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Research Progress of IBD Combined with Psychological Disorders

Jiaxin Yan[1,a], Yaping Cui[2,b,*]

[1]*Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712046, China*
[2]*The Second Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712046, China*
[a]*yykl999555@126.com*, [b]*1441164138@qq.com*
[*]*Corresponding author*

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Abstract: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is a chronic inflammatory disease mainly involving the gastrointestinal tract. The main clinical manifestations are acute pain, diarrhea and hematochezia. At the same time, IBD patients are often accompanied by psychological disorders such as anxiety and depression. IBD combined with psychological disorders not only aggravates the economic burden of patients, but also seriously affects the daily life of patients and brings great pain to patients. In recent years, there have been more and more researches on IBD combined with mental disorders. This article reviews the research status of the relationship between IBD and mental disorders, the mechanism and psychological intervention of IBD in recent years, so as to provide theoretical basis for the psychological treatment of IBD patients.

1. Introduction

Inflammatory bowel disease (IBD) is a chronic disease characterized by inflammation of the gastrointestinal tract, which is prone to recurrent attacks [1]. IBD includes ulcerative colitis and Crohn's disease [2], as shown in Figure 1. The clinical manifestations are often acute pain, diarrhea and bloody stool, which seriously affect the quality of life of patients [3]. The incidence of IBD is high in developed countries such as Europe and America, about 2‰. In Asia and Latin America, the incidence is low, about 0.1‰~1‰. The incidence of IBD in China is about 2.0/100 000. However, with the development of China's economy, the incidence of IBD has been increasing year by year, and the incidence has reached 11.6/100 000, which brings serious impact on the quality of life and social and economic benefits of patients [4]. IBD seriously affects the daily life of patients, which may hinder the career ideal, increase the economic burden, lead to social discrimination and damage the quality of life of patients [1]. Currently, the main treatment options for IBD include drugs (aminosalicylic acids, glucocorticoids, immunosuppressants, and biologics) and surgery, which is typically required in 70% to 80% of patients with Crohn's disease and 30% of patients with ulcerative colitis [1]. With the continuous progress of IBD research, some scholars believe that psychological factors have an impact on the onset, recurrence, and progression of IBD. At the same time, the symptoms of IBD also affect the mental health of patients [5].

Figure 1: Crohn's disease and ulcerative colitis

2. IBD combined with psychological disorders

2.1. Anxiety and depression

Many epidemiological studies have confirmed that the incidence of psychological complications in IBD is high. At the same time, psychological disorders can also aggravates the disease process of IBD and reduce the health quality of life (HRQOL) [6]. IBD is often associated with psychological disorders, such as anxiety and depression. S.Zhang conducted a statistical analysis of 159 IBD patients and found that compared with the healthy control group, the IBD group was more likely to have anxiety and depression. The average score of anxiety in IBD group was 41.88±7.05, and the incidence rate was 22.64%. The average score of depression was 49.96±9.73, and the incidence was 43.41%. There were 63 patients with anxiety or depression in IBD group, and the overall incidence rate was 39.62% [7]. One study found that 35% of 143 IBD patients were complicated with anxiety, 23.8% with depression, and 18.9% with both. The incidence of depression in UC group was significantly higher than that in CD group [8]. Y.Li et al. found that among 358 IBD patients, the proportion of anxiety and depression was 19.55% and 27.37%, respectively [9]. Yi Wang conducted a control study on 130 IBD patients and 84 healthy outpatients, and found that the incidence of anxiety and depression in IBD patients was significantly higher than that in controls, which confirmed that it can cause a certain degree of negative emotions [10]. Aolan Huang et al. investigated 200 patients with IBD and found that the psychological resilience of IBD patients was at a medium to low level, the quality of life was low, and the incidence of anxiety and depression was high [11]. Qin Cao found that the incidence of anxiety and depression in IBD patients was 97.4% and 91%, respectively. The high prevalence of anxiety and depression may be related to the severity of the disease and the measurement standard of anxiety and depression scale. In addition, disease activity is an important risk factor for anxiety and depressive symptoms in IBD patients [12]. W.Zhang analyzed the correlation between mental status and health education of 35 patients with inflammatory bowel disease and found that the incidence of anxiety, depression and somatization symptoms in patients with inflammatory bowel disease was high, indicating that the mental health of patients was not good, and health education based on patients' needs could significantly improve the mental health of patients [13]. In addition, there are also differences in anxiety and depression between UC and CD patients: the incidence of anxiety and depression in UC patients is higher than that in CD patients [14].

2.2. Psychosomatic symptoms

In addition to anxiety and depression, psychological stress can cause a range of somatic symptoms such as sleep disturbances, fatigue. Xu Zhang studied 216 IBD patients and found that only 61% of them had a normal level of stress. 40.7% of the patients had different degrees of anxiety. 46.3%

patients had poor sleep quality [15]. Xiangdian Bu investigated 127 IBD patients and found that UC and CD patients with anxiety or depression had sleep disorders, and the quality of life of these patients was not high [16]. Hui Liu et al. conducted a cross-sectional study on 164 IBD patients. The results showed that IBD patients had a high level of perceived stress, and sleep quality, self-efficacy, coping style and mental state were the main factors affecting the level of perceived stress of patients [17]. Sha Li et al. found that the total score of fatigue in IBD patients was (52.57 ±12.68), among which the physiological fatigue dimension scored the highest. In short, fatigue is a multi-dimensional symptom, and most IBD patients are plagued by fatigue symptoms [18]. Haiyuan Huang et al. also found that the quality of life and fatigue of patients with inflammatory bowel disease were at a moderate level, and the quality of life of patients with inflammatory bowel disease was negatively correlated with fatigue. The more severe the fatigue, the lower the quality of life of patients [19].

2.3. Sources of psychological stress

Firstly, due to the lack of science popularization of IBD in China, patients have insufficient understanding of the disease, which leads to patients missing the best treatment time and delaying the disease, which is more difficult for patients to accept. Secondly, traditional Chinese thinking shows that psychological problems are a bad disease, so the disease shame makes patients unwilling to reveal their true thoughts, and lack of correct methods to relieve bad emotions and stress management, which directly leads to negative emotions and affects their quality of life [11]. In addition, recurrent episodes of incontinence, cancer, surgery and IBD increase the rate of disability, increase the stigma of patients, and patients are prone to anxiety and depression, and some patients even feel hopeless [20].

3. The mechanism of IBD combined with psychological stress

3.1. Inflammation and immune response

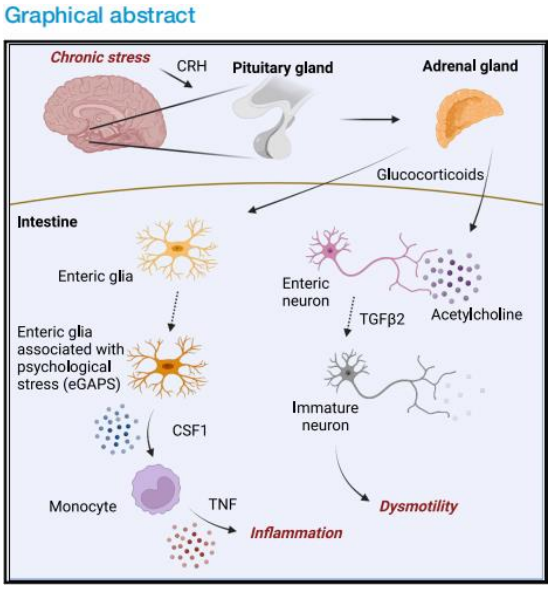

Figure 2: Psychological stress affects the mechanism of intestinal inflammation through the enteric nervous system (ENS)

Studies have shown that the progression of depressive symptoms in patients with depression is related to the level of inflammation, which is manifested as the increased expression of cytokines such as interleukin (IL)-1, Il-1β, IL-6, IL-8, TNF-α, interferon-γ (IFN-γ), and macrophage

inflammatory protein-1β (MIP-1β) in peripheral blood [21]. At the university of Pennsylvania microbiologist Christoph Thaiss recent studies have found that Psychological stress drives the generation of intestinal glial cell subsets through glucocorticoids, which promote monocyte aggregation by secreting CSF1, and monocytes secrete TNF to promote inflammatory response [22], as shown in Figure 2.

3.2. Brain-gut axis

Mental disorders are involved in the pathophysiological basis of IBD, which may be related to the brain-gut axis. As a continuous stress, mental disorders affect the brain-gut axis, activate the central nervous system, stimulate the HPA axis, stimulate the sympathetic nervous system, reduce the vagal tone, promote the secretion of glucocorticoids, epinephrine, norepinephrine and other hormones, and cause visceral hypersensitivity by activating mast cells, releasing inflammatory mediators, inducing excessive immune responses in the intestine. Increase the intestinal inflammatory reaction [23]. L.Jiang's research found that Locus coeruleus (LC) is involved in the regulation of stress: Green PRV was injected into the proximal colon of mice, and the results showed that LC also expressed the virus significantly. LC released norepinephrine in the whole central nervous system, indicating that there is a structural connection between this brain region and the colon and it is involved in the regulation of the organism's vigilance and anxiety [24].

3.3. Gut microbiota

Gut microbiota plays a key role in the intestinal environment. Studies have demonstrated the communication pathways between gut microbiota and the brain, including the vagus nerve, intestinal hormone signaling, immune system, tryptophan metabolism, and short-chain fatty acid metabolism [25]. Abundant evidence has shown that gut microbiota plays a corresponding role in neuropsychiatric diseases such as depression and anxiety, and is also one of the driving forces of these diseases. The pathways of intestinal flora imbalance causing psychological disorders in IBD mainly include the production of immune mediators, activation of vagus nerve, short-chain fatty acid (SCFA) and tryptophan metabolism [6]. By sequencing the V4-V5 region fragment of 16S rRNA gene in the feces of 23 depression patients and 31 healthy controls, it was found that there were differences in the composition of gut microbiota between the first-episode depression patients and healthy people. There was a significant correlation between the diversity of gut microbiota and depressive symptoms in the depression group, and there was a significant positive correlation between the relative abundance of desulfurizing Vibrio and depressive symptoms [26]. A study from Zhengzhou University found that patients with first-episode depression have a decrease in the content of a variety of intestinal flora and an increase in the levels of a variety of inflammatory cytokines, and there is a correlation between the content of intestinal flora and inflammatory cytokines. The lower the content of Bifidobacterium, the higher the TNF-α level, the lower the content of Escherichia coli, the higher the IL-6 level, and the lower the content of Lactobacillus, the higher the IL-2 level. The lower the content of Lactobacillus, the more severe the depressive symptoms [27].

4. Psychological intervention for IBD

4.1. Antidepressants

Antidepressants for IBD patients mainly include tricyclic antidepressants (TCAs) and serotonin reuptake inhibitors (SSRIs), which are suitable for patients with mild to moderate depression and anxiety. Many animal experiments and some clinical trials show that drugs antidepressant treatment

at the same time of improving mood may improve patients with IBD intestinal symptoms, even changes disease progression and reduces recurrence [7].

4.2. Psychological intervention

60 IBD patients were treated with structural psychological intervention. The results showed that the quality of life score of the patients after structural psychological intervention was significantly improved than that of the control group, indicating that the quality of life of the patients had been improved. The reasons were considered as the participation and spiritual support of the patient's family members relieved the patient's anxiety and depression, sublimated the emotional function, and accompanied by the improvement of intestinal function and systemic symptoms. Finally, the patient successfully returned to society, which further enhanced the confidence and thus improved the quality of life [28]. A total of 87 IBD patients were treated with conventional combined tele-care intervention. It was found that conventional combined tele-care intervention could effectively reduce patients' negative emotions, relieve patients' psychological pressure and improve their quality of life. Remote care intervention is a mobile device-based mode of dynamic and real-time management of patients, which is more effective in combination with conventional treatment [29]. A meta-analysis found that mindfulness-based intervention training can improve the anxiety and depression levels of patients with inflammatory bowel disease in the short term [30]. Mindfulness intervention, known as the "third wave of behavioral and cognitive therapy", has shown some effects in reducing stress levels and improving quality of life [31]. Psychological intervention based on written expression was carried out in 98 patients with IBD. It was found that psychological intervention based on written expression in the treatment of IBD patients could effectively help patients relieve negative emotions, guide them to form positive psychology and change their coping styles [32]. After 4 weeks of PPI based on written expression, compared with the control group, the hope and optimism levels of patients in the intervention group were significantly improved. After 8 weeks of intervention, the hope, optimism and subjective well-being levels of patients in the intervention group were higher than those in the control group. PPI based on written expression is helpful to improve the positive psychological status of IBD patients [33].

4.3. Music therapy

B.Li conducted a randomized controlled trial on 56 patients with inflammatory bowel disease and found that: Music therapy not only improved patients' fatigue symptoms, but also reduced their anxiety and depression levels. Music therapy is a highly feasible and effective tool to reduce the fatigue, anxiety and depression of patients with inflammatory bowel disease, relieve the negative emotions of patients with inflammatory bowel disease, provide a guarantee for the recovery or improvement of mental and physical health of patients with inflammatory bowel disease, and serve as a reference for the relief of other disease-related negative emotions [34].

4.4. Health education

Y.Zhu et al. investigated 106 IBD patients and found that the overall level of disease-related knowledge awareness of IBD patients was low, and they had a high demand for drug, non-drug treatment knowledge and complications knowledge [35]. Some studies have found that the content of health education needs includes drug, diet, nasointestinal tube management and related knowledge of complications. In the form of health education, patients prefer to learn through online and offline combined methods, and hope to be guided by different professional medical staff [36]. The popularization of mental health knowledge has a positive role in promoting IBD patients to establish

a correct view of the disease. Early intervention can even prevent the formation of mental and psychological disorders in IBD patients [37]. A study of 80 IBD patients found that the application of IBD TCM health education micro-course can significantly improve the TCM health literacy of IBD patients, promote patients to do disease self-management, reduce the incidence of complications, improve the quality of life, relieve patients' anxiety and depression, and increase patient satisfaction [38].

In conclusion, IBD, as a chronic inflammatory disease, is often combined with psychological disorders, which seriously affects the life and work of patients. IBD patients with psychological disorders are prone to symptoms of anxiety, depression, and even sleep disorders and fatigue. The mechanism of anxiety and depression in IBD patients is mainly related to inflammation and immune response, brain-gut axis and intestinal flora. In addition, there are many factors affecting the occurrence of anxiety and depression in IBD patients. However, few IBD patients receive psychotherapy in clinical practice, which may be related to patients' stigma or clinicians' neglect of psychotherapy. Although there is currently no consensus on the treatment of mood disorders in IBD patients, the treatment of psychological symptoms may have a positive impact on IBD patients, and further clinical intervention trials are needed in the future to explore whether psychological treatment can affect the prognosis of IBD patients. However, existing studies have found that psychological treatment is not only beneficial to improve the psychological and intestinal symptoms of IBD patients, promote the recovery of the disease, but also reduce the incidence of complications and reduce the recurrence rate. Therefore, in the treatment of IBD, it is necessary to improve the attention of clinicians and patients to mental health, and comprehensive treatment focusing on psychology should become a new trend in the treatment of IBD in the future.

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