

阿托伐他汀联合重组人脑利钠肽治疗急性心肌梗死合并心力衰竭的临床观察

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摘要 目的: 观察阿托伐他汀联合重组人脑利钠肽(rhBNP)治疗急性心肌梗死(AMI)合并心力衰竭的疗效和安全性。方法: 160例AMI合并心力衰竭患者随机分为A组和B组。A组患者给予肝素、阿司匹林、氯吡格雷等药物,同时限制钠水摄入,给予利尿药、 β 受体阻滞药,合并呼吸困难者给予面罩吸氧,合并肺感染患者给予抗菌药物等常规治疗;B组患者在A组治疗的基础上给予冻干rhBNP负荷剂量1.5 $\mu\text{g}/\text{kg}$,3 min内静脉推注完,后以0.007 5 $\mu\text{g}/(\text{kg}\cdot\text{min})$ 维持静脉滴注24 h,连用7 d+每晚睡前服用阿托伐他汀钙片40 mg,每日1次,连用14 d。两组疗程均为14 d。观察两组患者的临床疗效,治疗前后血清前胶原氨基末端肽(PⅢNP)、超敏C反应蛋白(hs-CRP)、去甲肾上腺素(NE)、血肌酐(Cr)、左心室射血分数(LVEF)、左心室舒张末期容积(LVEDV)、左心室收缩末期容积(LVESV)及不良反应发生情况。结果:B组患者总有效率显著高于A组,差异有统计学意义($P<0.05$)。治疗前,两组患者PⅢNP、hs-CRP、NE、Cr、LVEF、LVEDV、LVESV比较,差异均无统计学意义($P>0.05$)。治疗后,两组患者PⅢNP、hs-CRP、NE、Cr、LVEDV、LVESV均显著低于同组治疗前,且B组低于A组;LVEF显著高于同组治疗前,且B组高于A组,差异均有统计学意义($P<0.05$)。两组患者不良反应发生率比较,差异无统计学意义($P>0.05$)。结论:在常规治疗的基础上,阿托伐他汀联合rhBNP治疗AMI合并心力衰竭疗效显著,可有效提高心输出量,改善心室重塑,且安全性相当。

关键词 急性心肌梗死;心力衰竭;阿托伐他汀;重组人脑利钠肽;疗效;安全性

Clinical Observation of Atorvastatin Combined with Recombinant Human Brain Natriuretic Peptide in the Treatment of Acute Myocardial Infarction with Heart Failure

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ABSTRACT OBJECTIVE: To observe the efficacy and safety of atorvastatin combined with recombinant human brain natriuretic peptide (rhBNP) in the treatment of acute myocardial infarction (AMI) with heart failure. METHODS: 160 AMI patients with heart failure were randomly divided into group A and group B. Group A was given heparin, aspirin, clopidogrel, sodium intake was limited, diuretics and β -blockers were used for anti-heart failure, dyspnea patients were given oxygen masks, and lung infection patients were given antibiotics, and other conventional treatment; group B was additionally given loading dose 1.5 $\mu\text{g}/\text{kg}$ rhBNP by intravenous injection within 3 min, and maintained with 0.007 5 $\mu\text{g}/(\text{kg}\cdot\text{min})$ for 24 h, for 7 d+40 mg atorvastatin before bed, once a day, for continuous 14 d. The treatment course for both groups was 14 d. Clinical efficacy, serum procollagen amino-terminal peptide (PⅢNP), high-sensitivity C-reactive protein (hs-CRP), norepinephrine (NE), serum creatinine (Cr), left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV) before and after treatment, and the incidence of adverse reactions in 2 groups were observed. RESULTS: The total effective rate in group B was significantly higher than group A, the difference was statistically significant ($P<0.05$). Before treatment, there were no significant differences in the PⅢNP, hs-CRP, NE, Cr, LVEF, LVEDV and LVESV between 2 groups ($P>0.05$). After treatment, PⅢNP, hs-CRP, NE, Cr, LVEDV and LVESV in 2 groups were significantly lower than before, and group B was group A, LVEF was significantly higher than before, and group B was higher than group A, the differences were statistically significant ($P<0.05$). And there was no significant difference in the incidence of adverse reactions between 2 groups ($P>0.05$). CONCLUSIONS: Based on the conventional treatment, atorvastatin combined with rhBNP has certain efficacy in the treatment of AMI with heart failure, it can effectively improve cardiac output and ventricular remodeling, with similar safety.

KEYWORDS Acute myocardial infarction; Heart failure; Atorvastatin; rhBNP; Efficacy; Safety

随着人口老龄化,心血管疾病的发病率逐年上升,急性心肌梗死(Acute myocardial infarction, AMI)作为心血管疾病中重要的一类,其急性期病死率约为15%^[1]。AMI常伴有心肌收

缩功能障碍,因此急性期患者极易并发心力衰竭,据相关研究报道其发生率约为32%~48%^[2]。脑利钠肽(BNP)是心室肌分泌的多肽激素,在心脏循环容积和压力调节的保护性代偿机制中具有重要的作用。已有大量研究证实了重组人脑利钠肽(rhBNP)在心力衰竭治疗中的有效性和安全性^[3-4]。近年来

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研究发现,他汀类药物不仅具有调脂作用,而且还能影响神经体液的调节,改善心室重塑和内皮功能,降低急性冠状动脉发生率和病死率^[5-6]。李敬等^[7]证实,高剂量阿托伐他汀能明显改善AMI患者的血脂、冠状动脉粥样斑块和血管内皮功能。为此,在本研究中笔者在常规治疗的基础上观察阿托伐他汀联合rhBNP治疗AMI合并心力衰竭的疗效和安全性,以为临床治疗提供参考。

1 资料与方法

1.1 研究对象

选择2010年3月—2015年3月宜宾市第二人民医院心内科收治的160例AMI合并心力衰竭患者,其中男性85例,女性75例;年龄75~90岁,平均年龄(85.4±5.9)岁。按随机数字表法将所有患者均分为A组和B组。A组男性43例,女性37例;年龄77~88岁,平均年龄(84.3±6.5)岁;心功能分级:Ⅱ级30例,Ⅲ级35例,Ⅳ级15例。B组男性42例,女性38例;年龄79~90岁,平均年龄(86.3±4.7)岁;心功能分级:Ⅱ级32例,Ⅲ级33例,Ⅳ级15例。两组患者性别、年龄、心功能分级等基本资料比较,差异均无统计学意义($P>0.05$),具有可比性。本研究方案经医院医学伦理委员会审核通过,所有患者或其家属均签署了知情同意书。

1.2 纳入与排除标准

纳入标准:(1)均符合《急性心肌梗死诊断和治疗指南》^[8]中的诊断标准;(2)均合并心力衰竭;(3)发病时间 <12 h。排除标准:(1)既往有AMI及心力衰竭病史;(2)发病时间 >12 h;(3)合并肝肾功能不全、肿瘤;(4)对本研究所用药物过敏;(5)合并心源性休克、心脏骤停。

1.3 治疗方法

A组患者给予肝素、阿司匹林、氯吡格雷等药物,同时限制钠水摄入,给予利尿药、 β 受体阻滞药,合并呼吸困难者给予面罩吸氧,合并肺感染者给予抗菌药物等常规治疗;B组患者在A组治疗的基础上给予冻干rhBNP(成都诺迪康生物制药有限公司,规格:0.5 mg)负荷剂量1.5 μ g/kg,3 min内静脉推注完,后以0.007 5 μ g/(kg·min)维持静脉滴注24 h,连用7 d+每晚睡前服用阿托伐他汀钙片(大连辉瑞制药有限公司,规格:10 mg/片)40 mg,每日1次,连用14 d。两组疗程均为14 d。

1.4 观察指标

表2 两组患者治疗前后PⅢNP、hs-CRP、NE、Cr比较($\bar{x}\pm s$)

Tab 2 Comparison of PⅢNP, hs-CRP, NE and Cr between 2 groups before and after treatment($\bar{x}\pm s$)

组别	n	PⅢNP,ng/ml		hs-CRP,ng/ml		NE,ng/L		Cr, μ .mol/L	
		治疗前	治疗后	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
A组	80	159.85±6.31	109.86±7.64*	15.74±2.24	9.26±1.02*	598.87±105.26	360.35±46.81*	110.75±20.43	85.56±9.37*
B组	80	161.35±9.27	90.27±5.99**	16.13±1.99	5.34±1.11**	605.95±99.56	270.35±39.75**	107.35±16.54	67.75±7.66**

注:与治疗前比较,* $P<0.05$;与A组比较,** $P<0.05$

Note: vs. before treatment,* $P<0.05$; vs. group A,** $P<0.05$

治疗前,两组患者LVEF、LVEDV、LVESV比较,差异均无统计学意义($P>0.05$)。治疗后,两组患者LVEF显著高于同组治疗前,且B组高于A组;LVEDV、LVESV均显著低于同组治疗前,且B组低于A组,差异均有统计学意义($P<0.05$),详见表3。

2.4 不良反应

两组患者治疗期间均未见严重不良反应发生。A组患者出现1例皮疹,2例食欲不振、轻度恶心呕吐,1例轻度头晕,1例心动过速,不良反应发生率为6.25%;B组患者出现2例轻度恶心呕吐,2例轻度Cr增高,2例阵发性室上性心动过速,1例血压轻度下降,不良反应发生率为8.75%。两组患者不良发生比较,差异无统计学意义($P>0.55$)。

观察两组患者治疗前后血清前胶原氨基末端肽(PⅢNP)、超敏C反应蛋白(hs-CRP)、去甲肾上腺素(NE)、血肌酐(Cr)、左心室射血分数(LVEF)、左心室舒张末期容积(LVEDV)、左心室收缩末期容积(LVESV)及不良反应发生情况。采用Bayer ADVIA 2 400型全自动生化分析仪(德国西门子子公司)测定hs-CRP、NE、Cr;采用酶联免疫吸附法(ELISA)测定PⅢNP(试剂盒由杭州联科生物技术股份有限公司提供);采用IE33型超声心动图仪(荷兰飞利浦公司)测定LVEF、LVEDV、LVESV。

1.5 疗效判定标准^[9]

显著有效:心功能Ⅰ级或提高 ≥ 2 级,临床症状显著改善;有效:心功能提高1级,临床症状有所改善;无效:心功能无改善,临床症状无变化;恶化:心功能恶化,临床症状加重。总有效率=(显著有效例数+有效例数)/总例数 $\times 100\%$ 。

1.6 统计学方法

采用SPSS 20.0统计软件对数据进行分析。计量资料以 $\bar{x}\pm s$ 表示,采用 t 检验;计数资料以%表示,采用 χ^2 检验。 $P<0.05$ 为差异有统计意义。

2 结果

2.1 两组患者临床疗效比较

B组患者总有效率显著高于A组,差异有统计学意义($P<0.05$),详见表1。

表1 两组患者临床疗效比较(例)

Tab 1 Comparison of the clinical efficacy between 2 groups (case)

组别	n	显著有效	有效	无效	恶化	总有效率,%
A组	80	30	26	15	9	70.00
B组	80	38	30	10	2	85.00*

注:与A组比较,* $P<0.05$

Note: vs. group A,* $P<0.05$

2.2 两组患者治疗前后PⅢNP、hs-CRP、NE、Cr比较

治疗前,两组患者PⅢNP、hs-CRP、NE、Cr比较,差异均无统计学意义($P>0.05$)。治疗后,两组患者PⅢNP、hs-CRP、NE、Cr均显著低于同组治疗前,且B组低于A组,差异均有统计学意义($P<0.05$),详见表2。

2.3 两组患者治疗前后LVEF、LVEDV、LVESV比较

3 讨论

心肌梗死主要由于不稳定冠状动脉粥样斑块破裂,引起血管内凝血系统及血小板的活化,最终引发出血及血栓的形成,心肌由于冠状动脉管腔闭塞而引发持续性的缺血产生梗死^[10]。AMI后神经体液系统、交感神经系统和肾素-血管紧张素-醛固酮系统(RAAS)激活,心肌进一步损伤,引起心室重塑,产生收缩功能及血流动力学障碍,易产生心力衰竭^[11]。

血脂与AMI的发病密切相关,血脂水平增高,侵及冠状动脉壁,进入中膜,引起平滑肌细胞增生,进而影响冠状动脉通畅度及心肌灌注,而脂蛋白分解产物构成了粥样斑块的主要成分。阿托伐他汀能有效抑制羟甲基戊二酸单酰辅酶A还原酶,降低血液中胆固醇及三酰甘油浓度,上调低密度脂蛋白及

表3 两组患者治疗前后LVEF、LVEDV、LVESV比较($\bar{x} \pm s$)Tab 3 Comparison of LVEF, LVEDV and LVESV between 2 groups before and after treatment($\bar{x} \pm s$)

组别	n	LVEF,%		LVEDV,ml		LVESV,ml	
		治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
A组	80	31.61±5.22	36.26±6.13*	110.86±12.79	100.26±11.12*	63.87±10.33	52.35±12.06*
B组	80	32.35±4.97	39.39±5.37**	111.13±14.25	95.34±11.87**	64.75±11.17	45.75±10.37**

注:与治疗前比较,* $P<0.05$;与A组比较,** $P<0.05$

Note: vs. before treatment, * $P<0.05$; vs. group A, ** $P<0.05$

增加高密度脂蛋白水平。此外,阿托伐他汀还可以稳定冠状动脉粥样斑块,抑制血管内皮炎症,通过提高内源性一氧化氮(NO)合酶和血管内皮舒张因子,改善内皮功能,达到抗凝和抗血小板的目的^[12]。

本研究结果显示,治疗后两组患者PⅢNP均显著低于同组治疗前,且B组低于A组,差异均有统计学意义。这说明,阿托伐他汀能明显改善心室重塑,抑制心肌纤维化。两组患者hs-CRP均显著低于同组治疗前,且B组低于A组,差异均有统计学意义。这提示,阿托伐他汀具有明显的抗炎作用,进而影响心室重塑的进程。研究表明,阿托伐他汀能增加循环中内皮细胞含量,减轻其与白细胞的相互作用,促进新生血管形成,减少急性心肌梗死事件的发生率^[13]。

自rhBNP于2001年被美国食品与药品管理局(FDA)批准用于治疗急性左心心力衰竭以来,其安全性和可靠性已得到大量临床研究论证^[14-15]。BNP通过扩张小动脉和小静脉,降低外周循环阻力,减轻心脏前后负荷,同时调节RAAS系统及交感神经系统,改善心肌血供,降低心肌氧耗,抑制心肌纤维增生,具有保护心脏的作用。AMI合并心力衰竭患者血浆氮末端BNP前体浓度可随梗死面积增加而上升,AMI合并心力衰竭时,虽然可产生大量BNP,但很快就会被降解,外源性rhBNP能较好的维持患者血浆中BNP水平,选择性扩张冠状动脉,增加心肌血供,提高心肌抗缺血缺氧能力,改善心室重塑,提高心肌存活率,降低梗死面积^[16]。研究证实,rhBNP可能通过VEGF-PKD1-HDAC7及VEGF-PI3K/AKte-NOS途径调节内皮祖细胞的功能,而内皮祖细胞可参与心肌梗死后缺血区域新生血管形成及损伤血管的修复,进而改善心功能^[17-18]。

本研究结果还显示,治疗后,两组患者LVEF显著高于同组治疗前,且B组高于A组;LVEDV、LVESV均显著低于同组治疗前,且B组低于A组,差异均有统计学意义。这表明,rhBNP能有效提高AMI合并心力衰竭患者的心搏量。AMI合并心力衰竭后机体通过神经体液调节,收缩外周血管以保证心脑血管血液供应,肾脏无氧代谢增强,患者易产生少尿、无尿,这是AMI合并心力衰竭高病死率的一个重要原因。在本研究中,两组患者NE、Cr均显著低于同组治疗前,且B组低于A组,差异均有统计学意义。这提示,rhBNP能增加肾脏灌注,提高肾小管毛细血管压,肾小管液重吸收减少,增加尿量,改善肾功能。

综上所述,在常规治疗的基础上,阿托伐他汀联合rhBNP治疗AMI合并心力衰竭疗效显著,可有效提高心输出量,改善心室重塑,且安全性相当。由于本研究纳入的样本量较少,随访时间较短,且未统计所有患者的长期疗效,故此结论仍需进行大样本、高质量的随机研究加以证实。

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氢氯噻嗪联合酚妥拉明对高血压急症患者相关指标的影响

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摘要 目的:探讨氢氯噻嗪联合酚妥拉明对高血压急症患者相关指标的影响。方法:150例高血压急症患者随机均分为酚妥拉明组、氢氯噻嗪组和联用组。各组患者均给予卡托普利等常规治疗。在此基础上,酚妥拉明组患者给予甲磺酸酚妥拉明注射液20 mg,加入5%葡萄糖注射液250 ml中,静脉滴注,30~40滴/min;氢氯噻嗪组患者给予氢氯噻嗪片50 mg,口服;联用组患者给予甲磺酸酚妥拉明注射液(用法用量同酚妥拉明组)+氢氯噻嗪片(用法用量同氢氯噻嗪组)。各组患者均在治疗后10、30、60 min时观察收缩压(SBP)、舒张压(DBP)、平均动脉压(MAP)、心率(HR)、心脏指数(CI)以及外周阻力指数(TPRI),并记录不良反应发生情况。结果:治疗后,联用组和酚妥拉明组患者SBP、DBP、MAP、TPRI水平均显著低于同组治疗前,随治疗时间的延长逐渐降低,而联用组低于酚妥拉明组和氢氯噻嗪组;CI水平显著高于同组治疗前,随治疗时间的延长逐渐升高,且联用组高于酚妥拉明组和氢氯噻嗪组;氢氯噻嗪组患者仅治疗后60 min SBP、DBP、MAP、TPRI水平低于同组治疗前及治疗后10、30 min,CI水平高于同组治疗前及治疗后10、30 min,差异均有统计学意义($P < 0.05$)。各组患者不良反应发生率比较,差异无统计学意义($P > 0.05$)。结论:在常规治疗的基础上,氢氯噻嗪联合酚妥拉明能显著改善高血压急症患者的血压、心功能,且安全性较好。

关键词 氢氯噻嗪;酚妥拉明;高血压急症

Effect of Hydrochlorothiazide Combined with Phentolamine on Related Indicators of Hypertensive Emergency

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ABSTRACT OBJECTIVE: To explore the effects of hydrochlorothiazide combined with phentolamine on related indicators of hypertensive emergency. METHODS: 150 patients with hypertensive emergency were randomly divided into phentolamine group, hydrochlorothiazide group and combination group. All patients were given Captopril tablet and other Conventional treatment. Based on it, phentolamine group was given 20 mg Phentolamine mesylate injection, adding into 250 ml 5% Glucose injection by intravenous infusion, with drip rate of 30-40 mg/min; hydrochlorothiazide group was given 50 mg Hydrochlorothiazide tablet, orally. Combination group was given Hydrochlorothiazide tablet (the same dosage with hydrochlorothiazide group) + Phentolamine mesylate injection (the same dosage with phentolamine group). Systolic blood pressure (SBP), diastolic blood pressure (DBP), arterial pressure (MAP), heart rate (HR), cardiac index (CI) and the peripheral resistance (TPRI) in all groups were observed after 10, 30 and 60 min. RESULTS: After treatment, the SBP, DBP, MAP and TPR levels in combination group and phentolamine group were significantly lower than before and gradually decreased by time extension, and combination group was lower than phentolamine group and hydrochlorothiazide group, CI level was significantly higher than before and gradually increased by time extension, and combination group was higher than phentolamine group and hydrochlorothiazide group; after 60 min, SBP, DBP, MAP and TPRI levels in hydrochlorothiazide group were lower than before and after 10 and 30 min, CI level was higher than before and after 10 and 30 min, the differences were statistically significant ($P < 0.05$). And there was no significant difference in the incidence of adverse reactions ($P > 0.05$). CONCLUSIONS: Based on the conventional treatment, hydrochlorothiazide combined with phentolamine can significantly improve the blood pressure and cardiac functions, with good safety.

KEYWORDS Hydrochlorothiazide; Phentolamine; Hypertensive emergency

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