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## 阿托伐他汀对急性冠状动脉综合征介入患者血清 ox-LDL、hs-CRP 及 sICAM-1 水平以及心功能的影响

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**摘要 目的:**探讨阿托伐他汀对急性冠状动脉综合征(ACS)介入患者血清氧化低密度脂蛋白(ox-LDL)、高敏 C 反应蛋白(hs-CRP)及可溶性细胞间黏附分子-1(sICAM-1)水平以及心功能的影响。**方法:**选取 2015 年 2 月-2016 年 4 月在我院接受治疗的 ACS 患者 120 例作为研究对象,采用乱数表法将所有患者分为观察组和对照组,两组均 60 例。在常规治疗基础上,观察组患者给予大剂量阿托伐他汀口服,对照组给予小剂量阿托伐他汀口服,对比两组患者治疗前后 ox-LDL、hs-CRP 及 sICAM-1 水平以及治疗后的心功能指标,观察两组患者治疗后的不良反应。**结果:**两组患者治疗 2 周后 ox-LDL、hs-CRP 及 sICAM-1 较治疗前均有明显下降,且观察组治疗 2 周后 ox-LDL、hs-CRP 及 sICAM-1 明显低于对照组( $P<0.05$ )。治疗 2 周后观察组的 E 峰与 A 峰流速比值(E/A)、左心室射血分数(LVEF)均显著高于对照组,而收缩指数、舒张指数和 Tei 指数均显著低于对照组( $P<0.05$ )。两组患者均未出现严重不良反应。**结论:**大剂量阿托伐他汀治疗 ACS 介入患者能有效降低患者术后 ox-LDL、hs-CRP 及 sICAM-1 水平,抑制炎症反应,改善患者心功能,药物安全性与小剂量相当,值得临床推广应用。

**关键词:**阿托伐他汀;急性冠状动脉综合征;心功能;ox-LDL;hs-CRP;sICAM-1

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## Effect of Atorvastatin on Serum Levels of ox-LDL, hs-CRP and sICAM-1 and Cardiac Function in Patients with Acute Coronary Syndrome

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**ABSTRACT Objective:** To investigate the effects of atorvastatin on serum oxidized low density lipoprotein (ox-LDL), high sensitive C reactive protein (hs-CRP) and soluble intercellular adhesion molecule -1 (sICAM-1) level and heart function in patients with acute coronary syndrome (ACS). **Methods:** A total of 120 patients with ACS, who were treated in Dongfang Hospital of Beijing University of Chinese Medicine from February 2015 to April 2016, were selected and randomly divided into observation group ( $n=60$ ) and control group( $n=60$ ). On the basis of routine treatment, the patients in the observation group were given high dose of atorvastatin, and the control group was given low dose of atorvastatin orally. The levels of ox-LDL, hs-CRP and sICAM-1 before and after treatment, the indexes of cardiac function after treatment in the two groups were compared; and the adverse reactions after treatment in the two groups were observed. **Results:** The levels of ox-LDL and hs-CRP and sICAM-1 in the two groups after 2 weeks of treatment were significantly lower than those before treatment, and the levels of ox-LDL, hs-CRP and sICAM-1 in the observation group after 2 weeks of treatment were significantly lower than those in the control group ( $P<0.05$ ). The E peak and A peak velocity ratio (E/A) and left ventricular ejection fraction (LVEF) of the observation group were significantly higher than those of the control group after 2 weeks of treatment, while the contraction index, diastolic index and myocardial work index were significantly lower than the control group ( $P<0.05$ ). There were no serious adverse reactions in the two groups. **Conclusion:** High dose of atorvastatin for interventional patients with ACS can effectively reduce the levels of ox-LDL, hs-CRP and sICAM-1 after operation, inhibit inflammatory reaction and improve cardiac function, and drug safety is comparable to low dose, which is worthy of clinical application.

**Key words:** Atorvastatin; Acute coronary syndrome; Cardiac function; ox-LDL; hs-CRP; sICAM-1

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### 前言

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急性冠状动脉综合征 (Acute coronary syndromes,ACS)是一种常见的心血管疾病临床综合征,其病理基础为冠状动脉粥样硬化斑块侵袭或破裂、继发闭塞性血栓形成,ACS 是冠心病的严重类型,急性心肌缺血是其共同特征<sup>[1-3]</sup>。ACS 发病人群多为老年男性、绝经后女性,其危险因素有吸烟、高血压、糖尿病、高脂血症及冠心病家族史等。胸闷、发作性胸痛等症状是 ACS

患者常见临床表现,严重者可致心律失常、心力衰竭、甚至猝死,对患者生命健康构成严重威胁<sup>[4-6]</sup>。经皮冠状动脉介入治疗(PCI)是临床上缓解 ACS 临床症状的有效方法之一,但术后有明显的炎症反应,易引发患者二次冠状动脉狭窄<sup>[7,8]</sup>。临床研究显示,氧化低密度脂蛋白(ox-LDL)、高敏 C 反应蛋白(hs-CRP)及可溶性细胞间黏附分子-1(sICAM-1)在不同病程 ACS 患者中变化较大,是判断和治疗 ACS 的重要指标<sup>[9,10]</sup>。阿托伐他汀是一种常用的降脂药,能减少主要心血管病事件的发生率。ACS 患者术后使用阿托伐他汀能在调脂的同时有效控制并加速消退炎症,逆转 ACS 炎症病理生理过程<sup>[11,12]</sup>。本文旨在研究阿托伐他汀对 ACS 患者介入治疗后 ox-LDL、hs-CRP、sICAM-1 以及心功能的影响,以期为临床治疗 ACS 提供参考,现将研究结果报道如下。

## 1 资料与方法

### 1.1 一般资料

选取我院 2015 年 2 月-2016 年 4 月收治的 ACS 患者 120 例作为研究对象,纳入标准:(1)经心电图、超声心动图、冠状动脉造影确诊为 ACS 患者;(2)无他汀类药物过敏者;(3)近期未行重大手术者。排除标准:(1)肝肾功能不全患者;(2)孕妇及哺乳期妇女;(3)免疫血液系统疾病患者;(4)恶性肿瘤、内分泌疾病患者;(5)严重高血压疾病患者;(6)急慢性感染患者。采用随机数字表法将所有患者分为观察组和对照组各 60 例。观察组男 28 例,女 32 例,年龄 50-76 岁,平均年龄(62.66±8.09)岁,其中不稳定型心绞痛 30 例,急性非 ST 段抬高性心肌梗死 13 例,急性 ST 段抬高性心肌梗死 17 例。对照组男 31 例,女 29 例,年龄 52-77 岁,平均年龄(64.10±7.88)岁,其中不稳定型心绞痛 29 例,急性非 ST 段抬高性心肌梗死 16 例,急性 ST 段抬高性心肌梗死 15 例。两组患者一般资料无明显差异( $P>0.05$ ),具有可比性。

### 1.2 治疗方法

两组患者均给予扩张冠状动脉、抗血液凝集、调脂、抗血小板、改善心室重构及改善心功能等常规对症治疗,在此基础上,两组患者均给予阿托伐他汀钙片(浙江新东港药业股份有限公司,国药准字 H20163270,规格:20 mg)治疗,对照组患者晚餐后给予 20 mg 口服,1 次/d,观察组患者晚餐后给予 40 mg 口服,1 次/d。两组患者从入院至治疗 2 周后均需口服阿托伐他汀钙片,不得间断,同时监测患者服药期间神经系统及消化系统的不良反应,如出现血清总胆固醇  $<2.6$  mmol/L,天门冬氨酸氨基  $>$  正常高限 3 倍等严重不良反应时应及时停止用药。

### 1.3 观察指标

对比两组患者介入治疗前和治疗 2 周后采用酶联免疫吸附法检测 ox-LDL、hs-CRP 及 sICAM-1 水平,抽取所有患者的清晨空腹静脉血 6 mL,3000 r/min 离心 10 min 后取血清,检测试剂盒均购于北京义翘神州科技有限公司,操作均按照说明书指南进行。采用心脏超声检查测量心功能参数,主要包括心尖四腔心切面超声指标:E 峰与 A 峰流速比值(E/A),左心射血分数(LVEF);左室流出道超声指标:收缩指数、舒张指数、Tei 指数。记录两组患者治疗 2 周后的不良反应。

### 1.4 统计学方法

选用 SPSS19.0 对所有数据进行统计分析,计数资料以率(%)表示,进行卡方检验,计量资料以均值±标准差( $\bar{x} \pm s$ )表示,进行 t 检验,以  $\alpha=0.05$  为检验标准。

## 2 结果

### 2.1 两组患者治疗前后 ox-LDL、hs-CRP 及 sICAM-1 水平对比

两组患者治疗前的 ox-LDL、hs-CRP 及 sICAM-1 水平比较无统计学意义( $P>0.05$ );两组患者治疗 2 周后 ox-LDL、hs-CRP 及 sICAM-1 较治疗前均有明显下降( $P<0.05$ ),观察组治疗 2 周后 ox-LDL、hs-CRP 及 sICAM-1 明显低于对照组 ( $P<0.05$ ),详见表 1。

表 1 两组患者介入治疗后 ox-LDL、hs-CRP 及 sICAM-1 对比

Table 1 Comparison of ox-LDL, hs-CRP and sICAM-1 in two groups after treatment

| Groups            | n  | ox-LDL(mmol/L)   |                           | hs-CRP( $\mu$ g/L) |                           | sICAM-1( $\mu$ g/L) |                           |
|-------------------|----|------------------|---------------------------|--------------------|---------------------------|---------------------|---------------------------|
|                   |    | Before treatment | Two weeks after treatment | Before treatment   | Two weeks after treatment | Before treatment    | Two weeks after treatment |
| Observation group | 60 | 69.06±0.49       | 41.22±0.53 <sup>#</sup>   | 16.28±0.88         | 6.02±0.61 <sup>#</sup>    | 291.5±27.61         | 63.33±9.23 <sup>#</sup>   |
| Control group     | 60 | 68.91±0.51       | 47.33±0.91 <sup>#</sup>   | 16.03±0.94         | 10.01±0.51 <sup>#</sup>   | 295.3±25.51         | 127.29±8.98 <sup>#</sup>  |
| t                 |    | 1.643            | 44.941                    | 1.504              | 38.870                    | 0.791               | 38.556                    |
| P                 |    | 0.103            | 0.000                     | 0.135              | 0.000                     | 0.430               | 0.000                     |

Note: compared with before treatment, <sup>#</sup> $P<0.05$ .

### 2.2 两组患者治疗后心功能比较

治疗后观察组 E/A、LVEF 均显著高于对照组,而收缩指数、舒张指数和 Tei 指数均显著低于对照组( $P<0.05$ ),详见表 2。

### 2.3 两组患者介入治疗后不良反应对比

两组用药相对较安全,在用药期间定时监测血常规、肝、肾功能均属于正常范围,在消化反应、过敏反应及神经系统损害等方面治疗均未出现严重不良反应。

## 3 讨论

ACS 是一种常见的心血管疾病,其主要致病因素是血栓的形成和冠状动脉粥样斑块破裂,血栓形成导致冠状动脉完全或不完全闭塞,引起心肌缺血综合征,严重可致死亡<sup>[13-15]</sup>。近年来其发病率及死亡率逐年上升,并且出现年轻化趋势。若能及早发现并进行对应的治疗,可大幅度降低患者死亡率及并发症

表 2 两组患者治疗后心功能比较

Table 2 Comparison of cardiac function between two groups after treatment

| Groups            | n  | E/A        | LVEF(%)     | Contraction index | Diastolic index | Tei index  |
|-------------------|----|------------|-------------|-------------------|-----------------|------------|
| Observation group | 60 | 1.24± 0.21 | 60.24± 8.47 | 0.20± 0.04        | 0.23± 0.03      | 0.43± 0.08 |
| Control group     | 60 | 1.05± 0.19 | 56.64± 7.88 | 0.28± 0.06        | 0.31± 0.05      | 0.53± 0.07 |
| t                 | -  | 5.197      | 2.410       | 8.593             | 10.627          | 7.287      |
| P                 | -  | 0.000      | 0.017       | 0.000             | 0.000           | 0.000      |

的产生,改善患者预后<sup>[16,17]</sup>。作为目前临床上治疗 ACS 的常见治疗方式,PCI 通过经心导管技术使狭窄甚至闭塞的冠状动脉管腔得以疏通,从而达到改善心肌血流灌注的目的,能及时重建血运通道,相应的改善患者预后<sup>[18,19]</sup>。但 PCI 术会对冠状动脉血管产生刺激并损伤冠状动脉血管内膜,激活炎症因子,导致术后炎症反应明显,冠状动脉粥样硬化仍然持续,诱发新的血栓形成以及粥样斑块,继发组织再次发生血液微循环障碍,易导致心血管事件发生<sup>[20-22]</sup>。

ox-LDL 是晚期斑块脂质核心组成部分,具有极强的细胞毒性,不仅能直接损伤内皮细胞,还可使粘附于内皮细胞的单核细胞增加并向泡沫细胞转化,造成内皮细胞溃疡,血细胞、纤维蛋白继发沉积加速血栓形成,ox-LDL 异常表达是导致不稳定性心绞痛的重要诱因<sup>[23,24]</sup>。hs-CRP 是反应炎症过程的敏感指标,不仅是冠脉发生病变的预测指标,也是评价诊疗效果及预后的重要指标。sICAM-1 在冠状动脉病变过程中起着重要作用<sup>[25]</sup>,sICAM-1 出现异常可介入血管内皮细胞和单核细胞的粘附,增加血管内皮损伤,造成血管内血小板凝聚,形成血栓,也是反应冠脉损伤的重要指标。本次研究结果显示,两组患者使用阿托伐他汀介入治疗 2 周后 ox-LDL、hs-CRP 及 sICAM-1 较治疗前均有明显下降,且观察组介入治疗后 3 项指标明显低于对照组 ( $P<0.05$ ),说明大剂量阿托伐他汀的使用能有效降低 ACS 患者术后炎症因子水平,能更有效抑制患者炎症反应。且两组患者均未出现严重不良反应,说明两种用药方法的安全性相当。阿托伐他汀钙片的主要成分是阿托伐他汀,阿托伐他汀是 3- 羟基-3- 甲基戊二酸单酰辅酶 A 还原酶 (HMG-CoA)还原酶选择性、竞争性的抑制剂,通过干扰脂蛋白的生成,降低血清中 ox-LDL 含量,抑制细胞中信号的转导,降低 hs-CRP 的表达,抑制炎症细胞的粘附和集聚,降低 sICAM-1,从而达到有效控制炎症反应,提高内皮依赖性血管扩张功能,保护内皮细胞的目的<sup>[26,27]</sup>。本研究还显示,治疗 2 周后观察组的 E/A、LVEF 均显著高于对照组,而收缩指数、舒张指数和 Tei 指数均显著低于对照组 ( $P<0.05$ ),这说明观察组可以有效改善 ACS 患者的心功能。分析其中原因,主要有以下几点:① 炎症反应可损害心功能,活性氧可加速心衰,而阿托伐他汀具有抗炎抗氧化的作用,进而可以有效改善心功能。② 阿托伐他汀可抑制基质金属蛋白酶的生成,进而改善心肌重塑;③ 阿托伐他汀可以增强血管内皮功能,改善血流动力情况,进而改善心功能<sup>[28-30]</sup>。

综上所述,大剂量阿托伐他汀的使用能更有效的降低患者术后 ox-LDL、hs-CRP 及 sICAM-1ACS 水平,抑制炎症反应,改善心功能,药物安全性与小剂量相当,值得临床推广应用。

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