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沙库巴曲缬沙坦联合呋塞米治疗慢性心力衰竭的疗效研究*

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摘要 目的:探究沙库巴曲缬沙坦联合呋塞米治疗慢性心力衰竭的临床疗效。**方法:**选择2017年1月-2018年12月于我院诊治的慢性心力衰竭患者60例,随机将其分为两组。其中,对照组给予呋塞米进行治疗,研究组在对照组基础上联合沙库巴曲缬沙坦进行治疗,对比两组患者的治疗总有效率、治疗前后心功能、血清N端B型脑钠肽(NT-proBNP)、醛固酮(ALD)、细胞间黏附分子-1(ICAM-1)水平的变化及不良反应的发生情况。**结果:**治疗后,研究组患者的治疗总有效率[96.7%(29/30)]显著高于对照组[80.0%(24/30)]($P<0.05$)。两组患者治疗后的左心室射血分数(LVEF)均较治疗前显著升高,左心室舒张末期内径(LVEDD)、左心室收缩末期内径(LVESD)均较治疗前明显降低($P<0.05$),且研究组LVEF显著高于对照组,而LVEDD和LVESD明显低于对照组($P<0.05$);两组患者治疗后的血清NT-proBNP、ALD、ICAM-1水平均较治疗前显著降低($P<0.05$),且研究组以上指标均显著低于对照组低($P<0.05$)。对照组患者不良反应发生率[10.0%(3/30)]与研究组[13.3%(4/30)]比较无显著性差异($P>0.05$)。**结论:**沙库巴曲缬沙坦联合呋塞米治疗慢性心力衰竭的效果显著优于单用呋塞米治疗,其可有效改善患者的心功能且安全性较高,可能与其明显改善患者血清NT-proBNP、ALD、ICAM-1水平有关。

关键词:沙库巴曲缬沙坦;呋塞米;慢性心力衰竭;心功能

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Efficacy of Shakuba Valsartan Combined with Furosemide in the Treatment of Chronic Heart Failure*

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ABSTRACT Objective: To investigate the clinical effect of shakuba Valsartan combined with furosemide in the treatment of chronic heart failure. **Methods:** 60 patients with chronic heart failure who were treated in our hospital from January 2017 to February 2018 were randomly divided into two groups. Among them, the control group was treated with furosemide, and the study group was treated with shakuba valsartan on the basis of the control group. The total effective rate, the changes of cardiac function, serum NT-proBNP, ALD and ICAM-1 levels, and incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate in the study group was [96.7%(29/30)], which was significantly higher than that in the control group [80.0%(24/30)] ($P<0.05$). The LVEF levels of the twoboth groups were increased after treatment, while the LVEDD and LVESD were decreased ($P<0.05$), and LVEF was significantly higher in the study group than in the control group, while LVEDD and LVESD were significantly lower in the study group than in the control group ($P<0.05$). The serum levels of NT-proBNP, ALD and ICAM-1 in the two groups after treatment were significantly lower than those before treatment ($P<0.05$), and the above indexes in the study group were significantly lower than those in the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the control group [10.0%(3/30)] and the study group [13.3%(4/30)] ($P>0.05$). **Conclusion:** The effect of saponin and fluoxetine combined with furosemide in the treatment of chronic heart failure is significantly better than that of furosemide alone. This method can effectively improve the heart function of patients and have high safety. It may be related to significantly improve the patient's serum NT-proBNP, ALD, ICAM-1 levels.

Key words: Shakuba valsartan; Furosemide; Chronic heart failure; Cardiac function

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前言

心力衰竭是指机体心脏的舒张及(或)收缩功能出现障碍,导致静脉系统血液发生淤积,进而动脉系统血液灌注不足,引

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发心脏循环障碍,其根据发生的缓急程度可分为急性心衰和慢性心衰^[1,2]。其中,慢性心衰是指由心肌梗死、血流动力负荷增加、炎症等引起持续性心肌功能及结构的改变,进而使得心室充盈能力及射血功能异常,是各类心血管疾病发展的严重阶段^[3-5]。乏力、呼吸困难、水肿等是慢性心衰患者的主要临床症状。

目前,临床上治疗慢性心衰的方案主要包括利尿、扩血管、强心等短期措施^[6]及病因治疗、症状改善、抑制神经内分泌等长期修复性方案^[7]。呋塞米是一种广泛应用于治疗充血性心力衰竭和水肿的袢利尿药^[8],沙库巴曲缬沙坦作为首个国家食品药品监督管理局批准的血管紧张素受体脑啡肽酶抑制剂,常用于临床治疗慢性心衰^[9,10]。研究表明常规利尿、强心等短期治疗措施虽可有效缓解患者的临床症状和改善生活质量,但5年内的死亡率并未显著下降^[11]。因此,本研究主要探讨沙库巴曲缬沙坦联合呋塞米治疗慢性心力衰竭的疗效,以期临床用药提供更多参考依据。

1 资料与方法

1.1 一般资料

选择在我院治疗的60例慢性心力衰竭患者为研究对象,将所有患者随机分为两组。对照组30例中,男17例,女13例,年龄在54-79岁之间,平均年龄为65.1±5.3岁,病程在2-13年之间,平均病程为6.2±2.0年,NYHA分级:II级12例,III级18例;研究组30例中,男16例,女14例,年龄在55-79岁之间,平均年龄为65.5±5.1岁,病程在2-13年之间,平均病程为6.3±1.8年,美国纽约心脏病学会(NYHA)心功能分级:II级11例,III级19例。两组的一般临床特征比较差异均无统计学意义($P<0.05$),具有可比性。

1.2 纳入和排除标准

纳入标准:(1)符合西医慢性心力衰竭的临床诊断标准者;(2)入组前未使用过他汀类及β受体阻滞剂药物者;(3)年龄≤80岁;(4)自愿参与本次研究,均已签署《知情同意书》。

排除标准:(1)严重肝肾功能不全者;(2)先天性心脏病或心脏瓣膜病者;(3)急性心衰或心梗者;(4)对本次研究所用药物过

敏者;(5)伴发造血系统疾病者;(6)患有严重精神类疾病者;(7)患有自身免疫性疾病或肿瘤者。

1.3 治疗方法

两组患者均给予常规抗心衰治疗,对照组在此基础上给予呋塞米(批准文号:国药准字H31021074,生产企业:上海朝晖药业有限公司,产品规格:20mg*100s)进行治疗,起始剂量为20~40mg/次,每日1次,必要时6~8小时后追加20~40mg(1-2片);研究组在对照组基础上联合沙库巴曲缬沙坦(批准文号:国药准字J20171054,生产企业:北京诺华制药有限公司,产品规格:0.1g*14片/盒)进行治疗,起始剂量为50mg/次,每日两次,随后剂量每2周倍增一次,直至达到200mg/次,两组患者均治疗8w。

1.4 观察指标

(1)临床疗效^[12]:患者的乏力、呼吸困难、体液潴留等临床症状均显著改善,心功能分级改善至少2级即为显效;患者的乏力、呼吸困难、体液潴留等临床症状均有所改善,心功能分级改善至少1级即为有效;未达到上述标准者即为无效;(2)采用彩色多普勒超声检查两组治疗前后的LVEF、LVEDD、LVESD等心功能指标^[13];(3)采用酶联免疫吸附法检测并对比两组患者治疗前后的NT-proBNP、ALD、ICAM-1等血清学指标^[14],具体操作严格按照说明书进行;(4)两组患者治疗期间的不良反应发生率,包括头晕、头痛、便秘、心动过缓、低血压、高钾血症等。

1.5 统计学分析

采用SPSS20.0统计学软件对本次研究数据进行分析,计量资料以均数±标准差表示,组间对比经t检验;计数资料以百分比表示,组间对比经 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组治疗总有效率的对比

治疗后,研究组的治疗总有效率[96.7%(29/30)]显著高于对照组[80.0%(24/30)]($P<0.05$),见表1。

表1 两组治疗总有效率对比[例(%)]

Table 1 Comparison of the total effective rate of treatment between two groups[n (%)]

Groups	n	Significant effect	Effective	Invalid	Total effective
Research group	30	20(66.7)	9(30.0)	1(3.3)	29(96.7)*
Control group	30	14(46.7)	10(33.3)	6(20.0)	24(80.0)

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

2.2 两组治疗前后心功能的对比

治疗前,两组的心功能各项指标比较差异均无统计学意义($P>0.05$);治疗后,两组LVEF水平均较治疗前显著升高,LVESD、LVEDD指标均较治疗前显著降低($P<0.05$),且研究组LVEF显著高于对照组,而LVEDD和LVESD明显低于对照组($P<0.05$),见表2。

2.3 两组患者治疗前后血清 NT-proBNP、ICAM-1、ALD 水平的对比

治疗前,两组患者的血清 NT-proBNP、ICAM-1、ALD 水平

对比均无统计学差异($P>0.05$);治疗后,两组患者的上述指标均比治疗前显著降低($P<0.05$),且研究组以上指标显著低于对照组($P<0.05$),见表3。

2.4 两组治疗期间不良反应发生情况的比较

治疗期间,对照组有1例出现头晕、头痛,1例出现便秘,1例出现心动过缓,不良反应发生率为10.0%(3/30);研究组有1例乏力,1例头晕、头痛,1例低血压,1例高钾血症,不良反应发生率为13.3%(4/30)。两组不良反应的发生率比较差异无统计学意义($P>0.05$)。

表 2 两组治疗前后心功能对比(均数± 标准差)

Table 2 Comparison of the cardiac function indicators between two groups before and after treatment (mean ± standard deviation)

Groups	n	LVEF(%)		LVEDD(mm)		LVESD(mm)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	30	41.7± 6.9	55.2± 7.6 ^{#*}	61.8± 5.1	50.9± 4.8 ^{#*}	51.4± 5.8	40.2± 5.5 ^{#*}
Control group	30	41.2± 7.1	49.4± 7.5 [#]	62.0± 5.5	56.2± 5.0 [#]	50.9± 5.9	45.1± 5.6 [#]

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

表 3 两组患者治疗前后血清 NT-proBNP、ICAM-1、ALD 水平的对比(均数± 标准差)

Table 3 Comparison of the serum NT-proBNP, ICAM-1, ALD levels between the two groups before and after treatment(mean ± standard deviation)

Groups	n	NT-proBNP (pg/mL)		ICAM-1(ng/L)		ALD(pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	30	691.8± 45.1	413.2± 40.7 ^{#*}	66.5± 5.6	32.4± 4.9 ^{#*}	233.1± 35.0	161.4± 27.1 ^{#*}
Control group	30	690.4± 47.3	530.6± 43.8 [#]	65.9± 5.8	44.7± 5.2 [#]	232.6± 34.8	192.1± 30.2 [#]

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

3 讨论

慢性心力衰竭临床表现包括呼吸困难、乏力、腹部或腿部水肿、心脏扩大,心功能不全等^[15,16],高血压、冠心病和老年性退行性心瓣膜病是引发老年心力衰竭的重要原因^[17,18]。据资料显示,在 70-80 岁老年群体中,慢性心衰的发病率占 15%左右,且 3 年病死率约为 30%^[19-21],该数据与当今人口老龄化程度加深密切相关。因此,积极寻找安全、高效的治疗方案及药物对改善老年患者生活质量和降低病死率具有重要意义。

神经内分泌系统激活是慢性心衰的主要发病机制^[22],沙库巴曲缬沙坦作为全球首个血管紧张素受体-脑啡肽酶抑制剂,具有双靶点双重抑制神经内分泌系统的作用,作为一种长期、修复性治疗措施,该药物旨在改善心力衰竭患者心脏的生物学性质,是治疗慢性心衰的创新药物^[23,24]。本研究结果显示研究组患者的治疗总有效率显著高于对照组,两组患者的 LVEF 水平均升高,LVEDD、LVESD 指标均降低,且研究组更优,表明沙库巴曲缬沙坦联合呋塞米治疗慢性心力衰竭的效果显著,可有效改善患者的心功能。分析其原因为心力衰竭发生时,机体最快速的代偿机制为交感神经被激活,而沙库巴曲缬沙坦作为神经内分泌系统抑制剂,可直接、快速、高效的抑制已激活的神经内分泌系统,因此联合治疗效果更为显著。

NT-proBNP 是目前最重要的心脏功能生物标志物,常用于临床上心衰的诊断及疗效评估。ICAM-1 是介导黏附反应重要的一个黏附分子,可通过导致血栓引起心肌缺血进而影响心力衰竭^[25-28]。肾素-血管紧张素系统主要调节人体血压、水分、电解质和保持人体内环境的稳定性,其促进持续性 ALD 释放而造成钠潴留,因此检测 ALD 水平变化可鉴别和诊断慢性心衰^[29]。本研究结果显示两组患者治疗后的 NT-proBNP、ICAM-1、ALD 等血清学指标均比治疗前显著降低,且研究组更低,其原因与沙库巴曲缬沙坦的双靶向作用有关。此外,本研究结果还显示沙库巴曲缬沙坦联合呋塞米治疗慢性心力衰竭的安全性较好,该结果与 Boczar K^[30]等人一致。

综上所述,沙库巴曲缬沙坦联合呋塞米治疗慢性心力衰竭的效果显著优于单用呋塞米治疗,其可有效改善患者的心功能且安全性较高,可能与其明显改善患者血清 NT-proBNP、ALD、ICAM-1 水平有关。本研究还在一定的不足之处,例如病例选择较少、检测指标不完善等,后期应选择大样本量的研究对象和更具有针对性的检测指标做进一步的深入研究。

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