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重组脑钠肽对急性失代偿性心力衰竭患者炎症因子及肾素系统的影响*

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摘要 目的:探讨重组脑钠肽对急性失代偿性心力衰竭患者炎症因子及肾素系统的影响。**方法:**选择 2014 年 7 月~2016 年 7 月于我院就诊的急性失代偿性心力衰竭患者 160 例,80 例对照组行硝普钠治疗,80 例实验组行重组脑钠肽治疗,观察两组治疗前后肿瘤坏死因子- α (TNF- α)、超敏 C 反应蛋白(hs-CRP)、白细胞介素-6(IL-6)、脑钠肽(BNP)、醛固酮、血管紧张素 II、血浆肾素活性,血流动力学变化及心功能情况。**结果:**治疗前,实验组 TNF- α 、hs-CRP、IL-6、BNP 低于对照组,差异有统计学意义($P<0.05$)。实验组醛固酮、血管紧张素 II、血浆肾素活性低于对照组,差异有统计学意义($P<0.05$)。实验组血流动力学低于对照组($P<0.05$)。实验组心功能较对照组改善更明显($P<0.05$);实验组副反应少于对照组($P<0.05$)。**结论:**急性失代偿性心力衰竭患者应用重组脑钠肽治疗可降低患者炎症因子,改善肾素系统。

关键词:急性失代偿性心力衰竭;重组脑钠肽;炎症因子;肾素系统

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Effects of Recombinant Brain Natriuretic Peptide on Inflammatory Factors and Renin System in Patients with Acute Decompensated Heart Failure*

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ABSTRACT Objective: To research the effects of recombinant brain natriuretic peptide on inflammatory factors and renin system in patients with acute decompensated heart failure. **Methods:** 160 patients with acute decompensated heart failure who were treated in our hospital from July 2014 to July 2016 were selected and randomly divided into two groups, with 80 cases in each group. The patients in the control group were treated with sodium nitroprusside, while the patients in the experimental group were treated with recombinant brain natriuretic peptide. Then the serum levels of tumor necrosis factor alpha (TNF- α), hypersensitive c-reactive protein (hs-CRP), interleukin-6 (IL-6), brain natriuretic peptide (BNP), aldosterone, aldosterone II, plasma renin activity, hemodynamics and heart functions of patients between the two groups were observed and compared before and after the treatment. **Results:** After treatment, the serum levels of TNF- α , hs-CRP, IL-6 and BNP of the experimental group were lower than those of the control group, and the differences were statistically significant ($P<0.05$); After treatment, the levels of the aldosterone, aldosterone II and plasma renin activity of the experimental group were lower than those of the control group, and the differences were statistically significant ($P<0.05$); After treatment, the hemodynamics of the experimental group was lower than that of the control group, and the difference was statistically significant ($P<0.05$). The improvement of heart function of the experimental group was more obvious than that of the control group ($P<0.05$). The incidence of complications in the experimental group was lower than that of the control group ($P<0.05$). **Conclusions:** Recombinant brain natriuretic peptide has better clinical efficacy on the treatment of the acute decompensated heart failure, which can reduce the serum levels of the inflammatory factors, and improve the renin-angiotensin-aldosterone system.

Key words: Acute decompensated heart failure; Recombinant brain natriuretic peptide; Inflammatory factor; Renin system

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前言

急性心力衰竭是一种心力衰竭加重或者急性发作的临床综合征,且急性失代偿期是其严重阶段,可导致患者住院病死率增加^[1]。有报道发现,炎症因子能够促进心室重构,从而造成心力衰竭加剧^[2]。相关研究指出,急性失代偿性心力衰竭能够导

常激活内分泌系统,诱导肾素系统的异常表达,形成一种恶性循环,导致心力衰竭进一步加重^[3,4]。目前临床多采用扩血管、强心、利尿等对症治疗,但其抗心衰效果并不理想^[5]。重组脑钠肽是一种人工多肽,存在扩血管、利钠、抗纤维化等药物功效,现已逐步开展于心血管疾病治疗^[6]。本研究就急性失代偿性心力衰竭患者使用重组脑钠肽治疗对炎症因子及肾素系统的影响

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进行回顾性分析,现报告如下。

1 资料与方法

1.1 一般资料

选择 2014 年 7 月~2016 年 7 月于我院就诊的急性失代偿性心力衰竭患者,纳入标准:与急性失代偿性心力衰竭诊断标准相符^[7],且经临床表现、心电图等检查明确诊断;左室射血分数在 45%以下,且左室舒张末内径在 60 mm 以上;NAHA 心功能分级在 III~IV 级;发病至入院时间在 6 h 以内。排除标准:肝肾功能严重不全、急性感染或者创伤、自身免疫系统疾病、恶性肿瘤;心源性休克、瓣膜明显狭窄。对照组 44 例男性,36 例女性;年龄 45~72 岁,平均(65.41±1.18)岁;发病至入院时间 1~6 h,平均(2.54±0.38)h;基础病因:46 例缺血性心脏病,22 例高血压性心脏病,12 例扩张性心肌病。实验组 41 例男性,39 例女性;年龄 42~70 岁,平均(64.11±1.43)岁;发病至入院时间 1~6 h,平均(2.47±0.31)h;基础病因:42 例缺血性心脏病,26 例高血压性心脏病,12 例扩张性心肌病。比较两组基本资料无差异(P>0.05),有可比性。

1.2 方法

对照组行硝普钠治疗,起始予以患者 10 μg/mL 硝普钠静脉泵入,按照患者的心力衰竭及血压等缓解情况每 5~10 min 以 5 μg 增加用药剂量,直至血压、心率等达到临床效应。实验组行重组脑钠肽治疗,以 1.5 μg/kg 作为负荷剂量,予以患者静脉推注,再以 0.01 μg/kg·min 予以患者持续静脉泵入。两组均持续用药 48 h,同时予以 β 受体阻滞剂、利尿剂、洋地黄药物、血管紧张素 II 受体拮抗剂等基础治疗,并指导患者合理饮食。

1.3 观察指标

于治疗前及治疗结束时采集患者外周静脉血 2 mL,常规离心后,收集血清及血浆于 -80℃ 环境中待检。炎症因子包含 TNF-α;肿瘤坏死因子-α;hs-CRP;超敏 C 反应蛋白、IL-6;白细胞介素-6;BNP;脑钠肽使用放射比浊法检测,试剂盒分别由广州欧化药业有限公司、南昌市飞弘药业有限公司、甘肃定西扶正制药有限公司、云南南诏药业有限公司海口康力元制药有限公司提供。肾素系统:血管紧张素 II 及醛固酮使用酶联免疫双抗体夹心法检测,试剂盒分别由湖南正驰药业有限公司、甘肃益尔药业股份有限公司提供,以血管紧张素 I 的产生速率间接表示血浆肾素活性,试剂盒由上海安都制药有限公司提供。于用药期间置入 Swan-Ganz 漂浮导管监测血流动力学,包含肺毛细血管楔压、右心房压、中心静脉压。使用超声诊断系统评估患者左心功能,包含左室射血分数(LVEF)及左室舒张末内径(LVEDD)。观察两组用药期间的副反应,并详细记录。

1.4 统计学分析

选择 SPSS18.0 行数据统计,计量资料用均数±标准差($\bar{x} \pm s$)表示,用 t 检验比较,计数资料用[n(%)]表示,用 χ^2 检验比较,等级资料用秩和检验,P<0.05 有统计学意义。

2 结果

2.1 治疗前后两组患者炎症因子水平比较

治疗前,两组患者 TNF-α、hs-CRP、IL-6、BNP 水平比较,差异无统计学意义(P>0.05);治疗后,两组患者 TNF-α、hs-CRP、IL-6、BNP 均降低,组内比较差异明显(P<0.05),且实验组低于对照组,组间比较有统计学意义(P<0.05),见表 1。

表 1 治疗前后两组患者炎症因子水平比较($\bar{x} \pm s$)

Table 1 Comparison of levels of inflammatory factors between the two groups before and after the treatment

Groups	Time	TNF-α (ng/L)	hs-CRP (mg/L)	IL-6 (ng/L)	BNP (ng/L)
Control group (n=80)	Before treatment	6.87±1.84	7.32±2.17	89.62±12.70	2647.41±542.1
	After treatment	5.25±1.12 ^a	3.89±0.8 ^a	56.73±9.14 ^a	1682.65±511.4 ^a
Experimental group (n=80)	Before treatment	7.11±1.65	7.69±2.01	86.41±12.20	2643.91±568.42
	After treatment	4.93±0.85 ^{ab}	1.83±0.30 ^{ab}	43.69±8.51 ^{ab}	1240.69±405.2 ^{ab}

Note: compared with before treatment, ^aP<0.05; compared with control group after treatment, ^bP<0.05.

2.2 治疗前后两组患者肾素系统指标比较

治疗前,比较两组血管紧张素 II、醛固酮、肾素活性无统计学意义(P>0.05);治疗后,两组醛固酮、血浆肾素活性均降低,

组内比较有统计学意义(P<0.05),且实验组低于对照组,组间比较差异显著(P<0.05);两组血管紧张素 II 均上升,且实验组上升幅度更小,组间比较有统计学意义(P<0.05)。见表 2。

表 2 治疗前后两组患者肾素系统指标比较($\bar{x} \pm s$)

Table 2 Comparison of the renin-angiotensin-aldosterone system between two groups before and after the treatment

Groups	Time	Aldosterone (ng/L)	Angiotensin II (ng/L)	Plasma renin activity (ng/mL·H)
Control group (n=80)	Before treatment	170.81±39.27	82.20±15.69	4.39±1.15
	After treatment	67.94±18.42 ^a	114.60±19.20 ^a	1.36±0.35 ^a
Experimental group (n=80)	Before treatment	173.60±38.15	80.12±14.36	4.12±1.09
	After treatment	55.63±13.74 ^{ab}	105.60±17.93 ^{ab}	1.10±0.28 ^{ab}

Note: compared with before treatment, ^aP<0.05; compared with control group after treatment, ^bP<0.05.

2.3 治疗前后两组患者血流动力学比较

治疗前,比较两组血流动力学无统计学意义(P>0.05);治

疗后,两组血流动力学均降低,组内比较差异有统计学意义(见附表3)。
($P<0.05$),且实验组低于对照组,差异有统计学意义($P<0.05$),

表3 治疗前后两组患者血流动力学比较($\bar{x}\pm s$)
Table 3 Comparison of hemodynamics between two groups before and after the treatment

Groups	Time	Pulmonary capillary wedge pressure (mmHg)	Right atrial pressure (ng/L)	Central venous pressure (ng/mL·H)
Control group (n=80)	Before treatment	50.11± 7.21	147.89± 24.50	146.53± 25.80
	After treatment	36.85± 6.50 ^a	11.87± 1.70 ^a	12.84± 1.90 ^a
Experimental group (n=80)	Before treatment	52.87± 7.45	143.26± 24.10	144.76± 24.62
	After treatment	30.29± 5.36 ^{ab}	9.83± 1.68 ^{ab}	9.72± 1.60 ^{ab}

Note: compared with before treatment, ^a $P<0.05$; compared with control group after treatment, ^b $P<0.05$.

2.4 治疗前后两组患者心功能比较

治疗前,比较两组心功能无统计学意义($P>0.05$);治疗后,两组 LVEF 均上升,组内比较有统计学意义($P<0.05$),且实验

组高于对照组,组间比较有统计学意义($P<0.05$);两组 LVEDD 无改变,组内、组间比较均无统计学意义($P>0.05$)。见表4。

表4 治疗前后两组患者心功能比较($\bar{x}\pm s$)
Table 4 Comparison of cardiac function between two groups before and after the treatment

Groups	Time	LVEF (%)	LVEDD (mm)
Control group (n=80)	Before treatment	34.96± 6.10	64.47± 3.25
	After treatment	38.85± 6.54 ^a	63.75± 3.62
Experimental group (n=80)	Before treatment	33.56± 6.45	65.20± 3.60
	After treatment	42.50± 7.18 ^{ab}	64.21± 3.40

Note: compared with before treatment, ^a $P<0.05$; Compared with control group after treatment, ^b $P<0.05$.

2.5 两组患者副反应比较

对照组有12例胃肠道反应,4例低血压,不良反应发生率20.00%(16/80);实验组5例低血压,不良反应发生率6.25%(5/80);比较有统计学意义($\chi^2=6.6324, P=0.010$)。

3 讨论

急性失代偿性心力衰竭因心脏泵功能异常能够激活系列细胞及神经体液因子,其中肾素系统的异常激活是发病机制的主要因素,能够导致血管平滑肌出现收缩,增加阻力,使心室负荷加重,造成心血管系统对去甲肾上腺素的敏感性增强,利于醛固酮的分泌,导致心力衰竭出现恶化^[8,9]。内源性BNP是一种多肽,由心室及心房分泌,其中左心室是其主要分泌场所,能够起到扩张血管、减少水钠潴留、促进利尿排泄、抑制交感神经活性、拮抗肾素等作用,也能够介导心室的压力负荷及收缩功能,其分泌增加是机体心功能不全时的一种代偿机制^[10,11]。当机体发生急性失代偿性心力衰竭时能够减低其对BNP的敏感性,因此对神经激素无法起到拮抗作用。重组脑钠肽是一种具有活性的人工合成肽,是抗心衰的新型药物。诺普钠是临床上治疗心力衰竭的常用药物,对心衰有一定的改善作用^[12]。

近年来研究表明,心力衰竭和炎症反应联系紧密,TNF- α 、hs-CRP等炎症因子能够介导机体的炎症反应,从而对其他细胞因子造成影响,诱导心肌肥厚、心功能不全等^[13,14]。IL-6可由

多种活性细胞合成并分泌,是炎症反应中的主要介质,其可与心肌细胞的特定受体结合后形成复合物,起到细胞毒性及负性肌力的作用^[15]。有研究发现,重组脑钠肽能够使急性心肌梗死小鼠的炎症信号通路产生抑制,减轻缺血引起的再灌注损伤,提示重组脑钠肽能够起到抗炎作用^[16]。本研究显示,重组脑钠肽治疗后TNF- α 、hs-CRP、IL-6、BNP水平低于诺普钠治疗者,进一步证实重组脑钠肽能够降低炎症因子水平,进而减轻炎症反应对机体造成的损伤,延缓病情。本研究发现,急性失代偿性心力衰竭患者发病后血管紧张素II可有上升,但用药后可恢复至发病前水平,经重组脑钠肽治疗后血管紧张素II更低,且醛固酮和血浆肾素活性的改善均比较显著,表明重组脑钠肽对机体的肾素系统有良好的抑制作用,从而纠正机体的内分泌系统紊乱,缓解心力衰竭症状,可能与其能够导致外周交感神经受到抑制作用,使其神经兴奋性减弱,减少促肾上腺皮质激素及血管加压素的合成有关^[17]。

有研究指出,肾素系统的异常激活能够引起血流动力学变化,影响其稳定性,又进一步加剧内分泌系统紊乱,形成恶性循环^[18]。本研究显示,重组脑钠肽治疗后患者血流动力学显著降低,可能与其能够好血管内皮细胞和平滑肌受体作用,增加鸟苷酸环化酶的分泌,促进小动脉的扩张,减轻心脏负荷;其次能够增加肾小球对钠的吸收率,使钠排泄增强,从而起到利尿作用,导致外周体循环阻力减弱有关^[19]。有研究发现,重组脑钠肽

对急性失代偿性心力衰竭患者的心功能有改善作用。本研究显示经重组脑钠肽治疗后患者左室射血分数明显增高,但左心室收缩末期内径变化不明显,考虑与治疗前后对比时间较短,导致其变化不大^[20]。且经重组脑钠肽治疗后的副反应较少,安全性高,有较好的应用前景。

综上所述,急性失代偿性心力衰竭患者应用重组脑钠肽治疗可降低患者炎症因子,改善肾素系统。

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