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氯吡格雷联合阿司匹林对冠心病心绞痛患者血清 hs-CRP, TNF-α 及 IL-6 水平的影响 *

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摘要 目的:探讨氯吡格雷与阿司匹林对冠心病心绞痛患者血清炎症因子水平的影响及其临床疗效。**方法:**选择 2014 年 3 月 -2016 年 3 月在我院确诊为冠心病心绞痛患者 69 例作为研究对象,根据治疗方法不同,将患者随机分成研究组(39 例)和对照组(30 例)。对照组患者采用阿司匹林治疗,研究组患者在此基础上联合使用氯吡格雷治疗。观察并比较两组患者治疗前后血清高敏 C-反应蛋白 (high-sensitivity C-reactive protein, hs-CRP)、肿瘤坏死因子 -α (tumor necrosis factor-α, TNF-α) 及白细胞介素 -6 (interleukin-6, IL-6)水平的变化情况,以及临床疗效。**结果:**治疗前两组患者血清 hs-CRP,IL-6 及 TNF-α 水平比较,差异无统计学意义(P>0.05);治疗后两组患者血清 hs-CRP,IL-6 及 TNF-α 水平均低于治疗前,且研究组低于对照组,差异具有统计学意义(P<0.05)。研究组患者临床总有效率(94.7%)高于对照组(88.9%),差异具有统计学意义(P<0.05)。**结论:**氯吡格雷联合阿司匹林治疗冠心病心绞痛的临床效果显著,能够降低患者血清 hs-CRP,IL-6 及 TNF-α 炎症因子水平,值得临床推广应用。

关键词:冠心病;心绞痛;炎症因子;氯吡格雷;阿司匹林
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Effects of Clopidogrel and Aspirin on the Serum Levels of hs-CRP, TNF-α and IL-6 in Patients with Coronary Heart Disease and Angina Pectoris*

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ABSTRACT Objective: To investigate the effect of clopidogrel and aspirin on serum levels of inflammatory factors in patients with coronary heart disease and angina pectoris. **Methods:** 69 cases with angina pectoris and coronary heart disease who were diagnosed in our hospital from March 2014 to March 2016 were selected as the research objects, and according to the different treatment methods, the patients were randomly divided into the study group (39 cases) and the control group (30 cases). The patients in the control group were treated with aspirin, and the patients in the study group were treated with clopidogrel on the basis of the control group. Then the serum levels of high sensitive C-reactive protein (hs-CRP), tumor necrosis factor alpha (TNF-α) and leukocyte mediated IL-6 (IL-6) in patients between the two groups before and after treatment were observed and compared. **Results:** Before treatment, there was no statistically significant difference about the serum levels of hs-CRP, IL-6 and TNF-α between the two groups (P > 0.05); After treatment, the serum levels of hs-CRP, IL-6 and TNF-α in the two groups were lower than before, and the study group was lower than that of the control group, and the differences were statistically significant (P<0.05). The total effective rate in the study group was 94.7%, which was higher than 81.9% in the control group, and the difference was statistically significant (P<0.05). **Conclusion:** The clinical effect of clopidogrel combined with aspirin in the treatment of angina pectoris and coronary heart disease is significant, which can reduce the serum levels of hs-CRP, IL-6 and TNF- α, and it is worthy of clinical application.

Key words: Coronary heart disease; Angina pectoris; Inflammatory factors; Clopidogrel; Aspirin
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前言

冠心病(coronary heart disease,CHD)是机体血脂代谢异常导致的心肌功能障碍疾病,主要病因是冠状动脉粥样硬化[1,2]。冠心病最常见的类型是心绞痛,临床表现主要为胸骨后部的压榨性疼痛或憋闷并向左肩部及背部放射[3]。相关研究表明,冠状

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动脉血管内皮损伤、不稳定性斑块破裂出血、血小板聚集导致血栓形成阻塞冠脉管腔引起心肌缺血、缺氧反应是心绞痛发病的基础[4]。还有研究显示,动脉粥样板块含有大量的炎症细胞,当斑块破裂时,大量炎性因子被释放,破坏细胞外基质,促进血小板聚集成血栓,阻塞血管,导致急性心肌梗死的发生[5]。近年来研究发现,氯吡格雷与阿司匹林治疗冠心病心绞痛的临床效果显著,能够降低患者血清炎症因子水平[6]。因此,本研究通过观察氯吡格雷与阿司匹林对冠心病心绞痛患者血清炎症因子水平的影响,探讨其临床疗效。

1 资料与方法

1.1 临床资料

选择 2014 年 3 月 -2016 年 3 月在我院确诊为冠心病心绞痛患者 69 例作为研究对象,根据治疗方法不同,将患者随机分成研究组和对照组。其中研究组患者 39 例,包括男 14 例,女 25 例;年龄 38~60 岁,平均年龄(45.38± 5.66)岁;病程 1.29~10.01 年,平均病程(5.71± 0.55)年;心绞痛分级:Ⅰ级 8 例,Ⅱ级 13 例,Ⅲ级 11 例,Ⅳ级 7 例;其中 ST 段抬高者 13 例,压低者 26 例。对照组 30 例患者,包括男 18 例,女 12 例;年龄 41~64 岁,平均年龄(47.32± 5.54)岁,病程 1.05~8.19 年,平均病程(4.31± 0.62)年;心绞痛分级:Ⅰ级 5 例,Ⅱ级 12 例,Ⅲ级 10 例,Ⅳ级 3 例;其中 ST 段抬高者 9 例,压低者 21 例。两组患者的临床资料比较,差异无统计学意义(P>0.05),具有可比性。

1.2 纳入及排除标准

符合《内科学》[7]中对冠心病的诊断标准;胸口常有压迫感合并剧烈疼痛感,伴有向四肢及背部的放射性疼痛;患者采取舌下含服硝酸甘油后只能不完全性的缓解;患者出现静息痛或夜间痛;血脂异常;X 线、超声及冠状动脉造影等影像学检查示血管狭窄性或扩张性改变。排除妊娠或哺乳期妇女;心肌酶谱异常的心绞痛患者;严重肝肾疾病;心血管性疾病;恶性肿瘤患者;近期内行冠状动脉介入治疗或抗凝治疗者;近来服用过胆固醇类药物者;服药期间需服用炎症抑制药物或阿片类药物者及对药物过敏者。

1.3 治疗方法

两组患者均进行如饮食结构调整、生活作息改变等常规干预,同时对症处理糖尿病、高血压等合并症。对照组在常规治疗基础上给予阿司匹林肠溶片(拜耳医药保健有限公司,国药准字 H20120236) 100 mg /d,口服 1 次 /d。研究组在常规治疗基础上给予氯吡格雷(赛诺菲(杭州)制药有限公司,国药准字 J20130083)50 mg /d,口服 1 次 /d,联合阿司匹林(拜耳医药保健有限公司,国药准字 H20120236) 100 mg /d,口服 1 次 /d。两组患者疗程均为 4 周。

1.4 观察指标及检测方法

1.4.1 血清炎性因子水平检测 分别于治疗前后采集患者空腹外周静脉血 4 mL,3000 r/min 离心 10 min(离心半径 3 cm)取血清置于 -20 OC 冰箱保存待检。采用日立 7600 型全自动生化分析仪检测血清高敏 C- 反应蛋白(hs-CRP)、肿瘤坏死因子 -α(TNF-α)、白细胞介素 -6 (IL-6)含量。hs-CRP 采用乳胶增强免疫散射比浊法,TNF-α、IL-6 采用酶联免疫吸附实验法,所有试剂盒购自北京恒盛生物科技有限公司。

1.4.2 疗效判断标准 患者治疗后心绞痛症状消失,或患者心绞痛的发作频率前减少超过≥ 过频,心电图正常为显效;患者治疗后心绞痛发作频率减少在 50 % ~79 %之间,无心前区疼痛,心电图改善为有效;患者治疗后心绞痛症状及发作频率以及临床症状无改善甚至加重为无效。

1.5 统计学方法

计量数据采取($\bar{x}$± s)表示,行 t 检验,计数资料用率表示,应用卡方检验,数据分析使用 SPSS17.0 软件,P<0.05 认为差异具有统计学意义。

2 结果

2.1 患者治疗前后血清 hs-CRP 水平比较

对照组患者治疗前血清 hs-CRP 水平为(1.53± 0.51) ng/mL,研究组患者治疗前血清 hs-CRP 水平为(1.56± 0.41) ng/mL,两组比较,差异无统计学意义(P>0.05);研究组患者治疗后血清 hs-CRP 水平为(0.93± 0.33)ng/mL,对照组患者血清 hs-CRP 水平为(1.18± 0.46)ng/mL。与治疗前相比较,两组患者治疗后血清 hs-CRP 水平均降低,且研究组降低更显著,差异均具有统计学意义(P<0.05)。见表 1。

表 1 两组患者治疗前后血清 hs-CRP 水平比较(ng/mL, $\bar{x}$± s)

Table 1 Comparison of the serum levels of hs-CRP between two groups before and after treatment (pg/mL, $\bar{x}$± s)

Groups	Before treatment	After treatment
Study group	1.56± 0.41	0.93± 0.33*#
Control group	1.53± 0.51	1.18± 0.46*

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

2.2 患者治疗前后血清 TNF-α 水平比较

对照组患者治疗前血清 TNF-α 水平为(231.38± 51.31) ng/mL,研究组患者治疗前血清 TNF-α 水平为(236.10± 52.14) ng/mL,两组比较,差异无统计学意义(P>0.05);研究组患者治疗后血清 TNF-α 水平为(144.27± 31.95)ng/mL,对照组患者血清 TNF-α 水平为(170.21± 37.82)ng/mL。与治疗前相比较,两组患者治疗后血清 TNF-α 水平均降低,且研究组降低更显著,差异均具有统计学意义(P<0.05)。见表 2。

表 2 两组患者治疗前后血清 TNF-α 水平比较(ng/mL, $\bar{x}$± s)

Table 2 Comparison of the serum levels of TNF-α between two groups before and after treatment(pg/mL, $\bar{x}$± s)

Groups	Before treatment	After treatment
Study group	236.10± 52.14	144.27± 31.95*#
Control group	231.38± 51.31	170.21± 37.82*

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

2.3 患者治疗前后血清 IL-6 水平比较

对照组患者治疗前血清 IL-6 水平为(36.58± 6.35)ng/mL,研究组患者治疗前血清 IL-6 水平为(35.82± 6.16)ng/mL,两组

比较，差异无统计学意义（P>0.05）；研究组患者治疗后血清IL-6水平为(19.32± 3.43)ng/mL,对照组患者血清IL-6水平为(25.28± 4.29)ng/mL。与治疗前相比较，两组患者治疗后血清IL-6水平均降低,且研究组降低更显著,差异均具有统计学意义(P<0.05)。见表3。

2.4 两组患者的临床疗效比较

研究组患者临床总有效率高于对照组,差异具有统计学意义(P<0.05)。见表4。

表3 两组患者治疗前后血清IL-6水平比较(ng/mL, $\bar{x}\pm s$)

Table 3 Comparison of the serum levels of IL-6 between two groups before and after treatment(pg/mL, $\bar{x}\pm s$)

Groups	Before treatment	After treatment
Study group	35.82± 6.16	19.32± 3.43*#
Control group	36.58± 6.35	25.28± 4.29*

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

表4 两组患者的临床疗效比较 [n(%)]

Table 4 Comparison of the clinical curative effect between two groups [n(%)]

Groups	n	Excellent	Effective	Invalid	Total effect rate
Control group	30	7(38.9)	9(50.0)	2(11.1)	16(81.9)
Study group	39	8(42.1)	10(52.6)	1(5.3)	18(94.7)*

Note: compared with the control group, *P<0.05 .

3 讨论

氯吡格雷属于二磷酸腺苷受体拮抗类药物,是血小板聚集抑制剂，能够通过选择性地抑制ADP与血小板受体的结合及抑制ADP介导的糖蛋白GPⅡh/Ⅲa复合物的活化，从而达到抑制血小板聚集的目的,临床主要用于预防和治疗因血小板高聚集引起的心、脑及其他动脉循环障碍疾病[8]。有研究表明,氯吡格雷能明显改善不稳定型心绞痛患者血管内皮功能,降低炎性因子水平[9]。阿司匹林是临床常用的抗血小板药物,通过抑制环氧合酶活性,阻止血小板聚集和血管收缩,降低血黏稠度,预防和控制血栓形成[10]。

C反应蛋白(CRP)是一种急性反应蛋白,在炎症、局部缺血、组织损伤等过程中水平明显升高[11]。有研究表明,CRP是高度敏感的炎症标志物,为急性时相反应蛋白,在炎症、创伤时水平升高,因此在临床常用于判断炎症反应和组织损伤[12]。还有研究证实,hs-CRP等炎性因子参与急性冠脉综合症的发生与进展[13]。IL-6由184个氨基酸组成,能够对炎症反应进行中枢性的调节，主要由单核巨噬细胞、Th2细胞以及成纤维细胞等产生和分泌[14]。相关研究表明,IL-6能够对CRP的生成产生诱导作用,促进纤维蛋白原合成,以及血栓的形成,是机体在免疫应答过程中产生的一种重要介质[15]。还有研究显示,IL-6水平升高与心血管事件的发生关系密切,IL-6水平与粥样硬化斑块的不稳定性关系密切[16]。因此,临床可通过检测IL-6水平预测冠心病心绞痛。TNF作用于血管内皮细胞能够引起血管功能紊乱,形成血栓,阻断局部血流,导致出血、缺氧,甚至坏死[17]。有研究表明,血管内皮损伤、斑块破裂均可使局部炎性因子趋附,导致血清中肿瘤坏死因子-a水平升高[18]。

本研究结果表明，治疗前两组患者血清hs-CRP,IL-6及TNF-α水平比较,差异无统计学意义(P>0.05);两组患者治疗后血清hs-CRP,IL-6及TNF-α水平均低于治疗前,且研究组患者治疗后血清hs-CRP,IL-6及TNF-α水平降低更明显,差异具有统计学意义(P<0.05)。这与相关研究结果一致[19],说明氯吡格雷联合阿司匹林治疗有助于缓解冠心病心绞痛患者炎症水平。我们还发现，研究组患者临床总有效率（94.7%）高于对照组(81.9%),差异具有统计学意义(P<0.05)。这与相关研究结果相似[20],结果说明氯吡格雷联合阿司匹林治疗冠心病心绞痛具有显著的临床效果。

综上所述,氯吡格雷联合阿司匹林治疗冠心病心绞痛具有显著的临床效果，能够降低患者血清hs-CRP,IL-6及TNF-α水平,改善炎症反应,值得临床推广应用。

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