

Management of Overlap Syndrome between Functional Dyspepsia and Irritable Bowel Syndrome by Western and Traditional Chinese Medicine

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Abstract

The overlap syndrome of functional dyspepsia and irritable bowel syndrome (FD-IBS) is very common and difficult to treat. There are many risk factors of FD-IBS. Mental illness of FD-IBS patients is more serious. Functional dyspepsia and irritable bowel syndrome have some similarities in the aspects of pathophysiology, pathogenesis, and treatment. We should pay attention to two aspects of the treatment of overlap syndrome, one is simplifying medications, the other is using gastrointestinal motility drug with bidirectional regulative function when necessary. Traditional Chinese medicine in this respect shows some advantages. This review addresses the epidemiology, risk factors, clinical features, pathogenesis and management of FD-IBS.

Keywords

Functional Dyspepsia, Irritable Bowel Syndrome, Overlap Syndrome

1. Introduction

Both functional dyspepsia (FD) and irritable bowel syndrome (IBS) belong to functional gastrointestinal diseases (FGIDs). Recent data [1] suggested that overlap between functional dyspepsia and irritable bowel syndrome (FD-IBS) is very common, and there is a growing emphasis on it. The following is a review on epidemiology, risk factors, clinical features, pathogenesis and management of FD-IBS.

2. Epidemiology

The prevalence of FD-IBS is reported to be remarkably high in Asian countries.

Perveen *et al.* [2] carried out a 3,000-participant survey on the overlap of FD and IBS. The study demonstrated that approximately 27.1% of IBS patients and 42.1% of FD patients had FD-IBS, respectively. In addition, based on Rome III criteria, other epidemiology study [3] investigated 3,014 patients who responded to their questionnaires at a general gastroenterology outpatient clinic. The result showed FD-IBS overlap was observed in 5.0% of the patients, while 31.5% of IBS patients and 24.8% of FD patients had FD-IBS.

3. Risk Factors

Several studies reported that genetic factors were associated with the incidence of FD-IBS. The CC genotype of G-protein $\beta 3$ C825T may be related to FD and diarrhea-predominant IBS (IBS-D) [4]. In addition, it was found that poor sleep quality, smoking, anxiety, depression, female gender, abdominal distension, lose weight, visceral hypersensitivity and infection were all risk factors for FD-IBS [3] [5]-[10].

Kong and colleagues found that, when compared with single IBS group, mental factors, medications, fatty meal, cold food, climate-related factors and surgical trauma should be valued as predisposing factors of FD-IBS. In terms of drugs, the main cause are laxative agents as well as non-steroidal anti-inflammatory drugs. For example, for some patients with constipation-predominant irritable bowel syndrome (IBS-C), the onset was resulted from long-term use of Chinese and Western medicines such as phenolphthalein tablets, senna granules, and rhubarb soda tablet. Moreover, health care, cosmetics, such as intestinal tea and Paiduyangyan capsule are important factors in this disease [11].

4. Clinical Features

Fan *et al.* [12] reported that, in patients with FD and IBS overlap, postprandial distress syndrome (PDS) group overlap ratio of IBS-C was higher than that of epigastric pain syndrome (EPS) group, while EPS group overlap ratio of IBS-D was higher than that of the PDS group. Another study showed that, when compared with single FD or IBS patients, patients with FD-IBS scored significantly higher in the mental health test than patients with IBS only. Furthermore, the proportion of patients with anxiety and depression in FD-IBS group was higher than that of no overlapping symptoms group [13]. The results indicated that mental conditions of FD-IBS patients were more serious pointing to the notion that the treatment of mental and psychological factors should be strengthened.

5. Pathogenesis

Some studies [14] [15] [16] suggested that the mechanisms of FD-IBS include visceral hypersensitivity, gastrointestinal motility dysfunction, genetic susceptibility, psychiatric comorbidities, post-infection sensitization of gastrointestinal tract, and possibly sensitization of central nervous system (see **Table 1**) [15]. These study indicated that FD and IBS had some similarities in terms of their

Table 1. Levels of evidence for pathophysiological mechanisms common to functional dyspepsia (FD) and irritable bowel syndrome (IBS).

Mechanism	IBS	FD
Visceral hypersensitivity	+++	+++
Upper Gastrointestinal dysmotility	+	+++
Lower Gastrointestinal dysmotility	+++	+
Brain Processing abnormalities	++	?
Genetics	+	+
Psychiatric comorbidities	++	+
Post-infection	++	+
Serotonin Signalling abnormalities	+	+

+++ , strong evidence, numerous clinical studies in substantial agreement; ++, moderate evidence, clinical studies in agreement with preliminary data to be confirmed; +, weak evidence, isolated reports, data to be confirmed; ?, no evidence.

pathophysiology and treatment, Just one is located in the stomach, whereas the other is located in the intestines. In this regard, since FD and IBS have a lot of overlap in symptoms which sometimes are not being completely separated, some scholars advocates the expansion of the symptoms of IBS to upper digestive tract, and even called “one irritable gut” [17].

6. Medical Therapy

Taking into account the similarities of FD and IBS in pathophysiology and pathogenesis, as well as the complexity of FD-IBS in the clinical treatment, attention should be paid to two aspects of the treatment of overlap syndrome. First, to minimize the adverse drug reactions, medications must be simplified. We should strive for using some medicine which may have effect on both FD and IBS, so as to obtain satisfactory efficacy by using the least kind drugs. Secondly, because gastrointestinal motility disorders of FD and IBS may not be consistent, or even the opposite, gastrointestinal motility drug with bidirectional regulative function should be used. It is worth noting that traditional Chinese medicine in this respect shows some advantages. The following are to be described separately from the Western and Chinese medicine treatment.

6.1. Western Medicine Therapy

6.1.1. The Drugs with Effects on Both FD and IBS

1) Acid-Suppressive Drugs

The drugs include H₂ receptor antagonists (H₂-Rb) and proton pump inhibitors (PPI). They can inhibit gastric acid to relieve both the symptoms of FD patients with upper abdominal pain and IBS-D symptoms [18]. For example, the main mechanism of ranitidine in treatment of IBS-D is as follows. In patients with IBS, their intestinal mucosal mast cells are increased, activation and degranulation, and participate in the pathogenesis of IBS [19]. Ranitidine is a potent

histamine H₂ receptor blockers, and may alleviate the symptoms by inhibiting the release of histamine from intestinal mast cells [20]. Moreover, ranitidine acts with related receptors, resulting in reduced gastric acid secretion. By decreasing the secretion of gastric acid, it can not only reduce gastric acid irritation of the gastrointestinal tract slowing down small bowel peristalsis, but also reduce the overall gastrointestinal secretion of sodium and water leading to decreased gastrointestinal contents. Therefore it can effectively reduce stool frequency, and ultimately achieve the goal of diarrhea. Omeprazole may also play a role through anti-secreting effect. Furthermore, the chemical structure of omeprazole is similar to that of metronidazole, hence it can play a similar role through some antibacterial effect [21].

However, because of very strong acid suppressive effect of H₂-Rb and PPI, strong and sustained inhibition of gastric acid may have an impact on digestive function and intestinal microecology, and the longer the impact will be more obvious. And then it may appear adverse reactions such as small intestinal bacterial overgrowth (SIBO), Clostridium difficile-associated diarrhea and microscopic colitis. These may worsen IBS symptoms [22]. Therefore, close monitoring is required at the time of treatment.

2) Probiotics

Probiotics is not only for the treatment of irritable bowel syndrome, but also has the following three advantages. First, probiotics is able to inhibit Helicobacter pylori (H. Pylori) infection. The possible mechanisms include the downregulation of H. Pylori distribution density, secreting bacteriocins and other substances which kill H. Pylori directly, and inhibiting the in vivo immune response [23]. To our knowledge, H. Pylori is one of the important causes of FD. Secondly, probiotics itself can treat FD by relieving symptoms of FD [24]. Thirdly, probiotics can also prevent SIBO and other intestinal microflora disorders which are caused by PPI [25]. Thus the treatment of PPI can be carried out smoothly.

3) Gastrointestinal Motility Regulation Agents

For upper and lower gastrointestinal motility disorders whose motility changes are consistent with the same situation, such as the hypokinesis state of gastrointestinal tract when delayed gastric emptying FD appears simultaneously with IBS-C, or the hyperdynamic state of gastrointestinal tract when accelerating gastric emptying FD occurs with IBS-D, we can use gastrointestinal motility inhibitor or prokinetic drugs which have unidirectional regulative function. For upper and lower gastrointestinal motility disorders whose motility changes are in inconsistency or paradoxical situation, such as delayed gastric emptying FD combining with IBS-D, or accelerating gastric emptying FD combining with C-IBS, as well as FD combining with mixed type IBS (IBS-M), We recommend using gastrointestinal motility drugs which have bidirectional regulating function, such as trimebutine or pinaverium bromide [26] [27] [28] [29]. Moreover, there are few drugs which have inhibitory effect both on stomach and intestine peristalsis, and their adverse reactions are frequently observed. Hence, for FD-IBS patients with hyperdynamic state of gastrointestinal tract, trimebutine or

pinaverium bromide, or gastrointestinal motility inhibitor (effective only for IBS-D) can be used.

4) Antipsychotic Drugs

The pathogenesis of FD and IBS both include psychological abnormality and visceral sensitivity, and mental factors are even more serious when FD and IBS are overlap [13]. Therefore, antidepressants or anti-anxiety medications should be given. The use of those drugs improve the mental and psychological abnormality, increase the pain threshold to relieve upper abdominal or lower abdominal pain, and improve other symptoms of FD and IBS [30]. In addition, when necessary, those drugs can be combined with psychological therapy [31].

5) Gastrointestinal Mucosal Protective Agents

The drugs include glutamine [32] [33], rebamipide [34] [35], teprenone [36], and some others. They have a protective effect on gastrointestinal mucous membrane. Hence, they may improve symptoms of patients with FD-IBS. They can be used as appropriate.

6.1.2. The Drugs for FD or IBS

The drugs with specified properties, are used separately for FD or IBS. We should use them mainly in the condition when the symptoms of FD and IBS are serious or when the effect of drugs for both FD and IBS is poor. That is to say, according to the severity of FD or IBS, or according to the treatment effect, we should adjust or strengthen the use of drugs from a different focus on the basis of the above treatment. The principle of specific medication is as follows. If the patient's condition is serious, we could use these drugs immediately; and if the patient is not seriously ill, then we could decide whether to use these drugs based on efficacy.

1) Treatment of FD

The treatment of FD includes H. Pylori eradication, digestive enzymes, and gastric mucosal protective agents [37] [38].

2) Treatment of IBS

According to some recent reviews [39] [40], we can treat IBS as follows :for IBS-D, the drugs mainly include antidiarrheals, non-absorbable antibiotic, antispasmodics, and 5-HT₃ receptor antagonists; for IBS-C, the drugs mainly include fiber supplements ,laxative agents, 5-HT₄ receptor agonists, and prosecretory agents; and for IBS-M, the medications has been described previously.

Western medicine for the treatment of overlap syndrome of FD and IBS could be summarised as **Figure 1**.

6.2. Traditional Chinese Medicine Treatments

In view of the complexity in the treatment of FD-IBS, the vast majority of gastrointestinal motility drugs having unidirectional regulative effect, and only a few drugs (such as trimebutine and pinaverium bromide) having a bi-directional effect, we must try new approaches of treatment. Accordingly, traditional Chinese medicines have two features. First, there is a treatment method, namely homo

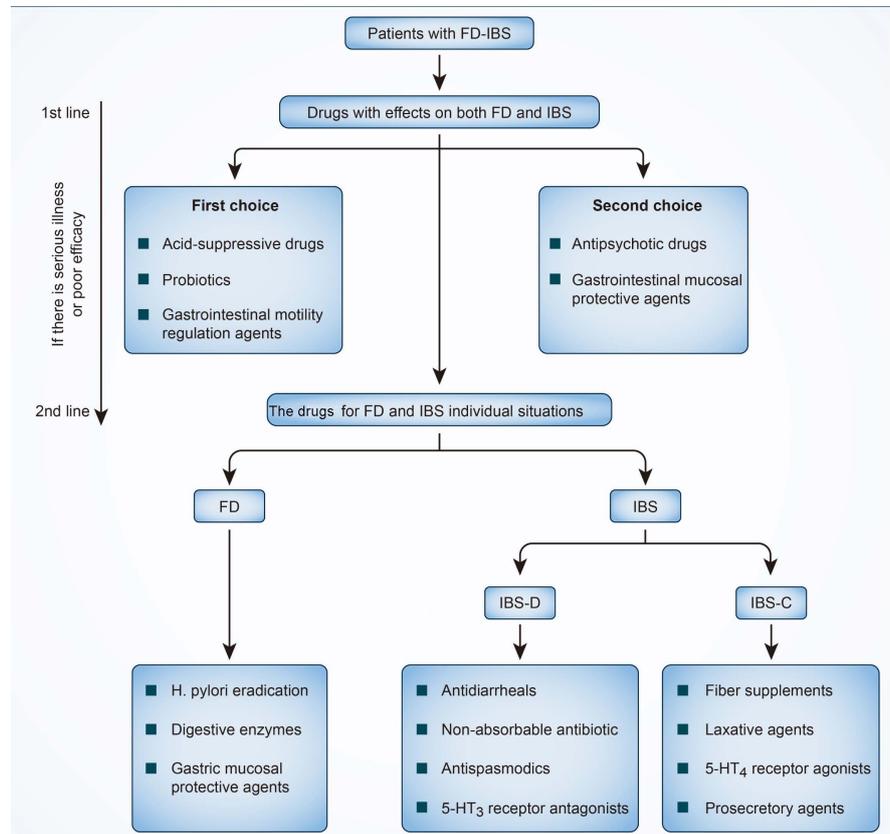


Figure 1. Therapeutic strategies of western medicine for FD-IBS.

therapy for heteropathy [41], which means treating different diseases with same drugs. Secondly, many Chinese herbs have a bidirectional regulative effect [42]. That is to say, according to different body state and/or different ways of medications, the same Chinese medicine and its components may play different roles or even contradictory roles. Therefore, the new treatment methods of FD-IBS can be tried from traditional Chinese medicine or integrated traditional Chinese and western medicines.

It is widely accepted that the basic pathogenesis of both FD and IBS is related to deficiency-weakness of spleen-Qi, and Liver-Qi stagnation and spleen. The only difference is that FD is located in the stomach, whereas IBS is located in the intestines [43]. The same or similar pathogenesis provides a theoretical basis for the occurrence of FD-IBS, and guide the clinicians to find the basic principles which is soothing the liver and strengthening the spleen. On the basis of the above basic principles, and through flexible medications, we could modify drugs according to the disease or symptoms [44] [45], avoiding the difficulty of taking into account the upper and lower digestive tract when lacking gastrointestinal motility drugs of bi-directional regulative function. If these can be done, we can, to a certain extent, achieve a balance between the upper and lower digestive tract and the optimal effects.

7. Conclusion

The complexity of FD-IBS symptoms and the similarity of FD and IBS in patho-

genesis, determines that their treatment have many unique aspects. We should simplify the medications, flexibly use gastrointestinal motility regulators, follow the principle of individualization, and give full play to the advantages of traditional Chinese medicine, benefitting the patient.

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