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替格瑞洛联合比伐芦定用于 STEMI 患者急诊行 PCI 术的疗效分析 *

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摘要 目的：分析替格瑞洛联合比伐芦定用于急性 ST 段抬高型心肌梗死(STEMI)患者急诊行经皮冠状动脉介入手术(PCI)的疗效。**方法：**回顾性分析 2016 年 10 月 -2017 年 10 月我院收治的 71 例行急诊 PCI 的 STEMI 患者，根据药物使用方案的不同分为研究组(n=35)和对照组(n=36)，两组术前均给予患者阿司匹林 300 mg 和替格瑞洛 180 mg 进行治疗，对照组术中采用肝素，研究组术中采用比伐卢定，对比两组患者的无复流发生率、内皮素(ET)、超氧化物歧化酶(SOD)、细胞间黏附分子 -1(ICAM-1)、C 反应蛋白(CRP)水平、心脏功能和主要不良心脏事件发生率。**结果：**研究组 PCI 术后的无复流发生率[8.6%(3/35)]显著低于对照组[27.8%(10/36)](P＜0.05)，术后左心室舒张末期内径(LVEDD)、左心室收缩末期内径(LVESD)、血清 ICAM-1、CRP、ET 水平均明显低于术前，且均显著低于对照组(P＜0.05)，术后左心室射血分数(LVEF)、血清 SOD 水平高于术前，且显著高于对照组(P＜0.05)。研究组术后 3 个月的主要不良心脏事件发生率[11.4%(4/34)]低于对照组[27.8%(10/36)](P＜0.05)。**结论：**在 STEMI 患者急诊行 PCI 术中，采用替格瑞洛联合比伐芦定进行治疗可有效降低患者的无复流发生率，减轻血管壁的炎性反应，改善心脏功能，且患者的主要不良心脏事件发生率较低。

关键词：替格瑞洛；比伐芦定；STEMI；PCI；无复流

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Analysis of the Efficacy of Ticagrelor Combined with Bivalirudin in the Treatment of STEMI Patients Undergoing PCI*

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ABSTRACT Objective: To analyze the efficacy of ticagrelor and bivalirudin in the emergency percutaneous coronary intervention (PCI) in patients with acute st-segment elevation myocardial infarction (STEMI). **Methods:** A retrospective analysis was conducted on the STEMI patients of 71 emergency PCI patients admitted to our hospital from October 2016 to October 2017. According to the different drug use regimens, they were divided into the research group (n=35) and the control group (n=36). Two groups of patients were treated with aspirin 300mg and ticagrelor 180mg before surgery, and heparin was used in the control group, and the research group was used for the treatment of the bivalirudin. Compared to two groups of patients the incidence of no reflow, endothelin (ET), superoxide dismutase (SOD) and intercellular adhesion molecule 1 (ICAM - 1), c-reactive protein (CRP) level and heart function and the incidence of major adverse cardiac events. **Results:** The incidence of uncomplicated flow after PCI in the research group was 8.6% (3/35), which was lower than 27.8% (10/36) in the control group (P<0.05). Left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), serum ICAM-1, CRP, and ET levels were significantly lower than those before surgery, and were significantly lower than those of the control group (P<0.05). The postoperative left ventricular ejection fraction (LVEF) and serum SOD levels were higher than those before surgery and significantly higher than those of the control group (P<0.05). The incidence rate of major adverse cardiac events in the research group was 11.4% (4/34), which was lower than 27.8% (10/36) in the control group(P<0.05). **Conclusion:** Ticagrelor combined with bivalirudin can effectively reduce the incidence of no reflow and reduce the inflammatory reaction of blood vessel walls, improve heart function and the incidence of major adverse cardiac events of STEMI patients undergoing PCI.

Key words: Ticagrelor; Bivalirudin; STEMI; PCI; No-reflow

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前言

急性 ST 段抬高型心肌梗死(STEMI)为临床上发病率、致残率、致死率均较高的冠心病类型之一，致病原因主要为冠状

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动脉血供急剧减少或中断引起心肌细胞缺血、坏死[1-3]。经皮冠状动脉介入手术(PCI)是一种安全、有效、快速的血运重建治疗手段,通过开通患者梗死的冠脉血管,在缓解临床症状、改善预后的同时,还可降低死亡率,被作为目前临床上治疗急性心肌梗死的首选方法[4-6]。但由于患者梗死相关动脉内血栓负荷较大,PCI 术中易出现心肌无复流现象,可加剧梗死的发展和再发生。因此,急诊 PCI 术前应用负荷剂量的抗血小板药物及术中使用抗凝药物,对预防和治疗术中无复流发生具有重要意义[7-9]。

替格瑞洛是一种不经肝脏代谢、可直接与血小板相关受体结合的 P2Y12 受体拮抗剂,具有快速、强效、安全等特点[10,11]。比伐芦定是一种凝血酶抑制剂,具有抗凝及部分抗血小板凝聚作用[12,13]。本研究通过分析替格瑞洛联合比伐芦定应用于 STEMI 患者急诊行 PCI 术的疗效分析,为临床合理用药提供参考,具体结果报道如下:

1 资料与方法

1.1 一般资料

回顾性分析 2016 年 10 月 -2017 年 10 月我院收治的 71 例行急诊 PCI 的 STEMI 患者,根据药物使用方案的不同分为研究组(n=35)和对照组(n=36)。其中,研究组中男 19 例、女 16 例,年龄在 30-73 岁,平均年龄为 52.6± 3.7 岁;病程在 2.5-9.4 年,平均病程为 6.2± 3.0 年,发病距就诊时间为 2.7-6.8 h,平均发病距就诊时间为 5.1± 2.3 h,疾病类型:高血压 18 例,高血脂症 11 例,糖尿病 12 例;对照组中男 21 例、女 15 例,年龄在 32-74 岁,平均年龄为 53.7± 3.6 岁;病程在 2.5-9.2 年,平均病程为 6.3± 3.1 年,发病距就诊时间为 2.9-6.9 h,平均发病距就诊时间为 5.2± 2.2 h,疾病类型:高血压 17 例,高血脂症 12 例,糖尿病 11 例。两组基础资料经统计学比较差异无统计学意义(P> 0.05),具有可比性。

1.2 排除及纳入标准

纳入标准:(1)临床资料完整者;(2)符合中华医学会心血管疾病分会关于 STEMI 诊断标准者;(3) 符合急诊 PCI 指征者;(4)发病至就诊时间≤ 12 h 者;(5)就诊前未进行静脉溶栓治疗者;(6)同意并支持本次研究者。排除标准:(1)既往有出血病史者;(2) 存在凝血功能障碍者;(3) 对本次研究所用药品过敏者;(4)肝、肾功能衰竭者;(5)年龄< 18 岁;(6)动静脉畸形或动脉瘤者。

1.3 处理方法

两组患者术前均给予阿司匹林 (拜耳医药保健有限公司,国药准字 H20120236)300 mg 和替格瑞洛 (AstraZeneca AB,国药准字 J20130020)180 mg 进行治疗。对照组:冠脉造影前动脉鞘管一次性注射 3000 U 肝素 (江苏万邦生化医药股份有限公司,国药准字 H32020612),PCI 前按总量 100 U/kg 补足肝素,检测活化凝血时间(ACT)> 300 s 时,开始 PCI 手术。研究组:冠脉造影前以 0.75 mg/kg 外周静脉注射负荷量比伐卢定,随后,以 1.75 mg/kg·h 静脉泵入,检测活化凝血时间(ACT)> 300 s时,开始 PCI 手术,以 1.75 mg/kg·h 静脉滴注比伐卢定至 PCI 结束。

1.4 观察指标

1.4.1 **无复流发生率** 统计两组患者术中无复流的发生率,诊断标准:球囊扩张或支架植入后血管造影显示前向血流 TIMI 血流分级≤ 2 级,即为无复流。

1.4.2 **血清 ICAM-1、CRP、ET、SOD 水平** 两组患者均于术前、术后 1 周清晨空腹采集静脉血 5 mL,离心分离血清,-20℃冰箱保存,经 Hitachi7600 模块式全自动生化分析仪检测内皮素(ET)、超氧化物歧化酶(SOD)、细胞间黏附分子 -1(ICAM-1)、C 反应蛋白(CRP)水平。

1.4.3 **心脏功能** 经心脏彩超检查,对比两组患者治疗前、治疗后 1 周的左心室舒张末期内径(LVEDD)、左心室收缩末期内径(LVESD)和左心室射血分数(LVEF)。

1.4.4 **主要不良心脏事件发生率** 统计两组患者 PCI 治疗后 3 个月内的主要不良心脏事件发生率,包括心源性死亡、再次心肌梗死、顽固性心绞痛和恶性心律失常等。

1.5 统计学分析

采用 SPSS20.0 统计学软件,两组计量资料($\bar{x}$± s)的比较采用 t 检验,计数资料(%)经卡方检验,以 P< 0.05 为差异存在统计学意义。

2 结果

2.1 两组术后无复流发生率的对比

研究组 PCI 术后出现无复流现象者 3 例,发生率为 8.6%(3/35);对照组 PCI 术后出现无复流现象者 10 例,发生率为 27.8%(10/36);研究组显著低于对照组(P< 0.05)。

2.2 两组术前和术后血清 ICAM-1、CRP、ET、SOD 水平的对比

研究组术后血清 ICAM-1、CRP、ET 水平均低于术前,且均显著低于对照组(P< 0.05);研究组术后血清 SOD 水平明显高于术前,且均明显高于对照组(P< 0.05)。见表 1。

表 1 两组术前和术后血清 ICAM-1、CRP、ET、SOD 水平的对比($\bar{x}$± s)

Table 1 Comparison of the serum ICAM-1, CRP, ET and SOD levels between two groups before and after operation($\bar{x}$± s)

Groups	n	Time	ICAM-1ET(ng/L)	CRP(mg/L)	ET(ng/L)	SOD(U/mL)
Research group	35	Before operation	1.72± 0.31	15.3± 3.6	101.7± 15.9	76.5± 6.1
		After operation	0.29± 0.05#*	8.6± 1.4#*	73.9± 10.2#*	88.0± 8.1#*
Control group	36	Before operation	1.73± 0.29	15.9± 3.9	102.6± 12.8	77.3± 6.4
		After operation	1.12± 0.11#	11.8± 2.5#	90.2± 9.4#	82.1± 7.6#

Note: compared with the before operation, #P<0.05; compared with the control group, *P<0.05.

2.3 两组术前和术后心脏功能对比

研究组术后 LVEF 水平高于术前,且高于对照组(P< 0.05);研究组术后 LVEDD、LVESD 水平均低于术前,且低于对照组(P< 0.05)。见表 2。

表 2 两组术前和术后心脏功能对比($\bar{x}\pm s$)

Table 2 Comparison of cardiac function between two groups before and after operation ($\bar{x}\pm s$)

Groups	n	Time	LVEF(%)	LVEDD(mm)	LVESD(mm)
Research group	35	Before operation	44.3± 3.8	56.9± 5.2	42.6± 3.8
		After operation	55.1± 4.6#*	47.8± 3.1#*	30.2± 2.6#*
Control group	36	Before operation	44.6± 3.9	57.1± 4.9	42.1± 3.9
		After operation	51.3± 4.2#	50.1± 3.5#	33.6± 2.5#

Note: compared with the before operation, #P<0.05; compared with the control group, *P<0.05.

2.4 两组术后 3 个月内主要不良心脏事件发生率对比

研究组术后 3 个月的主要不良心脏事件发生率[11.4%(4/34)]低于对照组[27.8%(10/36)](P＜0.05),见表 3。

表 3 两组术后 3 个月主要不良心脏事件发生率对比

Table 3 Comparison of the incidence of major adverse cardiac events between the two groups in 3 months after surgery

Groups	n	Myocardial infarction	Cardiac death	Refractory angina	Malignant arrhythmia	Total(%)
Research group	35	1	0	2	1	11.4*
Control group	36	2	2	5	1	27.8

Note: compared with the control group, *P<0.05.

3 讨论

PCI 手术具有再通率高、出血率低、再梗死率低等优点,是临床上治疗 STEMI 首选的方案,其中,快速、有效的抗血小板治疗在 STEMI 患者急诊行 PCI 术中意义重大[14-16]。虽然 PCI 手术可有效疏通心肌梗死患者的梗死相关血管,但往往 STEMI 继发于冠状动脉的粥样硬化,微栓子、血凝等动脉硬化碎屑均会导致远端血管的栓塞,继而产生无复流现象[17,18],可促进心肌梗死患者的心肌细胞进一步受到损害,且不可逆。同时,无复流现象可显著增加患者的并发症发生率[19,20],对其心功能的恢复具有一定的阻碍作用。本研究研究结果显示研究组 PCI 术后的无复流发生率低于对照组,表明于 PCI 术前给予替格瑞洛+比伐卢定可有效预防无复流现象的产生。分析原因可能为替格瑞洛联合比伐卢定对术中 TIMI 血流具有积极作用,通过改善血粘度、红细胞压积,且不干扰血小板,从而使得手术缺血区充分得到血液灌注,有效降低了无复流现象的发生率[21-23]。

ICAM-1 是介导黏附反应重要的黏附分子,在心肌细胞受到损伤时,含量会急剧升高[24]。CRP 是一种人体在应激状态下产生的急性相蛋白[25]。ET 是一种具有收缩血管和促进平滑肌细胞增殖等作用的多肽[26]。SOD 是一种能够催化超氧化物通过歧化反应转化为氧气和过氧化氢的酶[27]。本研究结果显示研究组术后 ICAM-1、CRP、ET 水平均低于术前,且低于对照组,研究组术后 SOD 水平高于术前,且高于对照组,表明 ICAM-1、CRP、ET、SOD 水平变化可作为评估冠状动脉病变程度的关键指标。

在对行急诊 PCI 的 STEMI 患者进行疗效评价时,仅关注血管再通而忽视微循环功能运作情况是没有临床意义的,心肌微循环的再灌注是 STEMI 患者行急诊 PCI 治疗的终极目标[28,29],本研究结果显示,研究组术后 LVEF 水平高于术前,且高于对照组,研究组术后 LVEDD、LVESD 水平均低于术前,且低于对照组,表明替格瑞洛联合比伐卢定对可有效清除微血栓,对改善机体的微循环提供了充分条件。此外,本研究结果显示研究组术后 3 个月的主要不良心脏事件发生率低于对照组,表明与肝素相比,联合比伐芦定可在一定程度上降低主要不良心脏事件发生率,安全性较高。其原因可能与比伐芦定不激活血小板、产生促凝物质有关[30,31]。

综上所述,在 STEMI 患者急诊行 PCI 术中,采用替格瑞洛联合比伐芦定进行治疗可有效降低患者的无复流发生率,减轻血管壁的炎性反应,改善心脏功能,且患者的主要不良心脏事件发生率较低。

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