearse en pacientes con diarrea en México? A propósito de la colitis microscópica

To the Editors:

We appreciate the interest of Carmona[1] in our article,[2] but it is very important to make some clarifications in response to his comments.

First, one must recognize his excellent and detailed description of the steps that must be taken for validating a diagnostic test.[1] However, we wish to reiterate that our brief communication[2] was not a validation of the anti-CdtB and anti-vinculin antibodies -which has now been published by Pimentel et al.,-[3] but rather, as Dr. Carmona himself stated at the beginning of his letter,[1] simply the presentation of our clinical experience with these antibodies at a private practice in Mexico.[2] In fact, our experience shows findings similar to those of the previous validation,[3] and our data also concur with those of Remes-Troche et al. in a much larger study in Veracruz.[4] The latter compared the results of 339 patients with Rome III irritable bowel syndrome (IBS) vs 274 controls, finding that these biomarkers were more prevalent in IBS-D and IBS-M, with significantly elevated levels only of anti-vinculin, indicating that this marker has greater importance in IBS in Mexico, and thus requiring further investigation.[4]

Second, the Rome criteria for diagnosing IBS-D, which have been universally accepted for the diagnosis of IBS in all the subtypes,[5] is criticized. Indeed, the recently published Mexican Consensus on Irritable Bowel Syndrome, of which Carmona is the main author, establishes the following for IBS diagnosis: ''The diagnostic symptom-based criteria enable the positive diagnosis of IBS in those patients without alarm symptoms and without risk factors.''[6] To the best of our knowledge, the Rome criteria ARE the available symptom-based criteria, and in addition, they are updated based on the evidence at hand, now resulting in the publication of the new Rome IV criteria.[5] The same consensus states: ''There is insufficient evidence for recommending a standard group of diagnostic tests in all patients meeting the symptom-based IBS criteria'' and it then says: ''It is recommendable to carry out complementary diagnostic tests in all patients that meet the symptom-based IBS clinical criteria and that present with alarm symptoms, refractory symptoms, or risk factors.''[6] Therefore, there is explanation that defends the statement that ''colonoscopy with biopsies should be carried out in many of the patients with IBS-D''.[1] Does ''many'' refer to the majority? We imagine that it refers to those patients with IBS-D that present with alarm symptoms, refractory symptoms, or risk factors, as recommended in the Mexican consensus on IBS,[6] but most definitely they are not the majority. In this sense, we did not intend to report our experience with the use of anti-CdtB and anti-vinculin in patients with alarm symptoms, or those that were refractory to treatment for IBS, or with risk factors for cancer of the colon, but rather as an initial test in patients with abdominal pain and diarrhea,[2] who precisely -according to a group of specialists surveyed in Mexico- have at least a 61.7% probability of having IBS-D.[7] Furthermore, the presence of a positive test showed us that it served as a positive inclusion biomarker for IBS-D or IBS-M in the patients with the Rome III criteria for those disorders.[2]

Third, it should be mentioned that the Rome Foundation also recently published the multidimensional clinical profile for characterizing patients with functional gastrointestinal disorders in all their dimensions, and this profile not only includes the Rome criteria as the first category, but also physiologic markers and biomarkers as one of the dimensions, when they are available.[5] These 2 categories should be complemented with the clinical modifiers, symptom impact, and psychosocial modifiers to determine a diagnosis and

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