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富马酸比索洛尔对老年慢性心力衰竭患者血清胆红素、NT-proBNP 及运动耐力的影响 *

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摘要 目的: 探究富马酸比索洛尔对老年慢性心力衰竭患者血清胆红素、N-末端 B 型利钠肽原 (N-Terminal pro-brain natriuretic peptide, NT-proBNP) 及运动耐力的影响。**方法:** 选择我院于 2017 年 1 月~2020 年 1 月收治的老年慢性心力衰竭患者 80 例, 根据入院顺序经随机数字表法分成两组, 对照组 40 例患者仅采用常规治疗方案进行治疗, 研究组 40 例患者在常规治疗基础上联合富马酸比索洛尔进行治疗。对比两组患者治疗总有效率、左心室射血分数 (left ventricular ejection fraction, LVEF)、心排量 (cardiac output, CO)、每搏输出量 (stroke volume, SV)、血清 NT-proBNP 水平、6 min 步行测试距离、总胆红素、直接胆红素水平。**结果:** 研究组的治疗总有效率 90.00 %, 显著高于对照组 72.50 % ($P < 0.05$); 治疗前, 两组的 LVEF、CO、SV 水平对比无差异 ($P > 0.05$); 治疗后, 两组的 LVEF、CO、SV 水平均升高, 且研究组更高 ($P < 0.05$); 治疗前, 两组的 NT-proBNP 水平及 6 min 步行测试距离对比无显著性差异 ($P > 0.05$); 治疗后, 两组的 NT-proBNP 水平比治疗前均显著降低、6 min 步行测试距离比治疗前均显著升高, 且研究组更优 ($P < 0.05$); 治疗前, 两组的总胆红素、直接胆红素水平对比无差异 ($P > 0.05$); 治疗后, 两组的总胆红素、直接胆红素水平均比治疗前显著降低, 且研究组显著低于对照组 ($P < 0.05$)。**结论:** 在常规治疗基础上联合富马酸比索洛尔治疗老年慢性心力衰竭的临床效果显著, 其可有效改善患者心功能及运动耐力, 值得推荐至临床广泛应用。

关键词: 富马酸比索洛尔; 老年慢性心力衰竭患者; 血清胆红素; NT-proBNP; 运动耐力

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Effects of Bisoprolol Fumarate on Serum Bilirubin, NT-proBNP and Exercise Tolerance in Elderly Patients with Chronic Heart Failure*

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ABSTRACT Objective: To investigate the effect of bisoprolol fumarate on serum bilirubin, NT-proBNP and exercise tolerance in elderly patients with chronic heart failure. **Methods:** A total of eighty elderly patients with chronic heart failure, who were admitted to Xinjiang Uygur Autonomous Region People's Hospital from January 2017 to January 2020, were selected as the research subjects and were randomly divided into two groups according to the order of admission. The 40 patients in the control group were only treated with conventional treatment, and the 40 patients in the study group were treated with bisoprolol fumarate based on the conventional treatment. The total treatment efficiency, left ventricular ejection fraction (LVEF), cardiac output (CO), stroke volume (SV), serum NT-proBNP level, 6-minute walking test distance, total bilirubin, and direct bilirubin levels were compared between the two groups. **Results:** The total effective rate of treatment in the study group was 90.00 %, which was significantly higher than that in the control group (72.50%, $P < 0.05$). Before treatment, there was no significant difference in LVEF, CO, and SV levels between the two groups of patients ($P > 0.05$); after treatment, the LVEF, CO, and SV levels of the two groups of patients increased, and the study group was higher ($P < 0.05$). Before treatment, there was no significant difference in NT-proBNP level and 6-minute walking test distance between the two groups of patients ($P > 0.05$). After treatment, the NT-proBNP levels of the two groups of patients were significantly lower than before treatment, the 6-minute walking test distance was significantly higher than before treatment, and the study group was better ($P < 0.05$). Before treatment, there was no significant difference in total bilirubin and direct bilirubin levels between the two groups of patients ($P > 0.05$). After treatment, the levels of total bilirubin and direct bilirubin in the two groups were significantly lower than before treatment, and the study group was significantly lower than the control group ($P < 0.05$). **Conclusion:** On the basis of conventional treatment, combined with bisoprolol fumarate in the treatment of elderly chronic heart failure has a significant effect, it can effectively improve the patient's heart function and exercise endurance, which is worth recommending to clinical application.

Key words: Bisoprolol fumarate; Elderly patients with chronic heart failure; Serum bilirubin; NT-proBNP; Exercise tolerance

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前言

心力衰竭是由于心肌梗死、心肌病、血流动力学负荷过重、炎症等引起的心肌损伤,造成心肌结构和功能的变化,最后导致心室泵血或充盈功能低下^[1,2]。临床上主要表现为活动时心慌、胸闷、憋喘、咳嗽咳痰,有的还出现少尿无尿等肾脏灌注不良,还有伴腹胀、纳差、恶心呕吐等胃肠道淤血的症状,体格检查可以发现患者血压偏低,双肺底闻及明显的湿啰音,肝脾肿大,有的合并胸腔腹腔积液,同时伴双下肢明显浮肿^[3-5]。慢性心力衰竭的患者,在临床上治疗主要包括生活方式的干预和规律服药治疗,患者可长期坚持服用利尿剂、 β 受体阻断剂、ACEI或者ARB等长期改善心衰预后的药物,必要的时候还需要加地高辛类强心药物^[6,7]。富马酸比索洛尔为 β 受体阻滞剂,对支气管和血管平滑肌的 β_1 -受体有高亲和力,从而使血管扩张,血压降低,广泛适用于高血压、冠心病、及中度至重度慢性稳定性心力衰竭等症^[8]。本文通过探究富马酸比索洛尔对老年慢性心力衰竭患者血清胆红素、NT-proBNP及运动耐力的影响,旨在为临床治疗提供参考依据。

1 资料与方法

1.1 一般资料

选择我院于2017年1月~2020年1月收治的老年慢性心力衰竭患者80例,根据入院顺序经随机数字表法分成两组,其中,对照组40例,男22例,女18例,平均年龄为70.77 $\pm$ 6.92岁,心功能分级包括II级12例,III级21例,IV级7例;研究组40例,男20例,女20例,平均年龄为71.54 $\pm$ 6.15岁,心功能分级包括II级13例,III级21例,IV级6例;两组的基础资料对比无差异($P>0.05$),具有可比性。

1.2 治疗方法

对照组采用血管紧张素酶抑制剂(ACEI)、利尿剂及血管扩张剂等常规治疗方案;观察组在常规治疗基础上采用富马酸比索洛尔(生产企业:Merck KGaA;批准文号:注册证号H20160474;规格:5 mg/片)进行治疗,初始剂量为1.25 mg,每日一次,随后根据患者血压、心率、心功能等情况逐渐增量至2.5 mg、3.75 mg、5.00 mg。疗程6个月。

1.3 观察指标

(1)对比两组治疗总有效率,治疗后,患者的心功能恢复正常或提高2级即为显效;患者的心功能未恢复正常,但提高1级即为有效;未达到上述标准者即为无效^[9];治疗总有效率=[(显效+有效)/总例数] $\times$ 100%;(2)对比两组左心室射血分数(LVEF)、心排量(CO)、每搏输出量(SV)水平,均采用GE Vivid E9彩超诊断系统测量^[10];(3)对比两组血清NT-proBNP水平及6 min步行测试距离,其中,血清NT-proBNP水平采用电化学发光双抗体夹心法测定^[11];(4)对比两组的总胆红素、直接胆红素水平,采用美国贝克曼公司全自动生化仪(LX20)进行检测^[12]。

1.4 统计学分析

采用SPSS 20.0,其中,计数资料以%表示,对比经卡方分析;计量资料以($\bar{x}\pm s$)表示,对比经t检验; $P<0.05$ 有统计学意义。

2 结果

2.1 两组疗效对比

研究组的治疗总有效率90.00%(36/40),显著高于对照组72.50%(29/40),对比有统计学意义($P<0.05$),见表1。

表1 两组疗效对比[例(%)]

Table 1 Comparison of treatment effect between two groups of patients [n (%)]

Groups	n	Effect	Effective	Invalid	Total excellent
Research group	40	24(60.00)	12(30.00)	4(10.00)	36(90.00)*
Control group	40	15(37.50)	14(35.00)	11(27.50)	29(72.50)

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

2.2 两组 LVEF、CO、SV 水平对比

治疗前,两组的LVEF、CO、SV水平对比无差异($P>$

0.05);治疗后,两组的LVEF、CO、SV水平均升高,且研究组更高($P<0.05$),见表2。

表2 两组 LVEF、CO、SV 水平对比($\bar{x}\pm s$)

Table 2 Comparison of LVEF, CO and SV levels between two groups ($\bar{x}\pm s$)

Groups	n	LVEF(%)		CO(L/min)		SV(mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	40	42.35 $\pm$ 5.06	53.74 $\pm$ 7.46**	4.16 $\pm$ 0.79	5.65 $\pm$ 0.89**	51.78 $\pm$ 8.30	62.52 $\pm$ 10.45**
Control group	40	42.42 $\pm$ 4.95	48.61 $\pm$ 7.68 [#]	4.20 $\pm$ 0.75	4.98 $\pm$ 0.85 [#]	51.76 $\pm$ 8.34	56.05 $\pm$ 9.62 [#]

Note: * $P<0.05$, compared with control group; [#] $P<0.05$, compared with preoperative.

2.3 两组 NT-proBNP 水平及 6 min 步行测试距离对比

治疗前,两组的NT-proBNP水平及6 min步行测试距离对比无差异($P>0.05$);治疗后,两组的NT-proBNP水平比治疗前均显著降低、6 min步行测试距离比治疗前均显著升高,且

研究组更优($P<0.05$),见表3。

2.4 两组血清胆红素水平对比

治疗前,两组的总胆红素、直接胆红素水平对比无显著性差异($P>0.05$);治疗后,两组的总胆红素、直接胆红素水平均

比治疗前显著降低,且研究组显著低于对照组($P<0.05$),见表4。

表 3 两组 NT-proBNP 水平及 6 min 步行测试距离对比 ($\bar{x}\pm s$)

Table 3 Comparison of NT-proBNP level and 6 min walking distance between two groups ($\bar{x}\pm s$)

Groups	n	NT-proBNP(ng/mL)		6 min Walking distance(m)	
		Before treatment	After treatment	Before treatment	After treatment
Research group	40	3.91±0.16	0.84±0.06 ^{#*}	108.86±22.29	162.05±45.49 ^{#*}
Control group	40	3.88±0.19	2.11±0.10 [#]	110.90±25.05	135.38±31.25 [#]

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

表 4 两组血清胆红素水平对比 ($\bar{x}\pm s$)

Table 4 Comparison of serum bilirubin levels between two groups of patients ($\bar{x}\pm s$)

Groups	n	Total bilirubin (μmol/L)		Direct bilirubin (μmol/L)	
		Before treatment	After treatment	Before treatment	After treatment
Research group	40	34.51±8.16	15.54±3.46 ^{#*}	18.16±3.19	5.45±1.49 ^{#*}
Control group	40	34.58±7.95	25.21±4.28 [#]	18.22±3.05	11.38±2.05 [#]

Note: * $P<0.05$, compared with control group; [#] $P<0.05$, compared with preoperative.

3 讨论

心力衰竭简称心衰,是各种心脏疾病进展至严重阶段引起的一种复杂的临床综合征。由于心脏的收缩功能和(或)舒张功能发生障碍,不能将静脉回心血量充分排出心脏,导致静脉系统血液淤积,动脉系统血液灌注不足,进而引起心脏循环障碍症候群^[13-15],在临床上主要表现为呼吸困难、乏力以及浮肿等三方面的临床表现^[16],严重威胁患者生命健康。富马酸比索洛尔是一种β受体阻滞剂,它可以选择性的阻断肾上腺素与β1受体结合,而不对β2受体产生影响,是一种对心脏具有高度选择性和亲和力的β1受体阻滞剂。临床上可用于降血压、控制心室率、治疗心力衰竭,改善心肌预后^[17-19]。本研究通过将其应用于老年慢性心力衰竭患者的治疗中,结果显示,研究组的治疗总有效率90.00%显著高于对照组;治疗前,两组的LVEF、CO、SV水平对比无显著性差异;治疗后,两组的LVEF、CO、SV水平均升高,且研究组更高;表明富马酸比索洛尔治疗老年慢性心力衰竭的效果显著与张依^[20]然等学者的研究类似,观察富马酸比索洛尔治疗老年慢性心力衰竭患者的临床效果,结果显示治疗6个月后,观察组治疗总有效率(88.64%)明显高于常规组(75.00%),同时结果显示该方法可显著降低患者血压、心率,并改善其心功能,提高心脏储备。

胆红素是人胆汁中的主要色素之一,主要是由于肝脏代谢体内衰老红细胞形成的^[21-23],胆红素偏高多提示肝脏功能异常或受损,一般可见于肝硬化、肝炎、脂肪肝,阻塞性黄疸、胆结石、胰头癌等肝胆疾病。而慢性心衰也可引起肝功能损害,患者主要表现为血清胆红素的轻度升高^[24,25]。本文研究结果还显示,治疗前,两组的总胆红素、直接胆红素水平对比无显著性差异;治疗后,两组的总胆红素、直接胆红素水平均比治疗前显著降低,且研究组显著低于对照组,表明,富马酸比索洛尔可有效改善老年慢性心力衰竭患者的胆红素水平。目前还没有报道富马酸比索洛尔治疗老年慢性心力衰竭患者与胆红素水平变化情

况。但是关于老年慢性心力衰竭与胆红素的相关性研究很多,如学者何凯^[26]等探讨老年慢性心力衰竭患者血清胆红素与NT-proBNP,超敏C反应蛋白(hs-CRP)的临床意义,结果显示老年慢性心力衰竭组血清胆红素,NT-proBNP,hs-CRP水平高于健康对照组,Pearson相关性分析发现总胆红素,直接胆红素,间接胆红素水平与NT-proBNP水平呈正相关,总胆红素,直接胆红素,间接胆红素水平与hs-CRP,左心室的射血分数(LVEF)水平呈负相关。NT-proBNP也就是N端脑钠肽前体,主要是用于评价心脏功能的指标,如果年龄在50岁以上,N端脑钠肽的数值大于900 g/L,如果NT-proBNP大于1500 ng/L,心力衰竭的可能性很大^[27-29]。心衰步行试验即6 min步行试验,这是一种简单、易行且安全、方便的检查,这种检查主要是通过评价心力衰竭患者的运动耐力,评价心力衰竭患者的病情严重程度以及治疗后的效果^[30,31]。本文研究结果显示,治疗前,两组NT-proBNP水平及6 min步行测试距离对比无显著性差异;治疗后,两组的NT-proBNP水平比治疗前均显著降低、6 min步行测试距离比治疗前均显著升高,且研究组更优;与孙淋霞^[32]等学者的研究类似,该学者探讨参附注射液联合富马酸比索洛尔片治疗慢性心力衰竭的临床疗效,结果显示治疗后两组6WMT距离均显著增加,且治疗组治疗后的6WMT距离显著优于对照组;治疗后两组血清NT-proBNP水平均显著降低,且治疗后治疗组血清学指标明显低于对照组。表明富马酸比索洛尔可有效改善老年慢性心力衰竭患者的心功能及运动耐力。同时,本研究尽管在一定程度上验证了联合用药在老年慢性心力衰竭患者治疗中的优势,但也存在一定不足,如样本量较少等,今后拟增加样本量进行更为全面的研究。

综上所述,在常规治疗基础上联合富马酸比索洛尔治疗老年慢性心力衰竭的效果显著,其可有效改善患者心功能及运动耐力,值得推荐至临床广泛应用。

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