Chinese Consensus on Psychosomatic Gastroenterological Clinical Practice

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Abstract :

Background and Aims: In the past decades, the changes of social running and human life styles were accelerating in mainland of China. Consistent with this, psychosomatic gastrointestinal diseases pose great challenges in clinical diagnosis and treatment. Unfortunately, most of the gastroenterologists know very little about psychosomatics. The previous version of the Consensus (2015) has greatly improved the ability of many physicians in management of psycho-gastrointestinal diseases. The objectives of this version were to integrate the important advance of psychosomatic gastroenterology and the updated viewpoints of Chinese experts, and to provide a relevant guide on this poorly understood condition for gastroenterologists working in mainland China.Methods: Hundreds of outstanding gastroenterologists from the Chinese mainland (all of whom are members of the Chinese Digestive Psychosomatic Union) gathered to discuss the viewpoints or experiences that are used to address difficult clinical challenges with the “socio-psycho-biological” holistic medical model in the clinical practice of gastroenterology. The consensus condenses the progress of the pathophysiological mechanisms of gastrointestinal diseases and psychosomatic diseases (in particular, the gut-brain interactions). Conclusions: This consensus includes 28 statements, along with the results of the vote for the statement.

Keywords:

Psychosomatics; gastroenterology; functional gastrointestinal diseases, refractory gastrointestinal disease; Chinese consensus; Chinese Digestive Psychosomatic Union.

Introduction

Chinese Consensus on Psychosomatic Gastroenterological Clinical Practice (Chinese edition, published in August 2015) is the first guideline in worldwide specialized for gastroenterologists dealing with digestive psychosomatic issues[1]. Based on the Consensus, the clinical skills of many gastroenterologists have been improved and thus numerous patients with digestive psychosomatic disorders have been benefited. To sum up, it has played an active role in improving the management of digestive psychosomatic diseases in the mainland of China. In the last three years, the social and clinic situations in China have

changed a lot, including ①The knowledge of gastroenterologists about digestive psychosomatic diseases progressed tremendously.②Chinese society and economy have witnessed great development. Accordingly, people's life behavior, interpersonal communication, and business model have changed dramatically. In this background, some clinical characters of digestive psychosomatic diseases also changed. Moreover, the rapid development of internet information technology has also changed the way by which doctors communicate with patients.③The government-driven reform of the medical system imposes more challenges to the clinical practice of gastroenterologists.④Since its foundation, the Chinese Digestive Psychosomatic Union (CDPU) regularly update the textbooks for continuing medical education, and update of this consensus is an important task. In response to above-mentioned reasons, update to the Consensus is necessary. This Consensus was written by experts of CDPU based on sufficient discussion and will be published exclusively in the inaugural issue of Psychosomatic Gastroenterology, the official journal of CDPU.

This Consensus was aimed to renew theory system of psychosomatic gastroenterology and to provide suggestions about how to comprehensively utilize therapy (medication particularly) of psychiatry, psychology, and psychosomatics as an essential complement to the management of gastrointestinal diseases.

This Consensus consists of three parts and twenty-eight Consensus statements. The strength of recommendations, level of evidence and experts' opinions on each Consensus statement are also included.

Part 1. The conception and tasks of psychosomatic gastroenterology

Consensus statement 1

Psychosomatic gastroenterology is a practical medicine to diagnose and treat digestive diseases based on theory and guidelines of psychosomatic medicine, which aims to improve the curative effect of these diseases. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Completely agree (90.3%)
B. Agree with some reservation (8.1%)
C. Disagree (1.6%)

Explanation:

At present, gastroenterological clinical practice based on biomedical model encounters formidable challenges. They include:① Refractory functional gastrointestinal diseases (FGIDs). According to traditional biomedical model, gastrointestinal motility dysfunction and visceral hypersensitivity are two leading mechanisms involved in the pathogenesis of FGIDs. However, medications targeting these mechanisms did not work satisfactorily. Most recently, Functional Gastrointestinal Disorders Rome Ⅳ Diagnostic Criteria updated the definition of gut brain interaction disorders, and proposed evaluation of multidimensional clinical profile (MDCP) from the perspective

of bio-psycho-social model. However, the relationship between FGIDs and mental health as well as guidelines of efficacious treatment algorithm were still not clearly addressed. In addition, MDCP evaluation proposed by Rome Ⅳ did not include enough vast disease spectrum[2].②As for those organic diseases with complex etiology and pathogenesis, e.g., inflammatory bowel diseases (in particular Crohn's disease)[3], current biomedical model-based pathogenesis-oriented therapy is confronted with a bottleneck.③How to deal with the sub-health status of the digestive system, including asymptomatic abnormal biological indicators found in routine health examination, healthcare behavior lacking scientific basis (including dietary behavior), over-treatment (invasive intervention for condition beyond indication, medication, etc.) or over-interpretion (e.g.,chronic slight inflammation and metaplasia of gastrointestinal mucosa) for certain clinical status. The reason for above-mentioned challenges is that current diagnostics and therapy fail to intervene pathophysiological processes of these sub-clinical statuses. Therefore, new diagnostic theory and practical skills, which will cover multifaceted factors of society, natural environment, cognition, behavioristics, physiology, and healthcare, are in urgent need.

Consensus statement 2

Psychosomatic gastroenterology emphasizes to comprehensively analyze and interpret pathophysiological status, natural environment, and the social situation concerning gastrointestinal disorders, and aims to optimize treatment strategies in an individualized manner. It organically integrated the new advances in basic and clinical researches on psychiatry, psychology, and psychosomatics. It aims to improve treatment of digestive diseases with disciplines of holistic medicine. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Completely agree (78.2%)

B. Agree with some reservation (11.7%)

C. Disagree (10.1%)

Explanation:

To improve practical skills in the treatment of digestive diseases, gastroenterologists should try to acknowledge the new advances in basic and clinical researches in this area. These include advances in mechanisms of esophageal motility dysfunction and anti-gastroesophageal reflux, the regulatory mechanism of gastric acid secretion, functional associations of stomach-duodenum-sphincter of Oddi, the regulatory mechanism of intestinal function, gut microbiota, gastrointestinal immune response, and neural-humoral regulatory mechanisms of above-mentioned processes[2]. A gastroenterologist should comprehensively consider all the probable factors related to the natural and social environment in which patients live and accurately establish the treatment strategies.

Consensus statement 3

At present, clinical issues that need to be solved based on the disciplines of psychosomatic gastroenterology include:①Certain functional or organic digestive diseases refractory to current biomedical model-based treatment algorithm;② Digestive diseases secondary to psychiatric, psychological and cognitive disorders;③ Mental health disorders resultant from digestive diseases;④ Co-morbidity of digestive diseases and mental health disorders;⑤ Digestive disorders related to society, natural environment and healthcare behavior.

The strength of recommendations:

strong. Level of evidence: medium. Vote:

A. Completely agree (78.7%)

B. Agree with some reservation (19.1%)

C. Disagree (2.1%)

Explanation:

①Refractory digestive diseases have complicated etiology and pathogenesis. The unsatisfactory effect of current therapy is mainly attributable to failure of targeting the pivotal pathogenic mechanisms. The major goal of clinical practice based on psychosomatic gastroenterology is to intervene the key pathophysiological processes.②Digestive diseases secondary to psychiatric, psychological and cognitive disorders belong to the scope of somatization symptoms and related disorders (Diagnostic and Statistical Manual of Mental Disorders, Fifth edition， DSM-5, published in 2013) [4,5]. According to present laws and regulations in China, doctors should recommend patients with these digestive diseases to visit psychiatric outpatient or hold a consultation with psychiatric specialists[6].③ In the biomedical model based treatment of mental health disorders resultant from digestive diseases, special attention should be paid to alleviate the psychiatrical and psychological, cognitive and behavioral complications and to prevent these complications aggravating the pre-existing mental problems.④In the treatment of co-morbidity of digestive diseases and mental health disorders, a gastroenterologist should comprehensively think over psychiatrical and psychological, cognitive, and behavioral abnormality as well as somatic disorders. Improvement of patients' quality of life and medical experience is a major therapeutic goal.⑤The digestive disorders related to society, natural environment and healthcare behavior involve a large scale of the disease spectrum. Treatment of these diseases should emphasize on education of appropriate healthcare, including increasing adaption ability to society and stressors, easing improper perception of diseases such as fear of disease, hypochondriasis and stigma, etc. Improvement of social and family support system should also be emphasized.

Part 2. Understanding of etiology and pathogenesis of digestive diseases based on psychosomatic gastroenterology

Consensus statement 4 Society- and natural environment-related factors contribute to the pathogenesis of digestive diseases, which should be emphasized in clinical practice. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Completely agree (89.4%)

B. Agree with some reservation (10.6%)

C. Disagree (0.0%)

Explanation:

Social factors include organization, communication, moral rules, laws and regulations, public medium and customs, etc. Social factors have a role in the development, progression, and outcome of digestive diseases through the impact on the degree of stress, biological rhythm, the perception of health status and healthcare. The natural environment refers to an environment composed of water and soil, territory, climate and other things of nature. The natural environmental factors have a non negligible influence on human's physical condition. It could affect the patients' awareness of the natural environment, psychological and behavioral responses to the environmental changes. As well, it could also affect the physical and chemical properties, nutritional ingredients and microbiota composition of food. The above-mentioned possible influences of the natural environmental factors may affect the development, progression, and outcome of digestive diseases. The social and natural environment in China are experiencing rapid changing. This should be paid special attention in clinical practice based on psychosomatic gastroenterology[7].

Consensus statement 5

Personality, cognition, and behaviors exert a profound influence on the development, progression and outcome of digestive diseases, especially on patients' adherence to treatment. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Completely agree (69.8%)

B. Agree with some reservation (21.2%)

C. Disagree (9.0%)

Explanation:

Personality, derived from Greek Persona, refers to the characteristics of a human to be distinct from other people, including peculiarity, uniformity, and functionality, etc. It's a subject with self-awareness and self-control and has the functionality of feeling, emotion, and will. It can exist away from the human body or material condition but independently exist in psychological dimension. Personality could exert influences on occurrence, progression, and outcome of digestive diseases through health-related cognition and behaviors. Cognition refers to a process of extrinsic information processing and subsequent conversion to mental activity, which affects human's behaviors. It consists of feeling, sense, memory, thinking, imagination, and language, etc. Cognitive bias could affect the occurrence and outcome of digestive diseases through improper perception of health status and characters of diseases[7].

Consensus statement 6

Psychological and emotional changes contribute to visceral and somatic hypersensitivity to noxious stimuli via centrally driven mechanisms. The strength of recommendations: strong.

Level of evidence: strong.

Vote:

A. Completely agree (83.2%)

B. Agree with some reservation (15.8%)

C. C. Disagree (1.0%)

Explanation:

Functional activation of brain areas in control of emotion (such as cingulate cortex, insula, amygdaloid nucleus, and hippocampus, etc.) could inhibit the analgesic function of certain midbrain nucleus and thus facilitate the regulatory effect of descending neuronal pathways on visceral and somatic pain responses through various mechanisms[8].

Consensus statement 7

The psychological and emotional disorders affect gastrointestinal function through disturbing the neuro endocrine function. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Completely agree (83.5%)

B. Agree with some reservation (11.4%)

C. Disagree (5.1%)

Explanation:

Cingulate cortex, insula, amygdaloid nucleus, and hippocampus are functionally associated with brain nucleus involving modulation of visceral pain (such as nucleus ambiguous and dorsal nucleus of vagal nerve). Therefore, excitability changes of psychology and emotion-related cortex, via affecting the function of these nuclei, can cause functional disturbance or dysfunction of sympathetic and parasympathetic nervous system (including vagus nerve), and thus lead to the abnormal gastrointestinal functions (including motility, secretion, and sensation). Moreover, these excitability changes can also influence the hypothalamic-pituitary-adrenal axis (HPA) and thus lead to changes in gastrointestinal functions[9]. Clinical evidence demonstrates that patients with functional dyspepsia (FD) or irritable bowel syndrome (IBS) exhibit abnormal functional activation in brain areas such as anterior cingulate cortex (ACC), insula, amygdaloid nucleus, and hippocampus, etc [8].

Consensus statement 8

Psychological and emotional factors play roles in the occurrence and outcome of digestive diseases through modulation of inflammatory response. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Completely agree (68.6%)

B. Agree with some reservation (19.5%)

C. Disagree (11.9%)

Explanation:

Changes in the psychology and emotion can affect the anti-infectious and anti-inflammatory mechanisms via neuro-endocrine disturbance[10], and thus closely relate to the occurrence and outcome of gut mucosal inflammation.

Consensus statement 9

The psychological and emotional disorders could affect the occurrence of gastrointestinal benign and malignant tumors through disturbing immunologic surveillance and immune killing function. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Completely agree (69.7%)

B. Agree with some reservation (21.6%)

C. Disagree (8.7%)

Explanation:

The results of basic and clinical researches indicate that tumor incidence is significantly higher in depressed and anxious population compared with the healthy controls. Meanwhile, abnormal anti-tumor function of the immune system is also more frequent in this population[11].

Consensus statement 10

The normal functional status of the digestive tract and the luminal environment (physical and biological) is important for mental health and the normal function of other organ systems. The strength of recommendations: strong.

Level of evidence: medium.

Voting results:

A. Fully agree (65.3%)

B. Accept with reservation (28.6%)

C. Disagree (6.1%)

Description:

Disorders of the gastrointestinal functions cause mental, cognitive, and behavioral abnormalities through the following mechanisms:①Symptoms of digestive diseases, such as painful experiences, trigger inappropriate cognitive and behavioral responses;②Changes in physical, chemical, and micro ecological factors, particularly in the metabolites of luminal nutrients and gut microbiota, could trigger the changes in systemic organ functions via neuro-endocrine pathways. The intervention of the dysregulated “gut-brain” pathway is a key point in the clinical practice based on psychosomatic gastroenterology[12].

Consensus statement 11

Physicians should pay attention to the new basic and clinical advances related to digestive diseases. These advances may be helpful in clinical practice based on psychosomatic gastroenterology. The strength of recommendations: strong.

Level of evidence: weak.

Vote:

A. Fully agree (86.1%)
B. Accept with reservation (10.7%)
C. Disagree (3.4%)

Description:

In many consensus or guidelines for the treatment of digestive diseases, the following mechanisms are not given enough emphasis, including gastric-duodenal Oddi sphincter dysfunction, low-grade inflammation of the proximal small intestinal mucosa, inflammation of the distal intestinal mucosa, and gut-liver interaction disorders. Gastric-duodenal-Oddi sphincter dysfunction can induce excessive bile acid exposure of the small intestine in fasting state, which may contribute to the pathogenesis of gastroesophageal reflux disease and gastric mucosal injury. This mechanism may also affect the digestion and absorption efficiency of the small intestine, leading to worsening of the intraluminal environment of the distal gut. This may be closely related to the development of the lower digestive tract diseases. However, the above mechanisms have not been mentioned in the latest consensus. Gut mucosal inflammation plays a role through neurological or humoral regulation pathways, and is associated with diseases of the liver and other systems. Thus, mucosal inflammation is a key target in the treatment of the related diseases. The new research advances in the interactions of gut microbiota-brain and systemic diseases should also be applied to clinical practice as soon as possible.

Consensus statement 12

The traditional Chinese medicine (TCM)'s theory system of visceral syndrome differentiation is highly compatible with the concept of psychosomatic medicine about digestive diseases. The theoretical system of TCM could provide inspiration for the clinical practice of psychosomatic gastroenterology. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Fully agree (89.4%)
B. Accept with reservation (10.6%)
C. Disagree (0.0%)

Description:

The digestive system corresponds to the "spleen" and "stomach" viscera in Chinese medicine. TCM believes that "Spleen governs blood, controls digestion and absorption, provides the indispensable material for the homeostasis of the body, and is the source of growth and development." In TCM, the digestive system has important associations with the "liver" (which is

responsible for mental emotions and neurological function), “kidney” (which is responsible for water metabolism and immune defense), “heart” (which promotes blood circulation and is related to “mind” or psychology-like cognition), and “lung” (which regulates the gas). The clinical experience obtained by Chinese medicine in thousands of years may have potential values in clinical practice of psychosomatic gastroenterology [13].

Part 3. Treatment strategy of digestive diseases based on psychosomatic gastroenterology

Consensus statement 13 The development of integrative medicine-based thought patterns is a prerequisite for accurately identifying digestive psychosomatic problems and for improving the treatment strategies of these problems. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Fully agree (91.5%)
B. Accept with reservation (8.5%)
C. Disagree (0.0%)

Description:

It has been nearly 40 years since Engel put forward the “bio-psycho-social medical model” on Science in 1977. Unfortunately, this medical concept has not been used consciously by most of the gastroenterological specialists in clinical practice [14]. Psychosomatic gastroenterology advocates that gastroenterological specialists should develop a medical concept of “biological-psycho-social medical model” in clinical practice, and actively and consciously adopt a comprehensive diagnosis and treatment thinking mode, that is, emphasizing the comprehensive analysis of the possible roles of mental and psychological factors and pathophysiological mechanisms in the development of digestive diseases. For each patient, the doctors shouldthink about and analyze the etiology and pathogenesis in three dimensions. The first is the biomedical dimension: understanding the history of the disease, analyzing the pathophysiological mechanisms of disease occurrence and development, emphasis of the interconnections and interactions of various biological systems. Second, the mental dimension of psychology: analyzing the etiology and pathogenesis of mental problem of patients and choosing the appropriate treatment strategy. Third, the social activity dimension: to understand the social factors which contribute to the patient’s clinical features. Finally, formulating a focused, comprehensive and detailed individualized treatment regimen after considering the contribution of various dimensions of pathogenic factors to patients’ clinical problems.

Consensus statement 14

The gastroenterologists should acknowledge the relevant theories of psychiatry. Moreover, the gastroenterologists are encouraged to use the self-rating scale to understand the mental state of the patients, and to use the somatic symptoms or the quality of life self-rating scales to assess the psychosomatics, and via doing so, to improve the ability to recognize mental health problems. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Fully agree (97.9%)
B. Accept with reservation (2.1%)
C. Disagree (0.0%)

Description:

Patients with digestive psychosomatic problems often choose the Department of Gastroenterology for outpatient service. Therefore, identification of their mental health problems is very important for the appropriate management of these problems. So, it is necessary for gastroenterologists to acknowledge the basic theory of psychiatry.

Consensus statement 15

A good clinician-patient relationship is a prerequisite for accurately identifying psychosomatic problems, choosing the appropriate treatment strategy, and achieving satisfactory results. In the clinical practice of psychosomatic gastroenterology, the following issues should be considered:①Figure out the patient's concerns. Try to use objective evidence to convince the patients that the digestive psychosomatic problems are not life-threatening and thus to eliminate their panic concerns.②Accurately grasp and distinguish the contributions of various pathogenic factors (including mental and psychological factors) to the symptoms, and help the patients to understand the pathophysiology of symptoms.③Help the patients to fully understand and persuade them to voluntarily accept the treatment strategy. Help the patients to master appropriate methods to cope with mental and psychological stress, to re-establish an appropriate lifestyle, to clarify the goals of behavior improvement, and to enhance compliance with treatment regimens. The strength of recommendations: strong.

Level of evidence: high.

Vote:

A. Fully agree (89.4%)
B. Accept with reservation (10.6%)
C. Disagree (0.0%)

Description:

Accumulating evidence shows that enough communication and trust between doctors and patients is beneficial in improving the short-term and long term efficacy of FGIDs [15]. Physicians should try to comprehensively

analyze the various possible etiological factors and their contributions to symptom development. These factors include gastrointestinal infection, mental stress, abdominal and/or pelvic surgery, recent dietary changes, and behavioral changes. To a certain extent, the patients' anxiety about the symptoms is one of the main causes for their behavior of seeking medical care, sometimes this anxiety emotion could contribute to the clinical manifestations more than the symptoms themselves do. The symptoms of some patients may be alleviated if the anxiety emotion can be alleviated. Studies have shown that good communications about the treatment strategies between the physicians and the patients can significantly improve the short-term and long term effects of placebo on IBS patients. Therefore, improvement of the ability and skills of physician patient communication should be encouraged. If necessary, the physicians can also communicate with the relatives of the patients and other accompanying staffs. When communicating with patients, empathy needs to be appropriate. Special attention should be paid to the indications and timing of the referral to a psychiatric specialist during communication (please refer to the relevant content below for details). Given the characteristics of our traditional culture and health philosophy, the way to help the patients to appropriately recognize the digestive psychosomatic problems should be individualized.

Consensus statement 16

The primary aim of clinician-patient communication is to reach a consensus on the state and prognosis of the disease and to establish an accurate therapeutic goal. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Fully agree (87.2%)
B. Accept with reservation (12.8%)
C. Disagree (0.0%)

Description:

Patients with digestive psychosomatic disorders often exhibit confused complaints, laboratory test results from different hospitals, and various unclear diagnosis. The doctors are encouraged to determine a therapeutic goal after sufficient communication with patients before the beginning of treatment. Of note, this goal should be approved by the patients.

Consensus statement 17

In the mainland of China, only cognitive therapy, behavioral therapy, psychological counseling, and medication, which can be adopted by non-psychiatric doctors, are recommended in the treatment of digestive psychosomatic diseases. Psychiatric therapies (such as hypnosis therapy), which can be only conducted by psychiatric specialists, is not recommended. Mastering the central and peripheral actions of neurotransmitters

modulating drugs is important for psychosomatic gastroenterological practitioners. The strength of recommendations: strong.

Level of evidence: medium.

Vote:

A. Fully agree with (83.0%)
B. Accept with reservation (17.0%)
C. Disagree (0.0%)

Description:

Gastroenterological specialists should obey the laws and regulations of *Law of the People's Republic of China on Medical Practitioners, Pharmaceutical Administration Law, Regulations on the Administration of Medical Institutions, Regulations on the Control of Narcotic Drugs and Psychotropic Drugs and Prescription Management Measures*. It should be noted that the gastroenterologists are not recommended to conduct a diagnosis or treatment regimen of psychiatric illnesses, which is only permitted by psychiatric specialists. It is recommended that gastroenterological specialists improve the skills related to cognitive therapy, behavioral therapy, and psychological counseling and utilize them to treat the comorbid mental health problems of patients with digestive diseases. According to the provisions of the above-mentioned laws and regulations, the medical practitioners who have obtained the qualifications of practicing doctors and completed registration can prescribe the central acting drugs in clinical practice in the medical institutions where they have the permission to practice. At present, doctors qualified as the attending physician or above are authorized to prescribe anesthetic drugs and the first class psychotropic drugs, with a prescribed dose for a 3-day treatment period. The prescribed dose for second class psychotropic drugs is limited to a 7-day treatment period. Other central acting drugs are not legally restricted.

Consensus statement 18

The characteristics of mental and emotional disorders are generally associated with the clinical features of gastrointestinal disorders:①The irritable emotional response is often accompanied with an exaggerated painful experience of the gut to noxious stimulation, uncoordinated enhancement of gastrointestinal motility and secretion, and excessive immune inflammatory response.②The inhibitory emotional response is usually accompanied with uncoordinated decrease in gastrointestinal motility, sensation, and secretion, as well as sustained infectious inflammation. These characteristics have implications for selection of neurotransmitter modulating agents in clinical practice of psychosomatic gastroenterology. The strength of recommendations: strong.

Level of evidence: weak.

Vote:

A. Fully agree (71.6%)
B. Accept with reservation (8.3%)
C. Disagree (20.1%)

Description:

The excitability changes in the cortex in control of emotional responses may cause changes in the pain response of peripheral organs to noxious stimuli, dysfunction of the nuclei in control of splanchnic nerve activity, and changes in systemic anti-infection and immune/inflammatory responses through the subcortical nerves. The clinical experience of gastroenterological experts shows that the irritable emotional response is often accompanied by an exaggerated painful experience of the gut to noxious stimulation. Uncoordinated enhancement of gastrointestinal functions such as motility and secretion often simultaneously exist. These include ①increased ineffective peristalsis of smooth muscles in the esophageal body and relaxation of lower esophageal sphincter, which lead to gastroesophageal reflux;②increased gastric acid secretion, which leads to peptic ulcer;③ increased duodenal peristalsis, Oddi sphincter relaxation, and luminal bile acid exposure during interdigestive phases, which may lead to bile acid reflux;④increased intestinal peristalsis leading to borborygmus and diarrhea. Conversely, the inhibitory emotional response is usually accompanied by visceral hypoesthesia and an uncoordinated decrease in gastrointestinal motility and secretion. These may cause achalasia of the cardia, gastrointestinal dysmotility, duodenal stasis, dry stool and so on [16]. For those patients with irritable emotional response, neurotransmitter modulating medicines with anti-panic and anti-anxiety activity and additional cholinergic antagonism can be chosen to improve the emotional responses and the coordination of gut functions. These include tricyclic antidepressants (TCA), certain selective serotonin reuptake inhibitors (SSRIs; e.g., paroxetine, fluvoxamine, etc.), noradrenergic and specific serotonergic antidepressants (NaSSAs; e.g., mirtazapine), norepinephrine and serotonin reuptake inhibitors (SNRIs) (e.g.,duloxetine), serotonin 1A receptor agonist (e.g., tandospirone), serotonin receptor antagonist/reuptake inhibitors (SARIs), and other drugs with similar anti-depressant and anti-anxiety activity. For those patients with inhibitory emotional response, the antidepressants that can improve mental state and gastrointestinal functions, such as some SSRIs (e.g.,fluoxetine, sertraline, citalopram, etc.) and SNRIs (e.g.,venlafaxine), and other antidepressants with similar activity, can be used.

Consensus statement 19

In clinical practice of psychosomatic gastroenterology, the treatment regimens with neurotransmitter modulating drugs differ from those adopted by psychiatric specialists because of the different pathogenesis of diseases and clinical therapeutic goals. This means that the kinds of drugs, dose, and course of treatment are different. For most of the patients with digestive disorders smaller doses and shorter treatment courses are suitable. The strength of recommendations: strong.

Level of evidence: weak.

Vote:

A. Fully agree (66.9%)
B. Accept with reservation (21.5%)
C. Disagree (11.6%)

Description:

Generally, there are three main therapeutic goals in clinical practice of psychosomatic gastroenterology. ①Amelioration of mental and psychological symptoms should be regarded as the leading therapeutic goal when the mental and psychological factors are the key pathogenesis of digestive disorders. Under these circumstances, the treatment strategies with neurotransmitter modulating agents should follow the guidelines of psychiatry specialty. The patients should be definitely diagnosed and detailedly evaluated the disease state by a psychiatric specialist. And the psychiatrist will make decisions about drug selection and treatment regimens. The gastroenterological specialists are recommended to treat the digestive disorders after holding a consultation with psychiatric specialists. The use of central acting drugs is mainly aimed to ameliorate the mental and psychological symptoms with minimal adverse reactions of the gastrointestinal tract. The effect of these drugs is usually dose dependent. The course of treatment should follow the guidelines and specifications of the psychiatric specialty. The drugs should be gradually withdrawn after a course of treatment of at least 6 months.②For patients seeking medical consultations because of their gastrointestinal disorders, psychosocial or mental problems are often accompanying symptoms. The severity of these symptoms do not yet meet the criteria for the diagnosis of mental and psychological disorders and cannot be identified as a major cause of clinical problems. Under these circumstances, neurotransmitter modulating drugs that can act on pathophysiological processes of both mental and psychological problems and digestive disorders should be chosen. It is recommended to start with a small dose, gradually increased to a dose at which an adequate effect can be achieved. The longer the onset of action, the longer the period of consolidation and gradual withdrawal may take. For those cases with rapid and satisfactory response, the discontinuation or on demand use of drugs can be conducted according to the guidelines for the treatment of digestive diseases. ③Some patients exhibit no identifiable psychiatric problems. However, they were refracted to routine treatment regimens for digestive symptoms. For these patients, a small dose of neurotransmitter modulating drugs can be used. It is supposed that these drugs can directly act on the peripheral nerves and/or gastrointestinal tract at small doses.

Consensus statement 20

I n t h e c l i n i c a l p r a c t i c e o f p s y c h o s o m a t i c gastroenterology, the first indication for the application of central acting agents is that patients have obvious mental and psychological disorders and their gastrointestinal symptoms can be regarded as the somatization of mental and psychological disorders. Once identified, central acting agents can be used on the first visit. It is recommended that the treatment regimens were conducted after consultation with psychiatric specialists. The strength of recommendations: strong.

Level of evidence:

high Vote:

A. Totally agree（59.6%）
B. Agree with reservation（38.3%）
C. disagree（2.1%）

Description:

Some patients visiting the gastroenterology outpatient have obvious presentations of mental and psychological disorders (including mental and psychological symptom complaints, paranoid health concepts, and significant cognitive bias of their clinical manifestations and health status). According to Chinese laws, it is recommended to refer them to the psychiatry clinic if these presentations can explain their digestive symptoms based on the descriptions of somatization and its related disorders in DSM-5. Under these circumstances, gastroenterologists should treat the accompanying digestive disorders with the assistance of psychiatric specialists.

Consensus statement 21

In the clinical practice of gastroenterological specialty, the second indication for the application of central acting agents is that gastrointestinal symptoms and mental and psychological disorders simultaneously exist, and the causal relationship between these two classes of symptoms is difficult to be determined. Mental and psychosocial factors can trigger and aggravate gastrointestinal symptoms. Neurotransmitter modulating drugs acting on both central nervous system and gastrointestinal tract are usually more effective than conventional drugs that only act on the gastrointestinal tract. The strength of recommendations: strong.

Level of evidence:

high Vote:

A. Totally agree（82.6%）
B. Agree with reservation（17.4%）
C. disagree（0.0%）

Description:

In the practice of psychosomatic gastroenterology, a considerable proportion of patients show both mental and psychological disorders and gastrointestinal symptoms. They often have experience of mental stress or sleep disorders. Mental and psychological factors aggravate gastrointestinal discomfort, while gastrointestinal symptoms aggravate mental and psychological disorders, thus forming a vicious circle. Evidence shows that mental and psychological disorders, such as high degree of mental stress, can exacerbate visceral hypersensitivity, thus worsening IBS symptoms [17].

Consensus statement 22

In the clinical practice of gastroenterological specialty, the third circumstance for the application of central acting agents is that some patients with FGIDs lack mental and psychological disorders, while they are refractory to 4-8 weeks treatment of conventional gastrointestinal acting drugs. The strength of recommendations: medium;

Level of evidence:

high Vote:

A. Totally agree（48.9%）
B. Agree with reservation（44.7%）
C. Disagree（6.4%）

Description:

The central acting agents exert a therapeutic and non therapeutic effect by altering the concentrations of neurotransmitters or acting on their receptors. These drugs have both central and peripheral effects. For example, the most commonly used antidepressants at present mainly regulate the actions of serotonin, norepinephrine, and dopamine. Besides acting centrally, these neurotransmitters are also regulators of gastrointestinal motility, secretion, sensation, and blood supply. It is not difficult to understand that in addition to the central effect, the improvement of gastrointestinal symptoms by antidepressants can be achieved by the peripheral effect. A growing number of studies has shown that low-dose tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) are effective in relieving IBS symptoms, even in those without obvious mental and psychological disorders [17].

Consensus statement 23

The mechanisms for the therapeutic effect of central acting agents on digestive psychosomatic disorders include:①Remove the mental and psychological causes of gastrointestinal dysfunction via acting on the central nervous system;②Alleviate visceral hypersensitivity via acting on the sensation-modulating pathways in the central and peripheral nervous system;③ Cause the changes in the concentration of neurotransmitters. Thus, the regulatory effect of these transmitters on gastrointestinal motility, secretion, and sensation via directly acting on receptors in the gastrointestinal tract can be enhanced. The strength of recommendations: strong.

Level of evidence:

high Vote:

A. Totally agree（64.8%）
B. Agree with reservation（22.6%）
C. C.disagree（12.6%）

Description:

Take the pathogenesis and clinical practice of FGIDs for example. First, dysfunction of the cerebral cortex in control of the emotional activity may play a role in visceral hypersensitivity related to FGIDs. Neurotransmitter modulating agents could improve the function of these regions. Second, the central acting agents cause the changes in the blood concentration of neurotransmitters. Thus, the regulatory effect of these transmitters on gastrointestinal functions via directly acting on receptors in the gastrointestinal tract can be enhanced. The mechanisms for the therapeutic effect of central acting agents on FGIDs are complicated, which are different from those for the treatment of mental and psychological problems. Therefore, when treating digestive psychosomatic gastroenterological disorders, the treatment regimens including drug type, onset dose, onset time, and course of treatment and withdrawal should be established according to the disease state. Copy of the treatment regimens of psychiatric medication is not recommended[16].

Consensus statement 24

In the treatment of digestive psychosomatic gastroenterological disorders, the dose of the central acting agents should be individualized. For those patients exhibiting obvious mental and psychological disorders and comorbid gastrointestinal symptoms (which are regarded as the somatization of mental and psychological disorders), it is recommended that small onset dose is used until to the dose recommended by the psychiatric specialists. For those patients with both gastrointestinal and mental and psychological disorders and those lacking mental and psychological disorders while refractory to 4-8 weeks treatment of conventional gastrointestinal acting drugs, a small dose (1/3 or 1/2 of the recommended dose for the treatment of psychiatric diseases) is recommended, and the dose can be adjusted according to the therapeutic effect. The strength of recommendations: medium;

Level of evidence:

medium Vote:

A. Totally agree（75.1%）
B. Agree with reservation（22.3%）
C. disagree（2.6%）

Description:

The central acting agents usually show a positive dose-effect relationship in the treatment of mental and psychological disorders. It is observed that the mental and psychological disorders of most of the patients with digestive psychosomatic disorders are mild. The leading therapeutic goal of digestive diseases is to ameliorate the gastrointestinal symptoms (but not mental and psychological disorders). So it is recommended to start with a small dose. For those patients with mental and psychological disorders that meet the diagnosis criteria of psychiatric diseases, it is recommended to refer them to the psychiatric specialist for diagnosis and treatment. As the effect of the central acting drugs on peripheral nerves and organs are quite complicated, the treatment regimens at different doses may yield different effects on pain regulation and gastrointestinal function. However, it should be noted that for patients with FGIDs, a satisfactory effect usually occurs only when the dose and course of treatment were similar to those adopted for the management of the psychiatric diseases. The establishment of a specific treatment strategy depends on the experience in practice.

Consensus statement 25

The treatment course of central acting agents for digestive psychosomatic disorders differs for different indications. For those patients exhibiting obvious mental and psychological disorders and comorbid gastrointestinal symptoms (which are regarded as the somatization of mental and psychological disorders), it is recommended to adopt the treatment regimens according to the advice of psychiatric specialists: a course of at least 6 months followed by reducing the dose gradually (reducing 1/4 to 1/2 per 2 weeks) until withdrawal. For those patients with both gastrointestinal and mental and psychological disorders, it is recommended to use these drugs for 3 to 6 months, with a gradual withdrawal of the drugs when stable efficacy is achieved and maintained for over one month. For those lacking mental and psychological disorders while refractory to 4-8 weeks

treatment of conventional gastrointestinal acting drugs, on-demand medication is acceptable according to the practical experience. The course of treatment still needs more clinical observation. The strength of recommendations: medium;.

Level of evidence:

medium Vote:

A. Totally agree（57.4%）
B. Agree with reservation（40.4%）
C. Disagree（2.1%）

Description:

For those patients exhibiting obvious mental and psychological disorders and comorbid gastrointestinal symptoms (which are regarded as the somatization of mental and psychological disorders) the therapeutic goal is to ameliorate the mental and psychological problems. Therefore, the treatment regimens are similar to those for the psychiatric disorders. For those patients with both gastrointestinal and mental and psychological disorders, the therapeutic goal is the amelioration of both mental and psychological problems and the gastrointestinal symptoms. The drug effect depends on both the central and peripheral nervous system. It is recommended to start with a small dose and adjust it according to the therapeutic effect. It has been reported that to the vast majority of such patients a satisfactory drug effect can be achieved at small doses. For those patients lacking mental and psychological disorders while refractory to 4-8 weeks treatment of conventional gastrointestinal acting drugs, drug effect is mainly exerted via directly acting on the gastrointestinal tract (the effect on the peripheral nervous system cannot be completely ruled out) by means of changing neurotransmitter concentration. Usually, a satisfactory drug effect can be achieved at a small dose. Of note, when SSRIs are used to promote gastrointestinal motility, sometimes it is necessary to increase the dose individually. In terms of dose, there is no high-level evidence or literature for reference. As for the course of treatment, amelioration of painful experiences such as abdominal pain and distension needs 2 to 4 weeks, while amelioration of other gastrointestinal symptoms such as defecation character and behavior needs 1 to 2 weeks.

Consensus statement 26

In the treatment of digestive psychosomatic disorders, the principle for selection of central acting drugs is not the same as that in the psychiatric specialty. When these drugs are used to treat digestive symptoms, the following principles should be followed.①Analyze the characters of psychological disorders and refer to the guidelines of psychiatric specialty.②Choose the drugs according to the roles of neurotransmitters in the pathophysiological mechanisms of gastrointestinal symptoms. The strength of recommendations: strong.

Level of evidence:

medium Vote:

A. Fully agree (89.4%)
B. Agree, but with reservations (10.6%)
C. Disagree (0.0%)

Description:

The principles for drug selection from the perspective of psychiatry are recommended to refer to those of psychiatric specialty. The pathophysiological mechanisms for gastrointestinal symptoms include visceral hypersensitivity, dysfunction of gastrointestinal m o t i l i t y a n d s e c r e t i o n , a n d t h e s u s t a i n e d gastrointestinal mucosal inflammation. Figuring out the pathophysiological mechanisms involving the central and peripheral nerves, the immune system and the gastrointestinal tract is the key point for proper selection of psychological medicine.

Consensus statement 27

In the treatment of digestive psychosomatic disorders it should be emphasized that psychological and physical problems are not mutually exclusive. When using the neurotransmitter modulating medicine mentioned in this Consensus, it is important to follow-up even if the therapeutic effect is satisfying. The strength of recommendations: high.

Level of evidence:

medium Vote:

A. Fully agree (91.5%)
B. Agree, but with reservations (8.5%)
C. Disagree (0.0%)

Description:

Investigation of the organic etiology and pathogenesis of the digestive disorders is an indispensable step before using central acting drugs to alleviate the symptoms. The time interval between the re examinations was recommended for 6 months based on the Rome IV criteria of FGIDs[2]. The ways for investigation are predominantly the routine examinations generally carried out by the secondary and tertiary medical institutions in China.

Consensus statement 28

This Consensus reflects the current knowledge of gastroenterolgical specialists on several problems found in the treatment of digestive psychosomatic diseases in the mainland of China. The experts involved in the research and discussion are all from the “Chinese Digestive Psychosomatic Union”. The suggestions in this Consensus are not mandatory and are not inconsistent with any existing laws or regulations. Experts who voted on time did not include all the experts who have insights in this field. This consensus is an open academic information. The author team will accept opinions and suggestions from scholars in this field at any time and will continuously revise and improve the Consensus. The strength of recommendations: strong.

Level of evidence:

medium Vote:

A. Fully agree (89.4%)
B. Agree, but with reservations (10.6%)
C. Disagree (0.0%) Supplementary explanations of the Consensus: Due to the limited publication length, the published 1 version of the Consensus does not include

the detailed description of the strength of the recommendations and the evidence level of the references, etc. The reference number has also been reduced.

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