

替罗非班降低急性心肌梗死患者经皮冠状动脉介入术后 PTX3 及 CD11b 表达^{*}

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摘要 目的:探讨替罗非班对急性心肌梗死(AMI)患者经皮冠状动脉介入术(PCI)后血清五聚素3(PTX3)及中性粒细胞表面粘附分子(CD11b)表达的影响。方法:选取2015年8月-2019年3月济南市槐荫人民医院收治的156例AMI患者,随机将其分成观察组和对照组,各78例。对照组患者行PCI术,观察组患者在对照组的基础上静脉注射替罗非班,应用生理盐水稀释终浓度为50 g/mL,前0.5 h以0.4 g/(kg·min)的速率静脉滴注,后以0.1 g/(kg·min)的速率持续静脉滴注至术后36 h。对比2组患者心肌再灌注情况、血PTX3、CD11b水平及主要不良心脏事件(MACE)等指标。结果:术后3 d,2组患者TIMI 3级血流比例比较,差异无统计学意义($P > 0.05$),观察组患者TMP 3级比例及ST段抬高回落(STR) > 50%占比明显高于对照组(91.02% vs 79.49%; 85.90% vs 70.51%, P 均 < 0.05);2组患者左室射血分数(LVEF)明显提高,且观察组明显高于对照组(P 均 < 0.05);2组患者左心室舒张末期内心径(LVEDD)明显降低,且观察组明显低于对照组(P 均 < 0.05);2组患者血PTX3和CD11b水平明显降低,且观察组明显低于对照组(P 均 < 0.05)。随访6个月,观察组患者MACE总发生率明显低于对照组(3.85% vs 15.38%, $P < 0.05$)。结论:替罗非班可有效提高AMI患者心肌灌注情况,恢复心功能,降低血PTX3、CD11b水平及MACE发生率。

关键词 替罗非班;急性心肌梗死;五聚素3;中性粒细胞表面粘附分子

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Tirofiban reduces the expression of PTX3 and CD11b after percutaneous coronary intervention in patients with acute myocardial infarction ZHANG Yu-qing¹, ZHAO Zhu¹, HU Xiu-fang¹, ZHANG Zai-ning¹, HU Bo².

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Abstract Objective: To explore the effect of Tirofiban on the expression of serum PTX3 and CD11b in patients with acute myocardial infarction undergoing percutaneous coronary intervention (PCI). Methods: Totally, 156 cases of acute myocardial infarction who underwent PCI in The People's Hospital of Huaiyin from August 2015 to March 2019 were selected as the observation subjects, and divided into the control group and the observation group according to the random number method, 78 cases in each group. The patients in the control group received PCI therapy, and those in the observation group were treated with Tirofiban on the basis of the control group. The treatment protocol was as follows: the final concentration was diluted to 50 g/mL with normal saline, intravenous drip at the rate of 0.4 g/(kg·min) in the first 0.5 h, and then continuous intravenous drip at the rate of 0.1 g/(kg·min) until 36 h after operation. Myocardial reperfusion, serum PTX3 and CD11b and major adverse cardiac events between the two groups were compared and analyzed. Results: At 3rd day after operation, there was no significant difference in the proportion of TIMI grade 3 between the two groups. The proportion of TMP3 grade and ST segment elevation reduction (STR) > 50% in the observation group was significantly higher than that in the control group (91.02% vs 79.49%; 85.90% vs 70.51%, all $P < 0.05$). The level of LVEF in the two groups was significantly increased, and that in the observation group was significantly higher than that in the control group ($P < 0.05$). The level of LVEDD in the two groups was significantly decreased, and that in the observation group was significantly lower than that in the control group ($P < 0.05$). The lev-

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els of PTX3 and CD11b in the two groups were significantly decreased, and those in the observation group were significantly lower than those in the control group ($P < 0.05$). During the follow-up of 6 months, the total incidence of MACE in observation group was significantly lower than that in control group (3.85% vs 15.38%, all $P < 0.05$). Conclusion; Tirofiban in the treatment of acute myocardial infarction can effectively improve myocardial perfusion, restore cardiac function, down-regulate the level of PTX3 and CD11b, and reduce the incidence of MACE.

Key words Tirofiban; Acute myocardial infarction; PTX3; CD11b

急性心肌梗死 (acute myocardial infarction, AMI)是指冠状动脉急性或持续性缺血缺血而诱发心肌组织坏死的心血管疾病,临床表现为胸骨后疼痛、低血压、心律失常甚至休克等症状,致死率高^[1,2]。临床以尽早疏通阻塞动脉和恢复损伤心肌再灌注为主要目标^[3],经皮冠状动脉介入术(percutaneous coronary intervention, PCI)是临床治疗 AMI的首选方法,但 PCI 术会增加血栓脱落、慢复流、微循环堵塞及心力衰竭等不良事件^[4],因而需联合抗血小板聚集药物以降低术后风险。替罗非班是常见的血小板糖蛋白受体拮抗剂,其可在阻止血小板聚集的基础上发挥抗血栓功效^[5]。五聚素 3 (PTX3)是保守、可溶的结构蛋白,主要由平滑肌细胞、巨噬细胞等分泌合成,并在白细胞介素-1 和肿瘤坏死因子等炎性因子的激活下大量增殖^[6]。中性粒细胞表面粘附分子 (CD11b) 归属于整合素类细胞粘附因子,其可介导机体的防御机制、炎症反应和血栓形成等病理生理反应,且其在 AMI 患者体内呈异常表

达^[7],二者均与 AMI 的发生、发展有一定的关联,本文探讨替罗非班对 AMI 患者血清 PTX3 及 CD11b 表达的影响。

资料与方法

一般资料 选取 2015 年 8 月-2019 年 3 月济南市槐荫人民医院收治的 156 例 AMI 患者,随机将其分成观察组和对照组,各 78 例。对照组患者行 PCI 术,观察组患者在对照组的基础上静脉注射替罗非班。比较 2 组患者年龄、性别、基础疾病、吸烟史、饮酒史、病变血管数目、入院时血压、梗死部位、入院至手术时间及冠脉病变特征等基线资料,差异无统计学意义(P 均 > 0.05),见表 1。

纳入标准:①符合 2010 年版本 AMI 诊断指南^[8],心电图出现动态变化,血清肌钙蛋白等指标水平超上限 2 倍,发病至入院时间 12 h 内;②符合 PCI 手术指征,且患者伴有持续性胸痛等症状;③首次发生 AMI,且近 3 个月未服用抗炎、糖皮质激素等

表 1 2 组患者基线资料比较

基线资料	观察组($n = 78$)	对照组($n = 78$)	t/χ^2	P
年龄(岁, $\bar{x} \pm s$)	60.46 \pm 5.10	59.50 \pm 6.55	0.727	0.469
病变血管数目(条, $\bar{x} \pm s$)	1.81 \pm 0.34	1.74 \pm 0.42	0.814	0.418
男性[例(%)]	41(52.56)	48(61.54)	1.282	0.258
冠状病变特征[例(%)]			0.525	0.769
前降支	41(52.56)	37(47.44)		
回旋支	23(29.48)	27(34.62)		
右冠状动脉	14(17.96)	14(17.94)		
梗死面积(cm^2 , $\bar{x} \pm s$)	9.03 \pm 1.01	8.92 \pm 0.99		
梗死部位[例(%)]			0.572	0.751
下壁	31(39.74)	27(34.62)		
前壁	25(32.05)	29(37.18)		
下壁合并右室	22(28.21)	22(28.20)		
入院时收缩压(mmHg, $\bar{x} \pm s$)	116.78 \pm 14.98	119.34 \pm 15.09	1.063	0.289
入院时舒张压(mmHg, $\bar{x} \pm s$)	76.98 \pm 5.67	77.45 \pm 6.09	0.499	0.619
入院至手术时间(h, $\bar{x} \pm s$)	6.09 \pm 1.01	6.13 \pm 0.97	0.252	0.801
高血脂[例(%)]	19(24.36)	15(19.23)	0.602	0.438
糖尿病[例(%)]	21(26.92)	16(20.51)	0.886	0.347
吸烟史[例(%)]	21(26.92)	17(21.79)	0.557	0.456
饮酒史[例(%)]	18(23.08)	15(19.23)	0.346	0.556

药物。

排除标准:①患有急性炎症疾病、恶性肿瘤、自身免疫疾病者;②心、肝、肾等器官严重损害者;③存在凝血功能障碍,近1年内存在活动性出血,血小板异常或有血小板减少病史;④对替罗非班等研究药物或冠脉造影剂过敏者;⑤哺乳或妊娠期妇女。本研究经医院伦理委员会审核批准,患者及家属均知情并签署同意书。

方法 所有患者入院后均行冠脉造影,以确诊病灶部位和病变血管数目,在发病后12 h内经股动脉或桡动脉穿刺下完成PCI术。对照组患者给予常规药物治疗,术前咀嚼阿司匹林肠溶片(拜耳医药保健有限公司,国药准字J20080078,规格:100 mg),首次负荷剂量为300 mg;口服硫酸氢氯吡格雷片[赛诺菲(杭州)制药有限公司,国药准字H20056410,规格:75 mg],首次负荷剂量为300 mg;术中应用肝素(50 U/kg),以发挥抗凝作用;术后持续口服阿司匹林和氯吡格雷片,剂量分别为100 mg/d和75 mg/d,同时术后所有患者均行抗心肌缺血常规治疗。观察组患者在对照组患者的基础上术前1 h静脉滴注替罗非班(山东新时代药业有限公司,国药准字H20090227,规格:12.5 mg),应用生理盐水稀释终浓度为50 g/mL,前0.5 h以0.4 g/(kg·min)的速率静脉滴注,后以0.1 g/(kg·min)的速率持续静脉滴注至术后36 h。

观察指标

1. 心肌再灌注指标。于术后3 d应用心肌梗死溶栓治疗,心肌梗塞溶栓治疗(thrombolysis in myocardial infarction, TIMI)血流分级、心肌灌注分级(TIMI myocardial perfusion, TMP)和心电图ST段抬高回落(ST-segment resolution, STR)评估梗死血管再灌注情况,并记录2组患者TIMI 3级、TMP 3级和STR > 50%的例数。TIMI具体标准^[9]:0级:无灌注,血管闭塞远端未见前向血流;1级:渗透,无灌注,仅有部分造影剂通过闭塞位置,远端血管未见明显充盈;2级:部分灌注,3个心动周期后,造影剂可全部充盈冠脉远端,但造影剂充盈或清除血管的速度较慢;3级:完全灌注,3个心动周期后,造影剂充盈完全,且充盈和速度恢复正常水平。TMP分级^[10]:0级:造影剂无法染色或通过血管;1级:心肌组织内存在造影剂染色现象,但无法正常排空;2级:心肌组织内造影剂排空速率较慢;3级:心肌组织造影剂正

常排空。STR是术前和术后2 h心电图ST段抬高总和的差值和术前ST段抬高总和的比例,STR > 50%表明回落正常,STR ≤ 50%表明回落异常^[11]。

2. 心功能。入院后次日空腹(术前)和术后3 d对所有患者行超声心动图检查,由高年资影像学技师测量患者左室射血分数(left ventricular ejection fraction, LVEF)和左心室舒张末期内径(left ventricular end diastolic dimension, LVEDD)等心功能指标,每名患者测量2次,取平均值,且变异度不超过10%。

3. PTX3和CD11b水平。于患者入院后次日(术前)和术后3 d采集患者空腹外周静脉血4 mL,加入EDTA-K2抗凝剂后,2 mL应用德国Sigma离心机以半径8 cm,3 000转/min,离心10 min,获得上清液,-70℃条件下贮存,应用美国BIOTEK全自动酶标仪酶联免疫吸附法测定血清PTX3水平,试剂盒购自上海钰博生物科技有限公司;2 mL外周血,与抗凝剂混匀后取100 μL全血,然后加入20 L藻红蛋白标记的抗CD11b单抗,混匀后静置30 min,加入2 mL专用溶血素(美国BD公司),去除红细胞后,应用德国Sigma离心机以1 000转/min,离心5 min,弃去上清液,加入1 mL磷酸盐缓冲液洗涤,继续以1 000转/min,离心10 min,加入0.5 mL磷酸盐缓冲液,待检测,应用FAC Scan型流式细胞仪(美国BD公司)测定CD11b相对表达水平。

4. 主要不良心脏事件(major adverse cardiovascular event, MACE)。随访6个月,记录2组患者出现再发心肌梗死、心律失常、心绞痛、心力衰竭、心源性休克及心源性死亡等不良事件。

5. 出血并发症及血小板减少症。术后30 d观察2组血小板减少症和出血性并发症的发生情况。血小板减少症:极重度为血小板计数(PLT) < 20 × 10⁹/L;重度为PLT < 50 × 10⁹/L;轻度为PLT < 100 × 10⁹/L。出血并发症按:大量出血:颅内出血或大出血,红细胞压积降低 ≥ 15%或血红蛋白(Hb)降低 ≥ 5 g/dL;少量出血:包括自发咯血、呕血及血尿,未察觉出血引起血红蛋白降低 ≥ 4 g/dL,但 ≤ 5 g/dL或红细胞压积降低 ≥ 12%但 ≤ 15%;极微出血:可察觉出血引起红细胞压积降低 ≥ 10%或Hb降低 ≥ 3 g/dL;不明显出血:失血未达上述标准。

统计学分析 采用SPSS 25.0统计学软件,计数资料以百分数(%)表示,采用 χ^2 检验;计量资料

导的动脉粥样硬化斑块破裂,进而诱发血管损伤和堵塞^[15]。PTX3是长链正五聚体蛋白,主要由血管单核细胞和内皮细胞合成并分泌,且储存于中性粒细胞中,其可由白细胞介素等炎性因子诱发而大量增殖。曲华清等^[16]报道,血清PTX3在AMI患者体内异常升高,且其动态变化与AMI诊断、预后评估有一定的关系。CD11b是常见的粘附因子,其正常情况下仅在中性粒细胞和单核细胞中低水平表达;而当机体发生炎症反应时,其可通过细胞粘附因子-1介导白细胞和内皮细胞,损伤血管,诱发心肌梗死、冠脉粥样硬化等病理改变。本研究表明,治疗后,2组患者血PTX3和CD11b水平明显降低,且观察组明显低于对照组($P < 0.05$),提示术前滴注替罗非班可有效降低PTX3和CD11b水平,改善患者炎症反应,优化患者病情状态。

综上所述,替罗非班可有效提高AMI患者心肌灌注情况,恢复心功能,降低PTX3、CD11b水平及MACE发生率。

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