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连续负荷量新活素治疗难治性心力衰竭患者的临床疗效观察

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摘要 目的：探讨连续负荷量新活素治疗难治性心力衰竭患者的临床疗效。**方法：**选取我院收治的65例难治性心力衰竭患者，随机分为两组。对照组在常规治疗的基础上加用硝酸甘油注射液，观察组在常规治疗的基础上加用新活素，比较两组的疗效，治疗前和治疗后24、36、48 h的肺动脉楔压(PAWP)、肺动脉压(PAP)、血清高敏C反应蛋白(hs-CRP)，脑利钠肽(BNP)水平的变化。**结果：**治疗后，观察组有效率为87.9%，显著高于对照组(65.6%，P<0.05)。两组患者治疗后24、36、48 h的PAWP和PAP降低值逐渐增加，且观察组PAWP和PAP降低值均显著高于对照组同时点(P<0.05)。两组治疗后24、36、48 h血清hs-CRP、BNP水平随着时间延长而逐渐下降(P<0.05)，观察组治疗后24、36、48 h的血清hs-CRP、BNP水平均低于对照组同时点(P<0.05)。**结论：**在基础治疗之上，给予连续负荷量新活素对于治疗难治性心力衰竭可提高治疗效果，减轻心脏前负荷，降低hs-CRP，BNP水平，改善心肌重构。

关键词：新活素；连续负荷量；难治性心力衰竭

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Effects of Continuous Loading Volume of New Living Factor on Patients with Refractory Heart Failure and Related Clinical Indicators

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ABSTRACT Objective: To investigate the clinical effects of continuous load volume new living factor on the refractory heart failure. **Methods:** 65 cases of patients with refractory heart failure patients were randomly divided into two groups. The control group was given conventional treatment and Nitroglycerin Injection, and the observation group was given new living factor with conventional treatment. The curative effect, changes of pulmonary artery wedge pressure (PAWP), pulmonary artery pressure (PAP), serum anti hs-CRP, brain natriuretic peptide (BNP) levels before treatment and at 24, 36, 48 h after treatment were compared between the two groups. **Results:** After treatment, the effective rate of observation group was 87.9%, which was higher than that of the control group (65.6%, P<0.05). The reduction value of PAWP and PAP levels of both groups were gradually increased at 24, 36, 48 h after treatment, which were significantly higher in the observation group than those of the control group at the same time points(P<0.05). At 24, 36, 48 h after treatment, the serum hs-CRP and BNP levels were decreased with the extension of treatment time (P<0.05), which were significantly lower in the observation group than those of the control group at the same time points (P<0.05). **Conclusion:** Based On the conventional treatment, continuous loading volume of new living factor can improve the therapeutic effect, and reduce cardiac preload, hs-CRP and BNP levels, improve the myocardial remodeling of patients with refractory heart failure.

Key words: New Live Hormone; Continuous Load; Refractory Heart Failure

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前言

心力衰竭是一种复杂的临床综合征，病程长，反复发作，发病率与患者年龄呈正相关。随着我国人口老龄化趋势加剧，心力衰竭患者数量也呈上升趋势[1-3]。这其中还包含了难治性心力衰竭患者，该类患者处于心力衰竭的终末阶段，具有治疗困难、病死率较高、医疗费用高昂等特点[2-6]。因此，积极治疗与预防难治性心力衰竭的发展具有重要的临床意义。传统治疗方式如正性肌力药物、硝酸甘油类药物效果有限[7-9]，不能较好地改善患者心肌收缩力，减轻心脏负荷。

新活素为重组人脑利钠肽，可以显著降低心脏前后负荷，增加心排出量，是理想的治疗药物。Hs-CRP和BNP均是心内科常用的用于心力衰竭的检测指标，两者可以较好地反映难治性心力衰竭的治疗效果。为了探究新活素与其他传统治疗方式联用的效果，本研究回顾性分析了65例来我院治疗的难治性心力衰竭患者的临床资料，现报道如下。

1 资料与方法

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1.1 病例资料

选取我院 2012 年 5 月 -2016 年 9 月收治的难治性心力衰竭患者 65 例，纳入标准：(1)符合欧洲心脏病学会的诊断标准[4]；(2)心功能在 3~4 级以上，左心室射血分数(LVEF)小于 25%；(3)通过休息、限钠、限水，给予利尿剂和强心剂治疗后，临床症状无明显缓解；(4)经本院伦理委员会批准，治疗前每位患者均签署书面知情同意书。排除标准：对新活素过敏，先天性心脏病，长期酗酒的患者。入院后随机分为两组，对照组(32 例)采用常规治疗方法联合硝酸甘油治疗，观察组(33 例)采用常规治疗方法联合新活素治。两组一般临床资料比较差异无统计学意义(P>0.05)，具有可比性，见表 1。

表 1 两组一般临床资料的对比

Table 1 Comparison of the baseline clinical information between two groups

Groups	n	Male/Female	Age	Course of Disease	Hypertension	Diabetes Mellitus	Coronary Disease	Heart Function	
								III	IV
Observationgroup	33	19/14	66.4± 14.2	12.4± 4.5	15	13	5	21	12
Control group	32	20/12	67.3± 15.4	11.3± 3.8	16	11	5	18	14

1.2 治疗方法

两组均常规给予抗心力衰竭治疗，由医师嘱咐患者注意多休息，少饮水，不要进行剧烈的活动，药物服用方面，选择利尿剂、β 受体阻滞剂、ACEI 药物进行抗心力衰竭治疗。观察组：常规治疗基础之上，给予新活素(成都诺迪康生物制药有限公司，规格：0.5 mg/ 500 U/ 瓶，批准文号：国药准字 S20050033)，负荷剂量 1.5 μg/kg，静脉注射，90 s 内注射完毕，然后以 0.01 μg·kg^{-1}·min^{-1} 的速度微量泵持续泵入 72 h。对照组：给予硝酸甘油(山东威高药业股份有限公司，规格：100 mL：硝酸甘油 10mg 与氯化钠 0.9g，批准文号：国药准字 H20052053)，静脉滴注，开始剂量 5 μg/min，根据病情每 10 min 增加 5μg/min，20 μg/min 为最大剂量。两组疗程均为 1 周。

1.3 观察指标

(1)疗效判定[5]：治疗 1 个疗程后进行疗效判定，显效：高度水肿、呼吸困难、四肢厥冷等症状基本消失，心功能改善程度大于Ⅱ级，有效：高度水肿、呼吸困难、四肢厥冷等症状减轻，心功能改善Ⅰ级；无效：症状无明显改善或恶化，心功能无变化或加重；(2)肺动脉楔压(PAWP)和肺动脉压(PAP)测定：床旁血流动力学监测，通过装满液体的管道将血管腔同外部压力换能器相连而测得，观察两组患者给药后 24、36、48 h 后的 PAWP 和 PAP 降低值；(3)血清 hs-CRP、BNP 水平检测：取患者外周静脉血，1000 r/min 离心 10 min，取上清液，-20 ℃冻存待测，全自动生化分析仪测定两组患者治疗前，治疗后 24、48、72 h 后的 hs-CRP、BNP 水平。

1.4 统计学分析

所有数据采用 SPSS 17.0 软件进行分析，计量资料以($\bar{x}$± s)表示，组间比较采用 t 检验，计数资料以%表示，组间比较采用 x^2 检验，以 P＜0.05 为差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后，观察组有效率为 87.9%，显著高于对照组(65.6%，P<0.05)，见表 2。

表 2 两组临床疗效的对比

Table 2 Comparison of the curative effect between two groups

Groups	n	Excellence	Availability	Invalid	Effective rate(%)
Observation group	33	21	8	4	87.9%
Control group	32	11	10	11	65.6%
P					0.033

2.2 两组治疗后不同时点血流动力学参数的对比

两组患者治疗后 24、36、48 h 的 PAWP 和 PAP 降低值逐渐增加，且观察组 PAWP 和 PAP 降低值均显著高于对照组同时点(P<0.05)，见表 3。

表 3 两组治疗后不同时点 PAWP 和 PAP 降低值的对比($\bar{x}$± s, mmHg)

Table 3 Comparison of the PAWP and PAP reduction at 24, 48,72h after treatment between the two groups($\bar{x}$± s, mmHg)

Groups	n	PAWP reductions			PAP reductions		
		At 24h after treatment	At 48h after treatment	At 72h after treatment	At 24h after treatment	At 48h after treatment	At 72h after treatment
Observation group	33	5.2± 2.4	6.4± 2.2	7.6± 3.1	6.4± 1.5	7.4± 2.1	8.2± 2.7
Control group	32	1.3± 0.4	2.3± 0.5	3.2± 0.7	3.5± 0.7	4.3± 1.6	5.7± 2.4
P		0.004	0.004	0.003	0.008	0.007	0.006

2.3 两组治疗后不同时点血清 hs-CRP 水平的对比

治疗前，两组血清 hs-CRP 水平相比差异无明显统计学意义(P>0.05)。治疗后 24、36、48 h，两组血清 hs-CRP 水平随着时间延长而逐渐下降(P<0.05)。观察组治疗后 24、36、48 h 的血清 hs-CRP 水平均低于对照组同时点(P<0.05)，见表 4。

表 4 两组治疗前和治疗后不同时点血清 hs-CRP 水平的比较 ($\bar{x}\pm$ s, mg/L)

Table 4 Comparison of the serum hs-CRP level between the two groups before treatment and at different time points after treatment($\bar{x}\pm$ s, mg/L)

Groups	n	Hs-CRP			
		Before treatment	At 24h after treatment	At 48h after treatment	At 72h after treatment
Observation	33	23.61± 8.53	21.17± 7.48*	14.64± 5.67*	8.46± 1.35*
Control	32	24.75± 8.27	23.52± 7.51	18.39± 6.35	16.45± 4.21
P			0.032	0.030	0.001

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

2.4 两组治疗后不同时点血清 BNP 水平的对比

治疗前，两组血清 BNP 水平相比差异无明显统计学意义(P>0.05)。治疗后 24、36、48 h，两组血清 BNP 水平随着时间延长而逐渐下降(P<0.05)。观察组治疗后 24、36、48 h 的血清 BNP 水平均低于对照组同时点(P<0.05)，见表 5。

表 5 两组治疗前和治疗后不同时点血清 BNP 水平的比较 ($\bar{x}\pm$ s, ng/L)

Table 5 Comparison of the serum BNP level between the two groups before treatment and at different time points after treatment ($\bar{x}\pm$ s, ng/L)

Groups	n	BNP			
		Before treatment	At 24h after treatment	At 48h after treatment	At 72h after treatment
Observation	33	722.7± 65.8	545.2± 48.3*	474.6± 42.3*	303.9± 32.6*
Control	32	719.8± 67.1	606.4± 53.9	548.7± 54.8	419.3± 42.7
P			0.000	0.000	0.000

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

3 讨论

心力衰竭是一种复杂的临床综合征，一般为各种心脏病发展的终末阶段。在我国的患病率约为 0.9%，男性患者发病率高于女性患者，而 65 岁以上人群的患病率高达 10%[6-8]。心力衰竭基本病因为心肌收缩、舒张功能障碍、心脏负荷过重引起，临床表现有三个较为明显的特征：劳累性呼吸困难，体液潴留，易感疲劳。心力衰竭是一种进展性疾病，很多慢性心力衰竭患者经过积极的药物治疗，仍然无法改善症状，最终发展成为难治性终末期心衰，这个阶段的心力衰竭具有死亡率高、发病率高、住院率高、医疗费用高，被称为难治性心力衰竭[10-13]。

对于难治性心力衰竭，临床一般提倡综合性治疗方法。首先，需要明确难治性心力衰竭的发病机制，导致心衰进展的两个关键过程，一为心肌收缩力下降，使心排血量下降，血流灌注量不足，不能满足机体的生理需要；二是神经内分泌系统过度激活导致，这里主要指的是交感神经系统及肾素 - 血管紧张素 - 醛固酮系统的激活[14]。以上两种系统能通过细胞因子的激活，使心肌发生重构，加重心衰。因此，切断这两个关键过程是心衰有效预防和治疗的基础[15]。脑利钠肽(BNP)是广泛存在于心肌细胞中的内源性活性因子，具有拮抗神经内分泌、抗心脏重塑的作用。心脏功能受损时，随心室容量扩增及压力负荷反应而分泌增加，起代偿性的心脏保护作用[14-16]，临床也常用此指标来检测心肌受损情况[17-20]。新活素是一种新型抗心力衰竭的治疗药物，结构与 BNP 相似，具有相同的作用机制[23-25]，临床采用连续负荷量的给药方式可起到如下效果：(1) 松弛血管平滑肌，扩张外周动静脉血管，降低血管阻力[26-28]；(2)提高肾小球滤过率，增强钠的排泄，产生明显的利尿作用，从而降低体循环阻力，减低心室的后负荷；(3) 阻断交感神经系统及肾素 - 血管紧张素 - 醛固酮系统兴奋，减少心肌耗氧量，改善心肌重构。与传统治疗心力衰竭的药物，如正性肌力药物，硝酸甘油类相比，在药代动力学方面具有较强的优势，药物半衰期短，2~15 min 起效，无肝首过效应，生物利用度较高，肝肾功能不全的患者也可使用[29-30]。

本研究中，采用传统治疗方法治疗的难治性心力衰竭患者疗效不如传统治疗方法加新活素治疗的患者，说明连续负荷量新活素能有效提高对难治性心力衰竭的治疗效果。PAP 和 PAWP 能反映左房舒张压或左室充盈压，即左心前负荷。新活素治疗的患者治疗后 24、36、48 h 肺动脉楔压(PAWP)和肺动脉压(PAP)降低值均明显高于同时点对照组。PAWP 和 PAP 的降低说明新活素给药后起效迅速，在较短时间内就能降低心脏前负荷，减少体循环阻力。hs-CRP 因其能和肺炎双球菌的细胞壁的 C 多糖起沉淀反应而得名，为肝脏合成的敏感急性炎症时相蛋白，hs-CRP 分泌与心肌受损程度呈正相关，对心力衰竭患者早期诊断和预后判断具有重要的价值。新活素治疗的患者在治疗后 24、36、48 h 血清 hs-CRP 和 BNP 水平显著下降，说明连续负荷量静脉滴注新活素，可以较好地控制病情，且随着治疗时间的延长，逐步稳定病情，使心肌受损情况得到改善。

总之，在基础治疗之上，给予连续负荷量新活素对于治疗难治性心力衰竭可提高治疗效果，减轻心脏前负荷，降低

hs-CRP，BNP 水平，改善心肌重构。

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