

阿托伐他汀联合依折麦布对非ST段抬高型急性冠脉综合征患者PCI围手术期Lp-PLA2的影响

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摘要 **目的** 评估强化阿托伐他汀和阿托伐他汀联合依折麦布对采用经皮冠状动脉介入治疗(PCI)的非ST段抬高型急性冠脉综合征(NSTE-ACS)患者围手术期脂蛋白相关磷脂酶A2(Lp-PLA2)水平的影响。**方法** 共纳入择期行PCI的NSTE-ACS患者193例,根据降脂方案,分为阿托伐他汀20 mg组(A20组)、阿托伐他汀40 mg组(A40组)、阿托伐他汀20 mg联合依折麦布10 mg组(A20+E10组)、阿托伐他汀40 mg联合依折麦布10 mg组(A40+E10组)。观察围手术期血浆Lp-PLA2和低密度脂蛋白胆固醇(LDL-C)水平的变化,随访30 d主要心血管不良事件和他汀类药物相关不良反应的发生情况。**结果** 析因分析结果表明,强化阿托伐他汀和依折麦布2个因素间无交互作用($P > 0.05$),强化阿托伐他汀和阿托伐他汀联合依折麦布均可显著降低术后血浆Lp-PLA2水平($P < 0.05$)。术前各组Lp-PLA2水平无统计学差异($P > 0.05$),术后各组Lp-PLA2水平均较术前降低($P < 0.001$)。对4组Lp-PLA2围手术期变化值进行两两比较,A40组、A20+E10组、A40+E10组均高于A20组,A40+E10组高于A40组($P < 0.05$),其余2组间比较无统计学差异($P > 0.05$)。术后与术前比较,各组LDL-C水平无统计学差异($P > 0.05$)。围手术期Lp-PLA2变化值与LDL-C变化值无相关性($P > 0.05$)。各组30 d主要心血管不良事件和他汀类药物相关不良反应的发生率无统计学差异($P > 0.05$)。**结论** 在进行PCI的NSTE-ACS患者中,与中等强度阿托伐他汀(20 mg)相比,高强度阿托伐他汀(40 mg)可进一步降低术后Lp-PLA2水平。与阿托伐他汀单药相比,阿托伐他汀联合依折麦布可进一步降低术后Lp-PLA2水平。围手术期强化阿托伐他汀和阿托伐他汀联合依折麦布对Lp-PLA2水平的降低作用不依赖于LDL-C变化。

关键词 非ST段抬高型急性冠脉综合征;经皮冠状动脉介入治疗;脂蛋白相关磷脂酶A2;阿托伐他汀;依折麦布

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Effect of atorvastatin combined with ezetimibe on perioperative Lp-PLA2 in patients with non-ST-segment elevation acute coronary syndrome after PCI

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Abstract **Objective** To investigate the periprocedural effects of atorvastatin plus ezetimibe and atorvastatin monotherapy on lipoprotein-associated phospholipase A2 (Lp-PLA2) levels in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS) after percutaneous coronary intervention (PCI). **Methods** In total, 193 patients with NSTE-ACS who underwent PCI were divided into four groups: 20 mg atorvastatin (A20 group), 40 mg atorvastatin (A40 group), 20 mg atorvastatin combined with 10 mg ezetimibe (A20+E10 group), and 40 mg atorvastatin combined with 10 mg ezetimibe (A40+E10 group). Changes in plasma Lp-PLA2 and low-density lipoprotein cholesterol (LDL-C) levels during the perioperative period were observed, and major adverse cardiovascular events (MACE) and statin-related adverse reactions were monitored for 30 d. **Results** Factorial analysis revealed no interaction between intensive atorvastatin and ezetimibe. Intensive atorvastatin and atorvastatin combined with ezetimibe significantly reduced the postoperative plasma Lp-PLA2 levels ($P < 0.05$). Plasma Lp-PLA2 levels were similar between the four groups before PCI and decreased significantly after PCI ($P < 0.05$). The changes in Lp-PLA2 during the perioperative period were compared between the four groups, and it was significantly higher in the A40 group than in the A20 group, in the A20+E10 group than in the A20 group, in the A40+E10 group than in the A20 group, and in the A40+E10 group than in the A40 group ($P < 0.05$). No significant difference in LDL-C levels and no significant correlation between the changes in LDL-C and Lp-PLA2 levels were observed between the four groups ($P > 0.05$). In addition, no significant differences in the incidence of major adverse cardiovascular event or statin-related adverse reactions were observed ($P > 0.05$). **Conclusion** Compared with atorvastatin (20 mg) monotherapy, both intensive atorvastatin (40 mg) and atorvastatin plus ezetimibe can further reduce postoperative

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Lp-PLA2 levels, independent of the changes in LDL-C in patients with NSTEMI-ACS undergoing PCI.

Keywords non-ST-segment elevation acute coronary syndrome; percutaneous coronary intervention; lipoprotein-associated phospholipase A2; atorvastatin; ezetimibe

经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)是非ST段抬高型急性冠脉综合征(non-ST-segment elevation acute coronary syndrome, NSTEMI-ACS)患者的重要治疗手段,但术后炎症细胞因子水平的变化与预后不良相关^[1]。目前,围手术期降脂治疗的获益尚不明确。研究^[2]表明,他汀类药物对行PCI的患者有益。目前,认为这种获益与其抗炎、改善内皮功能等多效性相关^[3]。依折麦布是一种胆固醇吸收抑制剂,IMPROVE-IT试验表明,在辛伐他汀基础上加用依折麦布能够进一步降低ACS患者的心血管事件发生率^[4]。

脂蛋白相关磷脂酶A2(lipoprotein-associated phospholipase A2, Lp-PLA2)是一种血管特异性新型炎症细胞因子。流行病学研究^[5-6]表明,Lp-PLA2在不稳定斑块和破裂斑块中高度表达,是冠状动脉粥样硬化性心脏病的独立危险因素。研究表明,他汀类药物预处理可降低PCI患者血浆Lp-PLA2水平^[7],依折麦布单药也可以降低Lp-PLA2水平^[8]。但强化阿托伐他汀以及阿托伐他汀联合依折麦布能否进一步降低术后Lp-PLA2水平,目前仍不明确。本研究的目的是评估强化阿托伐他汀以及阿托伐他汀联合依折麦布降脂方案对围手术期Lp-PLA2水平的影响。

1 材料与方法

1.1 研究对象和分组

连续纳入2020年3月至2021年3月间我科收治的择期行PCI的NSTEMI-ACS住院患者,共193例。纳入标准:(1)诊断为NSTEMI-ACS,NSTEMI-ACS的诊断符合《非ST段抬高型急性冠脉综合征诊断和治疗指南》;(2)接受PCI治疗;(3)年龄 ≥ 18 岁。排除标准:(1)既往他汀类药物或依折麦布治疗史;(2)他汀类药物和(或)依折麦布过敏史;(3)活动性肝病,即丙氨酸转氨酶(alanine transaminase, ALT)或天冬氨酸转氨酶(aspartate transaminase, AST) > 2 倍正常值上限或严重肝功能不全;(4)无法解释的肌酸激酶 > 1 倍正常值上限或血清肌酐 > 176 mmol/L;(5)甲状腺功能减退;

(6)诊断为稳定型心绞痛;(7)诊断为急性ST段抬高型心肌梗死。本研究经我院医学伦理委员会审核批准,所有患者知情同意。

入院后根据降脂方案,将193例患者随机分为阿托伐他汀20 mg组(A20组, $n = 57$)、阿托伐他汀40 mg组(A40组, $n = 53$)、阿托伐他汀20 mg联合依折麦布10 mg组(A20+E10组, $n = 41$)、阿托伐他汀40 mg联合依折麦布10 mg组(A40+E10组, $n = 42$)。

1.2 临床资料收集和血清学检测

1.2.1 临床资料收集:所有患者在入院后,测量身高和体重,详细记录年龄、性别、高血压史、糖尿病史、吸烟史、卒中史、既往心肌梗死史、PCI史、冠状动脉搭桥术史、用药史等重要的临床基本信息。

1.2.2 血清学检测:术前早晨和PCI术后早晨空腹抽取肘静脉血,于我院检验中心进行生化检测,检测指标包括心肌肌钙蛋白I(cardiac troponin I, cTn I)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、总胆固醇(total cholesterol, TC)、甘油三酯(triglyceride, TG)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)、ALT、AST、白细胞计数(white blood cell, WBC)、血红蛋白(hemoglobin, Hb)、血肌酐(creatinine, Cr)、脑钠肽(brain natriuretic peptide, BNP)、D-二聚体。

1.2.3 Lp-PLA2检测:将采集的血浆标本,在收集后30 min内,4 ℃、3 000 r/min离心10 min。离心后提取上清液,将其存于EP管中,-80 ℃保存。采用双抗酶联免疫吸附法试剂盒(深圳莱宝瑞生物科技有限公司)检测Lp-PLA2水平。

1.3 PCI和术后管理

所有患者术前口服阿司匹林300 mg和氯吡格雷300 mg,或阿司匹林300 mg和替格瑞洛180 mg。手术过程遵循《中国经皮冠状动脉介入治疗指南(2016)》进行。患者PCI术后冠状动脉的残余狭窄程度 $< 30\%$,且TIMI血流达到Ⅲ级,认定为手术成功。术后患者需继续术前抗栓药物治疗,并且原降脂方案治疗至少持续1个月。

1.4 30 d主要心血管不良事件 (major adverse cardiovascular event, MACE) 和他汀类药物相关不良反应

MACE包括心源性死亡、非致命性心肌梗死和卒中。他汀类药物相关不良反应包括他汀类药物相关性肌病(肌肉疼痛、肌炎和横纹肌溶解),无症状ALT升高>3倍正常值上限。术后30 d通过电话、门诊或住院随访,由3名独立的医师记录这些终点事件的发生情况。

1.5 统计学分析

采用SPSS 23.0软件处理数据。符合正态分布的计量资料用 $\bar{x} \pm s$ 表示,采用方差分析比较多组间差异,并采用LSD事后检验进行两两比较;不符合正态分布的计量资料用 $M(P_{25} \sim P_{75})$ 表示,采用Kruskal-Wallis H 检验进行比较,并采用Bonferroni校

正法进行两两比较。计数资料用百分比表示,采用 χ^2 检验或Fisher确切概率法进行比较。采用Pearson相关分析检验围手术期LDL-C变化值与Lp-PLA2变化值的相关性。采用析因设计,评估阿托伐他汀与依折麦布的主效应及交互作用。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 基线临床资料的比较

比较4组的基线临床资料,结果显示,年龄、男性比例、体重指数、入院收缩压和舒张压、高血压史、糖尿病史、卒中史、吸烟史以及药物治疗等均无统计学差异($P > 0.05$)。见表1。

2.2 基线血清学指标的比较

表1 4组患者基线临床资料的比较

Tab.1 Comparison of baseline clinical characteristics between the four groups

Item	A20 group (n = 57)	A20+E10 group (n = 53)	A40 group (n = 41)	A40+E10 group (n = 42)	P
Age (year)	63.14 ± 10.47	62.28 ± 9.60	63.12 ± 8.26	62.21 ± 8.23	0.857
Male [n (%)]	34 (59.6)	31 (58.5)	30 (73.2)	32 (76.2)	0.118
BMI (kg/m ²)	24.65 ± 3.45	21.27 ± 3.56	24.47 ± 2.66	24.12 ± 2.56	0.765
SBP (mmHg)	131.74 ± 21.12	131.61 ± 23.15	128.75 ± 21.56	134.15 ± 21.25	0.717
DBP (mmHg)	76.66 ± 15.02	74.57 ± 11.61	72.59 ± 12.46	74.79 ± 10.81	0.511
Current smoker [n (%)]	28 (49.1)	20 (37.7)	20 (48.8)	19 (45.2)	0.681
Hypertension [n (%)]	38 (66.7)	31 (58.5)	24 (58.5)	28 (66.7)	0.722
Diabetes mellitus [n (%)]	19 (33.3)	21 (39.6)	18 (43.9)	10 (23.8)	0.232
Stoke [n (%)]	6 (10.5)	3 (5.7)	4 (9.8)	4 (9.5)	0.797
Previous MI [n (%)]	12 (21.1)	12 (22.6)	13 (31.7)	5 (11.9)	0.185
Previous PCI [n (%)]	13 (22.8)	7 (13.2)	7 (17.1)	7 (16.7)	0.344
Previous CABG [n (%)]	1 (1.8)	1 (1.9)	0 (0)	1 (2.4)	0.829
LVEF (%)	59.75 ± 6.21	60.71 ± 5.51	60.75 ± 4.65	61.32 ± 4.32	0.654
SYNTAX score	18.23 ± 11.43	16.55 ± 9.67	16.52 ± 10.54	17.23 ± 10.34	0.712
Clinical diagnosis [n (%)]					
UA	36 (63.2)	41 (77.4)	30 (73.2)	29 (69.0)	0.414
NSTEMI	21 (37.8)	12 (22.6)	11 (26.8)	13 (31.0)	0.414
Medical treatment [n (%)]					
Aspirin	54 (94.7)	52 (98.1)	40 (97.6)	42 (100.0)	0.972
P2Y12 inhibitor	57 (100.0)	53 (100.0)	41 (100.0)	42 (100.0)	-
β-blocker	35 (61.4)	34 (65.4)	31 (75.6)	25 (53.7)	0.854
ACEI/ARB	35 (61.4)	33 (62.6)	27 (65.8)	28 (66.7)	0.949
CCB	15 (26.3)	17 (23.1)	12 (29.3)	11 (26.2)	0.503
Nitrate	51 (89.5)	48 (90.6)	36 (87.8)	38 (90.0)	0.972
Heparin	55 (96.5)	51 (96.0)	41 (97.8)	41 (98.0)	0.377

A, atorvastatin; E, ezetimibe; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; UA, unstable angina; NSTEMI, non-ST-segment elevation myocardial infarction; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium antagonist.

4组基线WBC、Cr、BNP、D-二聚体、ALT、ALT、LDL-C、HDL-C、TG、TC、Lp-PLA2等血清学指标的水平比较无统计学差异($P > 0.05$)。见表2。

2.3 手术特征的比较

表2 4组患者基线血清学指标的比较
Tab.2 Comparison of baseline serological indicators between the four groups

Item	A20 group (n = 57)	A20+E10 group (n = 53)	A40 group (n = 41)	A40+E10 group (n = 42)	P
WBC ($\times 10^9/L$)	6.33 ± 1.74	6.87 ± 2.01	6.88 ± 1.88	6.78 ± 1.61	0.754
Hemoglobin (g/L)	141.2 ± 15.5	135.5 ± 14.5	141.1 ± 15.3	141.3 ± 14.8	0.112
BNP (pg/mL)	55 (26–157)	44 (17–93)	29 (12–67)	43 (21–87)	0.114
D-dimer (mg/L)	0.28 (0.21–0.45)	0.31 (0.24–0.52)	0.37 (0.28–0.47)	0.31 (0.24–0.41)	0.233
Creatinine ($\mu\text{mol/L}$)	70.8 ± 20.7	69.2 ± 21.1	76.0 ± 21.4	71.7 ± 15.1	0.358
ALT (U/L)	33.2 ± 21.5	27.4 ± 17.2	26.3 ± 13.6	35.1 ± 31.5	0.128
AST (U/L)	25.1 ± 22.2	23.3 ± 14.2	21.5 ± 5.2	25.3 ± 14.3	0.492
LDL-C (mmol/L)	2.56 ± 0.43	2.32 ± 0.85	2.34 ± 0.42	2.32 ± 0.67	0.387
HDL-C (mmol/L)	0.89 ± 0.22	1.22 ± 0.24	0.89 ± 0.24	0.82 ± 0.23	0.832
TC (mmol/L)	4.11 ± 0.89	3.89 ± 0.91	3.89 ± 0.83	3.89 ± 1.21	0.387
TG (mmol/L)	1.89 ± 1.12	1.71 ± 0.78	1.76 ± 1.16	1.67 ± 1.21	0.483
Lp-PLA2 (ng/mL)	232.0 ± 32.1	242.1 ± 23.1	245.0 ± 33.1	237.7 ± 28.2	0.254

WBC, white blood cell; BNP, brain natriuretic peptide; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; Lp-PLA2, lipoprotein-associated phospholipase A2.

所有患者均植入药物涂层支架。4组处理的靶血管、病变血管数量、支架数量、支架直径、支架总长度等血管造影和手术特征比较均无统计学差异($P > 0.05$)。见表3。

表3 4组患者手术特征的比较
Tab.3 Comparison of procedural characteristics between the four groups

Item	A20 group (n = 57)	A20+E10 group (n = 53)	A40 group (n = 41)	A40+E10 group (n = 42)	P
Target vessel [n (%)]					
LAD	29 (50.9)	28 (52.8)	18 (43.9)	25 (59.5)	0.565
RCA	17 (24.6)	15 (28.3)	10 (24.4)	11 (26.2)	0.963
LCX	16 (46.1)	14 (26.4)	16 (39.0)	10 (23.8)	0.123
Number of target vessel [n (%)]					
One vessel	52 (91.2)	48 (90.6)	35 (85.4)	40 (95.2)	0.672
Two vessels	5 (8.8)	5 (9.4)	6 (14.6)	3 (7.1)	0.625
Stent number	1.48 ± 0.79	1.47 ± 0.76	1.53 ± 0.75	1.62 ± 0.82	0.928
Stent diameter (mm)	3.12 ± 0.48	2.98 ± 0.62	2.94 ± 0.49	3.09 ± 0.46	0.325
Total stent length (mm)	39.22 ± 22.48	41.11 ± 26.53	36.21 ± 22.17	38.10 ± 25.25	0.801

LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery.

2.4 围手术期血清学指标水平的变化

2.4.1 PCI前后Lp-PLA2变化值的析因分析:对PCI围手术期Lp-PLA2的变化值进行析因分析,结果显示,强化阿托伐他汀与依折麦布间无显著交互作用($P > 0.05$)。二者的主效应分析结果提示,强化阿托伐他汀和依折麦布对术后Lp-PLA2的影响均有统计

学意义(P 分别为0.045和0.003)。见表4。

2.4.2 PCI前后Lp-PLA2水平的变化:PCI前,各组基线Lp-PLA2水平的差异无统计学意义($P > 0.05$)。PCI后,4组Lp-PLA2水平均较术前明显降低($P < 0.05$)。对4组围手术期Lp-PLA2变化值进行比较,A40组、A20+E10组、A40+E10组均高于A20组,A40+

E10组高于A40组 ($P < 0.05$), 而A40+E10组与A20+E10组比较、A40组与A20+E10组比较, Lp-PLA2变化值的差异均无统计学意义 ($P > 0.05$)。见表5。

2.4.3 PCI围手术期 LDL-C水平的变化: 4组比较, PCI前和PCI后的 LDL-C水平以及PCI前后 LDL-C变化值的差异均无统计学意义 ($P > 0.05$)。见表5。

表4 析因分析
Tab.4 Factorial analysis

Variable	SS	df	MS	F	P
Atorvastatin	2 396.41	1	2 396.41	2.87	0.045
Ezetimibe	7 181.50	1	7 181.50	9.27	0.003
Atorvastatin and ezetimibe	87.67	1	87.67	0.12	0.748

表5 4组PCI围手术期 Lp-PLA2和LDL-C水平的比较
Tab.5 Comparison of perioperative levels of Lp-PLA2 and LDL-C between the four groups

Item	A20 group (n = 57)	A20+E10 group (n = 53)	A40 group (n = 41)	A40+E10 group (n = 42)	P
Lp-PLA2 (ng/mL)					
Pre-PCI	232.0 ± 32.1	242.1 ± 23.1	245.0 ± 33.1	237.7 ± 28.2	0.254
Post-PCI	168.0 ± 31.4 ¹⁾	157.1 ± 24.6 ¹⁾	163.0 ± 29.5 ¹⁾	148.9 ± 24.0 ¹⁾	0.008
Changing value	63.0 ± 42.1	84.0 ± 33.9 ²⁾	78.0 ± 41.8 ²⁾	90.1 ± 33.5 ^{2),3)}	0.004
LDL-C (mmol/L)					
Pre-PCI	2.62 ± 0.90	2.46 ± 0.80	2.45 ± 0.70	2.47 ± 0.80	0.396
Post-PCI	2.53 ± 0.70	2.38 ± 0.60	2.37 ± 0.50	2.34 ± 0.40	0.475
Changing value	0.07 ± 0.02	0.08 ± 0.03	0.07 ± 0.02	0.13 ± 0.02	0.374

Lp-PLA2, lipoprotein-associated phospholipase A2. 1) $P < 0.05$ vs. pre-PCI within group; 2) $P < 0.05$ vs. A20 group at the same time point; 3) $P < 0.05$ vs. A40 group at the same time point.

2.5 相关性分析

相关性分析结果显示, PCI围手术期LDL-C变化值与Lp-PLA2变化值无相关性 ($r = 0.039, P > 0.05$)。

组各发生非致死性心肌梗死2例; A20+E10组发生缺血性卒中1例。4组间不良事件的发生率无统计学差异 ($P > 0.05$)。见表6。

2.6 不良反应

2.6.1 MACE: 30 d内发生MACE 9例。其中, A20组和A40+E10组各发生心源性死亡1例; A20组和A40+E10组各发生非致死性心肌梗死1例; A20+E10组和A40

2.6.2 他汀类药物相关不良反应: 住院期间和术后30 d, 4组均未观察到他汀类药物相关性肌病和ALT升高>3倍正常值上限。

表6 4组MACE发生情况的比较[n (%)]
Tab.6 Comparison of the incidences of major adverse cardiovascular events between the four groups [n (%)]

Item	A20 group (n = 57)	A20+E10 group (n = 53)	A40 group (n = 41)	A40+E10 group (n = 42)	P
MACE	2 (3.4)	3 (5.6)	2 (4.9)	2 (4.8)	0.79
Cardiac death	1 (1.7)	0 (0)	0 (0)	1 (2.4)	-
Non-fatal myocardial infarction	1 (1.7)	2 (3.8)	2 (4.9)	1 (2.4)	0.50
Stroke	0	1 (1.8)	0	0	-

MACE, major adverse cardiovascular event; PCI, percutaneous coronary intervention.

3 讨论

本研究是一项2×2析因设计的病例对照研究,结果表明,强化阿托伐他汀以及阿托伐他汀联合依折麦布均可使PCI术后Lp-PLA2水平进一步下降,同时不增加他汀类药物相关不良反应的发生。

本研究发现,PCI后各组Lp-PLA2水平均较基线降低,这与既往研究^[9]结果一致。该研究检测了PCI术后即刻以及PCI术后1、3、7 d的Lp-PLA2水平,发现术后即刻Lp-PLA2水平较术前约下降22%,术后1 d较术前约下降25%,说明PCI可有效降低NSTE-ACS患者的Lp-PLA2水平。PROVE IT TIMI-22研究^[10]结果表明,ACS患者经过30 d强化阿托伐他汀治疗(80 mg/d)与中等强度普伐他汀(40 mg/d)治疗,Lp-PLA2水平分别下降20%和3.6% ($P < 0.05$),前者治疗后Lp-PLA2水平下降幅度更大。但是,目前鲜有研究探讨不同剂量他汀类药物治疗方案对围手术期Lp-PLA2的影响。本研究中,A40组与A20组比较,围手术期Lp-PLA2水平下降幅度更大,表明强化阿托伐他汀可进一步降低Lp-PLA2的水平。

我国的一项基础研究^[11]表明,单独使用依折麦布可使冠脉粥样硬化斑块缩小,其机制是通过降低血清胆固醇浓度,抑制巨噬细胞在病变内聚集,以及减少单核细胞趋化蛋白1和肿瘤坏死因子- α 等炎性细胞因子。还有研究^[12]表明,依折麦布可通过自噬来抑制巨噬细胞NLRP3炎性小体激活,并通过减少核因子 κ B活化等多种机制,实现改善脂肪性肝炎的作用。GRAVITY研究^[13]是一项多中心随机研究,患者接受不同剂量的瑞舒伐他汀和辛伐他汀治疗6周后再口服依折麦布10 mg,维持6周以上,结果发现,瑞舒伐他汀或辛伐他汀与依折麦布联合与他汀单药治疗相比,可更大程度降低Lp-PLA2的活性和浓度 ($P < 0.05$),但这种降低主要与LDL-C水平下降有关。本研究结果表明,在围手术期LDL-C明显降低前,阿托伐他汀联合依折麦布可进一步降低PCI术后Lp-PLA2水平。这表明阿托伐他汀和依折麦布除降脂作用外,可能具有抗炎作用,且阿托伐他汀联合依折麦布与阿托伐他汀单药治疗相比,这种抗炎作用更明显。欧洲心脏病学会动脉粥样硬化与血管生物学工作组发布了关于降脂治疗的抗炎反应专家共识文件^[14],阐明降脂具有抗炎和免疫调节的

特性,降脂药物也可以在不依赖血脂变化情况下起到减轻炎症的作用。此外,他汀类药物剂量加倍时LDL-C下降幅度仅约6%。最近的一项研究^[15]发现,在冠状动脉粥样硬化性心脏病患者中,中等剂量他汀类药物(瑞舒伐他汀10 mg)联合依折麦布10 mg与高剂量他汀类药物(瑞舒伐他汀20 mg)相比,在减少心血管事件发生方面无劣势,且不良反应发生率低于高剂量他汀类药物,提示联合降脂治疗在临床应用中更具优势。

综上所述,本研究表明,在择期行PCI的NSTE-ACS患者中,与中等强度阿托伐他汀相比,围手术期强化阿托伐他汀可进一步降低PCI后Lp-PLA2水平;与阿托伐他汀单药相比,阿托伐他汀联合依折麦布可进一步降低PCI后Lp-PLA2水平,且这种作用不依赖于LDL-C的变化。本研究具有单中心、开放标签的设计和样本量较小的局限性,未来需要大样本、前瞻性、随机对照研究验证研究结果的准确性。

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