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沙库巴曲缬沙坦联合曲美他嗪治疗老年慢性心力衰竭的疗效及相关炎症因子影响 *

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摘要 目的：探究沙库巴曲缬沙坦联合曲美他嗪治疗老年慢性心力衰竭的疗效及相关炎症因子影响。**方法：**随机选取 2018 年 1 月 ~2019 年 10 月期间在本院接受治疗的 60 例慢性心力衰竭老年患者，将其随机平分为对照组和研究组，每组各 30 例，其中对照组在常规治疗的基础上给予沙库巴曲缬沙坦进行治疗，研究组在对照组的基础上给予曲美他嗪进行治疗，两组患者均连续治疗 3 个月，对比两组治疗总有效率，两组治疗前后的心功能指标，两组治疗前后的炎性因子水平，两组治疗期间的不良反应发生率。**结果：**研究组的治疗总有效率显著高于对照组 (93.33 % vs.76.67 %，*P*<0.05)。治疗前，两组的左心室收缩末期内径（left ventricular end-systolic diameter, LVESD）、左心室舒张末期内径（left ventricular end-diastolic diameter,LVEDD）、左心室射血分数（left ventricular ejection fraction, LVEF）、血浆 N- 末端脑钠素前体(N-terminal pro-brain natriuretic peptide，NT-pro BNP)等心功能指标对比均无统计学差异（*P*>0.05）；治疗后，两组的 LVEDD、LVESD、NT-pro BNP 指标均比治疗前显著降低，LVEF 水平均比治疗前显著升高（*P*<0.05），且研究组更优（*P*<0.05）；治疗前，两组的超敏 C 反应蛋白（high-sensitivity C-reactive protein, hs-CRP）、白介素 6（interleukin 6, IL-6）、IL-1、肿瘤坏死因子 α（tumor necrosis factor α, TNF-α）等炎性因子水平对比均无统计学差异（*P*>0.05）；治疗后，两组的上述指标均比治疗前显著降低（*P*<0.05），且研究组更低（*P*<0.05）；治疗期间，对照组的不良反应发生率 10.0 %（3/30）与研究组 13.3 %（4/30）之间无显著性差异（*P*>0.05）。**结论：**沙库巴曲缬沙坦联合曲美他嗪治疗老年慢性心力衰竭的效果显著，该方法可有效改善患者的心功能和炎症因子水平，且不良反应未增加，值得临床推广使用。

关键词：沙库巴曲缬沙坦；曲美他嗪；老年慢性心力衰竭；炎症因子

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Efficacy of Shakuba Trvalsartan Combined with Trimetazidine in Elderly Patients with Chronic Heart Failure and the Effects of Related Inflammatory Factors*

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ABSTRACT Objective: To investigate the curative effect of sacurbactra valsartan combined with trimetazidine in elderly patients with chronic heart failure and the influence of related inflammatory factors. **Methods:** A total of 60 elderly patients with chronic heart failure who were treated in our hospital from January 2018 to October 2019 were randomly selected as research subjects, and they were randomly divided into a control group and an observation group, with 30 cases in each group. Among them, the control group was given Sakuba trvalsartan on the basis of conventional treatment, and the study group was given trimetazidine on the basis of control. The patients in two groups were treated continuously for 3 months. Compare the total effective rate of treatment of the two groups of patients, compare the cardiac function indicators of the two groups of patients before and after treatment, compare the levels of inflammatory factors before and after treatment, and compare the incidence of adverse reactions during the treatment of the two groups of patients. **Results:** The total effective rate of treatment in the study group was significantly higher than in the control group (93.33 % vs. 76.67 %, *P*<0.05). Before treatment, there was no significant difference in the LVESD, LVEDD, LVEF, NT-pro BNP and isocardial function in the two groups of patients (*P*>0.05). After treatment, the LVEDD, LVESD and NT-pro BNP indexes of the two groups of patients were significantly lower than before treatment, the LVEF level was significantly higher than before treatment (*P*<0.05), and the study group was better (*P*<0.05). Before treatment, the levels of inflammatory factors such as hs-CRP, IL-6, IL-1 and TNF-α were not statistically different between the two groups (*P*>0.05). After treatment, the above-mentioned indicators of two groups of patients were significantly

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lower than before treatment (P<0.05), and the study group was lower (P<0.05). During the treatment period, there was no significant difference in the incidence of adverse reactions between the control group patients at 10.0 % (3/30) and the study group at 13.3 % (4/30) (P>0.05). **Conclusion:** Sakuba trvalsartan combined with trimetazidine has a significant effect on elderly patients with chronic heart failure. This method can effectively improve the heart function and inflammatory factor levels of patients, and the adverse reactions have not increased. It is worthy of clinical popularization.

Key words: Shakuba trvalsartan; Trimetazidine; Chronic heart failure in the elderly; Inflammatory factors

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前言

心力衰竭是大多数心血管疾病的终末阶段，约 40 %的心血管疾病最终可发展为心力衰竭[1]，随年龄的不断增加，老年患者心力衰竭的发病率逐渐上升，是导致心血管疾病死亡的主要原因，据报道，其发病率及致死率高，严重危害人类的健康。据报道，心力衰竭患者 3 年、5 年生存率仅为 68 %、50 %。心力衰竭的治疗时间长、疗效不明显，给社会及家庭、个人带来了沉重负担，因此有效治疗心力衰竭是一个有待解决的公共健康问题[2,3]。心力衰竭发生机制复杂。目前，老年人心力衰竭，临床上主要针对病因进行治疗，控制高血压，通过药物、介入或手术治疗，改善冠心病心肌缺血、心瓣膜病的手术治疗等[4,5]。沙库巴曲缬沙坦是临床上比较新的治疗心力衰竭的一种药物，药品一般用于射血分数降低的慢性心力衰竭成人患者[6]，有资料报道称，它可以降低心血管死亡和心力衰竭住院的风险[7]。曲美他嗪属于细胞能量代谢调节药物，其主要作用是在细胞缺血或缺氧情况下，通过调节细胞内 ATP 水平，避免细胞内能量下降，维持细胞内离子泵能量供应，维持细胞的正常工作[8]。我国目前有关沙库巴曲缬沙坦联合曲美他嗪治疗老年慢性心力衰竭的临床疗效的文献报道较少。本文通过探究沙库巴曲缬沙坦联合曲美他嗪治疗老年慢性心力衰竭的疗效及相关炎症因子影响，旨在为临床提供更加科学治疗方案。

1 资料与方法

1.1 一般资料

回顾性选取 2018 年 1 月 ~2019 年 10 月期间在本院接受治疗的 60 例慢性心力衰竭老年患者。纳入标准：均符合慢性心力衰竭的诊断标准[9]；NYHA（纽约心脏学会）心功能分级：Ⅲ~Ⅳ。排除标准：低血压者；急性冠脉动脉综合征、肥厚性心肌病、甲状腺功能亢进、严重肝功能损害及血肌酐 ≥ 220 μmol/L 者；不配合治疗者；心力衰竭晚期；严重感染疾病。

将其随机平分为对照组和观察组，每组各 30 例。其中对照组男性 17 例，女性 13 例，年龄最大的 71 岁，年龄最小的 60 岁，平均年龄(65.25±3.74)岁，病程最长的 15 年，病程最短的 3 年，平均病程(9.05±2.18)岁。观察组男性 19 例，女性 11 例，年龄最大的 73 岁，年龄最小的 60 岁，平均年龄(66.30±3.68)岁，病程最长的 15 年，病程最短的 3 年，平均病程(9.09±2.03)岁。统计学对比两组的基础资料，无显著性差异（P>0.05），具有可比性。

1.2 研究方法

对照组：给予沙库巴曲缬沙坦（Novartis Singapore Pharmaceutical Manufacturing Private.Ltd（分装：北京诺华制药有限公司），国药准字 J20190001，规格：100 mg/ 片）进行治疗，25 mg/ 次，2 次 /d，根据患者耐受情况，逐渐递增，最大不超过 200 mg/ 次。

研究组：在对照组的基础上给予曲美他嗪片 (瑞阳制药有限公司生产，国药准字 H20066534，规格：20 mg/ 片) 进行治疗，20 mg/ 次，3 次 /d，餐后口服。

两组均连续治疗 3 个月。

1.3 观察指标

（1）疗效：治疗后患者症状均显著改善，心功能分级改善至少 2 级为显效；患者临床症状均有所改善，心功能分级改善至少 1 级为有效[10,11]；未达到上述标准者为无效；治疗总有效率 =[（显效＋有效）/ 总例数]×100 %。（2）采用彩色多普勒超声检查两组治疗前后的 LVESD、LVEF、LVEDD、NT-pro BNP 等心功能指标 [12]；（3）采用酶联免疫吸附法检测两组治疗前后的 hs-CRP、IL-6、IL-1、TNF-α 等炎性因子水平[13]；（4）对比两组治疗期间头晕、头痛、便秘、心动过缓、高钾血症等不良反应[14]。

1.4 统计学分析

应用 SPSS 20.0，计数资料以%表示，两组间对比采用卡方检验；计量资料以（$\bar{x}\pm s$）表示，两组间对比采用 t 检验，P<0.05 有统计学意义。

2 结果

2.1 两组疗效对比

研究组治疗总有效率为 93.33 %（28/30），对照组的治疗总有效率为 76.67 %（23/30），研究组的治疗总有效率显著高于对照组，两组对比差异有统计学意义（χ^2=9.617，P=0.002，P<0.05），见表 1。

表 1 两组疗效对比[例(%)]

Table 1 Comparison of efficacy between the two groups [n (%)]

Groups	n	Significant effect	Effective	Invalid	Total effective
Study group	30	19(63.33)	9(30.00)	2(6.67)	28(93.33)*
Control group	30	13(43.33)	10(33.33)	7(23.33)	23(76.67)

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

2.2 两组治疗前后心功能指标对比

治疗前，两组的 LVEF、LVEDD、LVESD、NT-pro BNP 等对比均无差异（P>0.05）；治疗后，两组的 LVEDD、LVESD、NT-pro BNP 均比治疗前显著降低，LVEF 水平均比治疗前显著升高（P<0.05），且研究组更优（t=3.340，P=0.001；t=4.158，P=0.000；t=3.414，P=0.001；t=16.773，P=0.000；P 均 <0.05）；见表 2。

表 2 两组治疗前后心功能指标对比（$\bar{x}\pm s$）

Table 2 Comparison of cardiac function indicators before and after treatment in two groups ($\bar{x}\pm s$)

Groups	n	LVEF(%)		LVEDD(mm)		LVESD(mm)		NT-pro BNP(pg/ml)	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Study group	30	38.54±5.25	55.24±7.26#*	61.85±5.24	50.92±4.84#*	51.02±5.85	40.23±5.57#*	2850.46±201.24	789.36±53.32#*
Control group	30	38.49±5.21	49.04±7.12#	62.02±5.15	56.23±5.05#	50.98±5.92	45.18±5.66#	2873.25±210.01	1084.82±80.41#

Note: *P<0.05 compared with the control group; #P<0.05 compared with the pretherapy.

2.3 两组的炎性因子水平对比

治疗前，两组的 hs-CRP、IL-6、IL-1、TNF-α 水平对比均无差异（P>0.05）；治疗后，两组的上述指标显著降低（P<0.05），且研究组更低（t=96.627，P=0.000；t=22.052，P=0.000；t=12.377，P=0.000；t=13.862，P=0.000；P 均 <0.05）；见表 3。

表 3 两组的炎性因子水平对比（$\bar{x}\pm s$）

Table 3 Comparison of inflammatory factor levels between two groups of patients ($\bar{x}\pm s$)

Groups	n	hs-CRP(mg/L)		IL-6(μg/L)		TNF-α(ng/L)		IL-1(μg/L)	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Study group	30	57.38±2.15	8.12±0.37#*	63.55±2.16	42.54±1.59#*	196.51±15.50	116.34±10.01#*	132.24±24.13	54.25±8.24#*
Control group	30	57.34±2.23	28.26±1.08#	63.49±2.28	52.27±1.82#	196.46±14.38	152.21±12.32#	133.13±24.12	89.46±11.21#

2.4 两组的不良反应发生率对比

在治疗期间，对照组中有 1 例头晕、头痛，1 例心动过缓，1 例便秘；研究组中有 1 例乏力，1 例头晕、头痛，1 例低血压，1例高钾血症。两组不良反应发生率之间无差异（13.3 % vs. 10.0 %，χ^2=0.162，P=0.866，P>0.05）。

3 讨论

慢性心力衰竭是指由于心脏的结构或功能的异常导致心排血量减少，引起外周的组织器官血流灌注不足，从而导致组织细胞缺血缺氧一系列临床综合征[15]。老年人心力衰竭是比较常见的疾病，多见于老年人合并有冠心病的患者。慢性心力衰竭为心脏病的终末期，一般较严重，各种心脏病发展到终末期[16]，即可造成心力衰竭、循环衰竭、多脏器功能障碍、多脏器功能衰竭，出现呼吸困难，危及患者生命[17]。

对于老年人心力衰竭的主要治疗方法，还是以口服药为主[18]。沙库巴曲缬沙坦钠片商品名叫诺欣妥，具有血管紧张素Ⅱ受体阻滞剂和脑啡肽酶抑制剂的作用，可作用于心功能Ⅱ-Ⅲ级，有症状的收缩期射血分数降低的慢性心力衰竭患者，具有降低心血管和心力衰竭住院的风险，对改善心功能有很大的帮助[19,20]，可以和其他治疗心力衰竭药如利尿剂，倍他受体阻滞剂，螺内酯合用，进一步减少心力衰竭的发病率及死亡率[21,22]。曲美他嗪是细胞能量代谢调节药物，其可通过改善心肌细胞能量代谢，抑制脂肪酸代谢途径，增加葡萄糖代谢途径，充分利用有限氧，具有抗心绞痛，对抗肾上腺素，去甲肾上腺素及血管加压素的作用[23]。临床上主要用于治疗慢性稳定型心绞痛，糖尿病伴有缺血性心肌病的临床效果良好[24]。本文通过将其联合应用于老年慢性心力衰竭的治疗过程中，研究组的治疗总有效率显著高于对照组，治疗后，两组的 LVEDD、LVESD、NT-pro BNP 均显著降低，LVEF 水平显著升高，且研究组更优，与国内普顺华等[25]学者的研究结果一致，该学着探讨沙库巴曲缬沙坦联合曲美他嗪治疗慢性充血性心力衰竭的临床疗效和安全性，发现治疗后 LVEF 水平显著增加，NT-proBNP 水平显著下降，同时 6MWT 距离延长，住院次数减少，国外目前还没有沙库巴曲缬沙坦联合曲美他嗪治疗慢性充血性心力衰竭，主要使用卡哌利特、基底膜衍生的基质胶蛋白等靶向治疗[26]。本研究表明两药联合治疗老年慢性心力衰竭效果显著，可有效改善心功能。分析原因沙库巴曲缬沙坦钠片改善患者的心功能，联合应用曲美他嗪，要进一步加强改善心肌细胞能量代谢，显著改善了患者的心功能。

老年人是慢性心力衰竭的高发人群，严重影响患者的生命健康和生活质量[27,28]。研究发现机体免疫及炎症反应与慢性心力衰竭的发生发展关系密切，因此有效改善慢性心力衰竭患者免疫功能和炎症因子水平已成为治疗的新方向[29-31]。本文研究结果还显示，治疗后，两组的上述指标均比治疗前显著降低，且

研究组更低，治疗期间，两组不良反应发生率无差异；与宋智[32]等学者研究类似，发现沙库巴曲缬沙坦联合曲美他嗪片治疗慢性心力衰竭患者血清炎症因子水平降低，且安全有效，表明两药联合可有效改善老年慢性心力衰竭患者炎症因子水平，分析其原因为曲美他嗪缓释片属于抗心绞痛类的心血管药物[33]，它的主要功能就是预防性治疗心绞痛发作，它的不良反应主要是胃肠道疾病、神经系统症状、皮肤病症状等。大部分副作用都可以在停药以后消失[34,35]。因此应用不会增加不良反应，安全有效。本研究创新性的将沙库巴曲缬沙坦联合曲美他嗪治疗老年慢性心力衰竭，疗效显著，且不良反应少，为临床治疗和探究老年慢性心力衰竭的机制提供了新的思路和靶点，值得借鉴应用。但是本研究也存在一定的不足，样本量少，且没有随访对比患者的生活质量，后续需要进一步扩大样本量，深入探究治疗机制。

综上所述，沙库巴曲缬沙坦联合曲美他嗪治疗老年慢性心力衰竭，效果显著，可有效改善心功能和炎症因子水平，且不良反应未增加，值得临床推广使用。

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