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## 大剂量血脂康在经皮冠状动脉介入术中的炎症抑制作用\*

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**[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:  $(5.44 \pm 1.57)$  mg/L vs  $(4.04 \pm 1.54)$  mg/L; B组:  $(5.42 \pm 1.36)$  mg/L vs  $(3.60 \pm 1.14)$  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 $(9.22 \pm 5.03)$  mg/L; B组升至 $(4.97 \pm 1.75)$  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

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

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**[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 [ $(5.44 \pm 1.57)$  mg/L vs  $(4.04 \pm 1.54)$  mg/L,  $P < 0.05$ ] and in group B [ $(5.42 \pm 1.36)$  mg/L vs  $(3.60 \pm 1.14)$  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  $\pm$   $5.03$  mg/L) and an obvious increase in groups B (up to  $4.97$  mg/L  $\pm$   $1.75$  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

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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<sup>[1]</sup>,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<sup>[2]</sup>。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<sup>[3]</sup>。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  $\chi^2$  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 ( $\bar{x} \pm s$ , $\times 10^9/L$ )	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 <sup>#</sup>	9.22 ± 5.03 <sup>*</sup>
B	92	5.42 ± 1.36	3.60 ± 1.14 <sup>#&amp;</sup>	4.97 ± 1.75 <sup>*&amp;</sup>

<sup>#</sup>P < 0.05 vs baseline; <sup>&</sup>P < 0.05 vs group A; <sup>\*</sup>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)% <sup>*</sup>
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%) <sup>*</sup>

<sup>\*</sup>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<sup>[4]</sup>。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<sup>[3]</sup>。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<sup>[5]</sup>;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<sup>[6]</sup>。

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<sup>[7]</sup>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。

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