Pathophysiologic Findings of Irritable Bowel Syndrome in China

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The mechanism of irritable bowel syndrome (IBS) is still incompletely understood in the world although large amount of investigations have been carried out on it. There are many studies on the pathophysiology of IBS in China, which has huge amount of population suffering from IBS with special ethnicity and culture, including Mainland China, Hong Kong and Taiwan. We collected the literatures to show the results and discuss whether there were any differences in the pathophysiologic findings between China and other countries, whether there were any differences among different subtypes and how the pathophysiology correlated with the manifestations of patients. Gene polymorphism, disturbances of gastrointestinal motility, visceral hypersensitivity, intestinal infection and inflammation, psychological disturbances, food hypersensitivity and intolerance, and altered gut microflora were reviewed in this paper. Some conflicting outcomes between China and other countries were noted although most of them were similar.

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Key Words
China; Irritable bowel syndrome; Pathophysiology

Introduction

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder (FGID) mainly manifested as abdominal pain and correlated changed bowel habits. The chief bowel pattern determines the classification of IBS subtypes, which was set through Rome III criteria in the recent years, including constipation predominant IBS (IBS-C), diarrhea predominant IBS (IBS-D), mixed IBS (IBS-M) and unsubtyped IBS (IBS-U). Since IBS can cause substantial decline in the quality of life for the patients and accounts for a great amount of hospital visits and economic burden for society, many investigations have been done on the mechanisms of pathophysiology for IBS. The commonly stated mechanisms include genetic factors, abnormal gastrointestinal (GI) motility, visceral hypersensitivity, psychological disturbances, intestinal inflammation and so on. However, the results of these investigations have often been conflicting and no specific pathophysiology has been demonstrated to be certain for IBS.

The prevalence of IBS is reported to be 2.9%-15.6% in Asian countries nowadays, which is nearly comparable to that in the Western countries. China is a great country with large amount of population, specific ethnicity and custom in Asia. IBS has been found to be common for Chinese in these years and many studies about IBS have been carried out recently. The results of these in-
vestigations on pathophysiology and differences in the results between China and other countries have not been comprehensively reported since most of the works in China were published in Chinese journals. To show the results from China and find out the answer, we collected the manuscripts on pathophysiology of IBS by searching for papers in Chinese databases and PubMed to comprise the studies from Mainland China, Hong Kong and Taiwan from 1989 to 2011. In this review, the investigations about pathophysiology in China would be shown from the aspects of genetic factors, disturbances of GI motility, visceral hypersensitivity, intestinal infection and inflammation, psychological disturbances, food hypersensitivity and intolerance, and altered gut microflora, which have been frequently reported. Furthermore, we intended to find out if there were any differences for mechanisms among different subtypes and how the pathophysiology correlated to the manifestations of IBS in China.

Gene Polymorphism

Lots of familial aggregation studies and twin studies have suggested that genetic factors perhaps influenced the susceptibility of IBS although the reports were somewhat conflicting. Up to now, the genes associated with serotonin, inflammation, adrenergic, mucosal barrier, and psychology which may play a role in IBS have been widely examined. In China, the investigations about gene polymorphism are extremely limited and most of them are involved in serotonin and inflammation. We tried to find out if there were any differences in the results of gene polymorphism between China and other countries. The main findings of the investigations from China and other countries were shown in Table 1.

Serotonin transporter (SERT) is a protein which reuptakes 5-hydroxytryptamine (5-HT) in synaptic cleft and then reduces the function of 5-HT such as inducing urgency, cramps, diarrhea and vomiting. The lower expression of SERT will indicate higher level of 5-HT, which may be associated with bowel symptoms in IBS patients. The 2 well investigated polymorphism regions are variable number tandem repeat (VNTR) and serotonin transporter linked polymorphic region (5-HTTLPR).

For the 5-HTTLPR region, there were different associations reported between the genotypes and various subtypes of IBS in different studies. But none of the investigations has found correlations between the genotypes and IBS overall which had not been categorized except for the study by Park. A meta-analysis comprising studies involving Caucasians or Asians also concluded that there was no association between 5-HTTLPR and IBS overall. The transcriptional activity of long (L) allele is apparently greater than short (S) allele in 5-HTTLPR for SERT, then L/L genotype has higher transcriptional efficacy than L/S and S/S genotypes. All of the studies about 5-HTTLPR in China showed that IBS-C patients had significantly higher frequency of L allele or L/L genotype than healthy individuals and patients of other subtypes. Besides, Zhang and Lin also exhibited that IBS-D patients had higher frequency of S allele and S/S genotype than healthy controls and patients of other subtypes. The outcomes of investigations from other countries exhibited some discordance. Lee et al found no correlation between the polymorphism of 5-HTTLPR and overall or each subtype of IBS in Korea. While another study by Park et al which was also from Korea showed that S/S genotype was more common in patients with IBS than healthy controls, especially in IBS-D subtype. The result of investigation by Kim et al from US was the same with Lee et al. Yeo et al found the frequency of S/S genotype to be higher in female IBS-D patients than healthy controls in US. However, the investigations from Turkey by Pata et al and from India by Sikander et al both found the contradictory result that S/S genotype was more common in IBS-C than controls. Niesler et al also showed that male IBS-D patients had lower frequency of S/S genotype than controls in UK. Therefore, from the various results above, we could not obtain a firm conclusion about the relationship between polymorphism of 5-HTTLPR and IBS subtypes. But the results of investigations from China were almost the same for L/L genotype associated with 5-HTTLPR almost which was contradictory to the investigations by Pata and Sikander et al. In addition, the explanations for the conflicting phenomenon by them were also different. Wang et al speculated that the L/L genotype for high expression of SERT caused 5-HT reuptake before the effects of 5-HT were shown and then attenuated the motility and secretion of intestine to cause IBS-C. However, Pata et al considered the S/S genotype responding to the low expression of SERT which might have caused the aggregation of 5-HT and then downregulated the 5-HT receptors, therefore led to IBS-C.

Racial difference might be one of the reasons for the variations of these results since the distribution of 5-HTTLPR gene polymorphism varied among different races and regions. Homozygous for the S allele in Asians (64% of patients) was reported to be markedly higher than that in Caucasians (22% of patients) in a meta-analysis. Xia J et al investigated the polymorphism regions of 5-HTTLPR for healthy individuals of Han Chinese and found the frequencies of S allele and S/S genotype to be pre-