

· 基金项目纵览 ·

半夏泻心汤治疗慢性萎缩性胃炎的机制研究进展

任小军¹, 张曼玲², 赵慧慧¹, 时昭红^{1,2}

(1. 湖北中医药大学, 湖北 武汉 430000; 2. 湖北中医药大学附属武汉市中西医结合医院, 湖北 武汉 430000)

摘要:慢性萎缩性胃炎是公认的胃癌前病变,既往研究显示其病理状态正处于“炎-癌”转换的关键时期。早期识别并恰当干预是截断病程、逆转萎缩、防止癌变的核心环节。现代医学和中医传统医学均对此疾病展开了大量研究,以期可以挖掘其内在机制,从而提高临床疗效。大量研究显示中医中药在防治萎缩性胃炎方面表现出了卓越的优势,尤其以“半夏泻心汤”为代表的经典方剂研究最为深入。越来越多的基础及临床研究从不同角度阐述了“半夏泻心汤”治疗萎缩性胃炎的内在机制,但其散乱地分散在大量文献中,缺少系统的归纳及整理,给后续研究者从整体上了解“半夏泻心汤”治疗此疾病的内在机制造成了一定困扰。文章将从“半夏泻心汤”对胃蛋白酶及胃泌素水平的调节、辅助根除幽门螺杆菌、调控炎症、凋亡、血管新生等多种生物学过程以及靶向抑制PD-1、改善胃内微环境等5个方面,将近年来以“半夏泻心汤”为核心方剂治疗慢性萎缩性胃炎的相关机制研究做一综述,以为后续研究提供参考。

关键词:慢性萎缩性胃炎; 半夏泻心汤; 作用机制; 胃癌前病变

中图分类号: R285 **文献标志码:** A **文章编号:** 1673-842X(2024) 10-0065-05

Research Progress on the Mechanisms of Banxia Xiexin Decoration (半夏泻心汤) in the Treatment of Chronic Atrophic Gastritis

REN Xiaojun¹, ZHANG Manling², ZHAO Huihui¹, SHI Zhaohong^{1,2}

(1. Hubei University of Chinese Medicine, Wuhan 430000, Hubei, China;

2. Hubei University of Chinese Medicine Affiliated Wuhan Integrated Chinese and Western Medicine Hospital, Wuhan 430000, Hubei, China)

Abstract: Chronic atrophic gastritis (CAG) is recognized as a precancerous lesion of gastric cancer, and previous studies have shown that its pathological state is at a critical stage of transition from inflammation to cancer. Early recognition and appropriate intervention are crucial in interrupting the disease progression, reversing atrophy, and preventing carcinogenesis. Extensive research has been conducted on this condition by both modern medicine and traditional Chinese medicine, aiming to explore its underlying mechanisms and improve clinical efficacy. Numerous studies have demonstrated the remarkable advantages of traditional Chinese medicine and herbal medicine in the prevention and treatment of CAG, with a particular focus on the in-depth investigation of classic formulas such as “Banxia Xiexin Decoration (半夏泻心汤)”. Increasing amounts of basic and clinical research have elucidated the underlying mechanisms of “Banxia Xiexin Decoration” in treating CAG from different perspectives. However, these findings are scattered across a large number of literature sources, lacking systematic summarization and organization, which poses challenges for researchers to comprehensively understand the mechanisms of “Banxia Xiexin Decoration” in treating this disease. In this paper, we aim to provide a comprehensive review of recent research on the mechanisms of “Banxia Xiexin Decoration” in treating CAG, with a focus on five aspects: regulation of gastric protease and gastrin levels, assisting in the eradication of *Helicobacter pylori*, modulation of inflammation, apoptosis, and angiogenesis, as well as targeted inhibition of PD-1 and improvement of the gastric microenvironment. By presenting the relevant mechanistic studies of “Banxia Xiexin Decoration” as a core formula for treating CAG, we hope to provide a reference for future research in this field.

Keywords: chronic atrophic gastritis; Banxia Xiexin Decoration (半夏泻心汤); mechanisms of action; precancerous lesions of gastric cancer

慢性萎缩性胃炎(chronic atrophic gastritis, CAG)是公认的胃癌前病变(precancerous lesions of gastric cancer, PLGC)^[1]。CAG在组织病理上一般表现为胃黏膜固有腺体萎缩,或伴有肠上皮以及假幽

门腺化生^[2]。目前诊断主要依靠胃镜结合病理活检的方法^[3]。现代医学治疗CAG以根除幽门螺杆菌(*helicobacter pylori*, HP)、补充叶酸、改善饮食习惯等治疗为主^[4-5]。中医传统医学从“整体观念”和“辨

基金项目: 国家重点研发计划项目(2017YFC1700601); 武汉市卫健委青年项目(WZ22Q28); 武汉市卫健委重点项目(WZ20A07)

作者简介: 任小军(1993-),男,四川达州人,博士在读,研究方向:中西医结合治疗消化系统疾病。

通讯作者: 时昭红(1967-),女,湖北武汉人,教授、主任医师,博士研究生导师,博士,研究方向:中西医结合治疗消化系统疾病。

证论治”角度出发,结合中药多途径、多靶点的优势,在治疗CAG方面取得了较好的临床疗效,且不良反应较少。半夏泻心汤作为经典名方,临床广泛应用于消化系统疾病的治疗,尤其近年来大量研究报道半夏泻心汤对CAG有较好的临床疗效。但其作用机制较为零散且复杂,目前尚无文献对其进行梳理,不利于后续研究的参考及开展。因此本文旨在查阅近年来半夏泻心汤治疗慢性萎缩性胃炎的相关文献,对其作用机制做一综述。

1 中西医对慢性萎缩性胃炎的认识

1.1 现代医学对慢性萎缩性胃炎的认识

胃癌是全球第五大常见的恶性肿瘤,也是全世界第三大癌症相关的死亡原因。经典的Correa途径早在1992年就阐释了肠型胃癌的发生、发展模式。其认为胃黏膜感染幽门螺杆菌后,会出现由浅表性胃炎-萎缩性胃炎-肠上皮化生-异型增生-胃癌这一连续转换过程^[6]。而萎缩性胃炎这一病理阶段在组织病理学上表现为胃固有腺体的萎缩,可伴有肠上皮化和假幽门腺的化生,是公认的胃癌前病变。荷兰的一项队列研究显示,在确诊萎缩性胃炎后的5年内,胃癌的年发病率是0.1%^[7]。而我国的一项多中心研究显示,我国慢性胃炎患者中慢性萎缩性胃炎的比例高达25.8%^[8]。因此,如何阻断慢性萎缩性胃炎进展为胃癌是目前研究的热点问题。幽门螺杆菌是一种微需氧革兰氏阴性菌,1994年就被世界卫生组织列为I类致癌物^[9]。它的感染与萎缩性胃炎、胃癌、消化性溃疡、胃黏膜相关淋巴瘤(MALT)关系密切^[10]。因此推荐慢性萎缩性胃炎的患者进行根除幽门螺杆菌治疗^[11]。研究显示,在根除幽门螺杆菌后早期胃癌患者异时性胃癌发生率明显降低,并且胃体萎缩程度较前明显改善^[12]。因此现代医学以根除幽门螺杆菌为治疗慢性萎缩性胃炎的核心手段,辅以补充叶酸、微量元素及改变饮食习惯等方式,在一定程度上可以使萎缩黏膜得到恢复。

1.2 中医传统医学对慢性萎缩性胃炎的认识

中医传统医学尚无萎缩性胃炎的名称,根据临床症状多命名为“胃痞”“胃脘痛”等。病性多属“本虚标实”,本虚以脾胃气虚和/或阴虚为主,标实则有血瘀、热毒、湿阻、气滞等,多呈兼夹之势^[13]。治疗则有“补虚祛瘀”“补虚清热”“补虚化湿”“补虚理气”等多种原则。半夏泻心汤首载于《伤寒论》,由“半夏、黄芩、黄连、干姜、人参、甘草、大枣”七味中药组成,全方具有安中补虚、调和寒热、清上温下的功效。方中“人参、大枣、甘草”补虚安中,“黄芩、黄连”清热燥湿,“半夏、干姜”祛湿温中,与萎缩性胃炎的病机相吻合。因此开展了大量有关半夏泻心汤治疗萎缩性胃炎的研究,取得了较好的临床疗效^[14]。研究表明,半夏泻心汤可以通过多种机制参与萎缩性胃炎的治疗过程。主要包括对胃肠激素的调节、辅助根除幽门螺杆菌、改善胃内微环境、调节多条信号通路、介导多种表型,阻断“炎-癌”转化等多种途径发挥治疗作用。

2 半夏泻心汤治疗萎缩性胃炎的机制研究

2.1 半夏泻心汤调节胃蛋白酶及胃泌素水平

血清胃蛋白酶原是临床广泛用来评价胃黏膜

分泌功能的标记物^[15-16],通过联合胃蛋白酶原-I(pepsinogen-I, PG-I)和蛋白酶原-II(pepsinogen-II, PG-II)的比例对萎缩性胃炎进行血清学诊断,表现出较好的效能^[17-19],被推荐作为萎缩性胃炎及胃癌的非侵入性筛查指标^[20-21]。胃泌素-17(G-17)广泛存在于血浆或胃窦黏膜组织中,其可以调节胃酸分泌以及胃黏膜生长^[22-23],是诊断慢性萎缩性胃炎的另一种非侵入性标记物^[24-26]。王菁等^[27]通过随机对照试验的方法评价了半夏泻心汤联合胃复春治疗萎缩性胃炎的疗效,结果提示:半夏泻心汤联合胃复春可明显改善萎缩性胃炎的临床症状及内镜下表现,其可能的机制是参与调节了胃蛋白酶的表达。马会妙等^[28]研究发现半夏泻心汤可以调节幽门螺杆菌感染相关性胃炎,胃蛋白酶原及胃泌素-17的表达。高艳青教授^[29]团队进一步评价了半夏泻心汤及其类方对大鼠胃蛋白酶活性的影响,结果提示:半夏泻心汤、生姜泻心汤、甘草泻心汤三方对胃蛋白酶活性的改变无显著影响,而甘草与大枣的配伍可显著降低胃蛋白酶活性。因此,半夏泻心汤可能通过调节胃蛋白酶及胃泌素水平来发挥治疗慢性萎缩性胃炎的作用,但对胃蛋白酶活性的影响可能不大。

2.2 半夏泻心汤辅助根除幽门螺杆菌

幽门螺杆菌感染与慢性萎缩性胃炎存在明确的因果关系^[30-31]。因此根除幽门螺杆菌是治疗慢性萎缩性胃炎的主流方法之一。但仍有部分患者存在对抗幽门螺杆菌治疗不敏感,甚至存在耐药、过敏等情况^[32]。因此中医中药发挥了重要的替代治疗作用。大量临床试验研究了半夏泻心汤对幽门螺杆菌感染相关萎缩性胃炎的临床疗效^[33-34],最近的一篇Meta分析提示:半夏泻心汤联合西药可明显缓解幽门螺杆菌相关萎缩性胃炎的临床症状,并且提高了幽门螺杆菌的清除率与单用西药组相比表现出了显著差异^[35]。进一步研究显示:半夏泻心汤可能通过削弱毒力因子Cag A、Vac A、 γ -GGT从而发挥作用^[36]。此外,半夏泻心汤在难治性幽门螺杆菌方面也表现出较好的临床疗效。方春芝等^[37]研究发现半夏泻心汤在分阶段综合治疗幽门螺杆菌感染方面,与对照组相比可明显提高幽门螺杆菌的清除率,且在症状改善方面也优于对照组。最新研究报道,半夏泻心汤对耐药幽门螺杆菌感染小鼠也表现出良好的治疗作用^[38]。因此,半夏泻心汤在辅助根除幽门螺杆菌方面有明确的疗效,且其发挥作用的机制可能是多方面的。尤其对耐药人群或者对抗幽门螺杆菌有相对禁忌的人群有明显的优势。

2.3 半夏泻心汤调节炎症、凋亡、血管新生等多种表型

炎症是萎缩性胃炎发生的使动因素之一,阻断炎症对黏膜的损伤是逆转萎缩的关键。TNF信号通路、PI3K-Akt信号通路、NF- κ B信号通路是治疗慢性萎缩性胃炎常见炎症相关通路,半夏泻心汤可以通过多条信号通路阻断炎症的发展,进而防止和逆转萎缩。SUN等^[39]通过网络药理学的方法,分析半夏泻心汤中共有的152个有效成分,富集分析表明半夏泻心汤参与治疗慢性萎缩性胃炎,主要是

通过调节TNF信号通路、PI3K-Akt信号通路、NF- κ B信号通路和影响细胞凋亡来实现的。刘洁教授^[40]团队进一步在动物模型上做了验证,结果提示:半夏泻心汤可以使大鼠胃黏膜中PI3K的表达升高,Akt、mTOR的表达降低,从而使HIF-1 α 的表达水平降低,由此提高p53水平降低Bcl-2的表达,达到治疗甚至逆转PLGC的目的。而针对半夏泻心汤中核心药组“黄连、半夏”的动物研究提示:黄连、半夏的主要成分可通过降低血清炎症因子水平,抑制JAK2/STAT3通路与血管新生,修复胃黏膜形态,从而防止萎缩性胃炎向恶性肿瘤演化^[41]。Notch信号通路与胃癌的发生关系密切^[42-43],在哺乳动物中Notch有4种受体亚型,其中Nothc 1和Nothc 2亚型在肿瘤组织中高表达^[44]。研究发现半夏泻心汤可能通过下调Nothc1/2来发挥对慢性萎缩性胃炎的治疗作用^[45]。Wnt/ β -catenin信号通路参与多种疾病的发生发展。研究显示,半夏泻心汤含药血清可以通过抑制Wnt/ β -catenin信号通路从而抑制胃癌细胞活性和克隆形成,促进氧化应激、诱导细胞凋亡参与胃癌治疗^[46]。因此,半夏泻心汤可能通过参与多条信号通路来阻断炎症的进展,促进凋亡、阻断血管新生与克隆形成来发挥逆转萎缩的作用。

2.4 半夏泻心汤靶向抑制PD-1

PD-1是一种负性共刺激受体,主要在活化的T细胞上表达。PD-1与其配体程序性细胞死亡配体1或2(PD-L1或PD-L2)的相互作用会抑制T细胞活化^[47]。PD-L1和PD-1之间的相互作用会抑制细胞毒性T细胞的活性、减少T细胞产生细胞因子并诱导Treg细胞生成^[48]。这种相互作用可以保护肿瘤细胞免受细胞毒性T细胞的破坏,并促进肿瘤细胞的增殖。有研究显示,半夏泻心汤通过多靶点、多途径调控胃癌主要癌基因,抑制PD-L1的表达从而影响细胞增殖和凋亡^[49]。后续研究提示:半夏泻心汤可以通过调节MGMT的表达影响胃癌细胞的药物敏感性。该过程通过PD-L1发挥作用,而PD-L1本身由IL-6/JAK/STAT3信号通路介导^[50]。慢性萎缩性胃炎作为癌前病变,亦具有恶性肿瘤的某些生物学特性。因此我们推测,半夏泻心汤有可能通过抑制PD-L1的表达发挥治疗萎缩性胃炎的作用。当然需要后续相关研究需要进一步进行验证。

2.5 半夏泻心汤可以改善胃内微环境

胃内微环境的改变通过多种途径介导胃癌及癌前病变的发生^[51]。既往研究表明,变形菌门、厚壁菌门、拟杆菌门、梭杆菌门和放线菌门在胃内占据主导地位,若微环境中细菌过度生长,则导致胃内微环境失衡,其代谢产物则会损伤胃黏膜,甚至诱发癌变^[52]。有研究通过测序的方法评价了慢性胃炎、肠化生和胃癌患者胃黏膜微生物菌群的差异,结果提示:胃癌患者胃黏膜的微生物组成与慢性胃炎和肠化生患者存在显著差异^[53]。目前认为中医药可以通过改善胃肠道微生态结构、保护胃肠道黏膜生物屏障、防止菌群移位、增强胃肠黏膜免疫功能等多种途径对胃肠道恶性肿瘤起到干预作用^[54]。半夏泻心汤中核心成分小檗碱可以调节肠道菌群结构,抑制具核梭杆菌的致肿瘤生成作用^[55];魏俊等^[56]对甘草泻心汤是否可以改善胃肠道肿瘤术后发生的肠道菌群

紊乱进行了研究,结果显示甘草泻心汤可明显减轻胃肠道术后的肠道菌群紊乱。推测甘草泻心汤可改善肿瘤手术造成的胃肠道微生态失衡,并有降低术后并发症发生率的作用。胃内微环境的改变与癌前病变的发生是研究的热点话题,通过测序技术大量的微生物被鉴定和分离,而中医的整体观念与微环境的概念存在某种程度的相似性,或许通过对微环境的改变可以解开中医治病的密码。因此,中医药和微环境的研究可能是将来重点突破的领域。

3 讨论

胃癌是全球第五高发的恶性肿瘤,也是恶性肿瘤相关死亡的第三大病因^[57]。而在我国,胃癌是我国发病率第一的消化道恶性肿瘤,在所有恶性肿瘤中发病率排第二位,病死率排第三^[58]。且大多数胃癌在初次诊断时已经处于进展期,进而导致5年生存率低^[59]。因此早期发现,早期阻断,早期治疗是提高疗效,改善预后的关键。慢性萎缩性胃炎处于“炎症-癌变”转换的关键环节,目前现代医学和中医传统医学均在此阶段做了大量研究,以期可以达到逆转萎缩,防止癌变的目的。然而现代医学以祛除病因、改善临床症状为主的治疗手段,虽可以在短时间缓解症状,但无法从根本上逆转“炎-癌”转换模式。而中医传统医学在“整体观念”及“辨证论治”理论框架的指导下,使用中医中药防治萎缩性胃炎等癌前病变表现出了巨大的潜力。研究报道,目前有多种中药复方及单体成分均在一定程度上可以改善炎症、逆转萎缩^[60],尤其以摩罗丹及胃复春为代表的中成药在改善萎缩方面获得了高级别循证医学证据支撑^[14,61]。

半夏泻心汤是治疗消化系统疾病的经典名方,对消化系统多种疾病表现出了较好的临床疗效^[62]。大量临床及动物实验均表明,半夏泻心汤可以通过多种途径改善胃黏膜萎缩,尤其以辅助根除幽门螺杆菌、改善胃内微环境以及调节胃肠道激素水平的研究较为深入。半夏泻心汤也可以通过激活或者抑制多种信号通路的关键蛋白及分子调节多种癌前病变相关表型。然而,因为萎缩性胃炎的病因及病机的复杂性,中医药治疗该疾病出现了各家学术争鸣的情况,导致很多针对机制的研究也不够深入,缺乏对疾病本质及核心机制的深入探索。

本研究系统综述了近年来以半夏泻心汤为核心方剂治疗萎缩性胃炎的相关机制,为后续研究提供了参考方向。但现在我们发现,现有的机制研究存在着研究面广,但机制研究不深、不透的情况。因此,后续研究可以在前期研究的基础上,对有可能发挥疗效的核心机制及靶点进行有针对性的、多维度的探究。◆

参考文献

- [1] KOULIS A, BUCKLE A, BOUSSIOUTAS A. Premalignant lesions and gastric cancer: Current understanding [J]. World journal of gastrointestinal oncology, 2019, 11 (9): 665-678.
- [2] 李军祥,陈諝,吕宾. 慢性萎缩性胃炎中西医结合诊疗共识意见(2017年)[J]. 中国中西医结合消化杂志, 2018, 26 (2): 121-131.
- [3] RUGGE M, CORREA P, DIXON M, et al. Gastric mucosal atrophy: interobserver consistency using new criteria for classification and grading [J]. Alimentary pharmacology therapeutics, 2002, 16 (7): 1249-1259.
- [4] VANNELLA L, LAHNER E, BORDI C, et al. Reversal of

- atrophic body gastritis after *H. pylori* eradication at long-term follow-up [J]. *Digestive Liver Disease*, 2011, 43 (4): 295-299.
- [5] LEI J, REN F, LI W, et al. Use of folic acid supplementation to halt and even reverse the progression of gastric precancerous conditions: a meta-analysis [J]. *BMC gastroenterology*, 2022, 22 (1): 1-9.
- [6] CORREA P. Human gastric carcinogenesis: a multistep and multifactorial process—first American Cancer Society award lecture on cancer epidemiology and prevention [J]. *Cancer research*, 1992, 52 (24): 6735-6740.
- [7] DE VRIES A C, VAN GRIEKEN N C, LOOMAN C W, et al. Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands [J]. *Gastroenterology*, 2008, 134 (4): 945-952.
- [8] DU Y, BAI Y, XIE P, et al. Chronic gastritis in China: a national multi-center survey [J]. *BMC gastroenterology*, 2014, 14: 1-9.
- [9] CANCER I A F R O. Schistosomes, liver flukes and *Helicobacter pylori*. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Lyon, 7-14 [J]. *IARC Monogr Eval Carcinog Risks Hum*, 1994, 61: 1-241.
- [10] KUSTERS J G, VAN VLIET A H, KUIPERS E J. Pathogenesis of *Helicobacter pylori* infection [J]. *Clinical microbiology reviews*, 2006, 19 (3): 449-490.
- [11] PIMENTEL-NUNES P, LIBÂNIO D, MARCOS-PINTO R, et al. Management of epithelial precancerous conditions and lesions in the stomach (maps II): European Society of gastrointestinal endoscopy (ESGE), European *Helicobacter* and microbiota Study Group (EHMSG), European Society of pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019 [J]. *Endoscopy*, 2019, 51 (4): 365-388.
- [12] CHOI I J, KOOK M-C, KIM Y-I, et al. *Helicobacter pylori* therapy for the prevention of metachronous gastric cancer [J]. *New England Journal of Medicine*, 2018, 378 (12): 1085-1095.
- [13] 赵静怡, 赵鲁卿, 张声生. 张声生以微观癥积论治慢性萎缩性胃炎伴低级别上皮内瘤变经验 [J]. *北京中医药*, 2020, 39 (1): 31-35.
- [14] WANG L, DING X, LI P, et al. Efficacy and safety of Weifuchun tablet for chronic atrophic gastritis: A systematic review and meta-analysis [J]. *Plos one*, 2023, 18 (4): e0284411.
- [15] BANG C S, LEE J J, BAIK G H. Diagnostic performance of serum pepsinogen assay for the prediction of atrophic gastritis and gastric neoplasms: Protocol for a systematic review and meta-analysis [J]. *Medicine*, 2019, 98 (4): e14240.
- [16] PARK Y H, KIM N. Review of atrophic gastritis and intestinal metaplasia as a premalignant lesion of gastric cancer [J]. *Journal of cancer prevention*, 2015, 20 (1): 25-40.
- [17] ADAMU M A, WECK M N, ROTHENBACHER D, et al. Incidence and risk factors for the development of chronic atrophic gastritis: Five year follow-up of a population-based cohort study [J]. *International journal of cancer*, 2011, 128 (7): 1652-1658.
- [18] WANG X, LU B, MENG L, et al. The correlation between histological gastritis staging- 'OLGA/OLGIM' and serum pepsinogen test in assessment of gastric atrophy/intestinal metaplasia in China [J]. *Scandinavian journal of gastroenterology*, 2017, 52 (8): 822-827.
- [19] LEE J Y, KIM N, LEE H S, et al. Correlations among endoscopic, histologic and serologic diagnoses for the assessment of atrophic gastritis [J]. *Journal of cancer prevention*, 2014, 19 (1): 47-55.
- [20] BANG C S, LEE J J, BAIK G H. Prediction of chronic atrophic gastritis and gastric neoplasms by serum pepsinogen assay: a systematic review and meta-analysis of diagnostic test accuracy [J]. *Journal of clinical medicine*, 2019, 8 (5): 657-693.
- [21] FOCK K M, TALLEY N, MOAYYEDI P, et al. Asia-Pacific consensus guidelines on gastric cancer prevention [J]. *Journal of gastroenterology hepatology*, 2008, 23 (3): 351-365.
- [22] REHFELD J F. The new biology of gastrointestinal hormones [J]. *Physiological reviews*, 1998, 78 (4): 1087-1108.
- [23] ROZENGURT E, WALSH J H. Gastrin, CCK, signaling, and cancer [J]. *Annual review of physiology*, 2001, 63 (1): 49-76.
- [24] SIPPONEN P, RANTA P, HELSKE T, et al. Atrophic gastritis serum levels of amidated gastrin-17 and pepsinogen i in atrophic gastritis: an observational case-control study [J]. *Scandinavian journal of gastroenterology*, 2002, 37 (7): 785-791.
- [25] SUN L, TU H, LIU J, et al. A comprehensive evaluation of fasting serum gastrin-17 as a predictor of diseased stomach in Chinese population [J]. *Scandinavian Journal of Gastroenterology*, 2014, 49 (10): 1164-1172.
- [26] WANG R, CHEN X-Z. Prevalence of atrophic gastritis in southwest China and predictive strength of serum gastrin-17: a cross-sectional study (SIGES) [J]. *Scientific reports*, 2020, 10 (1): 4523.
- [27] 王菁, 杨冰, 李丽, 等. 半夏泻心汤联合胃复春对慢性萎缩性胃炎患者血清表皮生长因子及血清胃蛋白酶原, 胃泌素表达影响 [J]. *辽宁中医药大学学报*, 2019, 21 (7): 154-157.
- [28] 马会妙, 马民凯, 吴立国, 等. 加减半夏泻心汤辅助治疗幽门螺杆菌相关性胃炎疗效及对胃肠激素, 氧化应激及炎症状态的影响 [J]. *现代中西医结合杂志*, 2021, 30 (24): 2681-2685.
- [29] 高艳青, 司银楚, 牛欣, 等. 半夏泻心汤及其类方不同配伍对正常大鼠胃液成分的影响 [J]. *北京中医药大学学报*, 2006, 29 (3): 168-171.
- [30] WECK M N, BRENNER H. Association of *Helicobacter pylori* infection with chronic atrophic gastritis: meta-analyses according to type of disease definition [J]. *International journal of cancer*, 2008, 123 (4): 874-881.
- [31] UEMURA N, OKAMOTO S, YAMAMOTO S, et al. *Helicobacter pylori* infection and the development of gastric cancer [J]. *New England journal of medicine*, 2001, 345 (11): 784-789.
- [32] LIU C, WANG Y, SHI J, et al. The status and progress of first-line treatment against *Helicobacter pylori* infection: a review [J]. *Therapeutic advances in gastroenterology*, 2021, 14: 1-12.
- [33] 吴欣欣. 半夏泻心汤治疗幽门螺杆菌相关性慢性萎缩性胃炎 [J]. *长春中医药大学学报*, 2013, 29 (5): 286-287.
- [34] 彭海平, 保继琼, 赵敏, 等. 加味半夏泻心汤治疗幽门螺杆菌相关性萎缩性胃炎 32 例 [J]. *西部中医药*, 2015, 28 (002): 94-96.
- [35] 李一桐, 尤佳, 宋瑶, 等. 半夏泻心汤治疗幽门螺杆菌相关性慢性萎缩性胃炎的 Meta 分析 [J]. *北京中医药*, 2021, 40 (10): 1143-1148.
- [36] 尹抗抗, 谭达全, 郭春秀, 等. 半夏泻心汤及其拆方抗幽门螺杆菌作用的研究 [J]. *湖南中医杂志*, 2012, 28 (6): 106-108.
- [37] 方春芝, 黄驭, 刘磊, 等. 半夏泻心汤在分阶段综合治疗难治性幽门螺杆菌感染的临床研究 [J]. *中医药学报*, 2021, 49 (11): 78-82.
- [38] LI X H, XU J Y, WANG X, et al. BanXiaXieXin decoction treating gastritis mice with drug-resistant *Helicobacter pylori* and its mechanism [J]. *World Journal of Gastroenterology*, 2023, 29 (18): 2818-2835.
- [39] CHANG C, FENG W, SUN M, et al. Mechanisms of Banxia Xiexin Decoction Underlying Chronic Atrophic Gastritis via Network Pharmacology, Molecular Docking, and Molecular Dynamics Simulations [J]. *Computational Mathematical Methods in Medicine*, 2022, 2022: 4237040.
- [40] 彭雪靖, 刘洁. 半夏泻心汤对 PLCG 大鼠胃黏膜 P13k/Akt/mTOR 通路的影响及其防治研究 [J]. *湖南中医杂志*, 2018, 34 (10): 155-157.
- [41] 向阳, 黄琼, 袁林. 黄连半夏药对治疗慢性萎缩性胃炎作用机制研究 [J]. *天然产物研究与开发*, 2022, 34 (11): 1822-1831.
- [42] BRZOZOWA M, MIELAŃCZYK Ł, MICHAŁSKI M, et al. Role of Notch signaling pathway in gastric cancer pathogenesis [J]. *Contemporary Oncology/Współczesna Onkologia*, 2013, 17 (1): 1-5.
- [43] HUANG T, ZHOU Y, CHENG A S, et al. NOTCH receptors in gastric and other gastrointestinal cancers: oncogenes or tumor suppressors? [J]. *Molecular cancer*, 2016, 15 (1): 1-12.
- [44] KELLY P N. Notch1 promotes cancer spread [J]. *Science*, 2017, 355 (6331): 1278-1279.
- [45] YU B, YONGCAN C, YU C, et al. Efficacy of Banxia Xiexin decoction in a rat model of chronic atrophic gastritis [J]. *Journal of Traditional Chinese Medicine*, 2019, 39 (6): 867-874.
- [46] SUN X, XUE D, ZHANG K, et al. Acrid-release and bitter-downbearing therapy and banxia xiexin decoction regulate Wnt/ β -catenin pathway, inhibit proliferation and invasion, and induce apoptosis in gastric cancer cells [J]. *American Journal of Translational Research*, 2021, 13 (6): 6211-6220.
- [47] FREEMAN G J, LONG A J, IWAI Y, et al. Engagement of the

《证治汇补》水肿诊疗理论框架研究

吕晓明, 尚冰, 傅海燕

(辽宁中医药大学, 辽宁 沈阳 110847)

摘要:《证治汇补》是由清代李用粹撰于康熙二十六年, 其对水肿病的认识非常丰富, 具有较高的临床价值。文章通过系统分析其对水肿病的因机证治理论, 构建《证治汇补》水肿诊疗理论框架。言明水肿病由诸湿肿满皆属于脾、肾虚水泛渗于皮肤, 肺失通调水液停聚所致, 同时肺肾相传。其辨治当分清阳水阴水、气肿水肿、风肿瘀肿、风水石水、水分血分等类型, 注重喘胀相因、水肿脉法和水肿死症。以“调中健脾”为治疗大法, 治分阴阳、治分汗渗、湿热宜清、寒湿宜温、阴虚宜补, 邪实当攻。四苓散加味为主方, 同时依据病情加减用药。成方亦选用金匱肾气丸、术附汤、地黄汤加味、椒仁丸和牵牛甘遂加味。外治法以商陆根加麝香、蝼蛄、田螺、大蒜、车前草等外敷。预防调护包括忌甘温药、戒针刺、绝酒色、却盐酱、戒忿怒。并根据上述内容绘制《证治汇补》水肿诊疗理论框架图谱, 进一步促进中医药古籍的利用, 开拓医生临床诊疗思路, 提高中医临床疗效。

关键词: 证治汇补; 水肿; 诊疗框架; 图谱

中图分类号: R256.51

文献标志码: A

文章编号: 1673-842X(2024) 10-0069-05

Study on the Theoretical Framework of Diagnosis and Treatment of Edema in Evidence and Treatment Supplement

LYU Xiaoming, SHANG Bing, FU Haiyan

(Liaoning University of Chinese Medicine, Shenyang 110847, Liaoning, China)

Abstract: The book *Zhengzhi Huibu* was written by LI Yongcui of the Qing Dynasty in the 26th year of Kangxi's reign. Its understanding of edema disease is very rich and has high clinical value. This article systematically analyzes the theory of etiology, mechanism, and treatment of edema disease, and constructs the theoretical framework of edema diagnosis and treatment in the book *Zhengzhi Huibu*. It is stated that edema disease is caused by various dampness and swelling, all of which belong to the spleen and kidney deficiency. Water seeps into the skin and the lungs lose circulation, leading to the stagnation of water

基金项目: 国家重点基础研究发展计划(973计划)项目(2013CB532004); 辽宁省科技计划联合计划基金-博士科研启动项目(2023-BSBA-227); 辽宁省教育厅高校基本科研项目(JYTQN2023475)

作者简介: 吕晓明(1993-), 男, 辽宁大连人, 讲师, 博士, 研究方向: 中医临床文献研究。

通讯作者: 傅海燕(1963-), 女, 辽宁沈阳人, 教授, 博士, 研究方向: 中医文献研究及中医名词术语研究。E-mail: fly8480@163.com。

尚冰(1974-), 男, 山东高密人, 教授, 博士, 研究方向: 中医文化基础研究与中医藏象研究。E-mail: 542747695@qq.com。

- PD-1 immunoinhibitory receptor by a novel B7 family member leads to negative regulation of lymphocyte activation [J]. The Journal of experimental medicine, 2000, 192 (7): 1027-1034.
- [48] ZHENG Z, BU Z, LIU X, et al. Level of circulating PD-L1 expression in patients with advanced gastric cancer and its clinical implications [J]. Chinese Journal of Cancer Research, 2014, 26 (1): 104-111.
- [49] FENG X, XUE F, HE G, et al. Banxia xiexin decoction inhibits the expression of PD-L1 through multi-target and multi-pathway regulation of major oncogenes in gastric cancer [J]. OncoTargets therapy, 2021, 14: 3297-3307.
- [50] FENG X, XUE F, HE G, et al. Banxia xiexin decoction affects drug sensitivity in gastric cancer cells by regulating MGMT expression via IL-6/JAK/STAT3-mediated PD-L1 activity [J]. International Journal of Molecular Medicine, 2021, 48 (2): 1-11.
- [51] NARDONE G, COMPARE D. The human gastric microbiota: Is it time to rethink the pathogenesis of stomach diseases? [J]. United European gastroenterology journal, 2015, 3 (3): 255-260.
- [52] FERREIRA R M, PEREIRA-MARQUES J, PINTO-RIBEIRO I, et al. Gastric microbial community profiling reveals a dysbiotic cancer-associated microbiota [J]. Gut, 2018, 67 (2): 226-236.
- [53] EUN C S, KIM B K, HAN D S, et al. Differences in gastric mucosal microbiota profiling in patients with chronic gastritis, intestinal metaplasia, and gastric cancer using pyrosequencing methods [J]. Helicobacter, 2014, 19 (6): 407-416.
- [54] 朱广辉, 桑毅婷, 李杰. 中医药在调节胃肠道菌群以防治胃肠道肿瘤中的作用和意义 [J]. 世界华人消化杂志, 2020, 28 (1): 1-8.
- [55] 于亚男. 大肠肿瘤发生中肠菌紊乱及小檗碱干预的研究 [D]. 上海: 上海交通大学, 2014.
- [56] 魏俊, 童仕伦. 甘草泻心汤对胃肠道肿瘤术后肠道菌群失调及血清白介素的影响 [J]. 四川中医, 2016, 34 (9): 85-88.
- [57] SUNG H, FERLAY J, SIEGEL R L, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. CA: a cancer journal for clinicians, 2021, 71 (3): 209-249.
- [58] 中国中西医结合学会检验医学专业委员会. 中国早期胃癌筛查检验技术专家共识 [J]. 中华检验医学杂志, 2023, 46: 347-359.
- [59] PETRILLO A S, ELIZABETH C. 27 years of stomach cancer: painting a global picture [J]. The Lancet Gastroenterology Hepatology, 2020, 5 (1): 5-6.
- [60] YANG L, LIU X, ZHU J, et al. Progress in traditional Chinese medicine against chronic gastritis: From chronic non-atrophic gastritis to gastric precancerous lesions [J]. Heliyon, 2023, 9 (6): e16764.
- [61] DECORATION X D, ZHOU L Y, ZHANG S T, et al. Randomized double-blind clinical trial of Muluodan (摩罗丹) for the treatment of chronic atrophic gastritis with dysplasia [J]. Chinese journal of integrative medicine, 2016, 22: 9-18.
- [62] WENGUANG H, XIAOLI L, YICHENG X. Theoretical basis and overview of Banxia Xiexin decoction in treatment of digestive diseases [J]. International Medicine and Health Guidance News, 2022, 28 (17): 2410-2413.