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幽门螺旋杆菌感染与慢性胃炎患者 IL-8、IL-10、CRP 水平以及血脂指标的关系研究 *

代金玉¹ 苏卫仙¹ 史增辉¹ 赵俊精¹ 伍东升²

(1 河北省廊坊市人民医院消化科 河北 廊坊 065000; 2 北京协和医院消化科 北京 100032)

摘要 目的:研究幽门螺旋杆菌(Hp)感染与慢性胃炎患者白细胞介素-8(IL-8)、白细胞介素-10(IL-10)、C反应蛋白(CRP)水平以及血脂指标的关系。**方法:**选择从2015年6月到2017年6月在我院接受治疗的慢性胃炎患者150例作为观察组,根据¹³C-尿素呼吸实验的结果将观察组患者分成HP阳性组71例和Hp阴性组79例,另选同期在我院进行健康体检的志愿者150例作为对照组,对比观察组以及对照组的炎症因子IL-8、IL-10、CRP及血脂指标[低密度脂蛋白(LDL-C)、高密度脂蛋白(HDL-C)、甘油三酯(TG)、总胆固醇(TC)]水平,并对比观察组不同HP感染情况的炎症因子及血脂指标水平,分析Hp感染与患者炎症因子及血脂指标水平的相关性。**结果:**观察组的IL-8、IL-10、CRP、LDL-C及TG水平均分别高于对照组,差异均有统计学意义(均 $P<0.05$)。Hp阳性组患者治疗前的IL-8、IL-10、CRP、LDL-C及TG水平均分别高于HP阴性组,但Hp阳性组患者治疗后的上述指标水平均分别低于HP阴性组,差异均有统计学意义(均 $P<0.05$)。两组治疗后的IL-10、CRP水平均分别低于治疗前,且Hp阳性组患者的IL-8、LDL-C及TG水平也低于治疗前,差异均有统计学意义(均 $P<0.05$)。Spearman相关性分析结果显示,Hp感染与患者IL-8、IL-10、CRP、LDL-C及TG水平均呈正相关(均 $P<0.05$),但Hp感染与HDL-C和TC并无明显的相关性($P>0.05$)。**结论:**Hp感染与慢性胃炎患者的炎症指标及血脂指标关系紧密,临床上可考虑将此类指标作为存在Hp感染的慢性胃炎患者的监测指标,从而更好地辅助临床诊治。

关键词:幽门螺旋杆菌;感染;慢性胃炎;白细胞介素-8;白细胞介素-10;C反应蛋白;血脂指标

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Relationship Between *Helicobacter Pylori* Infection and Levels of IL-8, IL-10, CRP and Blood Lipid Indexes in Patients with Chronic Gastritis*

DAI Jin-yu¹, SU Wei-xian¹, SHI Zeng-hui¹, ZHAO Jun-jing¹, WU Dong-sheng²

(1 Department of Gastroenterology, Langfang People's Hospital, Langfang, Hebei, 065000, China;

2 Department of Gastroenterology, Peking Union Medical College Hospital, Beijing, 100032, China)

ABSTRACT Objective: To study the relationship between *Helicobacter pylori* (HP) infection and the levels of interleukin-8(IL-8), interleukin-10(IL-10), C reactive protein (CRP) and blood lipid indexes in patients with chronic gastritis. **Methods:** A total of 150 patients with chronic gastritis, who were treated in Langfang People's Hospital from June 2015 to June 2017, were chosen as observation group. According to the experimental results of ¹³C-urea breath, the patients of observation group were further divided into Hp positive group (n=71) and HP negative group (n=79). At the same time, 150 volunteers, who underwent physical examination in this hospital, were chosen as control group. The levels of inflammatory cytokines such as IL-8, IL-10, and CRP and blood lipid indexes such as low density lipoprotein (LDL-C), high density lipoprotein (HDL-C), triglyceride (TG), total cholesterol (TC) were compared between the observation group and the control group. The levels of inflammatory factors and blood lipid indexes of the patients with different Hp infection in the observation group were compared. The correlation between HP infection and levels of inflammatory factors and blood lipid indexes of the patients were analyzed. **Results:** The levels of IL-8, IL-10, CRP, LDL-C and TG in the observation group were significantly higher than that in the control group, the differences were statistically significant($P<0.05$). The levels of IL-8, IL-10, CRP, LDL-C and TG of Hp positive group before treatment were significantly higher than those of HP negative group, but the above indexes of the HP positive group were lower than those of the Hp negative group, the differences were statistically significant($P<0.05$). The levels of IL-10, CRP of the two groups after treatment were significantly lower than those before treatment, the levels of IL-8, LDL-C and TG of Hp positive group were significantly lower than those before treatment, the differences were statistically significant ($P<0.05$). Spearman correlation analysis showed that Hp infection was positively correlated with the levels of IL-8, IL-10, CRP, LDL-C and TG of the patients ($P<0.05$), but there was no significant correlation between Hp infection and HDL-C and TC ($P>0.05$). **Conclusion:** Hp infection is closely related to inflammatory indexes and blood lipid indexes of the patients with chronic gastritis. The above indexes can be considered as a monitoring index

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作者简介:代金玉(1970-),女,本科,副主任医师,从事消化内科方面的研究,E-mail:yqwegu@163.com

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of chronic gastritis patients with Hp infection, so as to better assist clinical diagnosis and treatment.

Key words: *Helicobacter pylori*; Infection; Chronic gastritis; Interleukin-8; Interleukin-10; C reactive protein; Blood lipid; Relationship

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前言

幽门螺杆菌 (*Helicobacter pylori*, Hp) 是十分常见的一类致病菌,也是导致胃炎发病的重要因素, Hp 感染和许多胃肠道疾病有密切联系^[1]。同时,研究证实, Hp 感染会造成胃黏膜上淋巴细胞以及相关细胞因子水平上升, 包括白细胞介素 -8(interleukin -8, IL-8)、白细胞介素 -10(interleukin -10, IL-10)、C 反应蛋白(C reactive protein, CRP)等,进而趋化并激活机体中的中性粒细胞,发生非特异性炎症反应,导致胃黏膜受损^[2-4]。Hp 感染甚至和胃癌发病关系密切,其在胃部的分布情况可对患者胃酸分泌功能产生较大影响。近期有报道指出, Hp 感染还会引发多种胃肠道之外的疾病, 例如 Hp 感染和动脉粥样硬化(atherosclerosis, AS)具有一定联系,提示 Hp 感染和心血管类疾病存在一定相关性^[5-6]。因此, Hp 感染对人体危害较大,了解 Hp 感染和慢性胃炎患者各项炎症指标以及血脂指标等之间关系十分有必要,因此探索高效抗 Hp 治疗方法成为当前临床研究的重点。有学者指出^[7-8], 枳术宽中胶囊对于 Hp 阳性的慢性胃炎患者疗效显著。本文应用枳术宽中胶囊治疗法,针对 Hp 感染与慢性胃炎患者 IL-8、IL-10、CRP 水平以及血脂指标的关系进行研究,旨在为临床治疗慢性胃炎患者提供数据支持,现报道如下。

1 资料和方法

1.1 临床资料

选择从 2015 年 6 月到 2017 年 6 月在我院接受治疗的慢性胃炎患者 150 例作为观察组,纳入标准:(1)经胃镜检查确诊患有慢性胃炎者;(2)未应用质子泵抑制剂和铋制剂以及抗生素等药物行抗 HP 治疗者;(3)年龄 ≥ 20 岁;(4)患者均对此次研究知情同意,并且已经签署同意书。排除标准:(1)有严重的心、肝、肾等脏器的功能性不全者;(2)有消化道手术史者;(3)有消化型溃疡和出血以及穿孔等相关并发症者;(4)有恶性肿瘤或血液疾病者。观察组男 84 例,女 66 例,年龄 23~66 岁,平均(45.81 $\pm$ 8.13)岁。根据 ¹³C- 尿素呼吸实验的结果将患者分成 HP 阳性组 71 例和 HP 阴性组 79 例,其中 HP 阳性组中男 40 例,女 31 例,年龄 24~64 岁,平均(44.94 $\pm$ 8.62)岁。HP 阴性组中男 44 例,女 35 例,年龄 23~66 岁,平均(45.01 $\pm$ 8.55)岁。另选同期在我院进行健康体检的志愿者 150 例作为对照组,男 100 例,女 50 例,年龄 22~65 岁,平均(44.81 $\pm$ 8.33)岁。各组

研究对象在性别比例及年龄上的统计分析结果显示差异无统计学意义($P>0.05$)。关于本次研究,医院的伦理委员会已经作出了评审并通过。

1.2 研究方法

观察组的 HP 阳性患者给予以下药物治疗:埃索美拉唑(阿斯利康药业公司,国药准字:H20046379,规格:20 mg),剂量为 20 mg,2 次/d;克拉霉素(江西汇仁药业公司,国药准字:H20033513),剂量为 0.5g,2 次/d;阿莫西林(海口市制药厂公司,国药准字:H20083420,规格:0.25 g),剂量为 1 g,2 次/d;枸橼酸铋钾(丽珠集团丽珠制药厂,国药准字:H10920098),剂量为 0.6 g/次,2 次/d;枳术宽中胶囊(山西双人药业公司,国药准字:Z20020003,规格:每粒装 0.43 g),剂量为 1.29 g,3 次/d。观察组 HP 阴性患者予以枸橼酸铋钾(丽珠集团丽珠制药厂,国药准字:H10920098),剂量为 0.6 g/次,2 次/d。两组的疗程均为 14 d。

1.3 观察指标

对比观察组与对照组的炎症因子(IL-8、IL-10、CRP)及血脂指标(LDL-C、HDL-C、TG、TC),研究观察组不同 HP 感染情况的炎症因子及血脂指标水平,分析 HP 感染与患者炎症因子及血脂指标水平的相关性。观察组于治疗前及治疗 14d 后,对照组在入组前检测上述指标,分别采集受试者晨间的空腹静脉血 6 mL,对血标本实施 15 min 3500 r/min 的离心,而后提取上清,置于 -20℃ 条件下保存待测。血清 IL-8、IL-10、CRP 使用购自美国的 BIO-RAD680 酶标仪及酶联免疫法测定,血脂指标通过贝克曼 AU480 型全自动生化反应分析仪测定,有关试剂盒均购自武汉博士德公司,操作时需严格遵照说明书的步骤进行。

1.4 统计学方法

使用 SPSS21.0 统计软件实施处理和分析数据,若是计数资料,则用(n,%)表示,其比较选择 χ^2 检验。若是计量资料,则用($\bar{x}\pm s$)表示,其比较选择 t 检验。相关性的分析采用 Spearman 法, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组炎症因子及血脂指标水平的对比

观察组的 IL-8、IL-10、CRP、LDL-C 及 TG 水平均分别高于对照组,差异均有统计学意义(均 $P<0.05$)。两组 HDL-C 和 TC 水平相比,差异均无统计学意义(均 $P>0.05$),见表 1。

表 1 两组炎症因子及血脂指标水平的对比($\bar{x}\pm s$)

Table 1 Comparison of inflammatory factors and serum lipid levels between two groups

Groups	n	IL-8(ng/L)	IL-10(μ g/L)	CRP(mg/L)	LDL-C (mmol/L)	HDL-C (mmol/L)	TG(mmol/L)	TC(mmol/L)
Observation group	150	14.63 $\pm$ 4.32	11.75 $\pm$ 3.62	35.09 $\pm$ 8.92	3.12 $\pm$ 0.62	1.13 $\pm$ 0.28	1.91 $\pm$ 0.63	4.51 $\pm$ 0.88
Control group	150	5.29 $\pm$ 1.44	5.29 $\pm$ 1.46	3.48 $\pm$ 0.59	2.24 $\pm$ 0.33	1.16 $\pm$ 0.32	1.23 $\pm$ 0.25	5.03 $\pm$ 2.94
t	-	25.121	20.269	43.307	15.345	0.864	12.287	2.075
P	-	0.000	0.000	0.000	0.000	0.388	0.000	0.039

2.2 观察组不同 Hp 感染情况治疗前后的炎症因子及血脂指标水平对比

Hp 阳性组患者治疗前的 IL-8、IL-10、CRP、LDL-C 及 TG 水平均分别明显高于 Hp 阴性组, 但 Hp 阳性组患者治疗后的上述指标水平均分别低于 Hp 阴性组, 差异均有统计学意义

(均 $P < 0.05$)。两组治疗前后的 HDL-C 和 TC 水平相比, 差异均无统计学意义(均 $P > 0.05$)。两组治疗后的 IL-10、CRP 水平均分别低于治疗前, 且 HP 阳性组患者的 IL-8、LDL-C 及 TG 水平也低于治疗前, 差异均有统计学意义(均 $P < 0.05$), 见表 2。

表 2 观察组不同 HP 感染情况的炎症因子及血脂指标水平的对比($\bar{x} \pm s$)

Table 2 Comparison of inflammatory factors and blood lipid indexes of different HP infection in observation group

Groups	IL-8 (ng/L)		IL-10 (μ g/L)		CRP (mg/L)		LDL-C (mmol/L)		HDL-C (mmol/L)		TG (mmol/L)		TC (mmol/L)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment	treat- ment
Hp positive group (n=71)	15.87 $\pm$ 2.83	5.33 $\pm$ 1.39*	16.39 $\pm$ 3.92	5.22 $\pm$ 1.31*	38.32 $\pm$ 6.97	3.51 $\pm$ 0.57*	3.15 $\pm$ 0.46	2.01 $\pm$ 0.13*	1.15 $\pm$ 0.24	1.14 $\pm$ 0.11	1.93 $\pm$ 0.52	1.19 $\pm$ 0.17*	4.63 $\pm$ 0.83	4.58 $\pm$ 0.97
Hp nega- tive group (n=79)	6.39 $\pm$ 1.45	5.87 $\pm$ 1.02	8.81 $\pm$ 2.54	6.41 $\pm$ 1.19*	9.83 $\pm$ 3.23	5.99 $\pm$ 1.03*	2.22 $\pm$ 0.27	2.18 $\pm$ 0.21	1.16 $\pm$ 0.26	1.15 $\pm$ 0.14	1.27 $\pm$ 0.24	1.26 $\pm$ 0.11	5.17 $\pm$ 2.76	4.60 $\pm$ 0.93
t	26.199	2.731	14.191	5.830	32.648	17.963	15.281	5.882	0.244	0.483	10.145	3.023	1.585	0.129
P	0.000	0.007	0.000	0.000	0.000	0.000	0.000	0.000	0.808	0.630	0.000	0.003	0.115	0.898

Note: compared with before treatment, * $P < 0.05$.

2.3 Hp 感染与患者炎症因子及血脂指标水平的相关性分析

根据 SPearman 相关性分析后显示, Hp 感染与患者 IL-8、IL-10、CRP、LDL-C 及 TG 水平均呈正相关($r=0.709, 0.687, 0.642, 0.599, 0.614; P=0.000, 0.000, 0.000, 0.000, 0.000$), 但与 HDL-C 和 TC 并无明显的相关性($r=0.128, 0.204; P=0.107, 0.118$)。

3 讨论

慢性胃炎为临床十分高发的消化系统类疾病, 是由于多种原因导致胃黏膜发生炎症, 并伴随上皮细胞受损以及再生等症状^[9]。近年来, 慢性胃炎临床发病率不断上升, 并且多数是和 Hp 感染关系密切^[10]。研究证实, Hp 能够导致胃黏膜发生持续性慢性感染, 进而引起慢性胃炎以及消化性溃疡等^[11,12]。虽然 Hp 本身属于非侵袭性细菌类型, 但是能够引发严重炎症反应, 进而对免疫细胞造成刺激作用, 并导致相关免疫反应发生^[13]。另有研究指出, IL-8、IL-10 以及 CRP 可能与 Hp 感染导致的慢性胃炎存在一定联系, 并且其和血脂指标波动关系密切, 但其具体机制目前尚不明确, 仍需进一步研究探讨^[14-16]。本研究针对 Hp 感染和炎症因子以及血脂指标等之间的关系进行分析, 并对枳术宽中胶囊等药物治疗 Hp 阳性患者的临床疗效情况进行相关总结, 旨在为 Hp 感染相关的慢性胃炎临床治疗提供相关依据。

本文研究发现, 观察组的 IL-8、IL-10、CRP、LDL-C 及 TG 水平均分别高于对照组(均 $P < 0.05$), 这符合陶景德等人^[17,18]的报道结果, 提示了慢性胃炎患者的炎症指标及血脂指标水平均明显升高。分析原因, 主要可能是因为患者血管内皮在一定程度上损害干扰了 LDL-C 及 TG 的代谢, 而 Hp 对慢性胃炎患

者造成的持续性感染也可能会影响机体中 LDL-C 及 TG 的代谢, 而 IL-8、IL-10、CRP 三者能较好地呈现机体的炎症感染情况, 因此均出现了不同程度的水平上升^[19,20]。IL-8 属于多元性并且多功能性质的细胞因子, 能够帮助启动以及促进炎症反应。其主要通过淋巴细胞以及巨噬细胞等生成, 对特异性以及非特异性类型免疫细胞均具备十分强烈的趋化作用。其功能主要在于能够使嗜中性粒细胞进行趋化并激活, 并且对淋巴细胞也可以产生趋化作用。当发生炎症情况时, IL-8 会使中性粒细胞发生趋化以及脱颗粒, 进而导致粘膜局部出现炎症, 加剧溃疡发生以及发展^[21]。IL-10 则是人体一项重要细胞因子, 能够对免疫起到调节作用^[23]。其能够抗炎, 并且有利于抑制促炎介质的产生并抑制其活性, 和抗炎介质之间存在协同关系。研究显示内源性 IL-10 可以参与下调与 Hp 有关的慢性胃炎患者体内炎症反应, 因此, IL-10 能够对 Hp 感染起到防御反应, 是一种具有炎症抑制作用的因子^[24,25]。CRP 属于急性时相类型反应蛋白, 在正常情况下, 人体含量极低, 一旦发生炎症以及损伤或者肿瘤等情况时, 其水平会急速上升。因此, CRP 对于感染类疾病敏感性非常高, 可用于多种感染早期诊断。同时, CRP 水平还和感染微生物存在一定联系, 有研究证实, 通过对 Hp 阳性状态的慢性胃炎患者体内 CRP 情况进行分析, 发现其 CRP 水平显著上升, 并且和胃炎本身活动性直接相关^[26,27]。因此, 可将 CRP 作为临床判定胃炎患者疾病严重情况的辅助指标。本文还发现, 观察组 Hp 阳性组患者治疗前的 IL-8、IL-10、CRP、LDL-C 及 TG 水平均分别明显高于 Hp 阴性组, 但治疗后的上述指标水平均分别明显低于 Hp 阴性组(均 $P < 0.05$), Hp 阳性及 Hp 阴性两组治疗后的 IL-10、CRP 水平均分别明显低于治疗前, 且 Hp 阳

性组的 IL-8、LDL-C 及 TG 水平也明显低于治疗前 (均 $P < 0.05$)，上述结果提示了经过枳术宽中胶囊及抗 Hp 治疗的 Hp 阳性组患者的机体炎症症状及血脂水平均出现了明显下降。原因主要考虑是与枳术宽中胶囊的药理机制及抗 Hp 疗法发挥了较好的治疗作用有关。中医学研究发现，肝脾功能失常是导致 Hp 感染的重要发病基础，且脾胃湿热证以及肝胃郁热证等是较常见证型^[28,29]。与 Hp 感染相关的慢性胃炎通常伴有肝郁脾虚的病况，其胃肠动力多受到不良影响。因此，增加胃动力有助于改善患者病情。本研究所用的枳术宽中胶囊为中医著名方剂枳术丸配以柴胡和山楂而得，能够对肝脾功能失调起到较佳疗效。方剂中炒白术作为君药，具有健脾益气以及固护中焦等功效。而枳实作为臣药，能够下气、消痞以及除满。而柴胡作为佐药，起到疏解肝郁作用。并加之山楂相佐助，发挥消食化积的功效。此四味中药相合，可获得补而不滞以及疏且不利理想药效。以此治疗有利于减轻患者消化功能异常症状，进而减少 Hp 复发。而抗 Hp 疗法在根治 Hp 的同时也阻断了其对血管内皮造成的损伤，优化了血脂代谢过程，最终调节了炎症因子水平及血脂水平。此外，本文根据 SPearman 相关性分析后显示，Hp 感染与患者 IL-8、IL-10、CRP、LDL-C 及 TG 水平均呈正相关，但与 HDL-C 和 TC 并无明显的相关性。这再次表明了慢性胃炎患者的 Hp 感染与其机体的炎症水平及血脂状态均具有紧密关联。这在张颖等人^[30]的报道结果中也可发现类似的结论。

综上所述，Hp 感染与慢性胃炎患者的炎症指标及血脂指标关系紧密，临床上可考虑将此类指标作为存在 Hp 感染的慢性胃炎者的监测指标，从而更好地辅助临床诊治。

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