

左西孟旦联合主动脉球囊反搏可有效改善急性心肌梗死合并心源性休克患者的预后

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摘要 目的:本研究评估左西孟旦联合主动脉球囊反搏(IABP)对急性心肌梗死(AMI)合并心源性休克(CS)患者的疗效及安全性。方法:连续收集AMI合并CS植入IABP行急性经皮冠状动脉介入治疗(PCI)患者82例,随机分为观察组(左西孟旦+IABP)和对照组(单纯IABP),使用化学发光法检测2组血清N末端-脑钠肽前体(NT-proBNP)、肌钙蛋白I(cTnI)水平,使用酶联免疫吸附检测超敏C反应蛋白(HsCRP)的水平。统计患者IABP辅助时间、CCU入住天数及总住院天数;心肌梗死后30d心脏主要不良事件发生情况;再发心肌梗死、脑卒中、再次血运重建、死亡及再次住院率。结果:治疗5d后,与对照组比较,观察组患者NT-proBNP下降更加明显[(-3895.37±1589.59)pg/mL vs (-2568.53±1864.23)pg/mL, $P=0.0026$],hsCRP降低更加显著[(-42.56±20.35)mg/L vs (-25.63±12.69)mg/L, $P=0.0032$],肌钙蛋白峰值更低[(89.65±36.58)ng/mL vs (98.56±32.69)mg/L, $P=0.042$];观察组IABP持续时间更短[(4.5±2.5)d vs (6.5±3.5)d, $P=0.032$],CCU入住时间更短[(7.5±3.5)d vs (9.5±4.5)d, $P=0.039$],总住院时间明显降低[(10.5±5.5)d vs (13.5±6.5)d, $P=0.025$]。2组患者住院期间死亡率比较,差异无统计学意义($P=0.696$)。观察组30d内心血管主要不良事件发生率低于对照组(19.05% vs 25.00%, $P=0.515$),急诊就医次数更少[(1.2±0.8) vs (2.2±1.8), $P=0.042$],再次住院次数更少[(0.8±1.2) vs (1.5±1.6), $P=0.049$]。出院时,观察组标准EQ-5D-3L健康调查问卷评分低于对照组($P=0.038$),随访30d时继续保持降低($P=0.029$)。结论:左西孟旦联合IABP对AMI合并CS患者疗效肯定且安全可靠。

关键词 主动脉球囊反搏;左西孟旦;急性心肌梗死;心源性休克

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Levosimendan combined with aortic balloon counterpulsation could effectively improve the prognosis of patients with acute myocardial infarction complicated with cardiogenic shock WANG Jiang-you^{1,2}, CHEN Han³. ¹Department of Cardiology, Wuhan Asian Heart Hospital, Hubei Wuhan 430022, China; ²Department of Cardiology, Wuhan Asia General Hospital, Hubei Wuhan 430056, China; ³Department of Intensive Care Unit, Wuhan Asia General Hospital, Hubei Wuhan 430056, China
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Abstract Objective: To evaluate the efficacy of levosimendan combined with intra-aortic balloon counterpulsation (IABP) in patients with acute myocardial infarction (AMI) complicated with cardiogenic shock (CS) and safety. Methods: A total of 82 patients with AMI combined with CS implantation with IABP who underwent acute percutaneous coronary intervention (PCI) were collected and randomly divided into an observation group (traditional medicine + levosimendan) and a control group (traditional medicine). NT-proBNP, HsCRP and cTnI levels were detected. The IABP assistance time, CCU stay days and overall hospitalization days, the incidence of major adverse cardiac events 30 days after myocardial infarction (recurrent myocardial infarction, stroke, revascularization, death and rehospitalization rate) were observed. Results: After 5 days of treatment, as compared with the control group, the NT-proBNP (-3895.37±1589.59 vs. -2568.53±1864.23 pg/mL, $P=0.0026$), the HsCRP (-42.56±20.35 vs. -25.63±12.69 mg/L, $P=0.0032$) and peak troponin (89.65±36.58 vs. 98.56±32.69 mg/L, $P=0.042$) significantly decreased in the observation group. The observation group had shorter duration of IABP (4.5±2.5 vs. 6.5±3.5 days, $P=0.032$), shorter CCU stay time (7.5±3.5 vs. 9.5±4.5 days, $P=$

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0.039) and total hospital stay time (10.5 ± 5.5 days vs. 13.5 ± 6.5 days, $P=0.025$) than in the control group. There was no significant difference in mortality during hospitalization between the two groups ($P=0.696$). The main adverse cardiovascular events in the observation group within 30 days showed a decreasing trend as compared with the control group (19.05% vs. 25.00%, $P=0.515$). Within 30 days, the observation group had fewer emergency hospital visits (1.2 ± 0.8 vs. 2.2 ± 1.8 , $P=0.042$) and fewer readmissions (0.8 ± 1.2 vs. 1.5 ± 1.6 , $P=0.049$) than the control group. Standard EQ-5D-3L health questionnaire score in the observation group significantly decreased at discharge ($P=0.038$) and 30 days ($P=0.029$) as compared with the control group. Conclusion: Levosimendan combined with IABP is effective, safe and reliable in patients with AMI and CS.

Key words Cardiogenic shock; Acute myocardial infarction; Intra-aortic balloon pump; Levosimendan

近年来,随着冠心病监护室、再灌注技术和药物种类的改善,急性心肌梗死(acute myocardial infarction, AMI)患者的临床转归得到显著改善,但是心源性休克(cardiogenic shock, CS)院内死亡风险依然居高不下,仍是心肌梗死患者治疗的最大挑战^[1,2]。左西孟旦具有增加心肌收缩和血管舒张作用,可降低AMI患者心肌损伤,减少心肌细胞凋亡和炎症反应^[3]。主动脉球囊反搏(intra-aortic balloon pump, IABP)通过物理作用提高主动脉内舒张压,增加冠脉血供,改善心功能,目前在国内广泛应用于心脏病等危重患者的抢救和治疗^[4]。本研究旨在评价左西孟旦联合IABP治疗AMI的疗效和安全性。

资料与方法

1. 一般资料:选取2018年6月-2019年10月因急性胸痛症状就诊武汉亚洲心脏病医院最终诊断AMI合并CS并接受急诊经皮冠脉介入治疗(percutaneous coronary intervention, PCI)和IABP辅助的患者共82例。采用随机数字表法分为观察组(左西孟旦+IABP)42例和对照组(单纯IABP)40例。观察组给予左西孟旦12.5 mg加入5%葡萄糖45 mL用微量泵以 $0.1 \mu\text{g}/(\text{kg} \cdot \text{min})$ 连续泵入,持续24 h泵完。对照组接受相同体积的5%葡萄糖水溶液,持续24 h泵入。所有患者都接受针对AMI和CS的基线治疗,包括阿司匹林、替格瑞洛、肝素、 β 受体阻滞剂、血管紧张素转化酶抑制剂、利尿剂和硝酸脂类药物等。本研究经医院伦理委员会批准,患者或家属均知情并签署同意书。

纳入标准:①胸痛持续30 min以上,经舌下含服硝酸甘油治疗后仍未缓解;②心电图至少2个导联ST段抬高 ≥ 2 mm;③血清肌钙蛋白I升高至其上限至少2倍;④急性ST段抬高型心肌梗死(acute ST-segment elevation myocardial infarction, STEMI)患者发病12 h内急诊PCI,急性非ST段抬高型心肌梗死(acute non-ST-segment elevation myocardial infar-

ction, NSTEMI)患者为极高危组,2 h内接受急诊PCI;⑤入院时收缩压 < 90 mmHg;⑥超声心动图显示左室壁异常运动。

排除标准:①2度或3度房室传导阻滞;②严重心律失常;③急慢性炎症或感染性疾病;④心包疾病;⑤梗阻性心肌病;⑥原发性肾或肝损害(肌酐 > 2.5 mg/dL);⑦造影剂过敏;⑧低钾血症或高钾血症(钾 < 3.5 或 > 5.5 mmol/L);⑨怀孕、哺乳。

2. 方法:所有患者入组后详细记录年龄、性别、病程、吸烟史、糖尿病史、高血压病史等。所有AMI患者均成功接受急诊PCI。造影前,给予患者替格瑞洛180 mg或氯吡格雷600 mg、阿司匹林300 mg,酌情使用替罗非班。患者均经股动脉或桡动脉途径进行冠脉造影,行急诊PCI前,给予静脉内注射70~100 IU/10 kg的普通肝素进行抗凝处理。由手术者对冠状动脉造影进行评估,行PCI治疗(术中由术者根据血栓负荷情况,予以血栓抽吸)。术后均给予药物治疗,关注患者循环情况。超声心动图结果用立方公式计算左心室舒张末期内径(left ventricular end diastolic dimension, LVEDD)、左心室缩短分数(left ventricular shortening fraction, LVSF)和左心室射血分数(left ventricular ejection fraction, LVEF)。所有参数均取连续3个以上心动周期的平均值。EQ-5D-3L健康问卷包括以下5个指标:①行动能力;②自理能力;③日常活动能力;④疼痛或不适;⑤焦虑或抑郁。每个指标按程度分为1~3分:1分表示没有问题;2分表示有问题;3分表示问题严重。

3. 统计学分析:采用SPSS 17.0统计学软件。连续变量以($\bar{x} \pm s$)表示,通过Kolmogorov-Smirnov检验测试连续变量的正态分布,比较基于参数变量的Student's t-检验和非参数变量的Mann-Whitney U检验。分类变量以n(%)表示,采用 χ^2 检验或Fisher's精确 χ^2 检验进行比较。采用Spearman法对相关性进行分析。以 $P < 0.05$ 为差异有统计学意义。

结果

1. 基线资料: 观察组与对照组年龄 $[(62.78 \pm 15.35)$ 岁 vs (63.56 ± 12.58) 岁, $P=0.758$]、体重指数 $[(26.76 \pm 3.28)$ kg/m² vs (25.89 ± 3.16) kg/m², $P=0.825$]、性别、心血管危险因素、术后药物治疗方面比较, 差异无统计学意义(P 均 >0.05), 见表1。2组冠状动脉病变类型、手术特点、药物洗脱支架和术中并发症等比较, 差异无统计学意义(P 均 >0.05), 见表2~4。

表1 2组患者一般临床资料比较[例(%)]

项目	对照组 (n=40)	观察组 (n=42)	P值
男性	27(68)	28(67)	0.936
既往心肌梗死	6(15)	7(17)	0.836
既往PCI	8(20)	12(29)	0.366
既往搭桥手术	5(13)	8(19)	0.417
STEMI	30(75)	35(83)	0.352
NSTEMI	10(25)	7(17)	0.352
吸烟史	26(65)	30(71)	0.532
高脂血症	24(60)	28(67)	0.121
高血压	30(75)	34(81)	0.515
糖尿病	20(50)	22(52)	0.829
家族史	8(20)	7(17)	0.696
使用ACEI or ARB	28(70)	32(76)	0.527
使用 β blockers	25(63)	30(72)	0.390
使用CCB	13(33)	8(19)	0.163
使用阿司匹林	40(100)	42(100)	1.000
使用氯吡格雷	8(20)	6(14)	0.492
使用替格瑞洛	32(80)	36(86)	0.492
使用胰岛素	18(45)	20(48)	0.812
使用他汀类	40(100)	42(100)	1.000

注: ACEIs为血管紧张素转换酶抑制剂, ARBs为血管紧张素II受体阻滞剂, β blockers为 β 受体抑制剂, CCB为钙离子通道抑制剂

2. 实验室检查指标: 治疗5d后, 与对照组比较, 观察组NT-proBNP $[(-3895.37 \pm 1589.59)$ pg/mL vs (-2568.53 ± 1864.23) pg/mL, $P<0.05$], Hs-CRP $[(-42.56 \pm 20.35)$ mg/L vs (-25.63 ± 12.69) mg/L, $P<0.05$]下降更为显著, 肌钙蛋白I峰值较低 $[(89.65 \pm 36.58)$ ng/mL vs (98.56 ± 32.69) ng/mL, $P<0.05$]。随访30d, 与对照组比较, 观察组NT-proBNP值更低($P<0.05$), 见表5。

3. 心脏超声指标: 干预治疗30d后, 2组患者LVEF、LVEDd、LVFS均显著改善, 且观察组改善更为显著(P 均 <0.05), 见表5。

表2 2组患者冠状动脉病变特点[例(%)]

项目	对照组 (n=40)	观察组 (n=42)	P值
病变分类*			
A+B1	28(70)	25(60)	0.321
B2+C	12(30)	17(40)	0.321
罪犯血管			
左主干	5(13)	8(19)	0.549
前降支	22(55)	25(60)	0.679
回旋支	12(30)	10(24)	0.527
右冠状动脉	18(45)	20(48)	0.812
单支病变	12(30)	10(24)	0.527
双支病变	18(45)	21(50)	0.650
三支病变	10(15)	11(26)	0.902

注: *根据根美国心脏协会/美国心脏病学会分类

表3 2组患者冠脉介入手术特征($\bar{x} \pm s$)

项目	对照组 (n=40)	观察组 (n=42)	P值
支架长度(mm)	23.26 \pm 3.82	21.89 \pm 2.87	0.553
支架尺寸(mm)	2.82 \pm 0.64	2.93 \pm 0.58	0.686
总扩张时间(s)	38.42 \pm 8.96	42.32 \pm 5.75	0.162
支架个数(个)	1.85 \pm 1.68	1.98 \pm 1.29	0.785
扩张最大压力(atm)	14.36 \pm 3.67	15.42 \pm 4.26	0.737

表4 2组患者术中资料[例(%)]

项目	对照组 (n=40)	观察组 (n=42)	P值
TIMI血流分级			
\leq 1级	2(5)	3(7)	1.000
2级	5(13)	8(19)	0.417
3级	33(83)	31(74)	0.342
扩张期间ST改变	12(30)	15(36)	0.582
介入并发症			
边支闭塞	2(5)	3(7)	1.000
冠脉夹层	2(5)	2(5)	1.000
冠脉痉挛	8(20)	10(24)	0.677
冠脉血栓	1(3)	2(5)	1.000

4. 院内治疗时间及随访指标: 观察组患者IABP持续时间、CCU入住时间、总住院天数较短, 急诊次数和再住院次数较少, 标准EQ-5D-3L健康问卷评分更低(P 均 <0.05)。2组住院死亡率(20.00% vs 16.67%, $P=0.696$)和30d主要心血管不良事件(25.00% vs 19.05%, $P=0.515$)比较, 差异无统计学意义(P 均 >0.05), 见表6。

讨论

本研究中, 静脉注射左西孟旦联合IABP治疗

表5 2组患者心脏超声指标及实验室指标比较($\bar{x} \pm s$)

项目	观察组($n=42$)		对照组($n=40$)	
	基线	30 d	基线	30 d
NT-pro-BNP(pg/mL)	12857.00 ± 2589.29	798.64 ± 368.26 ^{*#}	12059.00 ± 3687.35	1326.98 ± 563.12 [*]
LVEF (%)	42.58 ± 5.63	48.58 ± 4.89 ^{*#}	43.59 ± 4.82	45.86 ± 3.29 [*]
LVEDd (mm)	52.62 ± 4.53	42.53 ± 5.84 ^{*#}	53.27 ± 3.86	47.46 ± 4.28 [*]
LVFS (%)	27.53 ± 3.59	35.53 ± 3.72 ^{*#}	28.31 ± 3.48	31.42 ± 3.26 [*]

注:FS为左室短缩分数;与基线比较,^{*} $P < 0.05$;与对照组比较,[#] $P < 0.05$

表6 2组患者院内治疗时间和随访指标的比较($\bar{x} \pm s$)

项目	对照组($n=40$)	观察组($n=42$)	P 值
IABP使用时间(d)	6.5 ± 3.5	4.5 ± 2.5	0.032
CCU入住时间(d)	9.5 ± 4.5	7.5 ± 3.5	0.039
总住院时间(d)	13.5 ± 6.5	10.5 ± 5.5	0.028
急诊就诊(次)	2.2 ± 1.8	1.2 ± 0.8	0.042
再住院(次)	1.5 ± 1.6	0.8 ± 1.2	0.049
EQ-5D-3L评分(分)	11.5 ± 3.2	8.5 ± 2.6	0.038

AMI合并CS患者,可降低院内及随访30d患者血浆NT-proBNP水平,降低LVEDd,增加LVFS及LVEF值,明显降低CCU住院时间和IABP使用时间。本研究中2组患者随访30d心血管不良事件发生率比较,差异无统计学意义,但观察组主要心脏不良事件的发生率低于对照组。

IABP是目前临床最常用的机械辅助循环方法,其可增加冠脉灌注,显著降低心脏收缩时的左心室压力负荷,增强心肌收缩力,可有效改善心肌供血,增加心输出量,在AMI合并心力衰竭患者中效果显著^[4,5]。IABP-SHOCK II研究的结果影响了欧洲心脏病学会关于血运重建指南,AMI合并CS患者的IABP推荐级别进一步降低^[6],主要与欧美国家存在更好心室辅助装置有关,因此,IABP推荐仅限于伴有机械并发症的AMI患者^[7]。IABP-SHOCK II研究存在诸多不足:①患者病情相对较轻;入选者的中位血压值为90/55 mmHg,血压相对较高;入选患者左室射血分数较高,多为轻中度心源性休克;其中86%患者在PCI期间没有接受IABP的血流动力学辅助支持。②对照组10%的患者采用IABP交叉;③大部分患者在PCI术后使用IABP;1/3的患者为NSTMI;5%~40%的患者在术前进行心肺复苏。这些因素导致最终IABP在CS患者使用出现阴性结局。本研究对AMI合并CS患者应用IABP有显著效果,能够降低住院死亡风险,改善心功能,缩短CCU住院时间。

左西孟旦是一种新型钙增敏剂,在心力衰竭急性期可维持血流动力学稳定,除正性肌力作用外,还具有扩张血管、拮抗神经内分泌、抗炎、抗凋亡、抗心肌顿抑作用,这些均对心肌梗死合并心力衰竭有利^[8,9]。目前,左西孟旦已发展成为急性心力衰竭或其他心源性疾病需要使用强心药物时的理想选择,其中的原因主要基于左西孟旦在增加心肌收缩力的同时,不影响舒张功能,亦不会引起心肌耗氧量增加和交感神经激活^[10]。左西孟旦产生血管舒张作用,使得冠状动脉阻力血管和静脉容量血管舒张,从而改善冠状动脉的血流供应,降低心肌缺血再灌注损伤中心肌细胞凋亡^[11]。左西孟旦能够增加心脏收缩功能,改善心室-血管耦合,改善外周血管舒张,增加组织灌注^[12]。Jia等^[13]研究发现,左西孟旦可改善AMI合并心力衰竭患者的预后。本研究发现观察组患者的心力衰竭指标、炎症指标及肌钙蛋白均明显低于对照组,再次验证左西孟旦可改善患者临床预后。

本研究2组不良事件发生率无显著性差异。证实左西孟旦联合IABP治疗AMI合并CS安全有效。

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少,且为回顾性横断面研究,对于揭示 HP 感染与 NAFLD 的关系只能表明是否存在影响,不能完全反应因果关系。本研究中诊断 NAFLD 采用的是超声诊断,可能对于 NAFLD 的诊断率偏低。而 γ -GT、ALT、AST、FIB-4、NFS 等生化指标相对肝穿刺活检,不能完全反应肝脏炎症及纤维化程度。

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