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# 黄连温胆汤联合聚普瑞锌颗粒治疗胆汁反流性胃炎疗效及对血清 GAS、5-HT 水平影响 *

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**摘要 目的:**探讨黄连温胆汤联合聚普瑞锌颗粒治疗胆汁反流性胃炎疗效及对血清胃泌素(GAS)、5- 羟色胺(5-HT)水平的影响。**方法:**选择 2019 年 5 月 ~2021 年 5 月 120 例胆汁反流性胃炎患者,随机分为两组各 60 例,对照组予以聚普瑞锌颗粒治疗,研究组在对照组基础上加黄连温胆汤治疗。评估两组治疗前后临床症状改善情况,评价临床症状疗效和胃镜疗效,检测血清 GAS、5-HT 水平,随访 6 个月内的复发率。**结果:**两组患者治疗后主要症状计分及总分均明显降低,而研究组明显低于对照组($P$<0.05)。研究组临床症状疗效明显高于对照组($P$<0.05)。研究组胃镜疗效明显高于对照组($P$<0.05)。两组患者治疗后血清 GAS、5-HT 水平明显升高,而研究组明显高于对照组($P$<0.05)。两组复发率对比无差异($P$>0.05)。**结论:**黄连温胆汤联合聚普瑞锌颗粒治疗胆汁反流性胃炎可有效提升疗效,调节胃肠激素水平。

**关键词:**胆汁反流性胃炎;黄连温胆汤;聚普瑞锌颗粒;胃泌素;5- 羟色胺

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# Therapeutic Effect of Huanglian Wendan Decoction Combined with Jupurui Zinc Granule on Bile Reflux Gastritis and Its Effect on Serum Gas and 5-HT Levels*

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**ABSTRACT Objective:** To investigate the curative effect of Huanglian Wendan Decoction Combined with jupurui zinc Granule on bile reflux gastritis and its effect on the levels of serum gastrin (gas) and 5-hydroxytryptamine (5-HT). **Methods:** 120 patients with bile reflux gastritis from May 2019 to may 2021 were randomly divided into two groups, 60 cases in each group. The matched group was treated with jupurui zinc granule, and the study group was treated with Huanglian Wendan Decoction on the basis of the matched group. The improvement of clinical symptoms before and post-treatment, the curative effect of clinical symptoms and gastroscopy, the levels of serum gas and 5-hydroxytryptamine (5-HT) were measured, and the recurrence rate within 6 months was followed up. **Results:** The scores of main symptoms and total scores in the two groups were lower post-treatment, while those in the study group were lower than those in the matched group ($P$<0.05). The curative effect of clinical symptoms in the study group was higher than that in the matched group ($P$<0.05). The curative effect of gastroscopy in the study group was higher than that in the matched group ($P$<0.05). The levels of serum gas and 5-HT in the study group were higher than those in the matched group ($P$<0.05). The recurrence rate of the two groups was not significant ($P$>0.05). **Conclusion:** Huanglian Wendan Decoction Combined with jupurui zinc granule in the treatment of bile reflux gastritis can effectively improve the curative effect and regulate the level of gastrointestinal hormones.

**Key words:** Bile reflux gastritis; Huanglian Wendan Decoction; Jupri zinc particles; Gastrin; Serotonin

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## 前言

正常情况下,胆汁由于幽门括约肌阻止不会进入胃。当幽门括约肌受损或功能障碍时,胆汁则会反流进胃,从而引发胆

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汁反流性胃炎。胆汁属强碱性,反流到胃会改变胃 pH 值,引起胃粘膜的化学刺激,长时间可导致胃粘膜炎症细胞增多,壁细胞减少,粘膜细胞增生,腺体形态改变,引起萎缩性胃炎及肠化生[1-3]。胆汁反流性胃炎常发生于手术后,如部分胃切除术、胆囊切除术、括约肌成型术、幽门成型术等[4,5]。目前临床治疗胆汁反流性胃炎并无特异性疗法,治疗药物仍以质子泵抑制药、胃黏膜保护剂、促胃肠动力药物为主,对胆汁反流性胃炎的疗效不尽理想[6,7]。研究表明,胆汁反流是导致质子泵抑制药治疗失败的一个重要因素,在使用标准剂量或双剂量质子泵抑制药仍有胃食管反流相关症状的患者中,胆汁反流明显比胃酸反流更常见[8,9]。中医学中并无 " 胆汁反流性胃炎 " 这一病名,但可归于 " 胃痛 "" 胃痞 "" 嘈杂 "" 胆瘅 " 等范畴[10]。本研究采用黄连温胆汤联合新型胃黏膜保护剂聚普瑞锌颗粒治疗胆汁反流性胃炎,报道如下。

## 1 对象与方法

### 1.1 研究对象

选择 2019 年 5 月 ~2021 年 5 月 120 例胆汁反流性胃炎患者,采用随机数字表法分为两组各 60 例,研究组:男 37 例,女 23 例;年龄 25~71 岁,平均年龄(49.53±6.24)岁,病程 2～13 个月,平均(9.22±2.73)个月,胆汁反流程度:Ⅱ度 26 例,Ⅲ度 34 例;对照组:男 35 例,女 25 例;年龄 28~74 岁,平均年龄(48.73±8.29)岁,病程 1～17 个月,平均(10.52±3.44)个月,胆汁反流程度:Ⅱ度 28 例,Ⅲ度 32 例;两组一般资料无统计学意义($P$＞0.05)。

纳入标准:① 符合《慢性胃炎中西医结合诊疗共识》中胆汁反流性胃炎的诊断标准[11];② 中医辨证胆热犯胃证。

排除标准:① 合并慢性萎缩性胃炎、消化道溃疡、出血及肠易激惹综合征等其它消化道疾病;② 合并肝肾功能障碍;③ 合并各类肝炎病毒感染;④ 合并严重高血压、慢性心律失常;⑤ 合并自身免疫性疾病;⑥ 幽门螺旋杆菌阴性阳性;⑦ 入组前使用过质子泵抑制药、胃黏膜保护剂、促胃肠动力药物等药物治疗。严重过敏体质。

### 1.2 治疗方法

对照组予以聚普瑞锌颗粒(吉林省博大伟业制药有限公司,国药准字 H20120091)治疗,每次 1 袋,每日 2 次。研究组在对照组基础上加黄连温胆汤治疗,药物组成:黄连 3 g、姜半夏 10 g、枳实 10 g、茯苓 10 g、陈皮 10 g、竹茹 10 g、生姜 2 g、炙甘草 10 g。胃痛甚者加延胡索、白芍;呃逆甚者加代赭石。上药由我院中药房代煎,每次服用 150 mL,每日 3 次。两组患者均连续治疗 4 周。

### 1.3 观察指标

治疗前后对两组患者的主要症状进行计分,包括胃脘胀痛、泛酸、烧心、嗳气口苦、呃逆等,评分标准为:无任何不适症状为 0 分;轻度,间断出现(＜3 次 /d),对饮食和日常活动基本无影响为 2 分;中度,发作较频繁(3~6 次 /d),对饮食和日常活动的影响较大为 4 分;重度,发作频繁(＞6 次 /d),严重影响饮食和日常活动为 6 分。各项计分之和为总分。

抽取清晨空腹静脉血 2 mL,采用 ELISE 法检测血清胃泌素(Gastrin, GAS)、5- 羟色胺(5-hydroxytryptamine, 5-HT)水平。电话或门诊随访 6 个月,了解复发情况[12,13]。

### 1.4 临床症状疗效判断标准

根据尼莫地平法,治疗前后症状总分减少 95 %以上为痊愈;70 %~94 %为显效;30 %~69 %为有效;不足 30 %为无效[6]。

### 1.5 胃镜疗效判断标准

胃镜示无任何异常,无胆汁反流物为痊愈;胃镜示活动性炎症减轻 70%以上,胆汁反流减少 1 个级度以上为显效;活动性炎症减轻 30%以上,胆汁反流减少 1 个级度为有效;活动性炎症和反流改善情况未达到有效标准或加重为无效。

### 1.6 统计学方法

采用 SPSS22.0 分析,计量资料以 表示,采用 t 检验,计数资料以率表示,用 $\chi^2$ 检验或者秩和检验。$P$<0.05 表示有统计学意义。

## 2 结果

### 2.1 主要症状计分比较

两组患者治疗后主要症状计分及总分均明显降低,而研究组明显低于对照组($P$<0.05)。见表 1。

表 1 主要症状计分比较($\bar{x}\pm s$,分)

Table 1 Comparison of main symptom scores ($\bar{x}\pm s$, score)

| Groups | Epigastric distension and pain | | Pantothenic acid | | Heartburn | | Belching and bitter taste | | Hiccup | | Total score | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Pretherapy | Post-treatment | Pretherapy | Post-treatment | Pretherapy | Post-treatment | Pretherapy | Post-treatment | Pretherapy | Post-treatment | Pretherapy | Post-treatment |
| Research group (n=60) | 5.16±0.52 | 1.77±0.61* | 5.18±1.26 | 1.09±0.73* | 5.32±1.23 | 0.95±0.33* | 4.42±1.32 | 0.70±0.23* | 3.27±1.53 | 0.53±0.19* | 22.36±2.43 | 4.82±1.52* |
| Matched group (n=60) | 5.08±0.69 | 2.57±0.95* | 5.22±1.60 | 1.94±0.58* | 5.13±1.79 | 1.78±0.82* | 5.01±1.63 | 1.51±0.67* | 3.21±1.63 | 0.94±0.24* | 23.41±3.77 | 8.93±1.80* |
| $t$ | 0.717 | 5.488 | 0.152 | 7.061 | 0.677 | 7.273 | 2.178 | 8.857 | 0.207 | 10.375 | 1.813 | 13.513 |
| $P$ | 0.475 | <0.001 | 0.879 | <0.001 | 0.499 | <0.001 | 0.031 | <0.001 | 0.835 | <0.001 | 0.072 | <0.001 |

Note: Compared with that Pretherapy, *$P$＜0.05, the same below.

### 2.2 临床症状疗效比较

研究组临床症状疗效较对照组高($P$<0.05)。见表 2。

表 2 临床症状疗效比较[n(%)]

Table 2 Comparison of clinical symptoms [n(%)]

| Groups | Heal | Effective | Valid | Invalid |
|---|---|---|---|---|
| Research group(n=60) | 34(56.67) | 19(31.67) | 5(8.33) | 2(3.33) |
| Matched group(n=60) | 21(35.00) | 15(25.00) | 14(23.33) | 10(16.67) |
| Z | 4.262 | | | |
| $P$ | <0.001 | | | |

### 2.3 胃镜疗效比较

研究组胃镜疗效较对照组高($P$<0.05)。见表 3。

表 3 胃镜疗效比较[n(%)]

Table 3 Comparison of gastroscopic efficacy [n(%)]

| Groups | Heal | Effective | Valid | invalid |
|---|---|---|---|---|
| Research group(n=60) | 28(46.67) | 28(46.67) | 4(6.67) | 0(0.00) |
| Matched group(n=60) | 14(23.33) | 23(38.33) | 18(30.0) | 5(8.33) |
| Z | 4.003 | | | |
| $P$ | <0.001 | | | |

### 2.4 血清 GAS、5-HT 水平比较

两组患者治疗后血清 GAS、5-HT 水平明显升高($P$<0.05),而研究组明显高于对照组($P$<0.05)。见表 4。

表 4 两组治疗前后血清 GAS、5-HT 水平比较($\bar{x}\pm s$, ng/L)

Table 4 Comparison of serum GAS and 5-HT levels ($\bar{x}\pm s$, ng/L)

| Groups | GAS | | 5-HT | |
|---|---|---|---|---|
| | Pretherapy | Post-treatment | Pretherapy | Post-treatment |
| Research group(n=60) | 68.42±21.72 | 125.48±38.96* | 44.70±14.25 | 94.25±30.27* |
| Matched group(n=60) | 67.96±25.31 | 106.32±20.84* | 46.93±21.39 | 71.09±27.53* |
| t | 0.087 | 3.332 | 0.672 | 4.384 |
| $P$ | 0.930 | <0.001 | 0.503 | <0.001 |

### 2.5 复发率比较

研究组复发 0 例,复发率为 0。对照组复发 3 例,复发率为 5.0%。两组复发率对比无差异($\chi^2$=3.701,$P$=0.054)。

## 3 讨论

胆汁反流性胃炎较难治愈,尚无统一治疗方法,停药后容易复发[14,15]。聚普瑞锌颗粒是一种锌 -L - 肌肽螯合物,具有胃黏膜保护、抗溃疡等作用,其中的机制涉及抗氧化、抗炎、清除自由基等多重途径[16-18]。研究表明,聚普瑞锌通过降低炎症细胞因子水平,增加抗氧化酶、生长因子和热休克蛋白的表达,表现出与瑞巴匹特相似的胃粘膜保护作用,而且其与质子泵抑制药联用具有增效作用[19]。

本结果采用聚普瑞锌颗粒单药治疗胆汁反流性胃炎,结果显示,患者治疗后的临床症状明显减轻,但对症状疗效的无效率达到 16.67 %,胃镜疗效的无效率达到 8.33 %,临床疗效远不及研究组。采用黄连温胆汤联合聚普瑞锌颗粒治疗胆汁反流性胃炎,结果显示,与对照组比较,研究组的症状改善更显著,临床症状疗效与胃镜疗效明显提高。分析可知:中医学认为胆汁反流性胃炎的病机与肝胆脾胃均有关。胆汁乃肝之余气所化生,贮藏于胆,具有促进消化的作用,对保持脾胃健运具有重要作用。脾胃居中焦,脾升则健,胃降则和。当人或七情不遂,或劳倦过度,或饮食不节,或外邪入侵,导致肝的疏泄功能失常,胆气郁滞,影响胆汁的分泌与排泄,犯脾克胃,脾胃升降失常,且胃气挟胆汁上逆,造成胆汁不循常道,反流至胃,灼伤胃络,最终发为本病[20,21]。本病的病位在胆胃,胆邪犯胃,胃失和降是发病的根本,其中邪包括气、火、痰、湿、食、瘀等,气机升降失调是发病的关键环节。因此,治疗的原则可以 " 利胆邪、和胃气 " 为基础随证加减化裁。黄连温胆汤为宋·陈言《三因极一病症方论》中温胆汤化裁方,临床应用广泛,现代研究表明,本方具有调节糖脂代谢、抗炎等药理活性。方中黄连苦寒清热,尤善清中焦湿热,可疏通中焦气机升降,降逆止呕;姜半夏辛温燥湿,理气健脾,化痰和胃,消痞散结,两药同为君药,辛开苦降,清热降胃。现代药理研究表明,黄连具有利胆、抑菌、调节免疫等作用。竹茹清热化痰,除烦止呕;枳实行气消积,健脾和胃,化痰散痞;

陈皮理气健脾，和胃降逆，同为臣药，可助脾升胃降之功。现代研究表明，陈皮具有调节胃肠道平滑肌功能、排除肠道积气、改善血液黏度等作用[27]。茯苓健脾渗湿；生姜既可温中止呕，又可监制寒凉之性，同为佐药。炙甘草调和全方为使药。诸药配伍，共奏清热化痰、利胆和胃、通利三焦、降逆止呕之功。

中医药治疗胃炎的靶点多，机制复杂，可能与调节胃液、胃黏膜血流、抑制幽门螺杆菌、调节免疫、调节胃肠道神经递质、脑 - 肠肽、胃肠电活动、Cajal 间质细胞等多方面机制有关[22,23]。为了掌握本治疗方案的内在机制，本研究选取了两种胃肠激素 GAS、5-HT 进行分析。结果显示：两组治疗后血清 5-HT 水平明显提高，而 GAS 水平明显降低；且随访 6 个月，研究组复发率为 1.7 %，对照组复发率为 5.0 %，两组的复发率均低，无明显差异。说明单用聚普瑞锌也能从某一途径改善胆汁反流性胃炎患者的胃肠动力，而联合中药治疗血清 5-HT 和 GAS 水平改善更显著。分析可知：胆汁反流性胃炎的发病与胃肠动力异常有密切关系。胃肠动力是消化系统重要的生理机能，正常生理下，胃十二指肠平滑肌有节律地收缩运动，将食物从胃推向肠腔，使胃排空，维持胃压的动态平衡[24,25]。而当幽门功能出现障碍，幽门开放，胃十二指肠压力增高，则会导致胆汁反流进胃而损伤胃黏膜屏障[26]。研究表明，反流越严重，胃排空时间越长，胆酸盐等物质在胃内滞留时间越长，胃黏膜损伤越严重。因此，改善胃肠动力是治疗胆汁反流性胃炎的一个重要思路[27,28]。5-HT 广泛存在于胃窦和十二指肠中，与受体结合后刺激神经末梢乙酰胆碱的释放促进胃肠道运动，加快胃排空，且不会使胃酸分泌增加[29]。GAS 由 G 细胞分泌，可促进胃肠平滑肌收缩，促进幽门括约肌收缩，提高幽门张力，阻止胆汁等反流物反流，同时亦具有一定的黏膜保护作用[30]。黄连温胆汤亦具有调节胃肠动力的作用，与聚普瑞锌合用二者的功效叠加，这可能是二药联合治疗效果提升的机制之一。中医通过辨证施治，调理脏腑，解决根本症结，由内及表，理论上疗效稳固。本研究证实了黄连温胆汤联合聚普瑞锌治疗胆汁反流性胃炎的近期疗效较好，但不足在于随访时间较短，远期疗效尚需进一步观察。

总之，黄连温胆汤联合聚普瑞锌颗粒治疗胆汁反流性胃炎可有效提升疗效，调节胃肠激素水平。

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