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氧化樟脑注射液联合厄贝沙坦治疗心力衰竭的疗效及对血清NT-pro-BNP、NE水平的影响*

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摘要 目的:探讨氧化樟脑注射液联合厄贝沙坦治疗心力衰竭的疗效及对血清氨基末端脑钠肽前体(NT-pro-BNP)、去甲肾上腺素(NE)水平的影响。**方法:**选择2015年3月-2017年3月我院收治的心力衰竭患者80例进行研究,根据随机数表法将其分为观察组(n=41)和对照组(n=39)。对照组给予厄贝沙坦治疗,观察组在对照组的基础上加用氧化樟脑注射液治疗。比较两组患者的临床疗效、治疗前后血清NT-pro-BNP、NE水平、左室舒张末期内径(LVEDD)、左心室收缩末期容积(LVESV)、左心室收缩末内径(LVESD)、左心室射血分数(LVEE)水平的变化及不良反应的发生情况。**结果:**治疗后,观察组总有效率为95.12%,显著高于对照组(71.79%,$P<0.05$)。两组患者治疗后血清NT-pro-BNP、NE、LVEDD、LVESD、LVESV水平均较治疗前显著降低,LVEE显著上升,且观察组血清NT-pro-BNP、NE、LVEDD、LVESD、LVESV水平明显低于对照组($P<0.05$),而LVEE显著高于对照组($P<0.05$)。观察组不良反应的发生率为4.88%,明显低于对照组(23.08%,$P<0.05$)。**结论:**氧化樟脑注射液联合厄贝沙坦治疗心力衰竭的临床效果显著优于单用厄贝沙坦治疗,其可有效改善患者NT-pro-BNP、NE水平,且安全性较高。

关键词:氧化樟脑注射液;厄贝沙坦;心力衰竭;氨基末端脑钠肽前体;去甲肾上腺素

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Curative Efficacy of Camphor Oxide Injection Combined with Irbesartan in the Treatment of Heart Failure and Its Effects on the Serum Nt-pro-bnp and NE Levels*

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ABSTRACT Objective: To study the curative efficacy of Camphor oxide injection combined with irbesartan in the treatment of-Heart failure and its effects on the serum Amino terminal brain natriuretic peptide precursor (NT-pro-BNP), norepinephrine (NE). **Methods:** 80 patients with heart failure admitted to our hospital from March 2015 to March 2017 were selected and divided into the observation group (n=41) and the control group (n=39) according to the random number table method. The control group was treated with irbesartan, and the observation group was treated with camphor oxide injection on the basis of control group. The clinical efficacy, serum nt-pro-bnp, NE level, LVEDD, LVESV, LVESD, LVEE and incidence of adverse reactions were compared between two groups. **Results:** After treatment, the total effective rate of observation group was 95.12%, which was significantly higher than that of the control group (71.79%, $P<0.05$). After treatment, the serum levels of nt-pro-bnp, NE, LVEDD, LVESD and LVESV in the two groups were significantly lower than those before treatment, while the LVEE was significantly higher. Moreover, the serum levels of nt-pro-bnp, NE, LVEDD, LVESD and LVESV in the observation group were significantly lower than those in the control group ($P<0.05$), while LVEE was significantly higher than those in the control group($P<0.05$). The incidence of adverse reactions in the observation group was 4.88%, which was significantly lower than that in the control group (23.08%, $P<0.05$). **Conclusion:** The clinical effect of oxidized camphor injection combined with irbesartan was significantly better than that of irbesartan alone in the treatment of heart failure, which could effectively improve the levels of nt-pro-bnp and NE in patients with high safety.

Key words: Camphor oxide injection; Irbesartan; Heart failure; Amino terminal brain natriuretic peptide precursor; Norepinephrine

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前言

心力衰竭是内科常见危重症,是各种疾病导致的心脏疾病的严重阶段,有较高的病死率,临通常是由于机体心脏功能的

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下降,导致呼吸困难和液体潴留。如果不及时治疗,病人的生命将受到威胁[1,2]。有研究显示 NT-pro-BNP、NE 在心力衰竭中发挥重要作用,可作为该病治疗的靶点[3]。临床通常使用厄贝沙坦治疗该病,其是血管紧张素Ⅱ受体抑制剂,能够抑制血管收缩和醛固酮的释放,但是其单一治疗效果一般,对心力衰竭患者心功能无明显改变[4,5]。

氧化樟脑注射液可以有效的清除血管内的氧自由基,从而改善患者心肌功能[7,8]。研究显示氧化樟脑注射液对心力衰竭效果明显,能明显改善患者的心功能[6]。但临床上关于氧化樟脑注射液对心力衰竭患者血清 NT-pro-BNP、NE 水平影响的相关报道较少。因此,本研究主要探讨了氧化樟脑注射液联合厄贝沙坦治疗心力衰竭的疗效,及其对患者血清 NT-pro-BNP、NE 水平的影响,现报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 3 月 -2017 年 3 月我院收治的心力衰竭患者 80 例进行研究。采用简单随机分组法分为 2 组,观察组男 27 例,女 14 例,年龄 41~75 岁,平均(56.65± 4.52)岁;对照组男 23 例,女 16 例,年龄 41~74 岁,平均(56.59± 4.63)岁。两组基线资料无显著差异(P >0.05),存在可比性。

纳入标准[9]:(1)符合《慢性心力衰竭诊断治疗指南》诊断标准;(2)精神正常,可以正常沟通;(3)有心力衰竭的症状和体征。排除标准:(1)合并免疫疾病者;(2)患有意识障碍、精神障碍者;(3)伴有恶性肿瘤患者。

1.2 方法

对照组采用厄贝沙坦治疗:厄贝沙坦(规格:75 mg;生产厂家:石家庄以岭药业股份有限公司;国药准字 H20060794)75 mg 口服,1 天 1 次。观察组在对照组的基础上加用氧化樟脑注射液治疗:氧化樟脑注射液(规格:2 mL:10 mg,厂家:长春大政药业科技有限公司,国药准字 H22026205)80 mg 加入 5%生理盐水 100 mL 静脉滴注,1 d 1 次。两组患者均治疗 2 周。

1.3 观察指标

采集空腹静脉血 5 mL,以 3000 r·min^{-1} 的速度进行离心,时间 10 min,提取上层血清后,置于零下 20℃的冷冻箱内存储以备检测,血清 NT-pro-BNP、NE 的测定采用双抗体夹心酶联免疫吸附法 (ELISA);使用超声心动图测量 LVEE、LVEDD 、LVESD 、LVESV 并记录不良反应发生情况。

疗效评定标准:显效:临床症状消失,心功能改善 2 级以上;有效:心功能分级提高一级,临床症状明显改善;无效:心功能无改善或加重,显效+有效 = 总有效率。

1.4 统计学分析

以 spss18.0 软件包处理数据,计量资料均用均数± 标准差($\bar{x}\pm s$)表示,组间比较使用独立样本 t 检验,计数资料以率表示,组间比较采用 x^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组疗效的比较

治疗后,2 组总有效率分别为 95.12%、71.79%,观察组显著高于对照组($P<0.05$),见表 1。

表 1 2 组疗效比较[例(%)]

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

Groups	n	Effective	Valid	Invalid	Total effective rate
Observation group	41	25(60.98)	14(34.15)	2(4.88)	39(95.12)
Control group	39	17(43.59)	11(28.21)	11(28.21)	28(71.79)
x^2 value					7.992
P value					0.005

2.2 两组治疗前后血清 NT-pro-BNP、NE 水平的比较

治疗后,2 组患者血清 NT-pro-BNP、NE 水平均较治疗前显著降低,且观察组以上指标均明显低于对照组($P<0.05$),见表 2。

表 2 两组治疗前后血清 NT-pro-BNP、NE 水平比较($\bar{x}\pm s$)

Table 2 Comparison of serum nt-pro-bnp and NE levels between the two groups($\bar{x}\pm s$)

Groups	n	NT-pro-BNP(ng/L)		NE(pg/mL)	
		Before the treatment	After treatment	Before the treatment	After treatment
Observation group	41	745.36± 63.61	245.34± 17.45	204.36± 25.41	123.85± 21.04
Control group	39	745.46± 64.25	329.56± 18.96	204.18± 25.89	184.36± 25.36
t value		0.007	20.687	0.031	11.638
P value		0.994	0.000	0.975	0.000

2.3 两组治疗前后心功能的比较

治疗后,观察组 LVEDD 、LVESD 、LVESV 水平低于对照组,LVEE 高于对照组($P<0.05$)($P<0.05$),见表 3。

2.4 两组不良反应发生情况的比较

2 组患者总发生率分别为 4.88%、23.08%,观察组显著高于缔造者($P<0.05$),见表 4。

表 3 2 组治疗前后心功能的比较($\bar{x}\pm s$)

Table 3 Comparison of the cardiac function levels between the two groups($\bar{x}\pm s$)

Groups	n	LVEE(%)		LVEDD(mm)		LVESD(mm)		LVESV(mL)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	41	42.35± 3.21	55.86± 4.47	64.27± 4.51	41.21± 1.56	52.34± 6.38	31.31± 2.41	156.78± 35.85	102.31± 19.13
Control group	39	42.27± 3.19	48.76± 4.41	64.29± 4.57	48.52± 1.64	52.29± 6.41	40.57± 2.41	156.81± 35.97	119.85± 19.42
t value		0.112	7.148	0.019	20.432	0.035	17.178	0.004	4.070
P value		0.911	0.000	0.984	0.000	0.972	0.000	0.997	0.000

表 4 两组不良反应发生情况比较[n(%)]

Table 4 Comparison of adverse reactions between the two groups[n(%)]

Groups	n	Creatinine increased	Low blood pressure	Other	Total incidence of
Observation group	41	0	1	1	2(4.88)
The control group	39	2	3	4	9(23.08)
x^2 value					5.582
P value					0.018

3 讨论

心力衰竭,是心室泵血的一种临床综合症,近年来,其发病率呈上升趋势,严重影响患者的生活质量[10,11]。有研究显示心力衰竭的发生是由一系列分子和细胞机制导致心肌结构的变化,细胞因子网络失衡发挥重要作用[12,13]。因此,临床上通常使用强心、扩血管等治疗为主[14,15]。厄贝沙坦属于血管紧张素Ⅱ受体抑制剂,能够延缓心肌重构,清除炎症因子,但是其单一用于治疗心力衰竭的效果不佳,故较多学者提出在此基础上联合治疗,以提高临床疗效[16,17]。氧化樟脑注射液是中枢系统兴奋药,具有增强心脏收缩能力,能够快速恢复患者心律,抑制心肌纤维化,从而改善患者心脏血液循环[18,19]。有研究显示氧化樟脑注射液用于治疗心力衰竭效果显著,其经抗氧化作用能抑制心肌纤维化的发生,从而改善心肌损伤[20,21]。本研究结果显示联合治疗总有效率明显高于单药治疗的患者,同时,不良反应发生更少,与 Kim H L[22]等研究结果相似,提示氧化樟脑注射液联合厄贝沙坦治疗心力衰竭能明显提高患者的临床疗效,且安全性较高。

NT-pro-BNP 主要是由心脏分泌的肽类激素,是评价心力衰竭的重要指标之一。NT-pro-BNP 是 BNP 激素原分裂后没有活性的 N 末端片段,能反映 BNP 通路的激活,同时反映心功能的状况[23,24]。NE 是肾上腺素去掉 N- 甲基后形成的物质,由交感节后神经元和脑内肾上腺素能神经末梢合成和分泌,通过α受体的激动作用,可引起小动脉和小静脉血管收缩[25,26]。有研究显示 NT-pro-BNP、NE 在心力衰竭患者中表达异常[27,28]。本研究结果显示联合治疗的患者 NT-pro-BNP、NE 水平明显低于单独使用厄贝沙坦的患者,与 van Veldhuisen D J[29]等研究结果相似。分析是因为厄贝沙坦能够延缓心肌重构与细胞凋亡,且直接作用于 BNP,使其活化并参与心血管调节;氧化樟脑注射液则能增强心脏收缩,提高每分钟心排出量,恢复机体正常血液循环的作用,同时保护血管内皮细胞的完整性,改善心肌超微结构损伤,延缓心肌耐缺氧作用。

Dondo T B[30]等研究表明氧化樟脑注射液能明显改善心力衰竭患者的心功能。本研究结果也显示联合治疗的患心功能高于单药治疗的患者,提示联合治疗疗效显著,使患者的心功能得到改善。分析是因为氧化樟脑注射液具有调节心血管系统功能的作用,还能提高患者心肌收缩力,降低血压高凝状态,减少氧自由基的生成,保护机体线粒,预防心肌缺血再灌注中的损伤形,从而改善患者的心功能。

综上所述,在心力衰竭患者中应用氧化樟脑注射液联合厄贝沙坦的治疗效果显著,可有效改善患者 NT-pro-BNP、NE 水平,减少并发症。

参 考 文 献(References)

[1] Dharmarajan K, Rich M W. Epidemiology, Pathophysiology, and Prognosis of Heart Failure in Older Adults [J]. Heart Failure Clinics, 2017, 13(3): 417

[2] Køber L, Thune J J, Nielsen J C, et al. Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure [J]. N Engl J Med, 2017, 375(13): 1221

[3] Jakovljevic D G, Yacoub M H, Schueler S, et al. Left Ventricular Assist Device as a Bridgeto Recovery for Patients With Advanced Heart Failure [J]. Journal of the American College of Cardiology, 2017, 69 (15): 1924-1933

[4] Saitoh M, Dos Santos M R, Emami A, et al. Anorexia, functional capacity, and clinical outcome in patients with chronic heart failure: results from the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF)[J]. Esc Heart Failure, 2017, 4(4): 448-457

[5] Tayal U, Prasad S, Cook S A. Genetics and genomics of dilated cardiomyopathy and systolic heart failure[J]. Genome Medicine, 2017, 9 (1): 20

[6] Matsue Y, Meer P V D, Damman K, et al. Blood urea nitrogen-to-creatinine ratio in the general population and in patients with acute heart failure[J]. Heart, 2017, 103(6): 407-413

[7] Melenovsky V, Hwang S J, Lin G, et al. Right heart dysfunction in

heart failure with preserved ejection fraction [J]. Journal of Cardiac Failure, 2017, 35(48): 3452-3462

[8] Testa G, Cacciatore F, Bianco A, et al. Chronic obstructive pulmonary disease and long-term mortality in elderly subjects with chronic heart failure[J]. Aging Clinical & Experimental Research, 2017, 29(6): 1-8

[9] Ciani O, Piepoli M, Smart N, et al. Validation of Exercise Capacity as a Surrogate Endpoint in Exercise-Based Rehabilitation for Heart Failure: A Meta-Analysis of Randomized Controlled Trials[J]. Jacc Heart Failure, 2018, 6(7): 596

[10] Kosiborod M, Cavender M A, Fu A Z, et al. Lower Risk of Heart Failure and Death in Patients Initiated on Sodium-Glucose Cotransporter-2 Inhibitors Versus Other Glucose-Lowering DrugsClinical Perspective: The CVD-REAL Study (Comparative Effectiveness of Cardiovascular Outcomes in New Users of Sodiu [J]. Circulation, 2017, 136(3): 249-259

[11] Tampaki E C, Tampakis A, Pantos C. Letter by Tampaki et al Regarding Article, "Lower Risk of Heart Failure and Death in Patients Initiated on Sodium-Glucose Cotransporter-2 Inhibitors Versus Other Glucose-Lowering Drugs: The CVD-REAL Study (Comparative Effectiveness of Cardiovascular Outcom [J]. Circulation, 2018, 137(9): 982

[12] Packer M, O'Connor C, Jjv M M, et al. Effect of Ularitide on Cardiovascular Mortality in Acute Heart Failure[J]. New England Journal of Medicine, 2017, 376(20): 1956

[13] Jorsal A, Kistorp C, Holmager P, et al. Effect of liraglutide, a glucagon-like peptide-1 analogue, on left ventricular function in stable chronic heart failure patients with and without diabetes (LIVE)-a multicentre, double-blind, randomised, placebo-controlled trial [J]. European Journal of Heart Failure, 2017, 19(1): 69-77

[14] Jinshan H, Xuebin L. Letter by Jin-shan and Xue-bin Regarding Article, "Lower Risk of Heart Failure and Death in Patients Initiated on Sodium-Glucose Cotransporter-2 Inhibitors Versus Other Glucose-Lowering Drugs: The CVD-REAL Study (Comparative Effectiveness of Cardiovascular[J]. Circulation, 2018, 137(9): 988-988

[15] Rogers J G, Pagani F D, Tatooles A J, et al. Intrapericardial Left Ventricular Assist Device for Advanced Heart Failure - NEJM[J]. N Engl J Med, 2017, 376(5): 451-460

[16] Tiburcy M, Hudson J E, Balfanz P, et al. Defined Engineered Human Myocardium with Advanced Maturation for Applications in Heart Failure Modelling and Repair[J]. Circulation, 2017, 135(19): 1832

[17] Melman Y F, Shah R, Danielson K, et al. Circulating MicroRNA-30d Is Associated With Response to Cardiac Resynchronization Therapy in Heart Failure and Regulates Cardiomyocyte ApoptosisCLINICAL PERSPECTIVE: A Translational Pilot Study [J]. Government Information Quarterly, 2017, 131(25): 2202-2216

[18] Kupsky D F, Ahmed A M, Sakr S, et al. Cardiorespiratory fitness and incident heart failure: The Henry Ford ExercIse Testing (FIT) Project [J]. Diabetes Care, 2017, 38(11): 35-42

[19] Obokata M, Ynv R, Pislaru S V, et al. Evidence Supporting the Existence of a Distinct Obese Phenotype of Heart Failure With Preserved Ejection Fraction[J]. Circulation, 2017, 136(1): 6

[20] Dos Santos M R, Saitoh M, Ebner N, et al. Sarcopenia and Endothelial Function in Patients With Chronic Heart Failure: Results From the Studies Investigating Comorbidities Aggravating Heart Failure (SICA-HF) [J]. Journal of the American Medical Directors Association, 2017, 18(3): 240-245

[21] King J B, Shah R U, Sainskinguyen A, et al. Effect of Inpatient Dobutamine vs. Milrinone on Out-of-Hospital Mortality in Patients with Acute Decompensated Heart Failure[J]. Pharmacotherapy the Journal of Human Pharmacology & Drug Therapy, 2017, 37(6): 662

[22] Kim H L, Kim M A, Choi D J, et al. Gender Difference in the Prognostic Value of N-Terminal Pro-B Type Natriuretic Peptide in Patients with Heart Failureã- A Report From the Korean Heart Failure Registry (KorHF)[J]. Circulation Journal, 2017, 81(9): 1329-1336

[23] Sartipy U, Dahlström U, Fu M, et al. Atrial Fibrillation in Heart Failure With Preserved, Mid-Range, and Reduced Ejection Fraction [J]. Jacc Heart Fail, 2017, 5(8): 565-574

[24] Sartipy U, Dahlström U, Fu M, et al. Atrial Fibrillation in Heart Failure With Preserved, Mid-Range, and Reduced Ejection Fraction [J]. Jacc Heart Fail, 2017, 5(8): 565-574

[25] Fedele F, Mancone M, Adamo F, et al. Heart Failure With Preserved, Mid-Range, and Reduced Ejection Fraction: The Misleading Definition of the New Guidelines[J]. Cardiology in Review, 2017, 25(1): 4

[26] Ezekowitz J A, O'Meara E, Mcdonald M A, et al. 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure[J]. Canadian Journal of Cardiology, 2017, 33(11): 1342

[27] Wisløff U, Lavie C J, Rognmo Ø. Letter by Wisløff, et al. Regarding Article, "High-Intensity Interval Training in Patients With Heart Failure With Reduced Ejection Fraction" [J]. Circulation, 2017, 136(6): 609

[28] Seferovic J P, Claggett B, Seidelmann S B, et al. Effect of sacubitril/valsartan versus enalapril on glycaemic control in patients with heart failure and diabetes: a post-hoc analysis from the PARADIGM-HF trial [J]. Lancet Diabetes & Endocrinology, 2017, 5 (5): 333

[29] van Veldhuisen D J, Ponikowski P, Van d M P, et al. Effect of Ferric Carboxymaltose on Exercise Capacity in Patients with Chronic Heart Failure and Iron Deficiency[J]. Circulation, 2017, 136(15): 1374-1383

[30] Dondo T B, Hall M, West R M, et al. β-Blockers and Mortality After Acute Myocardial Infarction in Patients Without Heart Failure or Ventricular Dysfunction [J]. Journal of the American College of Cardiology, 2017, 69(22): 2710-2720