

[文章编号] 1000-4718(2007)09-1703-03

大剂量血脂康在经皮冠状动脉介入术中的炎症抑制作用*

刘尊齐, 崔连群[△], 王勇, 孔庆赞, 刘继东, 李峰, 盖玉生, 赵传艳
(山东大学山东省立医院心内科, 山东 济南 250012)

[摘要] 目的: 研究不稳定型心绞痛(UA)患者在经皮冠状动脉介入(PCI)治疗前应用大剂量血脂康对炎症的抑制作用。方法: 对196例临床确诊为高危UA(心绞痛 Braunwald 分级为Ⅲ和ⅡB级, CRP >3 mg/L)的患者按随机原则分别入选A组和B组, 在相似常规治疗的基础上分别口服1.2 g/d和2.4 g/d血脂康治疗72 h。随后对所有病人进行冠状动脉造影和PCI治疗。测定在入院时、药物治疗3 d后(PCI术前)和PCI术后48 h的血浆CRP的水平, 并随访半年内的冠脉事件和左室射血分数。结果: 入院时2组血浆CRP水平无明显差别($P > 0.05$); 治疗3 d后, 两组血浆CRP水平明显低于入院时[A组: (5.44 ± 1.57) mg/L vs (4.04 ± 1.54) mg/L; B组: (5.42 ± 1.36) mg/L vs (3.60 ± 1.14) mg/L, $P < 0.05$]; PCI术后48 h, 两组血浆CRP水平显著高于术前[A组升至 (9.22 ± 5.03) mg/L; B组升至 (4.97 ± 1.75) mg/L, $P < 0.05$]。PCI术前及术后48 h, B组的血浆CRP水平明显低于同期A组($P < 0.05$)。术后半年主要冠脉事件B组明显少于A组[21/104 (20.2%) vs 9/92 (9.8%), $P < 0.05$], 左室射血分数B组明显高于A组[$55.41\% \pm 10.93\%$ vs $59.30\% \pm 9.99\%$, $P < 0.05$]。结论: PCI术前大剂量血脂康治疗对PCI术引起的炎症具有抑制作用, 抑制炎症可能是PCI术后冠脉事件减少和左室射血分数增加的重要因素。

[关键词] 血脂康; 中草药; 经皮冠状动脉介入; 心绞痛, 不稳定型; C-反应蛋白质

[中图分类号] R363 **[文献标识码]** A

Inhibitory effect of high-dose Xuezhikang on inflammatory response induced by percutaneous coronary intervention in patients with unstable angina

LIU Zun - qi, CUI Lian - qun, WANG Yong, KONG Qing - zan, LIU Ji - dong, LI Feng, GAI Yu - sheng, ZHAO Chuan - yan

(Department of Cardiology, Shandong Provincial Hospital, Shandong University, Jinan 250012, China. E-mail: liubmjs@yahoo.com.cn)

[ABSTRACT] **AIM:** To study the inhibitory effect of high-dose Xuezhikang, administered before percutaneous coronary intervention (PCI) on inflammatory response induced by PCI in patients with unstable angina (UA). **METHODS:** All patients with UA in class III and II B according to Braunwald classification were considered for inclusion in the present study. Finally, 196 patients received Xuezhikang treatment 72 h before coronary angiography and successfully performed PCI with elevated C-reactive protein (CRP) level (> 3 mg/L) were randomised to 2 groups: 1.2 g/d of Xuezhikang as group A, or 2.4 g/d of Xuezhikang as group B. The levels of CRP were measured at baseline, after 3 days of therapy (before procedure) and 48 hours after PCI. The patients were followed-up for 6 months for major adverse coronary events and left ventricular ejection fraction. **RESULTS:** There was no significant difference in the mean CRP level among the two randomized groups ($P > 0.05$), however, after three days of pharmacological treatment, there was significantly reduced CRP content in group A [(5.44 ± 1.57) mg/L vs (4.04 ± 1.54) mg/L, $P < 0.05$] and in group B [(5.42 ± 1.36) mg/L vs (3.60 ± 1.14) mg/L, $P < 0.05$] compared with admission. Measurements performed 48 hours after the procedure revealed a marked CRP level increase in group A (up to 9.22 mg/L ± 5.03 mg/L) and an obvious increase in groups B (up to 4.97 mg/L ± 1.75 mg/L, $P < 0.05$) compared with pre-procedure. The serum level of CRP in B group was distinctly lower than that in A group before ($P < 0.05$) and after the procedure ($P < 0.05$), respectively. Major adverse coronary events during the 6-month clinical follow-up occurred less in group A than that in group B [21/104 (20.2%) vs 9/92 (9.8%); patients, $P < 0.05$]. Follow-up echocardiography revealed lower left ventricular ejection fraction in group A than that in group B [$55.41\% \pm 10.93\%$ vs $59.30\% \pm 9.99\%$, $P < 0.05$]. **CONCLUSION:** High-dose Xuezhikang therapy, administered before PCI, has better inhibition effect than low-dose on inflammatory response

[收稿日期] 2006-01-17 [修回日期] 2006-06-23

* [基金项目] 山东省自然科学基金资助项目 (No. Y2005C17)

△ 通讯作者 Tel: 0531-88383321; E-mail: liubmjs@yahoo.com.cn

induced by PCI in patients with UA. Attenuation of inflammatory response may be crucial for the reduction of coronary events following invasive coronary interventions.

[KEY WORDS] Xuezhikang; Drugs, Chinese herbal; Percutaneous coronary intervention; Angina, unstable; C-reactive protein

有研究表明,在经皮冠状动脉介入(percutaneous coronary intervention, PCI)之前服用他汀类药物可抑制 PCI 术触发的炎症反应,降低血浆 C-反应蛋白(C-reactive protein, CRP)水平^[1],心绞痛患者服用血脂康治疗 6 周(1.2 g/d)可明显降低空腹 CRP 水平^[2]。但是,有关 PCI 术前应用大剂量血脂康对炎症的抑制作用还未见报道。

本研究拟观察短期应用不同剂量血脂康对 UA 患者 PCI 围手术期 C-反应蛋白的影响,观察术后半年心脏事件和左室射血分数,探讨 UA 患者 PCI 术后强化应用血脂康治疗的必要性。

材 料 和 方 法

1 研究对象

2004 年 8 月到 2005 年 7 月,参与本研究的 400 例 UA 患者为我科住院的患者,其中,220 例符合入选标准,排除退出及失访的病例 24 例,剩余的 196 例作为研究病例,男性 139 例,女性 57 例,年龄 31-77 岁,平均年龄(54.74 ± 10.75)岁,均签署了知情同意书。

患者在入院前 2 个月未服任何调脂药,入院次日抽血检查后分为 2 组:A 组 104 例,予以常规治疗加口服血脂康 1.2 g/d;B 组 92 例,予以常规治疗加口服血脂康 2.4 g/d。其它治疗根据病情需要调整。血脂康治疗后第 3 d 行 PCI 治疗。药物治疗前及 PCI 术后 48h 检测血脂、肝、肾功能、CK-MB、cTnI、cTnT 及 CRP 等生化指标,同时行心脏超声检查。

UA 诊断符合中华医学会心血管病学分会制定的标准^[3]。入选患者应同时具备以下 2 个条件:(1)入院前存在反复发作的静息性心绞痛,根据 Braunwald 分级属于 II B 或 III 级;(2)入院时血浆 CRP 浓度 >3 mg/L。排除标准:具备以下任何一个条件者均排除。(1)血浆 CRP ≤ 3 mg/L;(2)心肌梗死 6 个月内的患者;(3)合并明显的肝肾功能异常、肿瘤性疾病或其它能引起 CRP 升高的疾病;(4)不能耐受血脂康治疗或以前服用他汀类药物;(5)禁忌 PCI 治疗的患者;(6)拒绝参加本研究的患者。

2 检测方法

CRP 测定:采用免疫透射比浊法进行高敏 C-反应蛋白(hsCRP)测定,试剂盒由美国 Diagnostic System Laboratory 公司生产。严格按照试剂盒说明进行操作。批间及批内误差均小于 5%。

3 心脏事件观察及随访

对入选病例观察 PCI 术后心脏事件(包括急性

心肌梗死、心性死亡、顽固性心绞痛)。并对出院患者进行随访半年,采用门诊或电话随访。记录主要冠脉事件包括:死亡、急性心肌梗死,心绞痛复发;同时复查心脏超声,测定左心室射血分数。

4 统计学处理

采用 SPSS 12.0 统计软件对所有数据进行统计学分析。计量资料以 $\bar{x} \pm s$ 表示。组间及组内(不同时间点)比较采用 *t* 检验;计数资料以百分比表示,组间比较采用 χ^2 检验。

结 果

1 一般临床资料

B 组男性、吸烟和既往有高血压史的患者略多于 A 组,但差异无统计学意义;入选时两组的生化指标和白细胞计数无明显区别;两组在研究过程中使用的抗生素和服用的药物亦无明显不同,见表 1。

表 1 两组一般临床资料的比较
Tab 1 Basic clinical data between two groups

	Group A (n=104)	Group B (n=92)
Male [n (%)]	72 (69.23%)	67 (72.83%)
Age ($\bar{x} \pm s$, year)	54.24 ± 9.83	55.32 ± 11.73
Hypertension [n (%)]	33 (31.73%)	34 (36.96%)
Diabetes [n (%)]	22 (21.15%)	23 (25.00%)
Family history [n (%)]	27 (25.96%)	21 (22.83%)
Smoking [n (%)]	34 (32.69%)	36 (39.13%)
WBC ($\bar{x} \pm s$, ×10 ⁹ /L)	6.15 ± 1.36	6.12 ± 1.45

No significant difference between two groups in all the indexes. Group A: Xuezhikang 1.2 g/d; Group B: Xuezhikang 2.4 g/d.

2 血脂的变化

从患者就诊到随机分组予以血脂康干预的时间是(15.0 ± 7.2)h,PCI 术治疗前后血脂差异无显著,见表 2。

3 两组血浆 CRP 浓度比较

两组入院时 CRP 浓度相似;治疗 3 d 后,两组 CRP 浓度明显降低,B 组又明显低于 A 组;PCI 术后 48 h,两组 CRP 浓度有不同程度的升高,但 B 组明显低于 A 组(*P* < 0.05),见表 3。

4 两组患者心脏事件观察及随访结果比较

两组患者术前左室射血分数无明显差别,术后半年 B 组病人左室射血分数明显高于 A 组。住院期间和半年随访 B 组单项心脏事件少于 A 组,但差别不明显,总心脏事件发生率明显低于 A 组(*P* < 0.05),见表 4。

表2 两组 PCI 治疗前后血脂的变化

Tab 2 Changes of the serum cholesterol in two groups after PCI (mmol/L. $\bar{x} \pm s$)

Group	n		TC	TG	LDL - C	HDL - C
A	104	Before therapy	4.74 ± 1.05	1.92 ± 1.18	2.90 ± 0.78	1.18 ± 0.29
		After therapy	4.68 ± 0.95	1.77 ± 0.89	2.89 ± 0.73	1.17 ± 0.30
B	92	Before therapy	4.70 ± 0.80	1.88 ± 1.13	2.85 ± 0.66	1.22 ± 0.26
		After therapy	4.58 ± 0.80	1.72 ± 0.79	2.83 ± 0.67	1.20 ± 0.26

No significant difference between two groups in all the indexes.

表3 两组不同时间点血浆 CRP 浓度比较

Tab 3 The levels of CRP in the two groups in different time (mg/L. $\bar{x} \pm s$)

Group	n	Levels of CRP (mg/L. $\bar{x} \pm s$)		
		Baseline	3 d after therapy	48 h after PCI
A	104	5.44 ± 1.57	4.04 ± 1.54*	9.22 ± 5.03*
B	92	5.42 ± 1.36	3.60 ± 1.14**	4.97 ± 1.75**

*P < 0.05 vs baseline; **P < 0.05 vs group A; *P < 0.05 vs 3 d after therapy.

表4 两组患者心脏事件观察及左室射血分数比较

Tab 4 The adverse coronary events and left ventricular ejection fraction were compared between two groups ($\bar{x} \pm s$)

Time	Group A (n = 104)	Group B (n = 92)
LVEF		
Before procedure	(53.72 ± 12.22)%	(51.73 ± 14.20)%
Half year after procedure	(55.41 ± 10.93)%	(59.30 ± 9.99)%*
Duration of hospital stay		
Angina again	4/104(3.85%)	2/92(2.17%)
Myocardial infarction	2/104(1.92%)	1/92(1.09%)
Death	1/104(0.96%)	1/92(1.09%)
Follow up		
Angina again	10/104(9.62%)	4/92(4.35%)
Myocardial infarction	3/104(2.88%)	1/92(1.09%)
Death	1/104(0.96%)	0
The whole events	21/104(20.20%)	9/92 (9.80%)*

*P < 0.05 vs group A.

讨 论

CRP 作为炎症标志物,本身尽管为非特异性的,但大量研究显示,CRP 与 UA 患者 PCI 术后并发症有关^[4]。本结果显示,不稳定型心绞痛患者短期大剂量血脂康可明显降低 PCI 术后的血浆 CRP 浓度升高的幅度,且这种作用强度与血脂康的剂量大小相关,同时也降低 PCI 术后半年的冠脉事件发生率,并提高左室射血分数。

血脂康含有大量天然他汀类药物及其它成分,同样有他汀类药物的作用^[3]。UA 患者短期应用血脂康治疗后可降低 PCI 术前后血浆 CRP 浓度,可能是血脂康通过降低循环中调节 CRP 产生的介质如肿

瘤坏死因子和白细胞介素等,短期内即降低 CRP 水平^[5];改善血管内皮功能,增加血管内皮对 PCI 术的耐受性,从而降低了支架和球囊扩张对冠状动脉壁的损伤,这样一方面减少了 PCI 术后的炎症反应,减少肝脏 CRP 的生成;另一方面减少了局部 CRP 的产生^[6]。

PCI 术后继续强化血脂康治疗,明显减少了 PCI 术后半年的冠脉事件发生率,提高了左室射血分数,其原因除强化降脂带来的益处外,还可能与大剂量血脂康能更有效地抑制炎症反应,减少冠脉事件的发生率有关。另外,血脂康中的他汀成分同他汀类药物一样具有^[7]改善心室重塑的作用,包括减少心室扩张、代偿性的非梗死左室壁肥厚,可能有助于左室射血分数的提高。

参 考 文 献

- [1] Doo YC, Han SJ, Han SW, et al. Effect of preexisting statin use on expression of C - reactive protein, adhesion molecules, interleukin - 6, and antioxidantized low - density lipoprotein antibody in patients with unstable angina undergoing coronary stenting [J]. Clin Cardiol, 2005, 28 (2): 72 - 76.
- [2] Liu L, Zhao SP, Cheng YC, et al. Xuezhikang decreases serum lipoprotein(a) and C - reactive protein concentrations in patients with coronary heart disease [J]. Clin Chem, 2003, 49(8): 1347 - 1352.
- [3] 第一届全国内科学术会议心血管病组. 关于冠状动脉性心脏病命名及诊断标准的建议[J]. 中华心血管病杂志, 1981, 9(1): 75 - 76.
- [4] Buffon A, Liuzzo G, Biasucci LM, et al. Preprocedural serum levels of C - reactive protein predicts early complications and late restenosis after coronary angioplasty [J]. J Am Coll Cardiol, 1999, 34(5): 1512 - 1521.
- [5] Musial J, Undas A, Gajewski P, et al. Anti - inflammatory effects of simvastatin in subjects with hypercholesterolemia [J]. Int J Cardiol, 2001, 77(2 - 3): 247 - 253.
- [6] Inoue T, Kato T, Uchida T, et al. Local release of C - reactive protein from vulnerable plaque or coronary arterial wall injured by stenting [J]. J Am Coll Cardiol, 2005, 46 (2): 239 - 245.
- [7] 汤圣兴, 祁述善, 周胜华, 等. 阿托伐他汀对自发性高血压大鼠心室重塑的作用及机制 [J]. 中国病理生理杂志, 2006, 22(8): 1535 - 1539.