

doi: 10.13241/j.cnki.pmb.2017.11.026

贝那普利联合阿托伐他汀治疗慢性心力衰竭的临床疗效*

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摘要 目的:探讨贝那普利联合阿托伐他汀治疗慢性心力衰竭临床疗效及对患者血清炎症因子水平的影响。**方法:**收集我院 2014 年 12 月~2016 年 5 月确诊为慢性心力衰竭的患者 120 例,随机分为观察组和对照组,各 60 例。对照组采用口服贝那普利治疗,观察组采用贝那普利联合阿托伐他汀治疗。观察并比较两组患者治疗前后左室收缩末期容积指数(LVESVI)、左室舒张末期容积指数(LVEDVI)、左心室舒张末期内径(LVEDD)、左心射血分数(LVEF)及血清 NT-proBNP,hs-CRP,TNF- α ,白介素-6(IL-6)及白介素-8(IL-8)水平的变化情况。**结果:**观察组有效率优于对照组,差异具有统计学意义($P<0.05$);治疗后,两组患者 Pro-BNP、LVEDD、E/A 均降低,且观察组低于对照组($P<0.05$);治疗后,两组患者 LVEF 升高,且观察组高于对照组($P<0.05$);两组患者治疗后血清 hs-CRP,TNF- α ,IL-6 及 IL-8 水平均降低,且观察组低于对照组($P<0.05$)。**结论:**贝那普利联合阿托伐他汀治疗对慢性心力衰竭患者进行治疗,疗效显著,患者炎症反应小,是一种安全有效的治疗方法。

关键词:慢性心力衰竭;贝那普利;阿托伐他汀;炎症因子

中图分类号:R541.61 **文献标识码:**A **文章编号:**1673-6273(2017)11-2102-04

Effect of Benazepril and Atorvastatin on Treatment of Chronic Heart Failure*

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ABSTRACT Objective: To explore the clinical effects of benazepril and Atorvastatin on the treatment of chronic heart failure and the serum levels of inflammatory factors. **Methods:** 120 cases with chronic heart failure who were treated in our hospital from December 2014 to May 2016 were selected and randomly divided into the observation group and the control group, with 41 cases in each group. The patients in the control group were treated with benazepril, while the patients in the observation group were treated with benazepril and atorvastatin. Then the changes of the ventricular end-systolic volume index (LVESVI), the left ventricular end-diastolic volume index (LVEDVI), the left ventricular end diastolic diameter (LVEDD) the left ventricular ejection fraction (LVEF), and the serum levels of NT-proBNP, hs-CRP, TNF- α , IL-6 and IL-8 in the two groups were observed and compared before and after the treatment. **Results:** The effective rate of the observation group was obviously higher than that of the control group ($P<0.05$); After treatment, the levels of Pro-BNP, LVEDD and E/A were significantly decreased in the two groups, and the observation group was lower than that of the control group ($P<0.05$); After treatment, the LVEF was significantly increased in two groups, and the observation group was higher than that of the control group ($P<0.05$). After treatment, the serum levels of hs-CRP, TNF- α , IL-6 and IL-8 in the two groups were significantly decreased, and the observation group was lower than that of the control group ($P<0.05$). **Conclusions:** Benazepril and Atorvastatin have obvious clinical effects on the treatment of chronic heart failure, which can reduce the levels of the inflammatory factors and it is safe for clinical application.

Key words: Chronic heart failure; Benazepril; Atorvastatin; Inflammatory factors

Chinese Library Classification(CLC): R541.61 **Document code:** A

Article ID:1673-6273(2017)11-2102-04

前言

慢性心力衰竭(Chronic heart failure, CHF)是指心脏功能出现障碍而引起的运动耐力下降,腹部或腿部出现水肿现象及出现心脏扩大或心功能不全等临床症状,是各种心脏疾病发展的终末阶段。其常见的诱发因素有呼吸道感染、心率失常、心脏负荷较大、体力劳动过度及其他严重疾病等。近年来,慢性心力衰竭的发病率呈逐年升高趋势,对患者生命健康安全造成了严重

的威胁,因此及时治疗并控制病情十分重要^[1]。相关研究表明:他汀类药物不仅具有改善血管内皮功能及抗炎作用,还具有降脂的作用^[2,3],而贝那普利具有改善心功能、延缓心室重构、优化心肌代谢等作用。本文旨在探讨贝那普利联合阿托伐他汀治疗慢性心力衰竭临床疗效及对炎症因子的影响,现报道如下。

1 资料与方法

1.1 临床资料

* 基金项目:湖北省自然科学基金项目(2006ABA23)

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(收稿日期:2016-11-06 接受日期:2016-11-30)

收集我院 2014 年 12 月~2016 年 5 月确诊为慢性心力衰竭的患者 120 例。其中男性 50 例;女性 70 例。所有患者均符合世界心脏病协会和 WHO^[4]关于慢性心力衰竭的诊断标准,经我院伦理委员会审核通过,排除凝血功能异常及严重心血管系统患者,排除对研究所涉及药物的用药禁忌症及药物过敏者,排除严重心、肝、肾、肺等功能障碍或其他严重原发性疾病者,排除孕妇及哺乳期患者,排除脑器质性病变及严重躯体疾病患者。患者或家属签订知情同意书,积极配合此次研究。将 120 患者按随机数字表法分为对照组及观察组各 60 例。两组间基本资料具有可比性($P>0.05$)。见表 1。

表 1 两组患者一般资料比较($\bar{x}\pm s$)

Table 1 Comparison of general information in two groups($\bar{x}\pm s$)		
Items	Observation group (n=60)	Control group (n=60)
Age (year)	35.32 $\pm$ 1.51 [#]	37.45 $\pm$ 1.62
Sex (M/F)	34/26 [#]	36/24
Weight (Kg)	67.3 $\pm$ 5.42 [#]	68.7 $\pm$ 3.55
Course of disease (year)	2.5 $\pm$ 0.8 [#]	2.8 $\pm$ 0.5

1.2 方法

对照组患者给予贝那普利(深圳信立泰药业,规格 10 mg $\times$ 14 片/盒)治疗,口服贝那普利 10 mg,1 日 1 次。观察组在对照组基础上加用阿托伐他汀(北京嘉林药业,规格:10 mg $\times$ 7 片/盒)治疗,每晚口服阿托伐他汀 40 mg,1 晚 1 次,一个治疗周期为 4 周。

1.3 观察指标及方法

1.3.1 疗效评价 临床疗效参照卫生部抗菌药物临床药物实验标准^[5],显效:临床症状明显改善,相关指标恢复正常;有效:临床症状改善,临床指标改善良好,但并未恢复到正常水平;无效:临床症状无变化或加重。总有效率 = 显效率 + 有效率。

1.3.2 炎症因子水平检测 所有患者均于治疗前及治疗 4 周后空腹 12 h 后抽取 5 mL 静脉血,并将其置于 3000 r/min 离心机上行 5 min 离心,将分离出血清置于 -80 °C 冰箱中冷藏。采用快速免疫荧光(RAMP)法对血浆患者的 NT-proBNP 水平进行检测,同时采用酶联免疫吸附法对各组间患者的血清 hs-CRP、

TNF- α 、白介素 -6(IL-6)及白介素 -8(IL-8)水平进行检测,并进行对比分析。

1.3.3 心功能检测 对两组患者治疗前及治疗 4 周后均由专人对患者行心脏超声波检查,其中以心尖四腔心切面测量左室收缩末期容积指数(LVESVI)、左室舒张末期容积指数(LVEDVI)、左心室舒张末期的内径(LVEDD)并计算出患者的 LVEF(测量 3 次取平均值)同时在患者呼气末,采用多普勒分别在主动脉瓣口和二尖瓣及最大血流处进行取样(血流与取样线夹角应 $<200^\circ$),测得二尖瓣口舒张起的 E 峰和 A 峰,并计算出 E/A。记录患者不良反应的发生率并对其进行比较分析。

1.4 统计学分析

所有统计数据均统一整理,采用 SPSS17.0 软件包进行分析,符合正态性的计量资料采用均数 $\pm$ 标准差表示,两组患者指标水平对比予以配对样本 t 检验,临床疗效及不良反应状况采用百分率(%)表示,予以 RxC 卡方检验, $P<0.05$ 存在统计学意义。

2 结果

2.1 两组临床疗效比较

对照组临床总有效率为 75.00%(45/60),观察组临床总有效率为 95.00%(57/60),观察组有效率高于对照组,差异具有统计学意义($P<0.05$)。见表 2。

表 2 两组患者的临床疗效的比较[n(%)]

Items	Observation group (n=60)	Control group (n=60)
Markedly	46(76.67) [#]	20(33.33)
Effective	11(18.33) [#]	25(41.67)
Invalid	3(5.00) [#]	15(25.00)
Total efficiency	57(95.00) [#]	45(75.00)

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

2.2 两组患者治疗前后心功能指标比较

与治疗前比较,两组患者治疗后的 Pro-BNP、LVEF、LVEDD、E/A 指标均明显降低,且观察组明显低于对照组,差异存在统计学意义($P<0.05$)。见表 3。

表 3 两组患者治疗前后心功能指标比较($\bar{x}\pm s$)

Table 3 Comparison of the cardiac function before and after treatment between the two groups($\bar{x}\pm s$)			
Items	Time	Observation group (n=60)	Control group (n=60)
Pro-BNP(pg/l)	Before treatment	659.21 $\pm$ 40.57	657.09 $\pm$ 36.71
	After treatment	573.30 $\pm$ 82.45 ^{*#}	590.19 $\pm$ 69.51 [*]
LVEF(%)	Before treatment	47.31 $\pm$ 5.19	47.96 $\pm$ 5.85
	After treatment	52.01 $\pm$ 5.21 ^{*#}	50.53 $\pm$ 5.49 [*]
LVEDD(mm)	Before treatment	59.04 $\pm$ 5.75	58.31 $\pm$ 6.65
	After treatment	52.94 $\pm$ 6.67 ^{*#}	55.01 $\pm$ 6.99 [*]
E/A	Before treatment	5.67 $\pm$ 3.74	6.39 $\pm$ 4.75
	After treatment	4.19 $\pm$ 2.08 ^{*#}	5.21 $\pm$ 1.78 [*]

Note: Compared with before treatment, ^{*} $P<0.05$; compared with control group after treatment, [#] $P<0.05$.

2.3 两组患者治疗前后血清炎症因子水平比较

与治疗前比较,两组患者治疗后的 hs-CRP、TNF- α 、IL-6 及

IL-8 水平均明显降低,且观察组明显低于对照组,差异存在统计学意义($P < 0.05$)。见表 4。

表 4 两组患者治疗前后血清炎症因子指标比较($\bar{x} \pm s$)

Table 4 Comparison of serum levels of inflammatory factors before and after treatment between the two groups($\bar{x} \pm s$)

Items	Time	Observation group (n=60)	Control group (n=60)
hs-CRP (mg/L)	Before treatment	16.55 $\pm$ 7.91	16.31 $\pm$ 7.15
	After treatment	1.66 $\pm$ 0.38* [#]	1.82 $\pm$ 0.98*
TNF- α (ng/L)	Before treatment	10.22 $\pm$ 3.19	10.96 $\pm$ 3.85
	After treatment	6.98 $\pm$ 1.55* [#]	7.12 $\pm$ 3.85*
IL-6 (ng/L)	Before treatment	47.54 $\pm$ 18.75	48.31 $\pm$ 16.65
	After treatment	8.94 $\pm$ 2.67* [#]	10.01 $\pm$ 2.99*
IL-8 (ng/L)	Before treatment	15.67 $\pm$ 3.74	16.39 $\pm$ 4.75
	After treatment	6.21 $\pm$ 1.28* [#]	7.27 $\pm$ 1.99*

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

2.4 安全性评价

治疗后,患者均有不同层度的不良反应发作。主要有恶心呕吐、皮肤瘙痒、头痛乏力、腹泻和白细胞减少。其中观察组有 4 例(6.66%)患者出现恶心呕吐,2 例(3.33%)患者出现皮肤瘙痒,3 例(5.00%)患者出现头痛乏力,对照组有 5 例(8.33%)患者出现恶心呕吐,3 例(5.00%)患者出现皮肤瘙痒,2 例(3.33%)患者出现头痛乏力,组间相比无明显差异($P > 0.05$)。

3 讨论

心力衰竭是指由于心肌病、心肌梗死、炎症及血流动力负荷过重等原因导致的心肌受损,导致患者心肌功能及结构发生变化,最终引发心室充盈功能低下或泵血现象^[6,7]。临床症状多表现为:运动耐力下降、乏力、呼吸困难等。慢性心力衰竭是指患者长期处于心力衰竭状态^[8,9]。近年来,随着我国心血管疾病的发病率不断升高,其中慢性心力衰竭就是心血管疾病的终末期的症状表现,严重危害身心健康^[10-12]。有研究表明,慢性心力衰竭患者血清炎症因子水平呈异常状态,因此减少患者的炎症反应对于改善患者的心功能具有重要意义^[13]。

贝纳普利是一种血管紧张素转化酶抑制剂,其不但具有降压的作用,还具有减低心脏负荷的作用^[14],其治疗原理是贝纳普利水解后形成一种活力的血管紧张素转换酶抑制剂,降低血管紧张素 II 的作用强度,从而降低外周血管阻力,达到降低血压的作用,且不会引起代偿性液体潴留,同时还能减轻心室后负荷,不增加心率^[15]。阿托伐他汀能够有效降低脂蛋白水平,减少低密度脂蛋白生成及降低血浆胆固醇^[16]。其主要作用机制是通过抑制 HMG-CoA 还原酶和胆固醇在肝脏的生物合成,从而达到降低脂蛋白水平及血浆胆固醇水平的目的。临床研究发现,两种药物联合使用产生耐药反应较少,且临床疗效较高^[17]。本研究发现采用贝纳普利联合阿托伐他汀进行治疗的患者其治疗疗效更加优异,其有效率高达 95.00%。慢性心力衰竭由于冠状动脉硬化能够使心脏局部组织产生纤维化,导致左心室发生增厚,对于心脏正常的功能形成影响,引起心功能减弱^[18]。本研究提示,贝纳普利联合阿托伐他汀治疗后 LVEDD、LVESD 均有降低,且 LVEF 明显升高,表明贝纳普利联合阿托伐他汀能够抑制心肌肥厚,改善心功能。TNF- α 为机体重要的促炎性

因子,可介导炎性细胞的产生聚集、黏附,引发炎症,加速细胞凋亡、坏死,还可促进血管新生^[19]。MMP-9 可参与机体炎症反应、血管新生等病理反应,可使动脉粥样硬化的稳定性减弱,促进斑块产生分裂,利于血栓的形成 D。CRP 为炎症反应的急性蛋白,可参与动脉粥样硬化形成的整个过程。阿托伐他汀无需经代谢即可生成药物活性,容易被机体所吸收,其半衰期长,生物利用度高^[20]。本研究显示,采用贝纳普利联合阿托伐他汀治疗后患者的 TNF- α 、MM P-9、CRP 低于单独采用贝纳普利治疗的患者,表明阿托伐他汀存在抗炎作用,能够降低机体炎症介质,控制疾病的进展。两组患者均产生较轻微的不良反应,且经对应处理后不良反应消失。

综上所述,贝纳普利联合阿托伐他汀治疗慢性心力衰竭的疗效显著,降脂疗效好,促进患者心功能恢复,且炎症反应较小。

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