

# 中医药调控脑-肠轴治疗GERD伴焦虑抑郁症的临床研究进展<sup>Δ</sup>

王宇青<sup>1\*</sup>, 罗佐媚<sup>1</sup>, 陈南<sup>1</sup>, 韩冰洁<sup>1</sup>, 黎丽群<sup>2</sup>, 刘礼剑<sup>2</sup>, 陈广文<sup>2</sup>, 杨成宁<sup>2#</sup>(1. 广西中医药大学研究生院, 南宁 530001; 2. 广西中医药大学第一附属医院脾胃病科, 南宁 530001)

中图分类号 R285;R975+1;R971+4

文献标志码 A

文章编号 1001-0408(2024)18-2315-06

DOI 10.6039/j.issn.1001-0408.2024.18.22



**摘要** 胃食管反流病(GERD)是由胃内容物反流至食管引起反酸、烧心等症状的胃肠动力障碍性疾病。GERD的发生与患者焦虑、抑郁等心理障碍密切相关。脑-肠轴作为大脑与胃肠道双向联系的中介,在GERD伴焦虑抑郁症的发生发展中具有重要作用。中药复方内服疗法(平冲降逆汤、调中化湿汤等)、中医药内服外用联合疗法(连栀泄热汤联合穴位贴敷、针刺督脉背段联合疏肝利胆和胃中药等)、中西药内服联合疗法(健脾疏肝汤联合雷贝拉唑、雷贝拉唑联合建中降逆汤等)可通过调控脑肠肽、肠道菌群、炎症因子、胃肠激素等分子信号有效改善GERD症状及焦虑、抑郁状态,提升患者生活质量。

**关键词** 胃食管反流病;焦虑;抑郁;脑-肠轴;中医药;中西药结合

## Clinical research progress of traditional Chinese medicine in the treatment of GERD with anxiety and depression by regulating brain-gut axis

WANG Yuqing<sup>1</sup>, LUO Zuomei<sup>1</sup>, CHEN Nan<sup>1</sup>, HAN Bingjie<sup>1</sup>, LI Liqun<sup>2</sup>, LIU Lijian<sup>2</sup>, CHEN Guangwen<sup>2</sup>, YANG Chengning<sup>2</sup>(1. Graduate School of Guangxi University of Chinese Medicine, Nanning 530001, China; 2. Dept. of Spleen and Stomach Diseases, the First Affiliated Hospital of Guangxi University of Chinese Medicine, Nanning 530001, China)

**ABSTRACT** Gastroesophageal reflux disease (GERD) is a gastrointestinal motility disorder characterized by the reflux of gastric contents into the esophagus, leading to symptoms such as acid reflux and heartburn. The incidence of GERD is closely associated with psychological disorders, including anxiety and depression. The brain-gut axis, serving as a mediator of the bidirectional connection between the brain and the gastrointestinal tract, plays a crucial role in the occurrence and development of GERD with anxiety and depression. Various therapeutic approaches, including compound Chinese medicine internal therapy (such as Pingchong jiangni decoction, Tiaozhong huashi decoction, etc.), combination therapy of internal and external Chinese medicine (such as Lianzhi xiere decoction combined with acupoint application, acupuncture at the back segment of governor vessel plus Chinese medication of soothing the liver and gallbladder, etc.), and combination therapy of internal Chinese and western medicine (including Jianpi shugan decoction combined with rabeprazole, rabeprazole combined with Jianzhong jiangni decoction, etc.), have been shown to regulate brain-gut peptides, intestinal flora, inflammatory factors and gastrointestinal hormones, thereby effectively alleviating GERD symptoms, anxiety and depression, and enhancing patients' quality of life.

**KEYWORDS** gastroesophageal reflux disease; anxiety; depression; brain-gut axis; traditional Chinese medicine; integration of traditional Chinese and western medicine

胃食管反流病(gastroesophageal reflux disease, GERD)是一种由胃内容物反流至食管引起反酸、烧心等不适症状的胃肠动力障碍性疾病<sup>[1]</sup>。据调查,GERD的全球患病率为13%~25%,呈逐年上升趋势<sup>[2]</sup>。此外,随着社会的快速发展和人们生活节奏的加快,许多人面临

着巨大的压力和挑战,从而导致焦虑、抑郁、愤怒等负面情绪的产生。研究发现,GERD患者发生焦虑、抑郁的风险是非GERD患者的2.57倍,且GERD伴焦虑抑郁症患者数量是无心理疾病GERD患者的2.23倍<sup>[3]</sup>。可见,GERD的发生与患者心理障碍密切相关。目前,临床治疗GERD伴焦虑抑郁症以质子泵抑制剂联合抗焦虑抑郁药物为主,但质子泵抑制剂可刺激患者胃肠道,加之GERD症状易反复,难以完全治愈,若长期治疗还可能引发恶心、呕吐、焦虑、超敏反应、运动障碍等诸多不良反应。因此,研发新的GERD伴焦虑抑郁症治疗药物具有重要意义。

**Δ 基金项目** 广西自然科学基金面上项目(No.2024GXNSFAA99-9154);广西自然科学基金青年科学基金项目(No.2024GXNSFBA010-102);国家自然科学基金项目(No.82260900, No.82160877)

\* **第一作者** 硕士研究生。研究方向:中医药防治脾胃病。E-mail:578465452@qq.com

# **通信作者** 副主任医师,硕士生导师。研究方向:中医药防治脾胃病。E-mail:ychn1006@163.com

已有研究表明,GERD和焦虑抑郁症在神经生物学机制方面存在诸多相似之处,其中脑-肠轴是中枢神经系统和肠神经系统之间双向交流的重要桥梁<sup>[4]</sup>,已被证实在GERD伴焦虑抑郁症的发生发展中发挥了重要作用。因此,干预脑-肠轴生理机制可能是有效治疗GERD伴焦虑抑郁症的关键。中医学认为,GERD归“吐酸”“嘈杂”“呃逆”“食管瘴”等范畴<sup>[5]</sup>,其基本病机为脾失升健、胃失和降、胃气上逆<sup>[6]</sup>。焦虑抑郁症归“郁证”“梅核气”等范畴,其基本病机为气机阻滞、运行不畅<sup>[7]</sup>。GERD和焦虑抑郁症二者共病,可辨证为异病同治,其关键致病因素为“热、逆、郁”,病位在食管和胃,与脾、肝、心等脏腑气机失调关系密切<sup>[6]</sup>。肝郁不舒,横逆脾胃,脾气不能升,胃气不可降,致机体气机升降失司;气逆日久反复,上扰心神,气机阻滞,郁而化火,则心烦难眠、焦虑、抑郁<sup>[7]</sup>。因此,中医药治疗GERD伴焦虑抑郁症当以疏肝解郁、和胃降逆、补脾益胃、清热燥湿为主要治则。随着学界对中医理论探索的不断深入,通过中医药调控脑-肠轴治疗GERD伴焦虑抑郁症已成为研究热点。基于此,本文对脑-肠轴及其在GERD伴焦虑抑郁症中的作用及中医药调控脑-肠轴治疗该病的临床研究进行综述,旨在为GERD伴焦虑抑郁症的诊疗提供新思路。

## 1 脑-肠轴的概述

脑-肠轴是中枢神经系统和肠神经系统之间双向联系的中介,彼此相互影响、相互作用<sup>[8]</sup>。其由自主神经系统通过交感神经和迷走神经将信号转导给肠神经系统,进而传递给中枢神经系统,从而触发下丘脑-垂体-肾上腺(hypothalamic-pituitary-adrenal, HPA)轴调节<sup>[9]</sup>。脑-肠轴可参与神经传导、内分泌调节,涉及免疫因素、肠道菌群等多个方面<sup>[10]</sup>,其最核心的调控方式是脑肠互动,即脑-肠轴之间神经-内分泌系统的双向传导。

## 2 脑-肠轴与GERD伴焦虑抑郁症的关系

研究发现,GERD和焦虑抑郁症在神经生物学机制方面存在许多相似之处,且两者存在遗传基因的高度重叠<sup>[11]</sup>。脑肠肽是调控脑肠互动的重要小分子多肽类物质,是脑-肠轴各通路协调运转的关键基础,可通过胃肠激素直接作用于胃肠道<sup>[12]</sup>。脑肠肽包括胃泌素(gastrin, GAS)、胃动素(motilin, MTL)、5-羟色胺(5-hydroxytryptamine, 5-HT)、P物质(substance P, SP)等兴奋性脑肠肽,以及胆囊收缩素(cholecystokinin, CCK)、血管活性肠肽(vasoactive intestinal peptide, VIP)、一氧化氮(nitric oxide, NO)等抑制性脑肠肽<sup>[13]</sup>。脑肠肽可通过增加兴奋性激素水平而促进胃肠动力,可通过降低抑制性激素水平来缓解焦虑、抑郁情绪;同时,脑肠肽作为神经递质,可驱使中枢系统相关受体的表达,从而减少焦虑、抑郁样行为<sup>[13]</sup>。肠道菌群是脑肠互动的重要参与者,可间接参与中枢神经系统调控,从而与大脑形成双向互通的联络网<sup>[14]</sup>。肠道菌群可使革兰氏阴性菌中的促炎因子过

表达,从而触发NO,诱导食管括约肌松弛,最终引发GERD<sup>[15]</sup>。此外,肠道菌群失调可通过产生代谢物来影响中枢神经,改变神经递质水平,最终导致GERD伴焦虑抑郁症的发生<sup>[16]</sup>。5-HT是肠神经系统的重要神经递质,可通过调控紧密连接蛋白的表达来引发GERD<sup>[17]</sup>;同时,5-HT也是诱发精神疾病的主要神经递质,其系统调节异常是GERD伴焦虑抑郁症的重要病理机制<sup>[18]</sup>。GERD是一种免疫介导的炎症性疾病;同时,炎症也是精神心理障碍的重要诱因,是GERD伴焦虑抑郁症共病的机制之一<sup>[19]</sup>。研究显示,应激所致的HPA轴功能亢进可引起胃肠动力异常和内脏高敏感性<sup>[20]</sup>,且HPA轴功能亢进还可引发焦虑、抑郁等情绪障碍<sup>[9]</sup>,最终导致GERD伴焦虑抑郁症的发生。此外,食管高敏感可通过刺激外周和中枢神经来增强疼痛感知,从而加重GERD症状及焦虑、抑郁样反应<sup>[21-22]</sup>。综上所述,基于脑-肠轴的GERD伴焦虑抑郁症病理机制包括脑肠肽分泌异常、肠道微生态失调、5-HT系统调节异常、炎症细胞因子水平异常、HPA轴调节功能异常等。

## 3 中医药治疗GERD伴焦虑抑郁症的临床研究

基于中医辨证论治理论,GERD与焦虑抑郁症具有共病性,可辨证为异病同治。二者共病的基本病机为气机运行失司、升降不利,且该病多由情志不遂、饮食内伤、脾胃亏虚等因素所致,与肝、脾、胃三脏密切相关,热、逆、郁蕴结中焦,阻遏气机发为此病<sup>[7]</sup>。当前,中医药通过调控脑-肠轴来修复患者食管黏膜损伤、调节胃肠道分泌及胃动力、改善食管下括约肌压力(lower esophageal sphincter pressure, LESp)、降低食管高敏感性,已成为临床治疗GERD伴焦虑抑郁症的新选择(图1)<sup>[3]</sup>。常见的中医药治疗方法包括中药复方内服疗法、中医药内服外用联合疗法、中西药内服联合疗法。

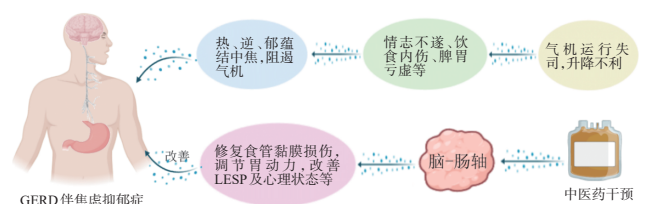


图1 GERD伴焦虑抑郁症的病理机制及中医药干预示意图

### 3.1 中药复方内服疗法

中药复方可通过多途径调节脑-肠轴分子信号水平,改善胃肠动力及LESp、调节食管高敏感性、减轻炎症、缓解抑郁,从而有效干预GERD伴焦虑抑郁症,疗法以疏肝解郁、和胃降逆和补脾益胃、清热燥湿为主。

#### 3.1.1 疏肝解郁、和胃降逆

戴琦等<sup>[23]</sup>运用平冲降逆汤治疗GERD伴焦虑抑郁症,治疗4周后,患者的总有效率(95.83%)和血清中GAS、MTL水平均显著高于对照组(雷贝拉唑钠肠溶胶

囊),汉密尔顿焦虑量表(Hamilton anxiety scale, HAMA)及汉密顿抑郁量表(Hamilton depression scale, HAMD)评分均显著低于对照组,可见平冲降逆汤用于GERD伴焦虑抑郁症的疗效确切,可调节患者胃肠激素水平,改善其焦虑抑郁症状,提高生活质量。唐丽明等<sup>[24]</sup>采用旋覆代赭汤加味治疗难治性胃食管反流病(refractory gastroesophageal reflux disease, RGERD)合并焦虑抑郁症,治疗后,患者的总有效率达90.0%,显著高于化学药对照组(莫沙必利联合埃索美拉唑),其HAMA、HAMD评分和CCK、VIP水平均显著低于化学药对照组,GAS、MTL水平均显著高于化学药对照组,可见旋覆代赭汤加味可调节患者胃肠激素水平,促进其食管下括约肌功能恢复,并改善胃肠道功能和焦虑、抑郁症状,疗效显著。孙叙敏等<sup>[25]</sup>运用柴胡疏肝散合旋覆代赭汤加减治疗GERD伴焦虑抑郁症,结果显示,该方案的疗效显著优于化学药对照组(奥美拉唑肠溶片联合氟哌噻吨美利曲辛片),且患者复发率显著低于化学药对照组,患者血清中VIP水平和肿瘤坏死因子 $\alpha$ (tumor necrosis factor- $\alpha$ , TNF- $\alpha$ )、白细胞介素1(interleukines-1, IL-1)、IL-6水平均显著降低,可见该方可促进患者胃肠排空,降低其胃肠食管敏感性,减轻炎症损伤,有效改善相关症状。王杰等<sup>[26]</sup>以疏肝降气、通调脾胃为治则,运用柴芍通降方治疗肝胃不和型非糜烂性反流病(non-erosive reflux disease, NERD)伴焦虑抑郁症,结果显示,患者的总有效率(91.67%)显著高于化学药组(雷贝拉唑钠肠溶片);同时,该方可降低患者的食管高敏感性,减轻其异常疼痛感知,缓解其焦虑、抑郁情绪。何美君等<sup>[27]</sup>运用疏肝降逆和胃方治疗肝胃不和型NERD伴焦虑抑郁症,结果显示,该方的临床疗效优于化学药(奥美拉唑肠溶片),患者的总有效率为86.49%;同时,该方能显著降低患者血清中神经生长因子水平和内脏高敏感性,促进食管黏膜修复,改善心理不良情绪。梁育仪等<sup>[28]</sup>运用柴胡陷胸汤加减治疗肝胃郁热型GERD伴焦虑抑郁症,患者的总有效率(93.3%)显著高于化学药组(艾司奥美拉唑镁肠溶片),HAMA-14评分明显低于化学药组;同时,该方可降低患者NO含量,提高GAS含量,减少胃酸分泌,改善GERD症状,缓解患者焦虑情绪。周燕等<sup>[29]</sup>运用建中降逆汤治疗NERD中虚气逆证,患者的总有效率(93.3%)显著高于化学药组(雷贝拉唑);同时,该方可通过升高患者GAS-17水平来改善其胃肠分泌功能,减轻患者躯体化症状及焦虑、抑郁状况。

### 3.1.2 补脾益胃、清热燥湿

杨成宁等<sup>[30]</sup>使用调中化湿汤治疗GERD伴焦虑抑郁症,患者的总有效率(90.0%)显著高于化学药组(枸橼酸莫沙必利分散片联合兰索拉唑肠溶片及氟哌噻吨美利曲辛片),HAMA-14、HAMD-17评分均显著低于化学药组;此外,该方可上调患者血清MTL、5-HT水平,促进胃

肠动力,提高LESP,从而改善患者的GERD症状及焦虑、抑郁状态。赵志勇<sup>[31]</sup>使用二陈平胃散加减治疗气郁痰阻型RGERD伴焦虑抑郁症,患者的总有效率(96.0%)显著高于化学药组(雷贝拉唑钠肠溶胶囊联合枸橼酸莫沙必利片);此外,该方能降低患者血清IL-6、TNF- $\alpha$ 含量,减轻炎症反应,促进胃动力,临床疗效确切。刘娟等<sup>[32]</sup>使用柴胡疏肝散与左金丸加味治疗GERD相关性胸痛,患者的总有效率(96.96%)显著高于化学药组(奥美拉唑肠溶胶囊联合潘立酮片),焦虑自评量表(self-rating anxiety scale, SAS)、抑郁自评量表(self-rating depression scale, SDS)评分均显著低于化学药组;此外,该方还可降低患者体内NO含量,改善患者GERD症状及不良情绪,效果优于化学药组。张贞鲁等<sup>[33]</sup>研究表明,加味四逆散治疗NERD伴焦虑抑郁症患者的总有效率(90.38%)显著高于化学药组(雷贝拉唑);此外,该方还可提高GAS、MTL、SP水平,降低VIP水平,抑制胃酸分泌,保护胃黏膜,舒缓压力和负面情绪。

### 3.2 中医药内服外用联合疗法

马可迅等<sup>[34]</sup>采用连枢泄热汤联合穴位贴敷治疗瘀热互结型RGERD伴焦虑抑郁症,结果表明,该组患者的总有效率(93.88%)显著高于化学药对照组(莫沙必利片联合奥美拉唑镁肠溶胶囊);同时该疗法可下调患者前列腺素E<sub>2</sub>水平,改善胃黏膜损伤,缓解胃黏膜高敏感性及胃反流症状,改善患者焦虑、抑郁状态。李华岳等<sup>[35]</sup>采用针刺督脉背段联合疏肝利胆和胃中药治疗NERD伴焦虑抑郁症,结果显示,该组患者的总有效率(98.6%)显著高于对照组(疏肝利胆和胃中药);同时该疗法可提高患者MTL、GAS水平和胃肠动力,促进胃排空,降低内脏高敏感性,缓解食管黏膜损伤。

### 3.3 中西药内服联合疗法

梁宇晗等<sup>[36]</sup>运用健脾疏肝汤联合雷贝拉唑治疗RGERD伴焦虑抑郁症,结果显示,该组患者的总有效率(90.5%)显著高于对照组(雷贝拉唑钠肠溶片联合枸橼酸莫沙必利片),HAMA评分显著低于对照组,且该疗法可上调患者血清中SP、GAS、MTL水平,降低CCK水平,促进食管括约肌运动,抑制胃酸反流,修复食管黏膜损伤,缓解负性情绪。吴银亚等<sup>[37]</sup>运用雷贝拉唑联合建中降逆汤治疗NERD,患者的有效率(91.18%)明显高于化学药组(雷贝拉唑),SAS、HAMD-17评分均显著低于化学药组,且该疗法可提高患者血清胃蛋白酶原I、GAS-17水平,改善胃肠分泌功能,缓解患者临床症状及负性情绪。归脾汤是治疗心脾两虚的代表方,曹燕飞等<sup>[38]</sup>在艾司奥美拉唑镁肠溶片的基础上加用归脾汤,结果显示,联合治疗组心脾两虚型NERD伴情绪障碍患者的总有效率(91.18%)显著高于化学药组(氟哌噻吨美利曲辛片联合艾司奥美拉唑镁肠溶片),SAS、HAMD-17评分均显著低于化学药组;同时,该联合治疗方案可降

低患者的VIP水平和内脏高敏感性,提高5-HT水平和LESP,促进胃肠动力,改善焦虑、抑郁情绪。翟昂帅等<sup>[39]</sup>使用气滞胃痛颗粒联合奥美拉唑治疗NERD伴焦虑抑郁症,结果显示,联合治疗组患者的总有效率(95.83%)显著高于化学药组(枸橼酸莫沙必利片联合奥美拉唑肠溶胶囊),SAS、SDS评分均显著低于化学药组;同时该联合疗法能降低患者食管高敏感性,促进胃肠动力,抑制胃酸分泌,缓解焦虑、抑郁情绪,改善其生活质量及心理状态。尹毅等<sup>[40]</sup>研究显示,柴胡温胆汤联合埃索美拉唑、氟哌噻吨美利曲辛可降低NERD伴焦虑抑郁症患者的内脏高敏感性,减轻胃酸反流,改善其自主神经功能,缓解其焦虑、抑郁状态,总有效率(90.91%)显著高于化学药组(埃索美拉唑联合氟哌噻吨美利曲辛),HAMD、HAMA评分均显著低于化学药组。何若瑜等<sup>[41]</sup>研究了归脾汤联合兰索拉唑治疗NERD伴焦虑抑郁症的疗效,结果显示,联合治疗组患者的总有效率(80.85%)显著高于化学药组(兰索拉唑联合氟哌噻吨美利曲辛片),HAMD-24评分显著低于化学药组;同时,该联合疗法可提高患者血清中5-HT水平,降低VIP水平,增强LESP,抑制胃酸反流,缓解不良情绪,临床疗效确切。

#### 4 结语

脑-肠轴被证实在GERD伴焦虑抑郁症的发生发展中具有重要作用。中医药临床治疗GERD伴焦虑抑郁症多以补脾益胃、疏肝解郁、和胃降逆、清热燥湿论治。上述研究证实,中药复方内服法(平冲降逆汤、调中化湿汤等)、中医药内服外用联合疗法(连翘泄热汤联合穴位贴敷、针刺督脉背段联合疏肝利胆和胃中药等)、中西药内服联合疗法(健脾疏肝汤联合雷贝拉唑、雷贝拉唑联合建中降逆汤等)可通过调控脑肠肽、肠道菌群、炎症因子、胃肠激素等分子信号来改善患者的GERD症状及焦虑、抑郁状态,从而提升患者生活质量。

中医药临床治疗GERD伴焦虑抑郁症具有重要的实用价值,但仍存在尚不明确且亟待解决的问题:(1)中药复方富含多种活性成分,组成复杂,导致其具体作用机制尚不明确,需要进一步进行物质基础和药理机制研究;(2)结合现代先进医学科技设备,统筹不同中医证型的疾病靶点及分子机制,以更好地了解GERD伴焦虑抑郁症的病理机制,并进行针对性治疗;(3)GERD与焦虑抑郁症二者共病的中医药干预研究有限,研究样本量小,且治法、方药等尚未形成完善体系。基于此,建议开展随机对照试验来评估GERD伴焦虑抑郁症的个体化治疗效果,为临床提供有力的科学证据。

#### 参考文献

[1] KATZ P O, DUNBAR K B, SCHNOLL-SUSSMAN F H, et al. ACG clinical guideline for the diagnosis and management of gastroesophageal reflux disease[J]. *Am J Gastroenterol*, 2022, 117(1):27-56.

[2] ZHANG D C, LIU S J, LI Z Q, et al. Global, regional and national burden of gastroesophageal reflux disease, 1990-2019: update from the GBD 2019 study[J]. *Ann Med*, 2022, 54(1):1372-1384.

[3] HE M J, WANG Q, YAO D, et al. Association between psychosocial disorders and gastroesophageal reflux disease: a systematic review and meta-analysis[J]. *J Neurogastroenterol Motil*, 2022, 28(2):212-221.

[4] RUTSCH A, KANTSJÖ J B, RONCHI F. The gut-brain axis: how microbiota and host inflammasome influence brain physiology and pathology[J]. *Front Immunol*, 2020, 11:604179.

[5] 刘凡, 张书, 郭洁, 等. 中医药治疗胃食管反流病特色与优势探讨[J]. *辽宁中医药大学学报*, 2021, 23(6):157-160.

LIU F, ZHANG S, GUO J, et al. Discussion on the characteristics and advantages of TCM in the treatment of gastroesophageal reflux disease[J]. *J Liaoning Univ Tradit Chin Med*, 2021, 23(6):157-160.

[6] 张声生, 朱生樑, 王宏伟, 等. 胃食管反流病中医诊疗专家共识意见:2017[J]. *中国中西医结合消化杂志*, 2017, 25(5):321-326.

ZHANG S S, ZHU S L, WANG H W, et al. Consensus opinion of TCM diagnosis and treatment experts on gastroesophageal reflux disease: 2017[J]. *Chin J Integr Tradit West Med Dig*, 2017, 25(5):321-326.

[7] 李仲贤, 彭乡敏, 徐海燕, 等. 调神固本整合针灸治疗轻度抑郁症共病胃食管反流病36例[J]. *中国针灸*, 2023, 43(11):1300-1302.

LI Z X, PENG X M, XU H Y, et al. Treatment of 36 cases of gastroesophageal reflux disease associated with mild depression by Tiaoshen guben integrated acupuncture and moxibustion[J]. *Chin Acupunct Moxib*, 2023, 43(11):1300-1302.

[8] 沈馨, 孙志宏. 微生物-肠-脑轴与神经系统疾病的研究进展[J]. *生物工程学报*, 2021, 37(11):3781-3788.

SHEN X, SUN Z H. Microbe-gut-brain axis and neurological disorders: a review[J]. *Chin J Biotechnol*, 2021, 37(11):3781-3788.

[9] 张云燕, 梁雅琳, 罗贞艺, 等. 基于脑肠轴探讨背俞指针疗法治疗胃食管反流病诊疗思路[J]. *辽宁中医药大学学报*, 2023, 25(4):195-198.

ZHANG Y Y, LIANG Y L, LUO Z Y, et al. Discussion on the therapeutic approach of Beishu pointer therapy in the treatment of gastroesophageal reflux disease based on brain gut axis[J]. *J Liaoning Univ Tradit Chin Med*, 2023, 25(4):195-198.

[10] CARABOTTI M, SCIROCCO A, MASELLI M A, et al. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems[J]. *Ann Gastroenterol*, 2015, 28(2):203-209.

- [11] ONG J S, AN J Y, HAN X K, et al. Multitrait genetic association analysis identifies 50 new risk loci for gastroesophageal reflux, seven new loci for Barrett's oesophagus and provides insights into clinical heterogeneity in reflux diagnosis[J]. *Gut*, 2022, 71(6): 1053-1061.
- [12] 范明明, 张湘龙, 刘佳鑫, 等. 基于脑-肠轴理论探讨功能性消化不良的中医研究进展[J]. *中南大学学报(医学版)*, 2019, 44(11): 1300-1305.  
FAN M M, ZHANG X L, LIU J X, et al. Research progress in functional dyspepsia relevant to traditional Chinese medicine based on the theory of brain-gut axis[J]. *J Cent South Univ Med Sci*, 2019, 44(11): 1300-1305.
- [13] 刘秦浪, 孙林梅, 孙慧, 等. 从脑肠轴探讨功能性便秘伴情绪异常发病机制的研究进展[J]. *世界中医药*, 2022, 17(4): 579-582, 589.  
LIU Q L, SUN L M, SUN H, et al. Research progress on the pathogenesis of functional constipation with emotional disorders from brain-gut axis perspectives[J]. *World Chin Med*, 2022, 17(4): 579-582, 589.
- [14] 郭小轩, 王珑, 邹伟, 等. 基于肠道菌群理论针灸抗抑郁机制研究进展[J]. *上海针灸杂志*, 2020, 39(11): 1473-1478.  
GUO X X, WANG L, ZOU W, et al. Research progress on antidepressant mechanism of acupuncture based on intestinal flora theory[J]. *Shanghai J Acupunct Moxibustion*, 2020, 39(11): 1473-1478.
- [15] DUAN X Y, CHEN P, XU X X, et al. Role of gastric microorganisms other than *Helicobacter pylori* in the development and treatment of gastric diseases[J]. *Biomed Res Int*, 2022, 2022: 6263423.
- [16] JANG S H, WOO Y S, LEE S Y, et al. The brain-gut-microbiome axis in psychiatry[J]. *Int J Mol Sci*, 2020, 21(19): 7122.
- [17] BROERS C, GEERAERTS A, BOECXSTAENS V, et al. The role of serotonin in the control of esophageal sensitivity assessed by multimodal stimulation in health[J]. *Neurogastroenterol Motil*, 2021, 33(3): e14057.
- [18] 马巾茹, 柴红, 宫璇, 等. 胃食管反流病患者合并焦虑、抑郁状态的研究进展[J]. *中国临床医生杂志*, 2023, 51(5): 533-537.  
MA J R, CHAI H, GONG X, et al. Research progress of patients with gastroesophageal reflux disease complicated with anxiety and depression[J]. *Chin J Clin*, 2023, 51(5): 533-537.
- [19] MENARD C, PFAU M L, HODES G E, et al. Social stress induces neurovascular pathology promoting depression[J]. *Nat Neurosci*, 2017, 20(12): 1752-1760.
- [20] 陈冬雪, 夏聪媛, 徐愿, 等. 从脑肠轴探讨胃食管反流病伴抑郁症发病机制的研究进展[J]. *临床医学工程*, 2020, 27(3): 383-384.  
CHEN D X, XIA C Y, XU Y, et al. Research progress in the pathogenesis of gastroesophageal reflux disease complicated with depression on the basis of brain-gut axis[J]. *Clin Med Eng*, 2020, 27(3): 383-384.
- [21] KATZKA D A, PANDOLFINO J E, KAHRILAS P J. Phenotypes of gastroesophageal reflux disease: where Rome, Lyon, and Montreal meet[J]. *Clin Gastroenterol Hepatol*, 2020, 18(4): 767-776.
- [22] SARKAR S, WOOLF C J, HOBSON A R, et al. Perceptual wind-up in the human oesophagus is enhanced by central sensitisation[J]. *Gut*, 2006, 55(7): 920-925.
- [23] 戴琦, 上官定, 杜艺婷. 平冲降逆汤治疗胃食管反流病合并轻中度焦虑抑郁临床研究[J]. *湖北中医药大学学报*, 2023, 25(4): 54-57.  
DAI Q, SHANGGUAN D, DU Y T. Clinical study on Pingchong jiangni decoction on gastroesophageal reflux disease with mild-to-moderate anxiety and depression[J]. *J Hubei Univ Chin Med*, 2023, 25(4): 54-57.
- [24] 唐丽明, 宋宁, 熊鹰, 等. 旋覆代赈汤加味治疗肝胃不和型难治性胃食管反流病的临床疗效及对胃肠激素的影响[J]. *辽宁中医杂志*, 2020, 47(11): 109-112.  
TANG L M, SONG N, XIONG Y, et al. Effect of modified Xuanfu daizhe decoction on refractory gastroesophageal reflux disease of disharmony between liver and stomach syndrome and its influence on gastrointestinal hormones[J]. *Liaoning J Tradit Chin Med*, 2020, 47(11): 109-112.
- [25] 孙叙敏, 张雅月, 尹璐. 柴胡疏肝散合旋覆代赈汤加减治疗伴焦虑、抑郁的胃食管反流病的临床疗效[J]. *中国实验方剂学杂志*, 2021, 27(8): 88-93.  
SUN X M, ZHANG Y Y, YIN L. Clinical efficacy of modified Chaihu shugansan combined with Xuanfu daizhe-tang on depression of patients of patients with gastroesophageal reflux disease[J]. *Chin J Exp Tradit Med Formulae*, 2021, 27(8): 88-93.
- [26] 王杰, 孙永顺. 柴芍通降方治疗肝胃不和证非糜烂性反流病的临床疗效观察[J]. *中国中西医结合消化杂志*, 2023, 31(7): 545-551.  
WANG J, SUN Y S. Clinical study on Chaishao tongjiang prescription in treating non-erosive reflux disease with liver-stomach dissonance[J]. *Chin J Integr Tradit West Med Dig*, 2023, 31(7): 545-551.
- [27] 何美君, 白光, 李晶, 等. 疏肝降逆和胃方治疗肝胃不和型非糜烂性胃食管反流病临床研究[J]. *陕西中医*, 2021, 42(11): 1539-1543.  
HE M J, BAI G, LI J, et al. Clinical study on Shugan jiangni hewei recipe in treating non-erosive gastroesophageal reflux disease with disharmony of liver and stomach[J]. *Shaanxi J Tradit Chin Med*, 2021, 42(11): 1539-1543.
- [28] 梁育仪, 吴波, 傅诗书. 柴胡陷胸汤加减治疗肝胃郁热型胃食管反流病的临床疗效观察[J]. *广州中医药大学学报*, 2021, 38(6): 1118-1123.

- LIANG Y Y, WU B, FU S S. Clinical efficacy observation of gastroesophageal reflux disease with liver and stomach stagnated heat type treated by modified Chaihu xianxiang decoction[J]. J Guangzhou Univ Tradit Chin Med, 2021, 38(6):1118-1123.
- [29] 周燕,李保良,曾志,等.建中降逆汤治疗非糜烂性胃食管反流病中虚气逆证临床研究[J].陕西中医,2022,43(6):740-743.
- ZHOU Y, LI B L, ZENG Z, et al. Clinical study on Jianzhong jiangni decoction in treatment of non-erosive gastroesophageal reflux disease with zhongxu qini type[J]. Shaanxi J Tradit Chin Med, 2022, 43(6):740-743.
- [30] 杨成宁,陈广文,黄晓燕,等.调中化湿汤治疗胃食管反流病伴焦虑抑郁患者的疗效及对血清MTL、5-HT、DA的影响[J].时珍国医国药,2021,32(4):899-902.
- YANG C N, CHEN G W, HUANG X Y, et al. Therapeutic effect of Tiaohuashi decoction on patients with gastroesophageal reflux disease complicated with anxiety and depression and its influence on serum MTL, 5-HT and DA [J]. Lishizhen Med Mater Med Res, 2021, 32(4):899-902.
- [31] 赵志勇.二陈平胃散加减治疗气郁痰阻型难治性胃食管反流病的临床疗效观察[J].中国现代药物应用,2022,16(7):150-152.
- ZHAO Z Y. Clinical efficacy of modified Erchen pingwei powder on refractory gastroesophageal reflux disease of Qi stagnation and phlegm obstruction type[J]. Chin J Mod Drug Appl, 2022, 16(7):150-152.
- [32] 刘娟,潘凤霞,张月.柴胡疏肝散与左金丸加味治疗胃食管反流病相关性胸痛的效果分析[J].当代医学,2022,28(6):158-160.
- LIU J, PAN F X, ZHANG Y. Effect of Chaihu shugan powder and Zuojin pills on chest pain related to gastroesophageal reflux disease[J]. Contemp Med, 2022, 28(6):158-160.
- [33] 张贞鲁,李静.加味四逆散治疗非糜烂性胃食管反流疗效及对患者睡眠质量的影响[J].陕西中医,2019,40(12):1683-1685.
- ZHANG Z L, LI J. Therapeutic effect of Jiawei sini powder on non-erosive gastroesophageal reflux and its influence on sleep quality of patients[J]. Shaanxi J Tradit Chin Med, 2019, 40(12):1683-1685.
- [34] 马可迅,杨梦坤,姚舜,等.连栀泄热汤联合穴位贴敷治疗难治性胃食管反流病痰热互结证的临床研究[J].环球中医药,2023,16(8):1654-1658.
- MA K X, YANG M K, YAO S, et al. Clinical study on the treatment of difficult to treat gastroesophageal reflux disease with blood stasis and heat stagnation syndrome by Lianzhi xiere decoction combined with acupoint application [J]. Global Tradit Chin Med, 2023, 16(8):1654-1658.
- [35] 李华岳,马昕宇.针刺督脉背段联合中药治疗非糜烂性胃食管反流疗效观察[J].上海针灸杂志,2018,37(11):1229-1234.
- LI H Y, MA X Y. Therapeutic observation of acupuncture at the back segment of governor vessel plus Chinese medication for non-erosive gastroesophageal reflux disease[J]. Shanghai J Acupunct Moxibustion, 2018, 37(11):1229-1234.
- [36] 梁宇晗,何慧彬,郑敏,等.中西医结合治疗难治性反流性食管炎的临床疗效及对脑肠肽指标的影响[J].中国中西医结合消化杂志,2023,31(6):456-462.
- LIANG Y H, HE H B, ZHENG M, et al. Clinical effect of integrated traditional Chinese and western medicine on refractory reflux esophagitis and its influence on brain-gut peptide index[J]. Chin J Integr Tradit West Med Dig, 2023, 31(6):456-462.
- [37] 吴银亚,汤小龙,马上吉,等.雷贝拉唑联合建中降逆汤治疗非糜烂性胃食管反流病的效果[J].中国医学创新,2022,19(21):78-81.
- WU Y Y, TANG X L, MA S J, et al. Effects of rabeprazole combined with Jianzhong jiangni decoction on non-erosive gastroesophageal reflux disease[J]. Med Innov China, 2022, 19(21):78-81.
- [38] 曹燕飞,何若瑜,王彦斐,等.归脾汤联合艾司奥美拉唑镁肠溶片治疗非糜烂性反流病伴情绪障碍患者的临床研究[J].浙江中医药大学学报,2021,45(10):1072-1079.
- CAO Y F, HE R Y, WANG Y F, et al. Effect of Guipi decoction combined with esomeprazole magnesium enteric-coated tablets on non-erosive reflux disease with emotional disorder[J]. J Zhejiang Chin Med Univ, 2021, 45(10):1072-1079.
- [39] 翟昂帅,曲娟.气滞胃痛颗粒对非糜烂性胃食管反流病患者焦虑抑郁情绪及睡眠质量的影响[J].继续医学教育,2021,35(11):159-162.
- ZHAI A S, QU J. Effects of Qizhi weitong granule on anxiety and depression mood and sleep quality in patients with non-erosive gastroesophageal reflux disease[J]. Continuing Med Educ, 2021, 35(11):159-162.
- [40] 尹毅,朱存成.柴胡温胆汤联合西药对非糜烂性胃食管反流病合并焦虑抑郁的疗效及对自主神经功能影响[J].辽宁中医杂志,2020,47(8):97-99.
- YIN Y, ZHU C C. Effect of Chaihu wendan decoction combined with western medicine on non-erosive gastroesophageal reflux disease combined with anxiety depression and its effect on autonomic nerve function[J]. Liaoning J Tradit Chin Med, 2020, 47(8):97-99.
- [41] 何若瑜,曹燕飞.归脾汤联合质子泵抑制剂治疗非糜烂性反流病伴抑郁患者的临床观察及对血清脑肠肽水平的影响[J].中国现代医生,2018,56(19):97-100.
- HE R Y, CAO Y F. Effect of Guipi decoction combined with proton pump inhibitor on patients with non-erosive reflux disease complicated with depression and its effect on serum brain-gut peptide levels[J]. China Mod Dr, 2018, 56(19):97-100.

(收稿日期:2024-04-02 修回日期:2024-08-26)

(编辑:邹丽娟)