Promising role of D-amino acids on Irritable bowel syndrome

Yuka Ikeda, Kurumi Taniguchi, Haruka Sawamura, Ai Tsuji, Satoru Matsuda

Abstract
Irritable bowel syndrome (IBS) is an important health care concern. Alterations in the microbiota of gut-brain axis may be linked to the pathophysiology of IBS. Some dietary intake could contribute to produce various metabolites including D-amino acids by the fermentation in gut microbiota. D-amino acids are the enantiomeric counterparts of L-amino acids, in general, which could play key roles in cellular physiological process against various oxidative stresses. Therefore, the presence of D-amino acids has been shown to be linked to the protection of several organs in a body. In particular, gut-microbiota could play significant roles on the stability of emotion via the action of D-amino acids. Here, we would like to shed light on the roles of D-amino acids, which could be used for the treatment of IBS.

Key Words: Irritable bowel syndrome; D-amino acid; gut-microbiota; colitis; probiotics; fecal microbiota transplantation


Core Tip: The potential efficacy of D-amino acids as a probiotics or a fecal microbiota transplantation (FMT) for the treatment of IBS has been shown here.
TO THE EDITOR

With great interest, we have read the article by Mamieva et al. [1]. As irritable bowel syndrome (IBS) could exacerbate the quality of the patients’ life, it is a considerable health care concern. Although the underlying pathophysiological mechanisms are not clear, the role of low-grade inflammation and the mucosal immune activation appear to be obvious in the signs of IBS. The IBS is a functional gastrointestinal disorder, and some probiotic supplementation may reduce the symptoms [2]. In addition, fecal microbiota transplantation (FMT) expects recommendations for the treatment of IBS, suggesting that alterations in gut microbiota-brain axis are linked to the pathophysiology of IBS. (Figure 1) It has been revealed that some cytokines and neurotransmitters as well as several microbial metabolites including short chain fatty acids (SCFAs) such as acetate, lactate, butyrate and propionate produced by the bacteria in the gut could modulate the integrity of brain-function [3]. The bidirectional communication between gut microbiota and brain is well-known as the gut-brain axis, which could play an important role on the stability of emotion [3]. As shown in the article by Mamieva et al [1], the microbiota could influence the pathogenetic factors of IBS through the production of several microbial metabolites. Here, we would like to add the efficacy of D-amino acids for the alteration of IBS condition.

Mice treated with D-serine prior to the induction of colitis exhibited a reduction in the colonic inflammation that is not seen in mice fed with L-serine [4]. In addition, D-serine efficiently suppressed the progression of chronic colitis. Therefore, D-serine might have effective properties as a prevention and/or a treatment for the colitis [4]. In addition, several studies have shown the significance of D-amino acids in clinical usage [5]. For example, D-methionine protects the intestinal damage through anti-oxidative and anti-inflammatory effects, which could improve the gut microbiome imbalance by enhancing the growth of beneficial bacteria [6]. Protective effects of low-dose D-serine have been also shown to suppress the renal damage, which may promote the proliferation of kidney epithelial cells [7]. In addition, D-cysteine administration could
defend the kidney from ischemia-reperfusion injury, which may be beneficial for the treatment of several renal diseases [8]. Gastro-protective effect with D-cysteine but not with L-cysteine has been shown via the effects of decreasing cellular damage, edema, and epithelium-loss [9]. Treatment with D-aspartate may bring positive effects in the nervous system [10]. Furthermore, D-cycloserine is a glutamatergic N-methyl-D-aspartate receptor-agonist which has been revealed to support the stability of emotion [11]. Furthermore, the activity of ovarian development with D-tryptophan is more effective rather than that with L-tryptophan [12]. These data suggest that D-amino acids could have beneficial and/or protective effects on various tissues, which might be favorable to the treatment of IBS. **(Figure 1)** In particular, the emotional stability via the action of D-amino acids seems to be important [13], because it has been shown that different types of physiological and/or psychological stressors are known to contribute to the development, maintenance, and exacerbation of IBS [14].

Gut microbiota have a large genetic capacity to produce D-amino acids which are utilized as nutrients to support bacterial growth [15]. D-amino acids are essential elements of peptidoglycans in the cell-wall of bacteria. Hence, higher levels of D-amino acids have been basically related to the mass of gut microbiota [16]. Many bacterial species encode specific racemases that can convert L-amino acids to D-amino acids, which are frequently present at the peptidoglycan-containing bacteria in gut microbiota [17]. Accordingly, the lumen of gastro-intestinal tract in mammals may be rich in free D-amino acids that might be derived from such bacteria or fermented foods. Probably, the source of D-amino acids in mammals may mostly be from their gut microbiota. For example, D-alanine production is linked to the relative abundance of bacterial species such as *Enterococcus* and *Lactobacillus* in gut microbiota [18]. Therefore, the metabolism of D-amino acids in a body might be modified by the alteration of gut bacterial communities affecting the host health and/or homeostasis [19]. Reduction of the amount of several D-amino acids may promote senescence through the increase of reactive oxygen species (ROS) production [20, 21].
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