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瑞舒伐他汀强化治疗对支架置入术后患者血管再狭窄的影响

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摘要 目的:探究瑞舒伐他汀强化治疗对行冠状动脉支架置入术后患者再狭窄率、血管内皮功能和血脂水平的影响。**方法:**选择2013年1月~2015年12月90例于我院行冠状动脉支架置入术后的患者。按照治疗方法的不同将患者随机分为观察组及对照组,每组45例。观察组患者术后给予20 mg/天瑞舒伐他汀强化治疗,对照组患者术后给予常规剂量(5~10 mg/天)瑞舒伐他汀治疗,连续服用6个月。比较两组患者治疗前后的血脂、C反应蛋白(CRP)、白介素8(IL-8)、一氧化氮合酶(eNOS)、内皮素-1(ET-1)水平及术后6个月支架内再狭窄率(ISR)。**结果:**治疗后,两组患者的胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白(LDL-C)水平均较治疗前显著降低($P<0.05$),且观察组患者以上指标均显著低于对照组($P<0.05$);观察组患者高密度脂蛋白(HDL-C)水平较治疗前增加明显($P<0.05$),而对照组该指标无明显改善($P>0.05$)。治疗后,两组患者的CRP、IL-8水平均较治疗前显著降低($P<0.05$),且观察组患者以上指标显著低于对照组($P<0.05$);观察组患者的一氧化氮合酶(eNOS)水平较治疗前显著提高,血管内皮素-1(ET-1)水平显著降低($P<0.05$),但对照组以上指标与治疗前相比无明显差异($P>0.05$)。术后6个月,观察组患者支架内再狭窄率(ISR)显著低于对照组($P<0.05$)。**结论:**瑞舒伐他汀强化治疗可通过显著改善患者血脂水平,减轻患者机体炎症状态,积极恢复内皮组织损伤,进而预防ISR的发生。

关键词:冠状动脉支架置入术;瑞舒伐他汀强化治疗;支架内再狭窄率(ISR);一氧化氮合酶(eNOS);内皮素-1(ET-1)

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The Influence of Rosuvastatin Intensive Therapy on the ISR of Patients with Placement of Stents in Coronary Artery

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ABSTRACT Objective: To explore the influence of rosuvastatin intensive therapy on the ISR, vascular endothelial function and level of blood lipid of patients with placement of stents in coronary artery. **Methods:** 90 patients with placement of stents in coronary artery treated in our hospital from January, 2013 to December, 2015 were randomly divided into the observation and control group with each group of 45 cases. Observation group was given rosuvastatin intensive therapy (20 mg/d), control group received conventional therapy (5~10 mg/d), the therapy last for 6 month. The blood lipid, level of IL-8, CRP, eNOS, ET-1 were compared in both groups. **Results:** After therapy, the level of TC, TG, LDL-C in both groups were obviously decreased compared with that of before therapy ($P<0.05$), and that of the observation group were significantly lower than the control group ($P<0.05$); the level of HDL-C in observation group increased obviously compared with that of before therapy ($P<0.05$), and that of control group showed no significant difference ($P>0.05$); the level of CRP, IL-8 in both group decreased obviously ($P<0.05$), and those of observation group were significantly lower than control group ($P<0.05$); in the observation group, the level of eNOS increased and ET-1 decreased significantly compared with those of before therapy, whereas the level of eNOS, ET-1 keep unchanged in control group; after treating for 6 months, the occurrence rate of ISR in observation group was significantly lower than control group. **Conclusion:** Rosuvastatin intensive therapy was effective methods in preventing the occurrence of ISR by improving blood lipid, down regulating levels of IL-8 and CRP, repairing endothelial tissue damage.

Key words: Placement of stents in coronary artery; Rosuvastatin intensive therapy; ISR; eNOS; ET-1

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前言

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自1986年世界第一例将网状金属支架用于冠状动脉,开创了介入治疗心血管疾病的新篇章^[1]。截至目前,冠状动脉支架置入术已成为有效治疗冠心病的措施之一,可显著改善患者临床及预后。然而,术后3~6个月内再狭窄的发生率较高(5~15%),再狭窄可引起症状复发、再次血运重建,是影响其远期疗效的主要问题之一^[2-4]。研究表明再狭窄与术后炎症反应及内皮功能受损等因素密切相关。因此,积极探究合理的药物干预方案对

于改善行冠状动脉支架置入术患者术后的临床疗效具有重要意义。他汀类药物具有抗炎、改善血管内皮功能、延缓动脉粥样硬化(AS)程度等作用^[5,6]。本研究旨在探究瑞舒伐他汀强化治疗对行冠状动脉支架置入术后患者的临床指标及生活质量的影响,以期为行冠状动脉支架置入术患者的用药方案提供参考依据。

1 资料与方法

1.1 一般资料

选择 2013 年 1 月~2015 年 12 月 90 例于我院行冠状动脉支架置入术后的患者。按照治疗方法的不同将患者随机分为观察组及对照组,每组 45 例。观察组包含男性 26 例,女性 19 例,平均年龄(64.28± 6.0)岁;对照组包含男性 25 例,女性 20 例,平均年龄(64.53± 5.53)岁。两组患者基线资料无显著差异(P>0.05),有可比性。纳入标准:① 所有患者在术前未服用过他汀类药物;② 病例资料完整,均与家属签署知情同意书。排除标准:① 合并严重肝肾功能异常;② 合并神经系统疾病,无法配合治疗;③ 对受试药物过敏;④ 合并恶性肿瘤。

1.2 治疗方法

观察组患者术后给予瑞舒伐他汀强化治疗,瑞舒伐他汀(AstraZeneca UK limited (英国),国药准字 J20120006),20 mg/天,连续服用 6 个月。对照组患者术后给予常规剂量(5~10 mg/天)瑞舒伐他汀治疗。

1.3 观察指标

1.3.1 血脂水平 检测所有患者在术前、术后 6 个月的血脂指标,包括甘油三酯(TG)、低密度脂蛋白(LDL-C)、胆固醇(TC)以及高密度脂蛋白(HDL-C)。采用全自动生化分析仪(日立全自动

生化分析仪 7020)检测上述指标。

1.3.2 炎症因子 检测两组患者术前、术后血清 C 反应蛋白(CRP)、IL-8 的水平,采用酶联免疫试剂盒测定(上海酶联生物有限公司)。

1.3.3 血管内皮功能 采用酶联免疫试剂盒测定 eNOS、ET-1 水平,试剂盒购于上海酶联生物有限公司,所有操作步骤均严格按照说明书。

1.3.4 再狭窄率发生情况 采用 CT 评价术后 6 个月是否存在支架狭窄程度。支架狭窄程度定义为:狭窄处近心端正常血管直径与狭窄处直径的差值比上狭窄处近心端正常血管直径,大于 50%即判定为支架内再狭窄(ISR)。

1.4 不良事件发生情况

1.5 统计学分析

使用 SPSS19.0 软件,,分别用卡方检验和 t 检验对计数资料和计量资料的进行统计学分析,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组患者治疗前后血脂水平的比较

治疗前,两组患者的血脂水平比较差异无统计学意义(P>0.05)。治疗后,两组患者的胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白(LDL-C)水平均较治疗前显著降低(P<0.05),且观察组患者以上指标显著低于对照组(P<0.05)。此外,观察组患者高密度脂蛋白(HDL-C)水平较治疗前增加明显(P<0.05),而对照组该指标无明显改善(P>0.05)。

表 1 两组患者治疗前后血脂水平比较($\bar{x} \pm s$, mmol/L)

Table 1 Comparison of the blood lipid level between two groups before and after treatment($\bar{x} \pm s$, mmol/L)

Groups	Number	TC		LDL-C		TG		HDL-C	
		Before therapy	After therapy	Before therapy	After therapy	Before therapy	After therapy	Before therapy	After therapy
Control group	45	5.93± 0.89	4.14± 0.72 ^a	3.71± 0.61	2.53± 0.42 ^a	2.82± 0.59	2.31± 0.60 ^a	0.85± 0.27	0.87± 0.21
Observation group	45	5.94± 0.91	3.92± 0.63 ^{ab}	3.73± 0.66	2.12± 0.47 ^{ab}	2.81± 0.62	2.27± 0.54 ^a	0.85± 0.22	0.96± 0.13 ^{ab}

Note: compared with before therapy, ^aP<0.05; compared with the control group after therapy, ^bP<0.05.

2.2 两组患者治疗前后血清 CRP、IL-8 水平的比较

治疗前,两组患者的血清 CRP、IL-8 水平比较差异无统计学意义(P>0.05)。治疗后,两组患者的血清 CRP、IL-8 水平均较

治疗前明显下降(P<0.05),且观察组患者以上指标显著低于对照组,差异具有统计学意义(P<0.05)。

表 2 两组患者治疗前后血清 CRP、IL-8 水平比较($\bar{x} \pm s$)

Table 2 Comparison of the serum CRP, IL-8 levels between two groups before and after treatment($\bar{x} \pm s$)

Groups	Number	CRP(mg/L)		IL-8(ng/L)	
		Before therapy	After therapy	Before therapy	After therapy
Control group	45	3.09± 1.10	3.74± 1.27 ^a	0.54± 0.21	0.46± 0.17 ^a
Observation group	45	3.14± 0.91	2.32± 0.73 ^{ab}	0.53± 0.23	0.23± 0.12 ^{ab}

Note: compared with before therapy, ^aP<0.05; compared with the control group after therapy, ^bP<0.05.

2.3 两组患者治疗前后血清 eNOS、ET-1 水平的比较

治疗前,两组患者的血清 eNOS、ET-1 水平比较差异无统计学意义(P>0.05)。治疗后,观察组患者的 eNOS 水平较治疗前显著提高,ET-1 水平明显降低 (P<0.05);对照组的 eNOS、

ET-1 水与治疗前相比无明显差异(P>0.05)。

2.4 两组患者支架内再狭窄(ISR)发生情况的比较

两组患者术后 6 个月经 CT 扫描检测结果显示:对照组 6 例患者出现(13.64%)再狭窄,观察组没有患者出现再狭窄,观

表3 两组患者治疗前后血清 eNOS、ET-1 水平比较[$\bar{x} \pm s$, ng/L]Table 3 Comparison of the serum eNOS, ET-1 levels between two groups before and after treatment [$\bar{x} \pm s$, ng/L]

Groups	Number	eNOS		ET-1	
		Before therapy	After therapy	Before therapy	After therapy
Control group	45	73.89 $\pm$ 22.30	72.62 $\pm$ 10.73	68.54 $\pm$ 18.71	67.46 $\pm$ 9.17
Observation group	45	73.74 $\pm$ 21.91	76.34 $\pm$ 11.27 ^{ab}	67.53 $\pm$ 18.23	57.73 $\pm$ 8.12 ^{ab}

Note: compared with before therapy, ^aP<0.05; compared with the control group after therapy, ^bP<0.05.

观察组 ISR 发生率显著低于对照组(P<0.05)。

3 讨论

冠状动脉支架植入术是目前而言治疗冠心病的有效方案,可显著改善患者的临床预后,然而支架内再狭窄发生率较高,影响其远期疗效。虽然随着药物洗脱支架的出现,再狭窄率明显降低,但仍维持在 5-15%,且患者在术后 1 年内易出现晚期追赶现象,即发生血管内膜增生、血栓形成而导致的继发靶病变血管重建(TLR)、心肌梗死(MI)和血栓的累计发生率逐渐接近金属裸支架。此外,再狭窄后的治疗方案也是临床上的难点^[7-10]。因此,探究科学合理的药物干预方案改善行冠状动脉支架置入术后患者的各项临床指征对于患者的预后意义深远。

炎症因子在机体发生炎症反应时明显升高,且与冠心病的发展关系密切,在早期动脉粥样病变阶段发现大量聚集的 CRP 通过激活补体系统,诱导血管内皮因子的合成与分泌进而对血管内膜组织造成损伤^[11-14]。另外,CRP 还能够促进单核细胞合成,大量释放组织因子,导致机体凝血-纤溶失衡引发心脏不良事件。国外研究结果已经证实 CRP 浓度升高是发生支架内再狭窄 (ISR)、心脏不良事件的独立危险因素^[15,16]。一氧化氮(NO) 和 ET-1 是调节和维持血管内皮功能的活性物质,eNOS 是关键 NO 合成酶,当机体的 ET-1 过多分泌或者 NO 合成过少时就会造成血管内皮损伤^[17,18]。现有的研究结果表明血管内皮功能损伤为导致 ISR 始发的主要诱因,尤其是行支架植入时已经一定程度地损害血管内皮,进而导致内膜组织明显增生^[19,20]。因此,有效控制炎症反应及修复内皮损伤对于降低 ISR 发生率具有重要的理论与实践意义。

本研究结果显示:与对照组相比,观察组(瑞舒伐他汀强化治疗组)患者治疗后的胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白(LDL-C)水平显著降低,高密度脂蛋白(HDL-C)水平明显增加。瑞舒伐他汀是一种选择性 3- 羟基-3- 甲基戊二酰辅酶 A (HMG-CoA)还原酶抑制剂,可抑制其向胆固醇前体转变,进而正向调节血脂水平。张兴凯^[21]等人的临床研究结果亦显示瑞舒伐他汀具有明显的降脂作用,降低心血管事件发生率。另外,他汀类药物还能够阻碍蛋白翻译后修饰过程,中断细胞内信号传导,产生抗炎,抗增殖,改善内皮等功能,这与本研究中发现经治疗后患者血清 CRP、IL-8、ET-1 水平显著降低,eNOS 水平明显增加的结果一致。

综上所述,瑞舒伐他汀强化治疗可显著改善支架置入术后患者的血脂水平,减轻其炎症状态,积极恢复内皮组织损伤,进而降低 ISR 发生率,改善患者的预后。

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