doi: 10.13241/j.cnki.pmb.2019.14.032

血府逐瘀汤联合四联疗法治疗 *Hp* 阳性慢性萎缩性胃炎的临床观察 *

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摘要 目的：探究血府逐瘀汤联合四联疗法治疗幽门螺旋杆菌(*Hp*)阳性慢性萎缩性胃炎的效果。**方法：**回顾性分析 2014 年 5 月-2017 年 12 月在我院进行诊治的 80 例 *Hp* 阳性慢性萎缩性胃炎患者的临床资料，按照其入院顺序经随机数字表分为研究组和对照组，每组各 40 例患者。其中，对照组患者采用四联疗法，研究组患者在对照组基础上联合血府逐瘀汤进行治疗，对比两组患者的 *Hp* 转阴率、治疗前后胃黏膜病理积分的变化情况、临床症状积分的变化情况和不良反应发生率。**结果：**治疗后，研究组患者的 *Hp* 转阴率[85.0%(34/40)]显著高于对照组[62.5%(25/40)]($P<0.05$)。两组上腹痛、纳差、上腹胀、反酸、嗳气等临床症状积分以及胃黏膜萎缩、肠化、不典型增生等病理积分均显著低于治疗前($P<0.05$)，且研究组以上指标均明显低于对照组($P<0.05$)。研究组患者的不良反应发生率[5.0%(2/40)]与对照组[12.5%(5/40)]无显著性差异($P>0.05$)。**结论：**血府逐瘀汤联合四联疗法治疗 *Hp* 阳性慢性萎缩性胃炎的效果显著优于单用四联疗法，其可有效改善患者的病变程度和临床症状，且无明显不良反应产生。

关键词：血府逐瘀汤；四联疗法；*Hp* 阳性慢性萎缩性胃炎；胃黏膜病理积分

中图分类号：R573.32 **文献标识码：**A **文章编号：**1673-6273(2019)14-2751-04

Effect of Xuefu Zhuyu Decoction Combined with Quadruple Therapy on the *Hp* Positive Chronic Atrophic Gastritis*

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ABSTRACT Objective: To explore the effect of Xuefu Zhuyu Decoction combined with quadruple therapy on the Helicobacter pylori (Hp)-positive chronic atrophic gastritis. **Methods:** 80 cases of patients with Hp-positive chronic atrophic gastritis who were treated in our hospital from May 2014 to December 2017 were selected and randomly divided into the study group and the control group according to the order of admission with 40 patients in each group. Patients in the control group were treated with quadruple therapy, and patients in the study group were treated with Xuefu Zhuyu Decoction on the basis of control group. The *Hp* negative rate, the changes of gastric mucosal pathological scores and clinical symptom scores before and after treatment as well as the incidence of adverse reactions were compared between two groups. **Results:** After treatment, the *Hp* negative rate of study group [85.0%(34/40)] was significantly higher than that of the control group [62.5%(25/40)]($P<0.05$). The scores of clinical symptoms such as abdominal pain, anorexia, upper abdominal distension, acid reflux and eructation, as well as gastric mucosal atrophy, intestinal metaplasia and atypical hyperplasia were significantly lower than those before treatment($P<0.05$). The above indicators of study group were significantly lower than those of the control group ($P<0.05$). The incidence of adverse reactions in the study group [5.0%(2/40)] was not significantly different from that in the control group[12.5%(5/40)]($P>0.05$). **Conclusion:** Xuefu Zhuyu Decoction combined with quadruple therapy is significantly better than quadruple therapy alone on Hp-positive chronic atrophic gastritis, which can effectively improve the degree of disease and clinical symptoms of patients and there was no obvious adverse reaction.

Key words: Xuefu Zhuyu Decoction; Quadruple therapy; Hp positive chronic atrophic gastritis; Gastric mucosal pathological score

Chinese Library Classification(CLC): R573.32 Document code: A

Article ID: 1673-6273(2019)14-2751-04

* 基金项目：北京中医药科技发展基金项目(JJ2015-16)

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(收稿日期：2018-11-06 接受日期：2018-11-30)

前言

慢性萎缩性胃炎是一种常发生于中老年群体并以胃黏膜萎缩和固有腺体减少为主要特征的消化系统疾病，患者常表现上腹部疼痛、胀满、嗳气等症状，该病具有发病率高、病程漫长、易反复发作、病情轻重不一、难治愈等特点[1-3]。幽门螺杆菌(*Hp*)是消化道常见的致病菌，*Hp* 感染是引起慢性萎缩性胃炎发生、发展的重要原因。目前，临床上常采用三联、四联疗法等根治*Hp*、保护胃黏膜和改善胃动力，具有一定的疗效[4,5]，但患者易产生耐药性及治疗后的不良反应发生率较高，临床疗效并不理想。

近年来，在中医辩证论治的指导下，中医药治疗慢性萎缩性胃炎具有自身独特的优势[6,7]，许多医家认为本病的病变部位在胃，但与脾、肝等脏器关系密切，治疗应以活血化瘀为主。血府逐瘀汤是一种由柴胡、当归、地黄、赤芍、红花、炒桃仁、麸炒枳壳、甘草、川芎、牛膝、桔梗等药物组成的中药汤剂[8-10]。本文通过回顾性分析我院收治的 80 例 *Hp* 阳性慢性萎缩性胃炎患者的临床资料，旨在探究血府逐瘀汤联合四联疗法治疗 *Hp* 阳性慢性萎缩性胃炎的效果。具体内容报道如下：

1 资料与方法

1.1 一般资料

回顾性分析于 2014 年 5 月 -2017 年 12 月在我院进行诊治的 80 例 *Hp* 阳性慢性萎缩性胃炎患者的临床资料，纳入标准：符合《中国慢性胃炎共识意见》中慢性萎缩性胃炎的诊断标准[11]和《中药新药临床研究指导原则》中脾胃血淤证的诊断标准[12]；13℃呼吸实验 *Hp* 呈阳性者；自愿参与本次研究，且签署《知情同意书》；排除标准：排除治疗期间胃粘膜脱落者；合并消化性溃疡、浅表性胃炎、糜烂性胃炎等疾病者；合并胃癌等其它恶性肿瘤者；合并严重心脑血管疾病者；对本次研究所用药物过敏者；妊娠及哺乳期妇女；严重精神障碍者。按照其入院顺序经随机数字表将所有患者分为两组：对照组 40 例患者中，男 22 例，女 18 例，平均年龄为 55.37± 6.91 岁，平均病程为 5.20± 1.16 年；研究组 40 例患者中，男 23 例，女 17 例，平均年龄为 55.42± 7.45 岁，平均病程为 5.16± 1.32 年。两组患者的一般临床资料比较差异无统计学意义($P>0.05$)，具有可比性。

1.2 治疗方法

对照组：采用四联疗法，口服阿莫西林胶囊 1.0 g，克拉霉素 0.5 g，均 2 次 /d，饭后 0.5 h 服用；雷贝拉唑片 20 mg，2 次 /d，饭前 0.5 h 服用；枸橼酸铋钾胶囊 0.6 g，3 次 /d，饭前 0.5 h 服用 14 天。

研究组：在对照组基础上，联合血府逐瘀汤进行治疗，药物组成为：柴胡 10 g、当归 15 g、地黄 15 g、赤芍 10 g、红花 10 g、炒桃仁 10 g、麸炒枳壳 10 g、甘草 10 g、川芎 10 g、牛膝 10 g、桔梗 10 g。将上述药物的全成分配方颗粒倒入杯中，取适量开水融化搅拌均匀后密闭 2-3 min，待充分溶解后服用，1 剂 /d，分早晚温服，连续治疗 3 个月。

1.3 观察指标

① 于治疗结束后 1 个月，通过 13C 呼吸实验检测两组患者的 Hp 转阴率；② 参照 2002 年《中药新药治疗慢性萎缩性胃炎的临床研究指导原则》制定证候分级量化标准，于治疗前、后分别对两组患者的临床症状进行评价，根据其改善程度分为无(计 0 分)、轻度(计 1 分)、中度(计 2 分)、重度(计 3 分)四个等级，其中，症状包括上腹痛、纳差、上腹胀、反酸、嗳气等；③ 参照 2009 年《慢性萎缩性胃炎中医诊疗共识意见》制定病理组织学分级量化标准，于治疗前后分别于胃窦、胃体、胃角处取 5 快胃粘膜活检标本。依据病变程度分为无(计 0 分)、轻度(计 1 分)、中度(计 2 分)、重度(计 3 分)四个等级，分别对胃黏膜萎缩、肠化、不典型增生等项目进行评价；④ 记录并对比两组患者的不良反应发生情况。

1.4 统计学分析

采用 SPSS19.0 统计学软件进行数据分析，计量资料($\bar{x}\pm s$)组间比较采用 t 检验，计数资料(%)组间比较采用 x^2 检验，以 $P<0.05$ 表明差异有统计学意义。

2 结果

2.1 两种 Hp 转阴率的对比

治疗后，研究组患者 *Hp* 转阴 34 例，转阴率为 85.0%(34/40)；对照组患者 *Hp* 转阴 25 例，转阴率为 62.5%(25/40)。研究组 *Hp* 转阴率显著高于对照组($P<0.05$)。

2.2 两组治疗前后临床症状积分对比

治疗前，两组患者的上腹痛、纳差、上腹胀、反酸、嗳气等临床症状积分对比差异无统计学意义($P>0.05$)；治疗后，两组患者的上述临床症状积分均较治疗前显著降低，且研究组显著低于对照组($P<0.05$)，详细结果见表 1。

表 1 两组治疗前后临床症状积分对比($\bar{x}\pm s$，分)

Table 1 Comparison of the clinical symptom scores before and after treatment between two groups($\bar{x}\pm s$, scores)

Detection item	Control group(n=40)		Research group(n=40)	
	Before treatment	After treatment	Before treatment	After treatment
Abdominal pain	2.41± 0.48	1.74± 0.35#	2.39± 0.49	1.03± 0.29#*
Anorexia	1.55± 0.42	1.06± 0.27#	1.54± 0.45	0.52± 0.19#*
Upper abdominal distension	2.19± 0.53	1.53± 0.38#	2.20± 0.48	0.74± 0.20#*
Acid reflux	2.02± 0.49	1.62± 0.41	1.98± 0.52	0.88± 0.29
Eructation	1.92± 0.37	1.25± 0.30	1.95± 0.38	0.78± 0.21

Note: compared with the control group, *$P<0.05$; compared with before treatment, #$P<0.05$.

2.3 两组治疗前后胃黏膜病理积分对比

治疗前,两组患者的胃黏膜萎缩、肠化、不典型增生等病理积分对比差异无统计学意义($P>0.05$);治疗后,两组患者的上述病理积分均较治疗前显著降低,且研究组以上指标均明显低于对照组($P<0.05$),详细结果见表 2。

表 2 两组治疗前后胃黏膜病理积分对比($\bar{x}\pm s$,分)

Table 2 Comparison of the pathological scores of gastric mucosabefore and after treatment between two groups($\bar{x}\pm s$, scores)

Detection item	Control group(n=40)		Research group(n=40)	
	Before treatment	After treatment	Before treatment	After treatment
Atrophy	2.65± 0.36	1.27± 0.25#	2.64± 0.39	0.34± 0.10#*
Intestinalization	1.59± 0.30	1.12± 0.24#	1.60± 0.29	0.81± 0.21#*
Atypical hyperplasia	1.14± 0.22	0.75± 0.16#	1.13± 0.25	0.33± 0.09#*

Note: compared with the control group, *$P<0.05$; compared with before treatment, #$P<0.05$.

2.4 两组治疗不良反应发生情况的对比

两组不良反应均较轻,给予对症处理后均能缓解。其中,对照组出现 1 例头晕头痛,2 例便秘,1 例口干,1 例恶心,不良反应发生率为 12.5%(5/40); 研究组出现 1 例便秘,1 例恶心,不良反应发生率为 5.0%(2/40)。两组患者的不良反应发生率无显著性差异($P>0.05$)。

3 讨论

流行病学资料显示我国慢性萎缩性胃炎的检出率约占受检人数的 14%左右,以 *Hp* 阳性慢性萎缩性胃炎患者居多。*Hp* 阳性慢性萎缩性胃炎患者多无特异性症状及临床体征,因此往往不能在疾病初期给予全面、系统的治疗[13-15],导致多数的患者因治疗不及时发展为重度慢性萎缩性胃炎,甚至癌变,严重影响患者的日常工作和生活质量。

慢性萎缩性胃炎在中医学中属 " 胃脘痛 "、" 胃痞 "、" 嗳气 " 等范畴,胃脘疼痛是其主要临床症状,且多以胀痛为主,痛有定处,甚至可在胃脘部形成痞块[16,17]。《医林改错》中指出 " 凡肚腹疼痛总不移是淤血 ",《诸病源候论》 中也指出 " 气血壅塞不通而成痞也 ",均可表明慢性萎缩性胃炎与血淤有关[18]。同时,慢性萎缩性胃炎具有病程较长、病情反复等特点,此为血瘀证形成、发展的重要基础,机体在外邪犯胃、情志失调、饮食不节、劳倦过度等致病因素作用下形成淤血, 淤血既是致病因素,亦为病理产物,一旦淤血形成,可使机体胃部出现络脉不畅,胃黏膜失养等不良后果,从而加速胃黏膜的进一步损害,长此以往会导致胃黏膜的萎缩性改变[19-21]。现代病理学研究结果也显示机体的血流变异常与胃黏膜萎缩的轻重程度成正相关,胃小弯和胃窦部的血管数目较少、血管径也较细,此部位也恰好是慢性萎缩性胃炎的好发部位,当血液处于高凝状态时,机体的局部微循环灌注会显著降低, 导致胃黏膜萎缩病变进一步加重[22-24],故在治疗过程中应运用活血化瘀的疗法[25]。

本研究所用血府逐瘀汤由柴胡、当归、地黄、赤芍、红花、炒桃仁、麸炒枳壳、甘草、川芎、牛膝、桔梗等药物组成,方中柴胡可解表退热,疏肝解郁,升举阳气;当归具有补血活血,调经止痛之功效;生地黄具有清热凉血、养阴生津之功效[26,27];赤芍可清热凉血,活血祛瘀;红花可活血通经、祛瘀止痛;桃仁可破血行瘀;枳壳具有理气宽胸、行滞消积之功效;川芎活血行气;牛膝活血通经;桔梗宣肺祛痰;甘草调和诸药;全方共奏活血化瘀、行气止痛之功效[28-30]。本研究结果显示研究组患者治疗后 *Hp* 转阴率显著高于对照组,胃黏膜萎缩、肠化、不典型增生等病理积分及上腹痛、纳差、上腹胀、反酸、嗳气等临床症状积分均显著低于对照组,但两组患者的不良反应发生率无显著性差异。表明血府逐瘀汤联合四联疗法治疗 *Hp* 阳性慢性萎缩性胃炎的效果显著优于单一四联疗法,且无明显不良反应产生。

综上所述,血府逐瘀汤联合四联疗法治疗 *Hp* 阳性慢性萎缩性胃炎的效果显著优于单用四联疗法,其可有效改善患者的病变程度和临床症状,且无明显不良反应产生。

参 考 文 献(References)

[1] Zhang J Z, Feng Q L, Hu Y L, et al. Correlation Study on Chinese Medical Syndrome Types of Chronic Atrophic Gastritis Patients, Hp, and IL-1 β2 Polymorphism [J]. China Medical Abstracts (Internal Medicine), 2016, 35(1): 1433-1436

[2] Chen P, Cui Y, Fu Q Y, et al. Positive relationship between p42.3 gene and inflammation in chronic non-atrophic gastritis [J]. Journal of Digestive Diseases, 2016, 16(10): 568-574

[3] Tong Y, Wu Y, Song Z, et al. The potential value of serum pepsinogen for the diagnosis of atrophic gastritis among the health check-up populations in China: a diagnostic clinical research [J]. Bmc Gastroenterology, 2017, 17(1): 88

[4] Takeoka A, Tayama J, Yamasaki H, et al. Impact of Helicobacter pylori Immunoglobulin G Levels and Atrophic Gastritis Status on Risk of Metabolic Syndrome[J]. Plos One, 2017, 11(11): e0166588

[5] Yamanaka K, Miyatani H, Yoshida Y, et al. Malignant transformation of a gastric hyperplastic polyp in a context of Helicobacter pylori -negative autoimmune gastritis: a case report [J]. Bmc Gastroenterology, 2016, 16(1): 130

[6] Zhang J, Huang K, Zhong G, et al. Acupuncture Decreases NF-κB p65, miR-155, and miR-21 and Increases miR-146a Expression in Chronic Atrophic Gastritis Rats [J]. Evidence-Based Complementray and Alternative Medicine, 2016: 1404629

[7] Yamada S, Tomatsuri N, Kawakami T, et al. Helicobacter pylori Eradication Therapy Ameliorates Latent Digestive Symptoms in Chronic Atrophic Gastritis[J]. Digestion, 2018, 97(4): 333

[8] Dore MP, Lu H, Graham DY. Role of bismuth in improving Helicobacter pylori eradication with triple therapy [J]. Gut, 2016, 65(5): 870

[9] Sipponen P, Kekki M, Siurala M. Atrophic chronic gastritis and in-

testinal metaplasia in gastric carcinoma. Comparison with a representative population sample[J]. Cancer, 2015, 52(6): 1062-1068

[10] Group E S. Risk factors for atrophic chronic gastritis in a European population: results of the Eurohepygast study [J]. Gut, 2015, 50(6): 779

[11] Prahalada S, Rhodes L, Grossman S, et al. Morphological and hormonal changes in the ventral and dorsolateral prostatic lobes of rats treated with finasteride, a 5-alpha reductase inhibitor [J]. Prostate, 2015, 35(3): 157-164

[12] Diakopoulos K N, Lesina M, Wörmann S, et al. Impaired Autophagy Induces Chronic Atrophic Pancreatitis in Mice via Sex- and Nutrition-Dependent Processes [J]. Gastroenterology, 2015, 148 (3): 626-638. e17

[13] Zhao C, Li P, Zhang L, et al. An Observational Study on Aberrant Methylation of Runx3 With the Prognosis in Chronic Atrophic Gastritis Patients[J]. Medicine, 2016, 95(20): e3356

[14] Castoro C, Moli R L, Arpi M L, et al. Association of autoimmune thyroid diseases, chronic atrophic gastritis and gastric carcinoid: experience from a single institution [J]. Journal of Endocrinological Investigation, 2016, 39(7): 1-6

[15] Jeong M, Park J, Han Y, et al. Dietary Intervention of Artemisia and Green Tea Extracts to Rejuvenate *Helicobacter pylori-Associated* Chronic Atrophic Gastritis and to Prevent Tumorigenesis [J]. Helicobacter, 2016, 21(1): 40-59

[16] Aasarød K M, Mosti M P, Stunes A K, et al. Impaired skeletal health in patients with chronic atrophic gastritis [J]. Scandinavian Journal of Gastroenterology, 2016, 51(7): 1

[17] Campana D, Ravizza D, Ferolla P, et al. Risk factors of type 1 gastric neuroendocrine neoplasia in patients with chronic atrophic gastritis. A retrospective, multicentre study[J]. Endocrine, 2016, 56(3): 1-6

[18] Lim T S, Kim D Y, Han K H, et al. Combined use of AFP, PIVKA-II, and AFP-L3 as tumor markers enhances diagnostic accuracy for hepatocellular carcinoma in cirrhotic patients [J]. Scandinavian Journal of Gastroenterology, 2016, 51(3): 344

[19] Yang Z, Wang C, Chen J, et al.Effects of moxibustion on cell proliferative factors in gastric mucosa in rats with precancerous lesions of chronic atrophic gastritis [J]. China Medical Abstracts (Internal Medicine), 2016, 35(1): 1269

[20] Yamasaki Y, Uedo N, Kanzaki H, et al. Investigation of mucosal pattern of gastric antrum using magnifying narrow-band imaging in patients with chronic atrophic fundic gastritis [J]. Annals of Gastroenterology, 2017, 30(3): 302-308

[21] Boyce M, Moore A R, Sagatun L, et al. Netazepide, a gastrin/CCK2 receptor antagonist, can eradicate gastric neuroendocrine tumours in patients with autoimmune chronic atrophic gastritis[J]. British Journal of Clinical Pharmacology, 2016, 83(3): 466-475

[22] Jeong S, Choi E, Petersen C P, et al. Distinct metaplastic and inflammatory phenotypes in autoimmune and adenocarcinoma-associated chronic atrophic gastritis[J]. United European Gastroenterology Journal, 2017, 5(1): 37

[23] Dai Y Q, Ye Z D, Huang H H. Long-term effect of *Helicobacter pylori* eradication combined with folate in patients with chronic atrophic gastritis [J]. World Chinese Journal of Digestology, 2017, 25 (19): 1777-1782

[24] Shi X, Zhu H, Zhang Y, et al. XuefuZhuyu decoction protected cardiomyocytes against hypoxia/reoxygenation injury by inhibiting autophagy [J]. Bmc Complementary & Alternative Medicine, 2017, 17 (1): 325

[25] Zhou J, Liu T, Cui H, et al. Xuefu zhuyu decoction improves cognitive impairment in experimental traumatic brain injury via synaptic regulation[J]. Oncotarget, 2017, 8(42): 72069-72081

[26] Wang X, Ling L, Li S, et al. The Diagnostic Value of Gastrin-17 Detection in Atrophic Gastritis:A Meta-Analysis [J]. Medicine, 2016, 95 (18): e3599

[27] Gao X, Zhang Y, Brenner H. Associations of *Helicobacter pylori* infection and chronic atrophic gastritis with accelerated epigenetic ageing in older adults [J]. British Journal of Cancer, 2017, 117 (8): 1211-1214

[28] Ma Z, Liu G, Zhang M, et al. *Helicobacter pylori* Infection Increases Frequency of PDCA-1(+) (CD317(+)) B-cell Subsets[J]. Archives of Medical Research, 2016, 47(2): 96-104

[29] Utiyama S R R, Bem R S D, Skare T L, et al. Anti-parietal cell antibodies in patients with autoimmune thyroid diseases [J]. Journal of Endocrinological Investigation, 2017, 8(5): 1-7

[30] Chen X Z, Schöttker B, Castro F A, et al. Association of *Helicobacter pylori* infection and chronic atrophic gastritis with risk of colonic, pancreatic and gastric cancer: A ten-year follow-up of the ESTHER cohort study[J]. Oncotarget, 2016, 7(13): 17182-17193