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Controversies about the use of serological markers in diagnosis of inflammatory bowel disease

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Abstract

The serological markers are increasingly used in diagnosis of inflammatory bowel disease (IBD). D-lactate and diamine oxidase are new indicators that can be used to reveal the damage to intestinal mucosa and permeability alteration in IBD. Although the two biological markers seem more sensitive, recent clinical trials and animal experiments have shown controversies about the use of them in diagnosis of IBD. Therefore, these markers should be interpreted cautiously and further prospective studies are needed to establish their clinical role in diagnosis of IBD.

Key words: Inflammatory bowel diseases; D-lactate; Diamine oxidase; Intestinal permeability; Diagnosis

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TO THE EDITOR

We read with great interest the article recently published in *World Journal of Gastroenterology* by Song *et al*[1], presenting that the serum levels of soluble intercellular adhesion molecule-1, D-lactate and diamine oxidase (DAO) can be used as major monitoring indices in diagnosis and treatment of inflammatory bowel disease (IBD). However, some points on designing the study and their conclusion about the markers in diagnosis of IBD may need further considerations.

First, the study was based on the view that the intestinal permeability (IP) is increased in the active phase of IBD so that D-lactate and DAO can enter blood through the dysfunctional barrier. A high serum level of the markers, which reflects the activity of IBD, can reveal the damage to intestinal mucosa. However, several studies have identified a subset of healthy relatives who also have increased IP but no CD[2-4]. Moreover, it has been shown that IP increases in remission of IBD, especially in CD[5].

Second, the authors stated that D-lactate could not be well metabolized as mammals have no D-lactate dehydrogenase for its decomposition. Therefore, plasma D-lactate can be used to reveal the damage to intestinal mucosa and permeability alteration in IBD. This conventional opinion is based largely on early experiments and continues to be quoted frequently. It has been reported that D-lactate is indeed metabolized[6]. The half-life of oral D-lactate (6.4 mmol/kg) is 21 min in blood of healthy humans while doubling this dosage increases its half-life to 40 min, most likely reflecting the saturation of its metabolism[7]. In addition, recent studies have identified D-lactate dehydrogenases in putative human and murine mitochondria[8,9]. These findings indicate that the plasma level of D-lactate is not a reliable marker of IBD.

Third, DAO activity in blood, as a diagnostic marker of IBD, should be interpreted cautiously. Actually, serum DAO enzyme activity is changed by several disorders including severe burn, gut injury, diverse enteropathy and abdominal surgery, chemotherapy and kidney injury. Furthermore, gender-related differences in DAO activity with a high inter-individual variability, demonstrate that abnormal serum DAO activity in women is not always associated with a pathological status[10].

Prerequisites for the clinical use of biomarkers in diagnosis of IBD include high sensitivity, specificity and cost-effectiveness. The rapidly expanding markers to the serologic IBD diagnostic algorithm will likely increase their sensitivity. Increased sensitivity, however, can often accompany decreased specificity, which must be carefully assessed and recognized. Further prospective clinical trials are needed to determine the role and importance of such markers in diagnosis of IBD.

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