

急诊 PCI 冠状动脉内注射替罗非班对糖尿病合并急性心肌梗死的影响

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【摘要】 目的:探讨急诊经皮冠状动脉介入治疗(PCI)时,冠状动脉内注射替罗非班对糖尿病合并急性心肌梗死(AMI)的近期疗效和安全性。 方法:选择接受急诊 PCI 的糖尿病合并急性 ST 段抬高型 AMI(STEMI)患者 133 例,随机分为替罗非班组($n=67$)和对照组($n=66$)。分别对两组的临床资料、冠状动脉病变特征、住院时间和并发症的发生率进行比较。 结果:替罗非班组 PCI 术后 TIMI3 级血流显著高于对照组($P<0.05$),TMPG 分级 0~1 级显著低于对照组,3 级显著高于对照组($P<0.05$)。替罗非班组的平均住院天数、梗死后心绞痛、严重心律失常、Killip III 级以上心功能显著低于对照组;皮肤黏膜出血显著高于对照组($P<0.05$)。 结论:替罗非班能够有效地改善糖尿病合并 AMI 患者的 TIMI 血流和 TMPG 灌注,减少恶性心律失常、心力衰竭等严重并发症的发生,并且不增加严重出血并发症。

【关键词】 糖尿病;急性心肌梗死;急诊经皮冠状动脉介入治疗;替罗非班

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Effects of coronary arterial injection of tirofiban on diabetes mellitus complicated with acute myocardial infarction during primary percutaneous coronary intervention LIU Yang, LIU Heng-liang, GENG Guo-ying, BA Ning, JIANG Song-bin, GUO Wei, ZHANG Zhi-fang. Department of Cardiology, the people's hospital of zhengzhou, Henan Province 450002, China

【Abstract】 Objective: To study the therapeutic effect and safety of intracoronary administration tirofiban in patients with diabetes mellitus complicated with acute myocardial infarction (AMI) during emergency percutaneous coronary intervention (PCI). **Methods:** This observational analysis was performed on 133 diabetes patients with ST segment elevated MI who underwent emergency PCI in our department from January 2010 to October 2012. The patients were randomly divided into tirofiban treatment group ($n=67$) and conventional treatment group ($n=66$). Their clinical data, coronary artery lesions, hospital stay time and complications were compared between the two groups, respectively.

Results: The blood stream of coronary thrombolysis in myocardial infarction trial (TIMI) grade 3 in tirofiban treatment group was significantly higher than in conventional treatment group after emergency PCI ($P<0.05$). The porprotron of patients with TIMI myocardial perfusion grade (TMPG) 0-1 in tirofiban treatment group was significantly lower than in conventional treatment group after emergency PCI ($P<0.05$). While porprotron of patients with TMPG 3 in tirofiban treatment group was significantly higher than in conventional treatment group after emergency PCI ($P<0.05$). Hospital stay time, and incidence of angina pectoris after MI, severe arrythemia and heart failure \geq Killip III in tirofiban treatment group was significantly lowerer than in conventional treatment group after emergency PCI ($P<0.05$). The incidence of minor bleeding in tirofiban treatment group was significantly higher than in conventional treatment group after emergency PCI ($P<0.05$). **Conclusion:** Intracoronary

injection of tirofiban in diabetes patients with AMI during emergency PCI can improve coronary flow and myocardial perfusion, and decrease the incidence of severe arrhythmia and heart failure, with no more bleeding occurrence.

【Key words】 Diabetes mellitus; Acute myocardial infarction; Emergency percutaneous coronary intervention; Tirofiban

不稳定斑块的破裂、血小板聚集、血栓形成是急性心肌梗死(AMI)的主要病理基础,糖尿病合并 AMI 患者急诊经皮冠状动脉介入治疗(PCI)后无复流、慢血流的发生率显著高于非糖尿病患者,这是糖尿病 AMI 患者心血管事件增加的主要原因之一^[1-2];盐酸替罗非班是一种强效血小板膜糖蛋白 II b/III a 受体拮抗剂,能有效改善 AMI 时心肌组织的再灌注,降低慢血流、无复流的发生率^[3-4]。本研究旨在探讨急诊 PCI 时冠脉内注射替罗非班对糖尿病合并 AMI 患者的疗效和安全性。

1 对象与方法

1.1 研究对象

选择 2010 年 1 月至 2012 年 10 月住院的糖尿病 AMI 患者 133 例为研究对象,随机分为两组。替罗非班组($n=67$),男 35 例,女 32 例,平均年龄(63.5 ± 9.8)岁;对照组($n=66$),男 31 例,女 35 例,平均年龄(62.6 ± 10.9)岁。入选标准:(1)STEMI 发病时间 ≤ 12 h;(2)已经确诊为糖尿病;(3)同意行急诊 PCI 术。排除标准:(1)STEMI 发病时间 ≥ 12 h;(2)怀疑主动脉夹层;(3)不能控制的高血压 $\geq 180/110$ mmHg;(4)溶栓治疗后补救性 PCI;(5)有脑出血史及 1 年内缺血性卒中史;(6)严重肝、肾功能不全;(7)有出血性疾病病史;(8)AMI 并发心源性休克、严重左心功能不全。

1.2 方法

患者入院后立即描记 18 导联心电图,给予心电监护,吸氧,查血糖、血脂、心肌酶、肌钙蛋白及其他相关生化和常规检验项目,同时给予阿司匹林 300 mg 和氯吡格雷 600 mg 嚼服。冠状动脉造影采用 Judksin 法,冠状动脉造影前经鞘管给予肝素 3000 U,造影结束,追加肝素 7000 U,指引导管到达冠脉开口,造影后若发现肉眼可见的血栓影,使用血栓抽吸导管抽吸血栓,然后指引导丝通过罪犯血管的闭塞病变。冠脉内注射替罗非班(欣维宁注射液,武汉远大制药集团有限公司),按 $10 \mu\text{g}/\text{kg}$ 的剂量,3 min 注射完毕,然后以 $0.15 \mu\text{g}/(\text{kg} \cdot \text{min})$ 持续静脉泵入 24 h;对照组不给予替罗非班。重复造影,了解冠脉血流情况,并根据病变情况行植入术。

术后复查心肌酶、肌钙蛋白、心电图、超声心动图、肝肾功能,继续服用阿司匹林 100 mg/d、氯比格雷 75 mg/d、他汀类药物、 β -受体阻滞剂和降糖药物。急诊 PCI 仅处理罪犯血管,其他血管如需处理于 7~14 d 后择期二次手术。

分析两组冠脉病变特点、治疗情况及术后并发症等。记录 PCI 后梗死相关血管的心肌梗死溶栓试验(thrombolysis in myocardial infarction trial, TIMI)血流分级及心肌灌注分级(TIMI myocardial perfusion grade, TMPG)情况。TIMI 血流分级标准:0 级为血管闭塞远端无前向血流;1 级对比剂部分通过闭塞部位,但不能充盈远端血管;2 级对比剂可完全充盈冠状动脉远端,但对比剂充盈及清除的速度较正常冠状动脉延缓;3 级为对比剂完全、迅速充盈远端血管并迅速清除。TIMI 0~1 级表明冠状动脉未再通, TIMI 2~3 级表明冠状动脉再通。TMPG 分级标准:0 级为对比剂注射和排空期间心肌极少染色或无染色;1 级为心肌染色缓慢,而且下一次注射对比剂时仅局部染色或心肌弥漫性点状染色;2 级为心肌可染色,但心肌染色或消退非常缓慢,以至在排空期末心肌染色仍然存在;3 级为血流正常,心肌被广泛染色,在排空期末染色仅轻度持续或无染色。

1.3 统计学分析

应用 SPSS13.0 统计软件,计数资料用 χ^2 检验,计量资料用 t 检验,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 一般临床资料比较

2 组患者性别、年龄构成、高血压、吸烟史、高脂血症、肾功能、既往 PCI 史、梗死前心绞痛、冠心病家族史均相似,无统计学差异($P > 0.05$)。

2.2 冠状动脉病变特征比较

两组单支、双支、三支及合并左主干病变和急诊 PCI 处理的靶血管无显著性差异($P > 0.05$);替罗非班组 PCI 术后 TIMI 3 级血流显著高于对照组, TMPG 分级 0~1 级替罗非班组显著低于对照组, 3 级显著高于对照组($P < 0.05$, 见表 1)。

表 1 冠状动脉病变特征比较 (n, %)

病变特点	替罗非班组	对照组	P 值
单支病变	7(10.45)	11(16.67)	0.43
双支病变	42(62.69)	39(59.1)	0.81
3 支病变	18(26.87)	26(39.39)	0.18
合并左主干病变	12(17.91)	12(18.18)	0.85
急诊 PCI 靶血管			
LAD	33(49.25)	37(56.06)	0.54
LCX	15(22.39)	12(18.18)	0.70
RCA	19(28.36)	17(25.76)	0.89
TIMI 分级			
术前 0~1 级	59(88.06)	58(87.88)	0.82
术后 3 级	65(97.01)	56(84.84)	0.03
术后 TMPG 分级			
0~1 级	1(1.49)	14(21.2)	0.00
2 级	3(4.48)	9(13.64)	0.12
3 级	63(94.03)	43(65.15)	0.00

2.3 治疗及并发症情况比较

两组间入院到球囊扩张平均时间、置入 2 个以上支架数、住院期间择期二次 PCI、住院期间再梗死、支架内血栓、心源性休克的发生率和 30 d 病死率无明显差异($P>0.05$)。平均住院天数、梗死后心绞痛、严重心律失常、KillipⅢ级以上心功能替罗非班组显著低于对照组;2 组间血小板减少、颅内和消化道等严重出血及输血例数无显著性差异,皮肤粘膜出血替罗非班组显著高于对照组($P<0.05$,见表 2)。

表 2 两组患者治疗及并发症情况比较 (n, %)

项目	替罗非班组	对照组	P 值
平均住院时间(d)	13.2±3.3	14.5±3.8	0.05
入院到球囊扩张时间(min)	87.7±28.2	82.9±39.8	0.70
置入 2 个以上支架	27(40.30)	24(36.36)	0.75
住院择期二次 PCI	34(50.75)	36(54.55)	0.74
梗死后心绞痛	16(23.88)	35(53.03)	0.004
再梗死	5(7.46)	9(13.64)	0.62
支架内血栓	0(0)	2(3.03)	0.88
严重心律失常	8(11.94)	21(31.82)	0.04
KillipⅢ级以上心功能	4(5.97)	13(19.70)	0.04
PCI 术后心源性休克	0(0)	2(3.03)	0.88
30d 病死率	1(1.49)	3(4.55)	0.88
出血			
血小板减少	1(1.49)	0(0)	0.99
颅内出血	1(1.49)	0(0)	0.99
消化道大出血	1(1.49)	1(1.52)	0.48
输血比例	2(2.99)	1(1.52)	0.99
皮肤黏膜出血	17(25.37)	4(6.06)	0.05
穿刺部位出血或血肿	9(13.43)	7(10.61)	0.88

3 讨论

及早、持续、充分的开通梗死相关血管是 AMI

最重要的治疗原则^[1,2]。糖尿病患者冠状动脉病变常常是多支血管受累,且常并发微血管病变和糖尿病型心肌病^[5-12]。糖尿病合并 AMI 患者急诊 PCI 无复流、慢血流发生率显著高于非糖尿病患者^[10-16]。与非糖尿病者相比,糖尿病患者有较高的死亡、心肌梗死、脑卒中和心力衰竭的发生率^[17-20]。

盐酸替罗非班是血小板膜糖蛋白Ⅱb/Ⅲa 受体的可逆性拮抗剂,能有效减少 PCI 时慢血流、无复流的发生^[3,16]。恢复梗死相关血管前向血流达到 TIMI 3 级曾被认为是再灌注治疗成功的金标准,但新近的研究证明,心肌组织水平的成功灌注才是再灌注成功的最终标准。TMPG 作为心肌水平的灌注标准,能更准确的评价心肌组织水平的灌注。研究表明,对于心外膜冠状动脉 TIMI 3 级血流的患者, TMPG 0~1 级(微血管闭塞)患者的病死率显著高于 TMPG 2~3 级的患者。本研究表明糖尿病合并 AMI 患者急诊 PCI 冠脉内应用盐酸替罗非班后 TIMI 3 级血流和 TMPG 3 级灌注明显高于对照组。

本研究中对照组严重心律失常的发生率高达 31%,原因可能是血糖升高加重内皮功能障碍、炎症反应和游离基诱导的再灌注损伤,增加 β 受体的兴奋性,易发生心律失常^[10-12]。糖尿病合并 AMI 时,胰岛素分泌相对或绝对不足,血浆游离脂肪酸浓度升高,脂肪酸使损伤心肌的耗氧量增加,增加梗死面积、加剧心室重塑,使心功能下降,诱发心力衰竭和心源性休克,增加病死率^[2,6,10]。替罗非班组心功能较对照组明显改善,可能与其改善微循环灌注,减少心肌细胞的死亡有关。

在阿司匹林和氯吡格雷双联抗血小板时,如果再加用替罗非班是否会引起血小板减少和出血并发症一直是心血管介入医师密切关注的问题。本研究替罗非班组轻度出血多于对照组,但严重出血并无显著增加。

合并糖尿病的 AMI 患者冠脉内给予替罗非班治疗,能够有效的改善 TIMI 血流和 TMPG 灌注,降低恶性心律失常、心力衰竭等严重并发症的发生。由于本研究是单中心研究,且未进行急诊 PCI 后长期随访,难免有一定的局限性。随着盐酸替罗非班临床应用经验的逐渐积累,糖尿病合并 AMI 患者的预后将有改善。

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