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左西孟旦对急性心衰患者心功能及 cTnT, hs-CRP, NT-proBNP 水平影响

宜海杰¹ 韩秀平² 丁国平¹ 姚翠娥³ 王 莉³

(1 延安大学附属医院急诊内科 陕西 延安 716000; 2 延安大学附属医院综合内科 陕西 延安 716000;

3 西京医院急诊科 陕西 西安 710032)

摘要 目的:观察左西孟旦对急性心力衰竭患者心功能及 cTnT、hs-CRP、NT-proBNP 水平影响。**方法:**选取在我院就诊的 327 例急性心力衰竭患者,按照治疗方式不同,分为观察组(常规治疗+左西孟旦)164 例和对照组(常规治疗)163 例,对比两组用药前及用药后 24 h 的左心射血分数(LVEF)、每搏输出量(SV)、肌钙蛋白 T(cTnT)、超敏 C 反应蛋白(hs-CRP)和氨基末端 B 型利钠肽前体(NT-proBNP)水平。**结果:**治疗前,两组 LVEF 和 SV 比较,差异无统计学意义($P>0.05$)。治疗后观察组 LVEF 和 SV 均显著高于治疗前($P<0.05$);对照组 LVEF 显著高于治疗前($P<0.05$),SV 与治疗前比较,差异无统计学意义($P>0.05$)。治疗后观察组 LVEF 和 SV 均显著高于对照组($P<0.05$)。治疗前两组 cTnT、hs-CRP、NT-proBNP 水平比较,差异无统计学意义($P>0.05$)。治疗后两组 cTnT、hs-CRP、NT-proBNP 水平均显著低于治疗前($P<0.05$)。治疗后观察组 cTnT、hs-CRP、NT-proBNP 水平显著低于对照组($P<0.05$)。两组不良反应比较差异无统计学意义($P>0.05$)。**结论:**左西孟旦治疗急性心力衰竭可明显增加心肌收缩力,抑制心肌重塑,减轻炎症反应,改善患者预后。

关键词:急性心力衰竭;左西孟旦;cTnT;hs-CRP;NT-proBNP

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Effect of Levosimendan on Cardiac Function and cTnT, hs-CRP and NT-proBNP Levels in Patients with Acute Heart Failure

YI Hai-jie¹, HAN Xiu-ping², DING Guo-ping¹, YAO Cui-e³, WANG Li³

(1 Emergency department, affiliated hospital of Yan'an University, Yan'an, Shaanxi, 716000, China; 2 Department of general internal medicine, affiliated hospital of Yan'an University, Yan'an, Shaanxi, 716000, China; 3 Emergency department, Xijing hospital, Xi'an, Shaanxi, 710032, China)

ABSTRACT Objective: To observe the effect of levosimendan on cardiac function and cTnT, hs-CRP and NT-proBNP levels in patients with acute heart failure. **Methods:** 327 cases of patients with acute heart failure in our hospital were selected in accordance with the different treatment modalities, 163 patients in the control group were given routine treatment and 164 cases in the observation group were given conventional treatment combined with levosimendan. The left heart shot ejection fraction (LVEF), stroke volume (SV), cardiac troponin T (cTnT) and ultra sensitive C reactive protein (hs CRP) and N-terminal pro-B-type natriuretic peptide (NT proBNP) level were detected before treatment and 24 h after treatment and compared between two groups. **Results:** There was no significant difference in LVEF and SV before treatment between the two groups ($P>0.05$). After treatment, LVEF and SV level were significantly higher than before treatment in the observation group, ($P<0.05$); and the LVEF level in control group was significantly higher than before treatment ($P<0.05$), but SV level was not statistically significant compared with before treatment ($P>0.05$). After treatment, the LVEF and SV level were significantly higher observation group than that of control group ($P<0.05$). The difference in the level of cTnT, hs-CRP, NT-proBNP was not statistically significant before treatment ($P>0.05$), and after treatment, the levels of cTnT, hs-CRP and NT-proBNP were significantly lower compared with before treatment ($P<0.05$), and they were significantly lower in the observation group than those of the control group ($P<0.05$). No significant differences in the rate of adverse reactions between the two groups ($P>0.05$). **Conclusions:** Levosimendan can significantly increase myocardial contractility, inhibit myocardial remodeling, reduce the inflammation and improve the prognosis of patients with acute heart failure.

Key words: Acute heart failure; Levosimendan; cTnT; hs-CRP; NT-proBNP

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前言

作者简介:宜海杰(1981-),男,本科,主治医师,研究方向:急诊内科学,电话:15891417171, E-mail: yihaijie_7171@sina.com
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急性心力衰竭是指由于各种原因引起的心脏结构或功能的异常,导致心脏泵血功能急剧下降,从而引起全身组织器官严重的灌注不足和急性淤血的一组临床综合征^[1]。急性心力衰竭再次住院率和死亡率均高于慢性心力衰竭^[2]。治疗心力衰竭

的传统药物存在很多问题^[9]。左西孟旦为钙离子增敏剂,是一种正性肌力药物,其通过直接与肌钙蛋白相结合,增加心肌收缩力^[10]。另外左西孟旦的扩血管效应可通过腺嘌呤核苷三磷酸(ATP)所敏感的K⁺通道而发挥作用^[9]。本研究通过观察左西孟旦对急性心力衰竭患者心功能及心肌肌钙蛋白T(cTnT)、超敏C-反应蛋白(hs-CRP)、N端前脑钠肽(NT-proBNP)水平影响,进一步探讨左西孟旦对急性心力衰竭患者临床应用疗效。

1 资料与方法

1.1 一般资料

选取在我院就诊的327例急性心力衰竭患者,按照治疗方式不同,分为观察组(常规治疗+左西孟旦)164例和对照组(常规治疗)163例。其中观察组男性90例,女性74例,年龄34~72岁,平均年龄(57.26±5.34)岁,对照组男性88例,女性75例,年龄36~75岁,平均年龄(56.27±6.21)岁。两组一般资料比较差异无统计学意义(P>0.05),具有可比性。

1.2 纳入标准

①NYHA心功能分级III-IV级,确诊为急性心力衰竭的患者;②超声心动图提示LVEF<40%;③无低血压(血压<90/60 mmHg或出现心源性休克)危险患者;④患者及其家属签署知情同意书,并经医院伦理委员会通过。

1.3 排除标准

①有急性脑血管病者;②对左西孟旦过敏者;③严重感染、风湿热、妊娠者;④有严重内分泌系统疾病、结缔组织疾病、恶性肿瘤等;⑤严重的肝肾功能不全者。

1.4 治疗方法

对照组:所有患者入院后均给予心电血压监护、休息、血氧饱和度监测,常规抗心力衰竭药物治疗。

观察组:在对照组基础上给予首次静脉注射6 μg/kg左西孟旦,维持量0.1 μg/kg/min,根据患者耐受情况,1 h后增加剂量到0.2 μg/kg/min,持续静脉泵入24 h。

1.5 观察指标与测定方法

观察指标:左心射血分数(LVEF)、每搏输出量(SV)、肌钙蛋白T(cTnT)、超敏C反应蛋白(hs-CRP)和氨基末端B型利钠肽前体(NT-proBNP)。

cTnT、hs-CRP、NT-proBNP水平的测定:患者入院后立即及治疗24 h后,肘静脉采血3 mL,全自动生化分析仪测定。

LVEF、SV的测定:采用彩色多普勒超声仪,所有患者均由同一位医师操作。

1.6 统计学方法

采用SPSS 18.0统计软件进行数据分析,计数资料以百分比表示,采用χ²检验,计量资料采用($\bar{x} \pm s$)表示,组间比较采用t检验,以P<0.05为差异具有统计学意义。

2 结果

2.1 两组治疗前后心功能改善情况比较

治疗前,两组LVEF和SV比较,差异无统计学意义(P>0.05)。治疗后观察组LVEF和SV均显著高于治疗前(P<0.05);对照组LVEF显著高于治疗前(P<0.05),SV与治疗前比较,差异无统计学意义(P>0.05)。治疗后观察组LVEF和SV均显著高于对照组(P<0.05)。

表1 两组治疗前后心功能改善情况比较

Table 1 Comparison of the improvement of cardiac function before and after treatment in two groups

Time	Observation group(n=164)		Control group(n=163)	
	LVEF(%)	SV(mL)	LVEF(%)	SV(mL)
Before treatment	29.12±8.11	58.51±15.94	28.78±7.98	62.44±18.44
After treatment	40.94±8.98* [#]	68.98±15.95* [#]	35.12±7.93*	62.21±17.68

Note: Compared with before treatment, *P<0.05; compared with the control group, [#]P<0.05.

2.2 两组治疗前后cTnT、hs-CRP、NT-proBNP水平变化比较

治疗前两组cTnT、hs-CRP、NT-proBNP水平比较,差异无统计学意义(P>0.05)。治疗后两组cTnT、hs-CRP、NT-proBNP

水平均显著低于治疗前(P<0.05)。治疗后观察组cTnT、hs-CRP、NT-proBNP水平显著低于对照组(P<0.05)。

表2 两组治疗前后cTnT、hs-CRP、NT-proBNP水平变化比较

Table 2 Comparison of cTnT, hs-CRP and NT-proBNP levels in two groups before and after treatment

Groups	time	cTnT(pg/mL)	hs-CRP(mg/L)	NT-pro BNP(pg/mL)
Observation group(n=164)	before treatment	96.12±48.88	8.13±1.53	2542.29±276.76
	after treatment	70.41±45.11* [#]	4.21±1.38* [#]	1268.63±213.65* [#]
Control group(n=163)	before treatment	93.21±58.90	8.21±1.64	2433.31±265.73
	after treatment	85.89±44.32*	5.99±1.08*	1923.71±205.69*

Note: Compared with before treatment, *P<0.05; compared with the control group, [#]P<0.05.

2.3 不良反应

观察组患者出现低血钾7例,给予静脉补钾后血钾恢复;血压明显降低2例,调整左西孟旦至0.075 μg/kg/min后血压逐步回升;出现交界性心动过速5例,后自行缓解;头晕、视物

模糊1例,停药后缓解。对照组患者低血钾1例,血压降低1例,心动过速1例。观察组不良反应发生率(9.14%)与对照组(1.84%)比较,差异无统计学意义(P>0.05)。

表 3 两组不良反应比较

Table 3 Comparison of adverse reactions between the two groups

Group	Low blood potassium	Low blood pressure	Tachycardia.	Dizziness, blurred vision	Adverse reaction rate (%)
Observation group(n=164)	7	2	5	1	9.14
Control group(n=163)	1	1	1	0	1.84

3 讨论

急性心脏病变引起心排量急剧显著地降低会导致急性心力衰竭^[6]。炎症反应是急性心力衰竭发生发展的一个重要环节,炎症细胞因子启动和参与心衰的过程主要通过介导心肌细胞的重塑、诱导心肌细胞的凋亡和抑制心肌细胞的收缩力等实现^[7]。hs-CRP 和 NT-pro BNP 越来越受到人们的重视其主要与心功能受损密切相关^[8,9]。hs-CRP 是急性炎症反应的标记物,hs-CRP 水平的升高与心血管的危险性和心肌细胞损伤的发展密切相关^[10]。NT-proBNP 是由心肌细胞合成的具有生物学活性的天然激素,主要在心室表达,在心室扩张及容量负荷过重时分泌增加,因其半衰期较 BNP 长,在临床诊断与应用中更广泛^[11]。可作为早期心功能损害的标志物,是判断心衰的重要指标^[12]。血清 cTnT 是反映心脏损伤的高敏感性、高特异性标志物,主要应用于诊断急性心肌缺血损伤,估计心肌损伤面积,判断心肌损伤程度,当心肌受到缺血、缺氧、氧自由基损伤、机械损伤等均可出现肌纤维溶解,甚至坏死,最终出现心室重塑,故心衰患者可因心肌损伤导致血清 cTnT 浓度增高^[13]。本研究中治疗前两组 cTnT、hs-CRP、NT-proBNP 水平比较,差异无统计学意义($P>0.05$)。治疗后两组 cTnT、hs-CRP、NT-proBNP 水平均显著低于治疗前 ($P<0.05$)。治疗后观察组 cTnT、hs-CRP、NT-proBNP 水平显著低于对照组($P<0.05$)。说明左西孟旦有抗炎及抑制心肌重构的作用。

治疗急性心力衰竭主要以控制基础病因和矫治引起心衰的诱因,稳定血流动力学状态,缓解症状为主^[14]。药物治疗的主要目的是降低心脏前后负荷、改善肺淤血,常用的药物包括扩张血管药物和利尿剂,但是其存在心输出量下降、神经内分泌系统和电解质紊乱甚至产生耐药性的缺陷^[15]。左西孟旦是一种钙离子增敏剂,属于正性肌力药物。与传统正性肌力药物相比,具有不增加细胞内 Ca^{2+} 浓度,不引起心肌钙超载和耗氧量增加,不影响心室舒张功能,不易导致恶性心律失常等优点^[16]。越来越多的应用于心衰的治疗。其主要是通过和肌钙蛋白 C (TnC)结合,增加 TnC 与 Ca^{2+} 复合物的构象稳定性,促进横桥与细肌丝的结合,增强心肌收缩力,有抑制心肌重构、抗细胞凋亡、抗炎以及抗氧化等作用^[17]。左西孟旦在增加心排量的同时,不增加交感神经的兴奋性^[18]。本研究中治疗前,两组 LVEF 和 SV 比较,差异无统计学意义($P>0.05$)。治疗后观察组 LVEF 和 SV 均显著高于治疗前($P<0.05$);对照组 LVEF 显著高于治疗前($P<0.05$),SV 与治疗前比较,差异无统计学意义($P>0.05$)。治疗后观察组 LVEF 和 SV 均显著高于对照组($P<0.05$)。表明左西孟旦对心功能的恢复具有较好的疗效,这和之前的研究结果也是一致的^[19]。左西孟旦常见的不良反应为低血压、低血钾以及室性心律失常等。本研究中两组不良反应比较差异无统计

学意义($P>0.05$)。表明左西孟旦具有良好的用药安全性。但也有报道建议应用左西孟旦治疗心衰连续不宜超过 24 h^[20],本研究并未进行长期的随访观察,我们的研究显示左西孟旦应用短期有效,而长期疗效以及药物效果维持时间,需要进行进一步随访观察。

综上所述,左西孟旦治疗急性心力衰竭可明显增加心肌收缩力,抑制心肌重塑,减轻炎症反应,改善患者预后,值得临床推广。

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