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复方谷氨酰胺联合四联疗法治疗消化性溃疡的临床研究*

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摘要 目的:探讨复方谷氨酰胺联合四联疗法治疗消化性溃疡的临床研究。**方法:**选取我院在2019年3月到2022年3月收治的80例消化性溃疡患者作为研究对象。将患者分为常规组与联合组,每组40例。常规组采用四联疗法,联合组在对照组的基础上联合复方谷氨酰胺进行治疗。对比两组患者临床疗效与临床指标,碳13呼气试验、炎症因子水平变化、生活质量以及复发率。**结果:**在本次研究80例患者经碳13呼气试验,两组患者Hp阳性率对比无差异($P>0.05$),治疗后两组患者Hp阳性率降低,且联合组低于常规组($P<0.05$);治疗后,联合组总有效率为95%,常规组总有效率为75%,联合组优于常规组($P<0.05$);治疗前,两组患者炎症因子水平对比无差异($P>0.05$),治疗后,两组患者hs-CRP、IL-6、TNF- α 水平均有所降低,且联合组优于常规组($P<0.05$);治疗前,两组患者生活质量各维度评分比较无明显差异($P>0.05$),治疗后两组患者各维度评分均有提升,且联合组高于常规组($P<0.05$);疗程结束后对两组患者进行随访,联合组溃疡复发率为5%,常规组溃疡复发率为25%,联合组低于常规组($P<0.05$)。**结论:**在临床治疗当中,采用复方谷氨酰胺联合四联疗法治疗,能够降低患者Hp阳性率,且能够有效降低机体炎症反应,提高患者生活质量水平,临床效果明显,且复发率低。

关键词:复方谷氨酰胺;四联疗法;消化性溃疡

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Clinical Study of Compound Glutamine Combined with Quadruple Therapy in the Treatment of Peptic Ulcer*

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ABSTRACT Objective: To investigate the clinical study of compound glutamine combined with quadruple therapy in the treatment of peptic ulcer. **Methods:** 80 patients with peptic ulcer treated in our hospital from March 2019 to March 2022 were selected as the research objects. The patients were divided into routine group and combined group, with 40 cases in each group. The conventional group was treated with quadruple therapy, and the combined group was treated with compound glutamine on the basis of the control group. The clinical efficacy and clinical indicators, carbon 13 breath test, changes in inflammatory factor levels, quality of life and recurrence rate were compared between the two groups. **Results:** Before the carbon 13 breath test of 80 patients in this study, there was no significant difference in the positive rate of HP between the two groups($P>0.05$). After treatment, the positive rate of HP in the two groups decreased significantly, and the combined group was lower than the conventional group($P<0.05$); After treatment, the total effective rate was 95% in the combined group and 75% in the conventional group. The combined group was better than the conventional group ($P<0.05$); Before treatment, there was no significant difference in the level of inflammatory factors between the two groups ($P>0.05$). After treatment, hs CRP, IL-6, TNF- α The combined group was better than the conventional group ($P<0.05$); Before treatment, there was no significant difference in the scores of each dimension of quality of life between the two groups ($P>0.05$). After treatment, the scores of each dimension of the two groups were improved, and the combined group was higher than the conventional group ($P<0.05$); After the course of treatment, the patients in the two groups were followed up. The ulcer recurrence rate in the combined group was 5%, and that in the conventional group was 25%. The ulcer recurrence rate in the combined group was lower than that in the conventional group ($P<0.05$). **Conclusion:** In clinical treatment, Compound Glutamine Combined with quadruple therapy can reduce the HP positive rate of patients, effectively reduce the inflammatory reaction of the body, and improve the quality of life of patients. The clinical effect is obvious, and the recurrence rate is low.

Key words: Compound glutamine; Quadruple therapy; Peptic ulcer

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前言

消化性溃疡是一种常见的消化疾病,指在各种致病因子的互相作用下,黏膜出现的炎性反应与脱落、坏死形成的溃疡^[1,2]。大多数消化性溃疡是由于胃肠道黏膜被胃蛋白酶或胃酸自身消化而引起的。该病可出现在食管、胃、十二指肠等位置,其中胃溃疡与十二指肠溃疡最为常见。据不完全统计^[3],全球约5%~10%的人群终生患有消化性溃疡。该病发病率高、病程长,易反复发作,对患者的生活质量造成严重的影响。有调查研究显示^[4,5],消化性溃疡的发生与幽门螺旋杆菌的感染密切相关,目前临床对于该疾病的治疗多采用质子泵抑制剂联合抗生素,临床效果明显。四联疗法是用于幽门螺杆菌相关的消化性溃疡的治疗^[7,8]。该疗法可对胃酸分泌与幽门螺杆菌有较好的抑制作用,但幽门螺杆菌抵抗会导致幽门螺杆菌的根除率受到影响,不利于溃疡愈合,而患者对于抗生素的不良反应也会影响治疗的依从性。复方谷氨酰胺中的主要成分L-谷氨酰胺,可增强胃粘液的分泌,对溃疡的愈合有一定的促进作用^[9,10]。因此,本研究选取我院在2019年3月到2022年3月收治的80例消化性溃疡患者作为研究对象,探讨复方谷氨酰胺联合四联疗法治疗消化性溃疡的临床效果。

1 资料与方法

1.1 一般资料

选取我院在2019年3月到2022年3月收治的80例消化性溃疡患者作为研究对象。本研究经我院伦理委员会批准。根据数字随机法将患者分为常规组与联合组,每组40例。其中常规组男25例,女15例,平均年龄(41.78±3.98)岁,平均病程(3.38±1.23)年,其中十二指肠溃疡22例,胃溃疡18例;联合组男26例,女14例,平均年龄(41.28±3.38)岁,平均病程(3.18±1.63)年,其中十二指肠溃疡23例,胃溃疡17例;两组患者资料相比无差异($P>0.05$),具有可比性。

纳入标准:(1)经胃镜检查并确诊为消化性溃疡且碳13呼气实验为阳性的患者;(2)意识清晰、有沟通能力;(3)近两周内未服用过抗生素及复方谷氨酰胺胶囊;(4)自愿参与本研究并在知情书上签字。

排除标准:(1)精神疾病者;(2)病历资料不全;(3)沟通障碍者;(4)有胃肠道手术史;(5)哺乳期或妊娠期妇女;(6)对本次研究所用药物过敏者;(7)严重肝、肾功能不全者;(8)恶性肿瘤患者。

1.2 方法

阿莫西林胶囊(华北制药股份有限公司,国药准字:H13020726),0.25 g/粒,1 g/次,2次/日;克拉霉素片(广东东阳光药业有限公司,药准字:H20183466),0.25 g/片,0.5 g/次,2次/日;连续用药2周。

艾司奥美拉唑肠溶胶囊(广东东阳光药业有限公司,国药准字:H20203210),20 mg/粒,20 mg/次,2次/日;胃铋镁颗粒(弘美制药(中国)有限公司,国药准字:H20045610),2袋,2次/日;连续用药8周。

联合组在常规组的基础上联合复方谷氨酰胺肠溶胶囊治疗。具体如下:给予复方谷氨酰胺肠溶胶囊(地奥集团成都药业

股份有限公司,国药准字:H51023598)口服,2粒/次,3次/日,服用后不可大量饮水。连续用药8周。

两组患者在治疗过程中均规律睡眠,按时就餐。饮食禁辛辣、刺激等事物。

1.3 观察指标

①观察两组患者的临床疗效。显效:胃镜检查显示治疗后胃黏膜溃疡基本消失,且炎性反应基本消失;有效:胃镜检查显示治疗后胃黏膜溃疡面积缩小30%以上,且炎性反应改善明显;无效:胃镜检查显示治疗后胃黏膜溃疡面积无变化或缩小低于30%,且炎性反应无变化,甚至加重。总有效率=显效率+有效率。

②治疗结束1月后,对两组患者进行碳13呼气试验来检测Hp。具体方法如下:让患者隔夜空腹后进行,收集100 mL气体,并服用含有13C-尿素的底物75 mg和100 mL水,随后静坐30 min后,再次收集100 mL气体进行送检,检查有无Hp感染,将DOB<4判定为阴性,DOB>4判定为阳性。

③观察两组患者治疗前后炎症因子水平变化情况。具体方法如下:在治疗前、后分别取患者5 mL空腹静脉血,离心后置低温环境。采用酶联免疫吸附法对超敏C反应蛋白(Hyper-sensitive C-reactive protein, hs-CRP)、白细胞介素-6(Interleukin-6, IL-6)以及肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)进行测定。

④观察两组患者治疗前后生活质量。具体方法如下:在治疗前、治疗后采用健康调查简表(Health survey summary, SF-36)分别对两组患者的生活质量水平进行评估。该量表包括36个项目,8个维度,总分0~100分,分数越高说明健康相关的生活质量越好。

⑤观察两组患者治疗后复发情况。疗程结束后对患者进行3个月的随访,并记录复发情况。

1.4 统计学方法

采取SPSS 23.0进行分析,计数资料以(n/%)表示,进行 χ^2 检验;计量资料用($\bar{x}\pm s$)表示,采用t检验;以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 临床疗效对比

治疗后,联合组总有效率优于常规组($P<0.05$)。如表1所示。

2.2 碳13呼气试验对比

在本次研究80例患者经碳13呼气试验前,两组患者Hp阳性率对比无明显差异($P>0.05$),治疗后两组患者Hp阳性率明显降低,且联合组低于常规组($P<0.05$),如表2所示。

2.3 炎症因子水平变化情况对比

治疗前,两组患者炎症因子水平对比无差异($P>0.05$)。治疗后,两组患者hs-CRP、IL-6、TNF- α 水平均有所降低,且联合组优于常规组($P<0.05$)。如表3所示。

2.4 生活质量对比

两组患者治疗前生活质量评分比较无差异($P>0.05$),治疗后两组患者各维度评分均有提升,且联合组高于常规组($P<0.05$)。见表4。

表 1 两组患者临床疗效对比[n(%)]

Table 1 Comparison of clinical efficacy between the two groups of patients [n (%)]

Groups	n	Excellence	Valid	Invalid	Total effective
Joint group	40	23(57.50%)	15(37.50%)	2(5.00%)	38(95.00%)
Conventional group	40	17(42.50%)	13(32.50%)	10(25.00%)	30(75.00%)
χ^2	-	-	-	-	6.275
<i>P</i>	-	-	-	-	0.012

表 2 两组患者碳 13 呼气试验对比[n(%)]

Table 2 Comparison of carbon 13 breath test between the two groups [n (%)]

Groups	n	Positive rate before treatment	Positive rate after treatment
Joint group	40	28(70.00%)	6(15.00%)
Conventional group	40	25(62.50%)	15(37.50%)
χ^2		0.503	5.230
<i>P</i>		0.478	0.022

表 3 两组患者治疗前后炎症因子水平变化情况对比($\bar{x} \pm s$)

Table 3 Comparison of changes in the levels of inflammatory factors before and after treatment in the two groups of patients ($\bar{x} \pm s$)

Indexs		Joint group(n=40)	Conventional group(n=40)	t	<i>P</i>
hs-CRP(mg/mL)	Before therapy	18.72± 1.72	18.52± 1.64	0.532	0.596
	After treatment	8.12± 0.63	13.54± 1.82	17.798	0.000
IL-6(ng/L)	Before therapy	23.89± 2.31	23.71± 2.28	0.351	0.727
	After treatment	9.75± 1.61	15.12± 1.74	14.327	0.000
TNF-α(μg/L)	Before therapy	3.78± 0.71	3.82± 0.82	0.233	0.816
	After treatment	1.63± 0.21	2.84± 0.32	19.994	0.000

表 4 两组患者治疗前后生活质量对比($\bar{x} \pm s$,分)

Table 4 Comparison of quality of life before and after treatment in the two groups of patients ($\bar{x} \pm s$, points)

Indexs		Joint group (n=40)	Conventional group (n=40)	t	<i>P</i>
General health	Before therapy	62.33± 7.35	63.57± 8.23	0.711	0.479
	After treatment	78.71± 9.52 ¹⁾²⁾	70.36± 8.34 ¹⁾	4.173	0.000
Somatic function	Before therapy	72.43± 8.25	73.25± 7.35	0.469	0.640
	After treatment	86.24± 9.22 ¹⁾²⁾	80.86± 8.13 ¹⁾	2.768	0.007
Somatic function	Before therapy	63.73± 8.46	64.24± 7.63	0.283	0.778
	After treatment	84.87± 7.56 ¹⁾²⁾	78.38± 8.51 ¹⁾	3.606	0.001
Somatic pain	Before therapy	74.77± 7.55	75.36± 8.22	0.334	0.739
	After treatment	89.42± 7.93 ¹⁾²⁾	79.36± 9.22 ¹⁾	5.232	0.000

Note: ¹⁾ Comparison with the same group before treatment: *P*<0.05; ²⁾ Comparison with the conventional group: *P*<0.05.

2.5 疗程结束后复发情况对比

疗程结束后对两组患者进行随访,联合组溃疡复发率为 5%,常规组溃疡复发率为 25%,联合组低于常规组(*P*<0.05)。见表 5。

3 讨论

消化性溃疡是消化系统常见的病症,是指胃肠道粘膜被胃蛋白酶或胃酸等自身消化而造成的溃疡,多发于胃部与十二指肠。该病的致病因素主要是由于胃酸分泌过多,造成胃黏膜功能下降以及幽门螺杆菌感染^[12-14]。消化性溃疡患者常常会出现上腹部疼痛,严重的患者还会出现穿孔、出血,甚至癌变的情况发生。该病病程长且治疗难度大^[15-17]。采用质子泵抑制剂为主的

四联疗法治疗消化性溃疡效果明显。但对于反复发作或病期较长患者来说,反复用药会使机体对药物的敏感性降低,药物疗效也随之降低。复方谷氨酰胺胶囊是一种新型的治疗胃肠道疾

病的复合制剂,能够促进受损胃黏膜的修复,改善胃肠道环境。因此,本研究探讨复方谷氨酰胺联合四联疗法治疗消化性溃疡的临床效果。

表 5 两组患者疗程结束后复发情况对比
Table 5 Comparison of recurrence after the course

Groups	n	Ulcer recurrence(n)	Recurrence rate (n,%)
Joint group	40	2	2(5.00)
Conventional group	40	10	10(25.00)
χ^2	-		6.275
P	-		0.012

在本次研究 80 例患者经碳 13 呼气试验前, 两组患者 *Hp* 阳性率对比无明显差异($P>0.05$), 治疗后两组患者 *Hp* 阳性率明显降低, 且联合组低于常规组($P<0.05$)。由此证明, 应用复方谷氨酰胺联合四联疗法治疗消化性溃疡能够降低患者 *Hp* 阳性率。有研究显示^[18-21], *Hp* 与消化性溃疡、胃炎、胃癌及与胃黏膜相关的淋巴组织病变均有关系。*Hp* 分泌的酶、细胞毒素等物质, 可引发各种炎症介质发生, 致使胃部炎症、消化性溃疡的发生。该检测结果与陈瑾等人^[22]的研究一致, 即 *Hp* 是引起消化性溃疡的主要原因。本次研究治疗后患者 *Hp* 阳性率均降低, 且联合组低于对照组, 分析可能是因为联合治疗效果更好, 进一步提升治疗效果的同时, 降低 *Hp* 阳性率。

本次研究显示, 治疗后, 联合组总有效率为 95%, 常规组总有效率为 75%, 联合组优于常规组($P<0.05$); 由此证明, 复方谷氨酰胺联合四联疗法治疗消化性溃疡, 可有效缓解患者临床症状, 疗效显著。分析认为, *Hp* 可生成毒素、酶等物质, 降解黏液, 损伤胃肠道黏膜, 增加胃黏膜通透性, 导致胃黏膜层的保护作用减弱, 使胃黏膜屏障受损, 导致消化性溃疡的发生^[23-25]。目前临床对于 *Hp* 的治疗多采用抗生素, 但由于过去人们对抗生素的认识不足, 导致抗生素滥用的情况发生, 致使 *Hp* 耐药性变强, 使治疗难度增加。四联疗法可有效对 *Hp* 进行清除, 加快溃疡愈合。其中克拉霉素可与细菌核糖体的 50S 亚基结合, 抑制蛋白质的合成从而产生抑菌的作用。质子泵抑制剂能抑制胃酸分泌, 隔离溃疡部位与胃蛋白、胃酸接触, 保护受损部位, 促进溃疡的修复与愈合, 可同时抑制 *Hp* 尿素酶活性。复方谷氨酰胺胶囊的 L- 谷氨酰胺可增强胃粘液中的葡萄糖胺含量, 使胃粘液的分泌增多, 促使溃疡部位的修复与愈合^[26-28]。

治疗后, 两组患者 hs-CRP、IL-6、TNF- α 水平均有所降低, 且联合组优于常规组($P<0.05$)。由此证明, 复方谷氨酰胺联合四联疗法治疗消化性溃疡可有效抑制炎症反应。分析认为, 在 *Hp* 感染后, 胃黏膜上皮细胞坏死、变性以及炎症细胞被浸润, 进而可激活中性粒细胞, 释放反应性蛋白溶解酶、反应性氧化代谢物, 导致机体出现炎症反应。四联疗法中的药物可直接作用于 *Hp* 细胞壁, 出现空泡样胞浆, 加速 *Hp* 消杀, 并在炎症表面形成保护膜, 隔离因胃酸所造成的损害, 减轻炎症反应。复方谷氨酰胺胶囊具有水溶性, 服用后, 在胃肠道内迅速溶解, 与胃黏膜充分接触, 抑制炎症反应, 同时促进上皮形成、肉芽新生。这与张莉等人^[29]的研究一致, 即复方谷氨酰胺可有效调节机体炎

性因子, 提高疗效。

治疗后两组患者生活质量评分均有提升, 且联合组高于常规组($P<0.05$)。疗程结束后对两组患者进行随访, 联合组溃疡复发率为 5%, 常规组溃疡复发率为 25%, 联合组低于常规组($P<0.05$)。由此证明, 复方谷氨酰胺联合四联疗法治疗消化性溃疡, 可提升患者生活质量, 且复发率低。分析原因, 单独使用四联疗法对幽门螺杆菌相关的消化性溃疡进行治疗, 长期使用易出现耐药性, 导致病情复发。这与 SHI Yuhua 等人^[30]的研究相符, 根据 SHI Yuhua 等人的随访记录发现, 两组患者四联疗法复发率较高。而本研究联合复方谷氨酰胺治疗, 增加药物效果, 稳定疗效, 复发率低。

综上所述, 在临床治疗当中, 采用复方谷氨酰胺联合四联疗法治疗, 能够有效缓解患者临床症状, 降低炎症反应, 提高其生活质量水平, 临床效果明显, 且复发率低, 值得临床应用。

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