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胃苏颗粒联合四联疗法对幽门螺杆菌相关性消化性溃疡患者血清炎症因子、胃肠激素及生活质量的影响*

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摘要 目的:探讨胃苏颗粒联合四联疗法对幽门螺杆菌(*Hp*)相关性消化性溃疡患者血清炎症因子、胃肠激素及生活质量的影响。**方法:**选取2018年3月~2019年12月期间我院收治的*Hp*阳性消化性溃疡患者124例,根据奇偶数字法将患者分为对照组、联合组,各62例。对照组给予四联疗法,联合组给予胃苏颗粒联合四联疗法,疗程均为4周。对比两组疗效、*Hp*根除率、炎症因子水平、胃肠激素水平、生活质量及不良反应。**结果:**联合组*Hp*根除率、临床总有效率高于对照组($P<0.05$)。联合组治疗4周后SF-36量表各维度评分较对照组更高($P<0.05$)。联合组治疗4周后血清降钙素原(PCT)、白介素-6(IL-6)、超敏C反应蛋白(hs-CRP)水平低于对照组($P<0.05$)。联合组治疗4周后胃泌素(GAS)、胃动素(MTL)低于对照组($P<0.05$)。两组不良反应发生率对比差异无统计学意义($P>0.05$)。**结论:**胃苏颗粒联合四联疗法治疗*Hp*相关性消化性溃疡患者,可有效改善患者体内血清炎症因子及胃肠激素水平,并提高其生活质量和*Hp*根除率,疗效优于单纯四联疗法。

关键词:胃苏颗粒;四联疗法;幽门螺杆菌;消化性溃疡;炎症因子;胃肠激素;生活质量

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Effect of Weisu Granule Combined with Quadruple Therapy on Serum Inflammatory Factors, Gastrointestinal Hormones and Quality of Life in Patients with *Helicobacter Pylori* Associated Peptic Ulcer*

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ABSTRACT Objective: To investigate the effect of Weisu granule combined with quadruple therapy on serum inflammatory factors, gastrointestinal hormones and quality of life in patients with *helicobacter pylori* (*Hp*) associated peptic ulcer. **Methods:** 124 cases of *HP* positive peptic ulcer patients who were admitted in our hospital from March 2018 to December 2019 were selected, they were divided into control group, combined group according to odd even number method, 62 cases per group. The control group was given quadruple therapy, and the combined group was given Weisu granule combined with quadruple therapy, the course of treatment was 4 weeks. The efficacy, *HP* eradication rate, levels of inflammatory factors, levels of gastrointestinal hormones, quality of life and adverse reactions were compared between the two groups. **Results:** *HP* eradication rate, clinical total effective rate of the combined group were higher than those of the control group ($P<0.05$). The SF-36 scale scores of each dimension in the combined group were higher than those of the control group after 4 weeks of treatment ($P<0.05$). The levels of serum procalcitonin (PCT), interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs CRP) in the combined group were lower than those of the control group after 4 weeks of treatment ($P<0.05$). The gastrin (GAS), motilin (MTL) in the combined group was lower than those of the control group after 4 weeks of treatment ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Weisu granule combined with quadruple therapy in the treatment of *HP* related peptic ulcer, can effectively improve the levels of serum inflammatory factors and gastrin indexes of the patients, and improve their quality of life and *HP* eradication rate, the curative effect is better than simple quadruple therapy.

Key words: Weisu granule; Quadruple therapy; *Helicobacter pylori*; Peptic ulcer; Inflammatory factors; Gastrointestinal hormone; Quality of life

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前言

消化性溃疡以节律性、周期性的慢性上腹部疼痛为主要症状,具有缠绵难愈、反复发作的特点,严重影响患者生活质量^[1]。

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现代医学认为^[2],幽门螺杆菌(*Hp*)是引起机体发生消化性溃疡的主要病原菌,临床上约有80%以上的消化性溃疡患者均为*Hp*阳性。因此,清除*Hp*可显著加速溃疡的愈合,降低该病的复发率^[3]。阿莫西林、泮托拉唑、克拉霉素、胶体果胶铋四联疗法是治疗消化性溃疡的一线治疗方案,但*Hp*的根除率已到达瓶颈,疗效有待进一步优化^[4,5]。胃苏颗粒是由香附、佛手、陈皮、鸡内金、香橼等多味中药材制成的一种中成药,有研究表明其对于治疗活动期胃溃疡和慢性胃炎疗效显著^[6-8]。本研究选取胃苏颗粒联合四联疗法,探讨该治疗方案对*Hp*阳性消化性溃疡患者血清炎症因子、胃肠激素及生活质量的影响,以期为该病的临床诊治提供一定支持,结果报道如下。

1 资料与方法

1.1 一般资料

选取我院于2018年3月~2019年12月期间收治的124例*Hp*阳性消化性溃疡患者,纳入标准:(1)诊断参考《消化性溃疡中西医结合诊疗共识意见(2017年)》^[9],经内窥镜确诊;(2)经¹⁴C尿素呼气试验或快速尿素酶试验确认为*Hp*阳性;(3)家属签署知情同意书;(4)患者对治疗药物没有过敏史。排除标准:(1)既往胃部手术者或胃部恶性肿瘤者;(2)精神疾患无法交流者;(3)妊娠或哺乳期妇女;(4)合并糖尿病、高血压、高血脂等疾病者;(5)合并胃出血等并发症者;(6)合并重度异型增生、穿凿性溃疡、癌前病变者;(7)合并肝、心、肾等器官病变严重者;(8)入组前1个月内有质子泵抑制剂、抗生素服用者。根据奇偶数字法将患者分为对照组、联合组,各62例。对照组男35例,女27例,年龄25~61(38.67±3.51)岁;病程8个月~3(1.78±0.24)年;溃疡部位:胃部24例、复合型20例、十二指肠18例;体质量指数20~28(24.18±0.96)kg/m²。联合组男38例,女24例,年龄27~64(39.83±4.69)岁;病程10个月~3(1.96±0.37)年;溃疡部位:胃部22例、复合型21例、十二指肠19例;体质量指数21~27(23.95±0.79)kg/m²。对比两组一般资料无差异($P>0.05$),具有可比性。本研究已获取我院伦理学委员会批准进行。

1.2 方法

对照组采用四联疗法治疗,于早餐前服用泮托拉唑(永信药品工业(昆山)股份有限公司,国药准字H20052585,规格:40mg)40mg/次,1次/d;阿莫西林(规格:0.375g(阿莫西林0.25g;克拉维酸0.125g),昆明贝克诺顿制药有限公司,国药准字H19994016)100mg/次,2次/d;克拉霉素(规格:0.125g(12.5万单位),朝阳富祥药业有限公司,国药准字H19990221)500mg/次,1次/d;胶体果胶铋(规格:50mg(以Bi计算),湖南迪博制药有限公司,国药准字H20063655)100mg/次,1次/d。在上

述基础上,给予联合组胃苏颗粒(规格:每袋装5g(无蔗糖),扬子江药业集团江苏制药股份有限公司,国药准字Z10950007)治疗,3袋/次,3次/d,用开水冲调后服用。两组疗程均为4周。

1.3 观察指标

(1)记录两组治疗4周后的总有效率。疗效判定标准如下:胃镜观测下溃疡消失、疤痕愈合视为治愈;患者临床症状基本消失,胃镜下可见溃疡基本愈合视为显效;胃镜观测下溃疡数目减少一半以上,患者临床症状有改善视为有效;胃镜观测下溃疡数目减少未达一半,患者临床症状未见改善视为无效。治愈率、显效率及有效率之和即为总有效率^[10]。(2)记录两组*Hp*根除率,*Hp*根除情况经¹⁴C尿素呼气试验或快速尿素酶试验检测,检测为*Hp*转阴则判定为*Hp*已根除。(3)于治疗前、治疗4周后采用健康调查简表(SF-36)^[11]评价两组患者生活质量,其中SF-36包括8个维度(每维度100分),分别为生理机能、生理职能、躯体疼痛、一般健康状况、精力、社会功能、情感职能以及精神健康。患者所得分数愈高,则认为其生活质量愈好。(4)提取两组治疗前、治疗4周后的空腹静脉血,采血量为5mL,经离心处理(离心半径8cm,3500r/min离心12min)后取上清液,采用酶联免疫吸附试验检测降钙素原(PCT)、白介素-6(IL-6)、超敏C反应蛋白(hs-CRP),采用放射免疫法测定胃泌素(GAS)、胃动素(MTL),严格按照试剂盒(上海桑戈生物工程有限公司)说明书步骤进行。(5)记录两组便秘、恶心、食欲减退等不良反应。

1.4 统计学方法

采用SPSS20.0软件进行统计分析。计数资料以率的形式表示,行卡方检验。计量资料以($\bar{x}\pm s$)的形式表示,行t检验,以 $\alpha=0.05$ 为统计学检验水准。

2 结果

2.1 两组*Hp*根除率对比

对照组*Hp*转阴45例,*Hp*根除率为72.58%(45/62),联合组*Hp*转阴54例,*Hp*根除率为87.10%(54/62),联合组*Hp*根除率高于对照组($\chi^2=4.058, P=0.044$)。

2.2 两组疗效对比

治疗4周后,对照组的临床总有效率为72.58%,联合组的临床总有效率为90.32%,联合组的临床总有效率较对照组更高($P<0.05$),见表1。

2.3 两组生活质量对比

治疗前对比两组SF-36量表各维度评分无差异($P>0.05$),治疗4周后两组SF-36量表各维度评分比治疗前更高,且联合组较对照组更高($P<0.05$),见表2。

表1 两组疗效对比[例(%)]

Table 1 Comparison of effect efficacy of the two groups[n(%)]

Groups	Clinical recovery	Obvious effect	Effective	Invalid	Total effective rate
Control group (n=62)	9(14.52)	19(30.65)	17(27.42)	17(27.42)	45(72.58)
Combined group(n=62)	14(22.58)	24(38.71)	18(29.03)	6(9.68)	56(90.32)
χ^2					6.459
P					0.011

表 2 两组生活质量对比($\bar{x}\pm s$,分)

Table 2 Comparison of quality of life between the two groups($\bar{x}\pm s$, score)

Groups	Time points	Physiological maneuver-ability	Mental health	Physiological function	Physical pain	General health	Energy	Social function	Emotional function
Control group (n=62)	Before treatment	59.25±6.73	60.53±5.84	58.30±7.24	53.44±6.63	56.24±7.74	56.32±7.57	57.69±6.44	56.37±8.73
	After 4 weeks of treatment	72.67±8.04*	74.52±8.03*	73.25±7.02*	75.10±6.45*	77.51±6.69*	74.12±6.78*	75.04±7.76*	72.86±6.21*
Combined group(n=62)	Before treatment	59.58±7.52	60.27±7.69	58.61±7.59	53.81±8.32	56.03±8.58	56.97±7.54	57.23±8.68	56.21±7.59
	After 4 weeks of treatment	84.25±7.35**	85.30±6.95**	83.24±6.13**	84.32±7.95**	86.32±7.25**	87.24±8.65**	87.35±8.09**	83.34±6.67**

Note: Compared with before treatment in the same group, * $P<0.05$, compared with the control group after 4 weeks of treatment, ** $P<0.05$.

2.4 两组血清炎症因子水平对比

对比两组治疗前血清炎症因子无差异($P>0.05$),两组治疗

4 周后血清 PCT、IL-6、hs-CRP 水平较治疗前更低,且联合组较对照组更低($P<0.05$),见表 3。

表 3 两组血清炎症因子水平对比($\bar{x}\pm s$)

Table 3 Comparison of serum inflammatory factor levels between the two groups($\bar{x}\pm s$)

Groups	Time points	PCT($\mu\text{g/L}$)	IL-6(ng/L)	hs-CRP(mg/L)
Control group (n=62)	Before treatment	3.77±0.63	25.59±2.58	10.64±1.55
	After 4 weeks of treatment	2.39±0.54*	18.34±2.40*	6.51±1.42*
Combined group(n=62)	Before treatment	3.72±0.58	25.17±2.35	10.43±1.21
	After 4 weeks of treatment	1.61±0.51**	12.20±2.79**	3.45±0.86**

Note: Compared with before treatment in the same group, * $P<0.05$, compared with the control group after 4 weeks of treatment, ** $P<0.05$.

2.5 两组胃肠激素指标对比

对比两组治疗前血清 GAS、MTL 水平对比差异无统计学意义 ($P>0.05$), 两组患者治疗 4 周后 GAS、MTL 较治疗前降

低,联合组治疗 4 周后 GAS、MTL 较对照组更低($P<0.05$),见表 4。

表 4 两组胃肠激素指标对比($\bar{x}\pm s$)

Table 4 Comparison of gastrointestinal hormone indexes between the two groups($\bar{x}\pm s$)

Groups	Time points	GAS($\mu\text{g/dl}$)	MTL(ng/L)
Control group (n=62)	Before treatment	97.04±6.55	174.10±19.42
	After 4 weeks of treatment	81.87±6.68*	129.08±22.35*
Combined group(n=62)	Before treatment	97.75±9.10	173.23±24.03
	After 4 weeks of treatment	64.17±8.86**	96.55±21.87**

2.6 不良反应发生率

用药期间对照组发生 4 例不良反应,包括便秘 1 例、恶心 2 例、食欲减退 1 例;联合组用药期间发生 6 例不良反应,包括便秘 1 例、恶心 2 例、食欲减退 3 例;对照组不良反应发生率为 6.45%(4/62),与联合组的 9.68%(6/62)对比差异无统计学意义 ($\chi^2=0.435, P=0.510$)。

分泌产生细胞毒素、空泡毒素、脂多糖和尿素酶等蛋白质,进而引起胃黏膜上皮细胞产生免疫和炎症反应^[14,15]。因此,治疗消化性溃疡的同时行有效的 Hp 根除治疗,不仅可保护胃黏膜血液循环,还可减少胃酸的的过量分泌,促进胃溃疡愈合。

3 讨论

消化性溃疡是一种酸性相关性疾病,溃疡愈合与胃酸抑制程度相关^[12]。消化性溃疡的发病机制未明确, Hp 感染作为导致胃溃疡的重要因素,该细菌生存能力极强,可在强酸性环境中生存,是目前已知的唯一能够在胃里面生存的细菌^[13]。Hp 可以

本研究采用了阿莫西林、泮托拉唑、克拉霉素、胶体果胶铋四联疗法,其中胶体果胶铋与溃疡面有较好的亲和力,可形成保护膜,促进溃疡愈合;同时胶体果胶铋可引起 Hp 细胞质内空泡样变,使细胞壁破裂,进而杀灭细菌^[16]。泮托拉唑是质子泵抑制剂,临床证实其具有较好的抑制胃酸作用^[17]。克拉霉素是红霉素衍生物,可通过抑制蛋白质合成来发挥其抑菌作用^[18]。阿莫西林是一种合成的光谱青霉素类抗生素,可通过抑制细胞壁的合成而产生杀菌效果,对 Hp 有较强的抗菌活性^[19]。虽然四

联疗法在临床使用已较为普遍,但同时也存在效果不稳定、耐药性高等问题。胃苏颗粒具有和胃止痛、理气消胀的功效,其中佛手理气和中、止呕消胀,香附理气宽中、疏肝理气、调经止痛,陈皮疏肝健脾、理气燥湿,鸡内金健胃消食、通淋化石,香橼消胀降痰、理气宽中,诸味中药相辅相成,达到和胃止痛、理气消胀的功效^[20,21]。

本研究在四联疗法治疗的基础上引入胃苏颗粒,结果显示,相比四联疗法治疗,胃苏颗粒联合四联疗法治疗 *Hp* 相关性消化性溃疡患者,*Hp* 根除率更高,疗效显著,且不增加不良反应发生率。这是因为胃苏颗粒具有抑制胃酸分泌,促进胃黏膜修复,降低胃酶活性的作用^[22],进而强化四联疗法杀灭 *Hp*、修复胃黏膜损伤、抑制消化性溃疡的作用,从而提高治疗效果。另外在本研究中,两组治疗方案均可降低 PCT、IL-6、hs-CRP、GAS、MTL 水平,且联合组相比对照组的改善效果更佳。消化性溃疡作为一种炎症性疾病,多种炎症因子参与着溃疡的发展进程。其中 IL-6 可激活炎症反应,加剧胃黏膜损伤,PCT、hs-CRP 在机体发生组织损伤、黏膜破损和细菌感染时,水平会迅速升高^[23]。GAS 作为一种胃肠激素类多肽,可刺激盐酸和胆汁盐的分泌,调节胃肠道蠕动^[24]。MTL 可以促进胃酸、胆汁和胰液分泌,其与溃疡等胃部炎症的产生存在密切联系^[25]。赵瑛瑛等研究显示^[26],胃苏颗粒改良四联方案可有效改善 *Hp* 阳性胃溃疡患者体内的血清炎症因子水平及临床症状。药理研究也证实胃苏颗粒可抑制胃酸分泌、促进胃肠蠕动以及修复胃黏膜功效,可以更好的满足胃溃疡活动期间需要保护和进攻同时实施的治疗原则,具体还可表现为甲基陈皮苷具有较明显的抗溃疡和抗炎作用,陈皮中的挥发油可以促进消化液分泌、佛手具有抗菌、抗炎的作用等^[27,28]。另研究显示胃苏颗粒联合四联疗法可提高患者生活质量,可能是因为联合治疗可促进溃疡症状改善,症状的明显改善可缓解患者的焦虑、抑郁情绪,改善其日常活动期间的心理和社会功能,从而帮助患者提高整体生活质量。

综上所述,胃苏颗粒联合四联疗法治疗 *Hp* 相关性消化性溃疡患者,可有效改善患者体内血清炎症因子及 GAS、MTL 水平,并提高其生活质量和 *Hp* 根除率,疗效优于单纯四联疗法。

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