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小剂量甲状腺素联合厄贝沙坦氢氯噻嗪治疗老年重症心力衰竭的效果观察 *

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摘要 目的：探究使用小剂量甲状腺素联合厄贝沙坦氢氯噻嗪治疗老年重症心力衰竭（CHF）中的治疗效果。**方法**：将 37 例本院老年 CHF 患者随机分做实验组（19 例）及对照组（18 例）。对照组予厄贝沙坦氢氯噻嗪片及美托洛尔治疗；实验组予厄贝沙坦氢氯噻嗪片、美托洛尔及左旋甲状腺素钠片治疗。对比治疗前后两组患者心力衰竭症状、心功能及甲状腺素水平的变化。**结果**：实验组总有效率(94.7%)高于对照组(77.8%)，差异具有统计学意义（P<0.05）；两组患者左心室射血分数（LVEF）水平及胱抑素 C 水平增加，纽约心脏病协会分级（NYHA）及 B 型脑钠肽水平均降低（P<0.05）；与对照组相比，实验组 LVEF 及胱抑素 C 水平较高，NYHA 分级及 B 型脑钠肽水平较低，差异存在统计学意义（P<0.05）；两组血清三碘甲状腺原氨酸（T3）、血清甲状腺素（T4）水平均升高（P<0.05），与对照组相比，实验组血清 T3、T4 水平较高，差异具有统计学意义（P<0.05）。**结论**：小剂量甲状腺素联合厄贝沙坦氢氯噻嗪治疗老年 CHF 的效果显著，可以明显改善心力衰竭症状、提高 LVEF 水平，降低 NYHA 分级及血清中 B 型脑钠肽水平。

关键词：重症心力衰竭；厄贝沙坦氢氯噻嗪；甲状腺素；老年患者

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Efficacy of Small Dose Thyroxine Combined with Irbesartan and Hydrochlorothiazide in the Treatment of Senile Severe Heart Failure*

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ABSTRACT Objective: To investigate the effects of small dose thyroxine combined with irbesartan and hydrochlorothiazide in the treatment of elderly patients with severe heart failure (CHF). **Methods:** 37 elderly patients with CHF who were treated in our hospital were selected and randomly divided into experiment group (19 cases) and control group (18 cases). The patients in the control group were treated with irbesartan and hydrochlorothiazide tablets and metoprolol, and the patients in the experiment group were treated with irbesartan, hydrochlorothiazide, metoprolol and levothyroxine sodium tablets. Then the heart failure symptoms and heart function and thyroxine levels of the two groups were observed and compared before and after treatment. **Results:** The total effective rate of the experiment group was 94.7% which was higher than 77.8% of the control group, and the difference was statistically significant (P<0.05); Compared with before treatment, the left ventricular ejection fraction (LVEF) and cystatin C levels of the two groups increased after treatment, while the New York heart association (NYHA) classification and b-type brain natriuretic peptide levels decreased (P<0.05); Compared with the control group, the levels of the LVEF and cystatin C in the experiment group were higher, and the NYHA classification and b-type brain natriuretic peptide levels were lower, and the differences were statistically significant (P<0.05); Compared with before treatment, the serum triiodothyronine (T3) and serum thyroxine (T4) levels of the two groups increased after treatment (P < 0.05); Compared with the control group, the serum T3 and T4 levels of the experiment group were higher, and the differences were statistically significant (P<0.05). **Conclusion:** Small dose thyroxine combine with irbesartan and hydrochlorothiazide in the treatment of elderly patients with CHF can obviously improve the symptoms of heart failure, increase the level of LVEF, decrease the NYHA classification and serum b-type brain natriuretic peptide levels, and improve the levels of serum T3 and T4.

Key words: Severe heart failure; Irbesartan and hydrochlorothiazide; Thyroxine; Elderly patients

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前言

重症心力衰竭(Congestive heart failure,CHF)是引发老年患者死亡的重要原因,多见于心血管疾的终末阶段[1]。因心肌细胞的损伤、血管壁弹性下降等原因使老年人的心脏泵血功能下降,诱发呼吸衰竭、神经内分泌功能紊乱等并发症。CHF 的病死率较高,约有 33%的初发患者会在 6 个月内死亡,而大多数慢性 CHF 患者的生存率也仅有 5 年[3]。因此,在疾病发生早期,有效缓解及减慢心室的重塑对患者的进一步预后具有重要意义。厄贝沙坦氢氯噻嗪片是治疗原发性高血压的重要药物,对血管紧张素 -II 受体(AT1 亚型)达到选择性拮抗,从而降低血清醛固酮升高血管紧张素 -II 含量[4]。氢氯噻嗪能够影响肾小管的重吸收,增强肾素活性减少血液容量,加快排泄而降低血压[5]。甲状腺素是体内重要的激素,能够促进细胞的代谢,当 CHF 发生时,会引起神经内分泌功能的紊乱,造成血清中甲状腺素水平下降,使用左旋甲状腺素片进行治疗,能够有效改善内分泌失衡对机体功能的影响 [6]。本实验通过测定患者治疗前后 LVEF、B 型脑钠肽、T3、T4 及 NYHA 分级水平, 探究小剂量甲状腺素联合厄贝沙坦氢氯噻嗪对老年 CHF 患者进行治疗时的临床效果。

1 资料与方法

1.1 病历选择

收集我院收治的老年重症心力衰竭患者 37 例, 把患者随机分做对照组及使实验组。对照组 18 例,其男性 11 例,女性 7 例,年龄为 63~82 岁,平均(68.4± 7.1)岁;实验组 19 例,男性 10 例,女性 9 例,年龄为 62~85 岁,平均(71.1± 7.3)岁。两组的性别、年龄及病因等比较,差异不存在统计学意义(P>0.05)。两组一般情况的对比不具有统计学意义(P>0.05)。本次研究获得本院伦理委员会批准,告知患者并已签署知情同意书。患者符合《内科学》中 CHF 的诊断标准,行超声心动图检查时可见患者左心室扩大 LVEF≤ 50%; 具有明显心力衰竭表现及体征患者;;年龄在 60~85 岁间。排除近一个月服用过对甲状腺素代谢有影响药物;具有严重的肝脏或肾脏疾病患者;患有心肌梗死或心绞痛患者;甲状腺功能异常;药物过敏者,依从性不好者。

1.2 方法

两组患者收入院治疗后均予常规心电监护监测血压等生命体征,予低流量吸氧必要时行机械通气,输液治疗电解质与酸碱平衡的失调。对照组予厄贝沙坦氢氯噻嗪片(安博诺,国药准字 H20130007)每次 1 片,每日 1 次,酒石酸美托洛尔片(倍他乐克,阿斯利康制药有限公司,国药准字 H32025391)25 mg,初始予 12.5 mg/ 日, 口服每日 2 次, 没有首剂反应后加至 25 mg/ 日,每日 2 次口服;实验组予厄贝沙坦氢氯噻嗪片(安博诺,国药准字 H20130007)每次 1 片,每日 1 次,酒石酸美托洛尔片 (倍他乐克, 阿斯利康制药有限公司, 国药准字 H32025391)25 mg,初服药时 12.5 mg/ 日,每日 2 次口服,在没有首剂反应后加至 25 mg/ 日, 每日 2 次, 左旋甲状腺素钠片(泽宁, 扬子江药业集团四川海蓉药业有限公司, 国药准字 H20041605),12.5 μg/ 日, 连续治疗 3 日后, 改为服用 25 μg/ 日,持续治疗 14 日后在 9 天内逐渐减量并停用。以 28 天一个疗程。

1.3 检测方法

治疗前后均采集两组 3 mL 空腹肘静脉血, 采好后装进有 EDTA 的抗凝采血管按 3000 r/min 转速,离心 10 min 后收集上层血清于 EP 管, 放入冰箱在 -20℃中保存备用。检测并对比 T3、T4 水平,B 型脑钠肽及 LVEF 等指标。B 型脑钠肽采用 ELISA 方法进行测定,选用由南京基蛋生物科技有限公司生产的试剂盒进行测定,T3、T4 值的测试根据上海樊克生物科技有限公司生产的试剂盒测量,胱抑素 C 选用由桂林英美特生物技术有限公司生产抗体,所有操作均严格依照操作说明及步骤进行检测。LVEF 选择上海然哲仪器设备有限公司生产的心室压力 - 容积测定系统。NYHA 分级由 2 名临床经验丰富的心内科医师进行评定。

1.4 疗效评价

根据心功能分级变化分为显效、有效和无效三个等级。显效:患者肺水肿、呼吸困难症状好转,LVEF 水平提高≥ 10%,心功能分级好转了 2 级或以上; 有效: 患者呼吸困难症状减轻,LVEF 水平提高≥ 5%,心功能分级好转 1 级;无效:患者休克及肺水肿等症状无明显变化,心功能分级未见明显缓解,LVEF 水平无明显提高。总有效率 =(显效患者数 + 有效患者数)/ 总例数× 100%。严密观察实验组及对照组患者呼吸、血压及心率的变化,对于出现的药物不良反应予对症治疗。

1.5 统计学方法

数据分析选用统计学软件 SPSS 19.0,"$\bar{x}$± s" 来记录呈正态分布的数据,选择 t 检验的方式进行验证差异,百分率(%)计数资料,得出 P<0.05,说明差异具有统计学意义。

2 结果

2.1 两组患者的临床疗效比较

实验组总有效率(94.7%)高于对照组(77.8%),差异存在统计学意义(P<0.05)。见表 1。

表 1 两组患者的临床疗效比较[n(%)]

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

Groups	Case	Excellence	Effective	Invalid	Clinical effect rate
Control group	18	6(33.3)	8(44.4)	4(22.2)	14(77.8)
Experiment group	19	7(36.8)	11(57.9)	1(5.3)	18(94.7)*

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

2.2 两组患者治疗前后心功能及肾功能比较

与治疗前比较,两组患者治疗后 LVEF 及胱抑素 C 水平增

加，NYHA 分级及 B 型脑钠肽水平均降低(P<0.05)；与对照组相比，实验组患者治疗后 LVEF 及胱抑素 C 水平较高，NYHA 分级及 B 型脑钠肽水平较低，差异存在统计学意义(P<0.05)。见表 2。

表 2 两组患者治疗前后 LVEF，NYHA，B 型脑钠肽及胱抑素 C 水平比较($\bar{\chi}\pm$ s)

Table 2 Comparison of the levels of LVEF, NYHA, B - type natriuretic peptide and serum cystatin C between two groups before and after treatment($\bar{\chi}\pm$ s)

Groups	LVEF(%)		NYHA		BNP(pg/mL)		cystatin C(mg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	36.8± 3.6	41.1± 5.2*	3.4± 0.4	2.7± 0.3*	1036.3± 105.6	766.7± 79.8*	0.8± 0.1	1.2± 0.1*
Experiment group	37.7± 1.4	54.7± 5.6*#	3.2± 0.4	1.8± 0.2*#	1037.5± 107.8	496.6± 54.7*#	0.8± 0.1*	1.5± 0.1*#

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

2.3 两组患者治疗前后血清 T3 及 T4 水平比较

与治疗前比较，两组患者治疗后血清 T3 及 T4 水平均升高(P<0.05)；与对照组相比，实验组患者治疗后血清 T3 及 T4 水平较高，差异具有统计学意义(P<0.05)。见表 3。

表 3 两组患者治疗前后 T3 及 T4 水平比较($\bar{\chi}\pm$ s)

Table 3 Comparison of the levels of T3 and T4 between two groups before and after treatment($\bar{\chi}\pm$ s)

Groups	Case	T3(nmol/L)		T4(nmol/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	18	0.8± 0.1	0.9± 0.1*	89.2± 9.4	93.3± 9.7*
Experiment group	19	0.9± 0.1	1.2± 0.1*#	91.4± 9.6	123.5± 12.4*#

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

3 讨论

心力衰竭多因各种原因引起的心脏收缩功能出现障碍导致心排血量明显降低以至于不能满足全身代谢所需要的血流量，血流动力学的异常激活神经系统分泌激素异常，从而发生的一系列综合征[7]。在年龄逐渐上升时，老年人多存在心血管系统疾病，使心脏泵血量减少，血管弹性下降，导致患者心脏收缩功能障碍，出现一系列并发症导致重症心力衰竭(CHF)的发生[8]。当发生 CHF 时，易引起呼吸系统出现衰竭及神经内分泌系统的分泌变化，病死率高，早期及时治疗十分关键。CHF 发生时患者常表现晕厥、休克、急性肺水肿及心脏骤停。心脏排血功能减退使得患者脑部出现短暂的意识丧失，当代偿不及时时会造成周围血管显著收缩，就会出现晕厥及休克等并发症[9]。而当左心功能出现异常时会出现急性肺水肿，因左心室排血量的减低使得肺泡甚至气道内都充满液体，导致出现端坐呼吸等呼吸衰竭表现，呼吸系统功能的变化易并发呼吸衰竭而增高患者的病死率[10]。CHF 的发生不仅损伤心脏组织也会对神经内分泌功能造成影响，使血清中甲状腺素的含量降低。

人体内正常水平的甲状腺素能够促进细胞代谢，促进氧的消耗利于肠道中葡萄糖的吸收，CHF 患者体内甲状腺素水平降低，可能会加重患者水肿，同时甲状腺素也会影响左心室的功能及交感肾上腺素系统的功能[11-13]。CHF 患者大多存在血清甲状腺素水平的异常而无甲状腺功能的减退表现，心功能越差的患者血清甲状腺素水平越低，这说明甲状腺素能够对心脏的收缩功能产生影响[14]。通过舒张外周血管降低阻力，提高细胞膜钠钾泵活性，增强心肌细胞的收缩功能，提高心输出量[15]。CHF 患者服用小剂量甲状腺后，能够有效降低血管阻力及心脏后负荷增强收缩力，增加体内血清甲状腺素水平，平衡体内激素水平紊乱，达到对心力衰竭的缓解及纠正[16]。

厄贝沙坦氢氯噻嗪片常用于原发性高血压的治疗，其中氢氯噻嗪能够激活体内的肾素 - 血管紧张素及交感神经系统，降低体内血钾的含量达到降压的作用[17]。厄贝沙坦可以减轻由氢氯噻嗪引起的血尿酸增高及血钾降低，并且依据对血管紧张素转换酶 1 受体进行选择性的阻断而达到降压的作用，加强利尿剂的作用效果，减轻心脏负荷有效缓解心力衰竭的程度[18-20]。本研究结果显示，实验组总有效率 94.7%高于对照组 77.8%，差异存在统计学意义(P<0.05)。结果说明，实验组患者心力衰竭症状及心功能改善优于对照组。实验组患者的 LVEF、胱抑素 C 及血清 T3、T4 水平较高，NYHA 分级及 B 型脑钠肽水平较低，差异存在统计学意义(P<0.05)，说明实验组在使用小剂量甲状腺素治疗后，改善了患者体内紊乱的神经内分泌功能，升高已下降的血清甲状腺素水平，使心输出量增加，减轻肾脏的负担及损伤。

综上所述，小剂量甲状腺素联合厄贝沙坦氢氯噻嗪治疗老年重症心力衰竭患者时，能达到明显改善临床症状、提高 LVEF 及降低 NYHA 分级的目的，适合广泛使用。

参 考 文 献(References)

[1] Zsebo K, Yaroshinsky A, Rudy J J, et al. Long-term effects of AAV1/SERCA2a gene transfer in patients with severe heart failure analysis of recurrent cardiovascular events and mortality [J]. Circulation research, 2014, 114(1): 101-108

[2] Menasché P, Vanneaux V, Hagè ge A, et al. Human embryonic stem cell-derived cardiac progenitors for severe heart failure treatment: first

clinical case report [J]. European heart journal, 2015, 36 (30): 2011-2017

[3] McMurray J J V, Packer M, Desai A S, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure[J]. New England Journal of Medicine, 2014, 371(11): 993-1004

[4] Pitt B, Pfeffer M A, Assmann S F, et al. Spironolactone for heart failure with preserved ejection fraction [J]. New England Journal of Medicine, 2014, 370(15): 1383-1392

[5] Packer M, McMurray J J V, Desai A S, et al. Angiotensin receptor neprilysin inhibition compared with enalapril on the risk of clinical progression in surviving patients with heart failure [J]. Circulation, 2015, 131(1): 54-61

[6] Damman K, Valente M A E, Voors A A, et al. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis [J]. European heart journal, 2014, 35(7): 455-469

[7] Ambrosy A P, Fonarow G C, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries [J]. Journal of the American College of Cardiology, 2014, 63(12): 1123-1133

[8] Goel S S, Bajaj N, Aggarwal B, et al. Prevalence and outcomes of unoperated patients with severe symptomatic mitral regurgitation and heart failure: comprehensive analysis to determine the potential role of MitraClip for this unmet need [J]. Journal of the American College of Cardiology, 2014, 63(2): 185-186

[9] Borer J S, Böhm M, Ford I, et al. Efficacy and safety of ivabradine in patients with severe chronic systolic heart failure (from the SHIFT study)[J]. The American journal of cardiology, 2014, 113(3): 497-503

[10] Takeda K, Naka Y, Yang J A, et al. Outcome of unplanned right ventricular assist device support for severe right heart failure after implantable left ventricular assist device insertion [J]. The Journal of Heart and Lung Transplantation, 2014, 33(2): 141-148

[11] Braunwald E. The war against heart failure: the Lancet lecture[J]. The Lancet, 2015, 385(9970): 812-824

[12] Mortensen S A, Rosenfeldt F, Kumar A, et al. The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial[J]. JACC: Heart Failure, 2014, 2(6): 641-649

[13] Mathiasen A B, Qayyum A A, Jørgensen E, et al. Bone marrow-derived mesenchymal stromal cell treatment in patients with severe ischaemic heart failure: a randomized placebo-controlled trial (MSC-HF trial)[J]. European heart journal, 2015, 36(27): 1744-1753

[14] Gronda E, Seravalle G, Brambilla G, et al. Chronic baroreflex activation effects on sympathetic nerve traffic, baroreflex function, and cardiac haemodynamics in heart failure: a proof of concept study [J]. European journal of heart failure, 2014, 16(9): 977-983

[15] Florea V G, Cohn J N. The autonomic nervous system and heart failure[J]. Circulation research, 2014, 114(11): 1815-1826

[16] Asbury A K, Aldredge H, Hershberg R, et al. Oculomotor palsy in diabetes mellitus: a clinico-pathological study [J]. Brain, 2016, 93(3): 555-566

[17] Greenberg B, Yaroshinsky A, Zsebo K M, et al. Design of a phase 2b trial of intracoronary administration of AAV1/SERCA2a in patients with advanced heart failure: the CUPID 2 trial (calcium up-regulation by percutaneous administration of gene therapy in cardiac disease phase 2b)[J]. JACC: Heart Failure, 2014, 2(1): 84-92

[18] Melenovsky V, Hwang S J, Lin G, et al. Right heart dysfunction in heart failure with preserved ejection fraction [J]. European heart journal, 2014, 35(48): 3452-3462

[19] Pfeffer M A, Claggett B, Assmann S F, et al. Regional variation in patients and outcomes in the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist (TOPCAT) trial[J]. Circulation, 2015, 131(1): 34-42

[20] Mc Murray J V, Packer M, Desai A S, et al. Baseline characteristics and treatment of patients in Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM HF)[J]. European journal of heart failure, 2014, 16(7): 817-825

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[14] Eid R E, Wang L, Kuzman M, et al. Endoscopic versus open saphenous vein graft harvest for lower extremity bypass in critical limb ischemia[J]. Journal of vascular surgery, 2014, 59(1): 136-144

[15] Scotton M F, Miot H A, Abbade L P F. Factors that influence healing of chronic venous leg ulcers: a retrospective cohort [J]. Anais brasileiros de dermatologia, 2014, 89(3): 414-422

[16] Stroud W, Whitworth J M, Miklic M, et al. Validation of a venous thromboembolism risk assessment model in gynecologic oncology[J]. Gynecologic oncology, 2014, 134(1): 160-163

[17] Van den Bos R R, Malskat W S J, De Maeseneer M G R, et al. Randomized clinical trial of endovenous laser ablation versus steam ablation (LAST trial) for great saphenous varicose veins [J]. British Journal of Surgery, 2014, 101(9): 1077-1083

[18] Lynch N P, Clarke M, Fulton G J. Surgical management of great saphenous vein varicose veins: A meta-analysis[J]. Vascular, 2015, 23 (3): 285-296

[19] Liu Z, Gao N, Shen L, et al. Endovascular treatment for symptomatic iliac vein compression syndrome: a prospective consecutive series of 48 patients[J]. Annals of vascular surgery, 2014, 28(3): 695-704

[20] Poredos P, Spirkoska A, Rucigaj T, et al. Do blood constituents in varicose veins differ from the systemic blood constituents? [J]. European Journal of Vascular and Endovascular Surgery, 2015, 50(2): 250-256