

doi: 10.13241/j.cnki.pmb.2019.19.041

rh-BNP 联合阿托伐他汀治疗急性心梗后心衰的临床疗效及对患者血清 cTn-I、Myo、CK-MB 水平的影响 *

袁晓红¹ 李 鹏^{2Δ} 胡彦超¹ 李雨微³ 刘军辉²

(1 西安交通大学第二附属医院 检验科 陕西 西安 710004; 2 西安交通大学第一附属医院 检验科 陕西 西安 710061;
3 西北妇女儿童医院 遗传中心 陕西 西安 710061)

摘要 目的:研究重组人脑利钠肽(rh-BNP)联合阿托伐他汀治疗急性心梗后心衰的临床效果及对患者血清心肌肌钙蛋白(cardiac troponin, cTn-I)、肌红蛋白(Myoglobin, Myo)、肌酸激酶同工酶(CK-MB)水平的影响。**方法:**选择我院 2017 年 2 月~2019 年 1 月收治的 72 例急性心梗后心衰患者,按随机数字表法分为观察组 38 例,对照组 34 例。对照组给予阿托伐他汀治疗,观察组在对照组基础上另加 rh-BNP,观察和比较两组的临床疗效,治疗前后血清 cTn-I、Myo、CK-MB 水平的变化及治疗后不良反应的发生情况。**结果:**治疗后,观察组总有效率明显高于对照组($P<0.05$),血清 cTn-I、Myo、CK-MB 水平均显著低于对照组[(0.23 ± 0.10) vs. (0.16 ± 0.08)、(27.54 ± 3.86) vs. (21.62 ± 2.54)、(70.82 ± 9.25) vs. (61.28 ± 8.33)]($P<0.05$)。观察组治疗后不良反情况总发生率为 7.89%,明显低于对照组(26.47%, $P<0.05$)。**结论:**与单用阿托伐他汀治疗相比,静脉注射 rh-BNP 联合阿托伐他汀治疗急性心梗后心衰可显著提高临床疗效和安全性,有效减低血清 cTn-I、Myo、CK-MB 水平。

关键词:静脉注射;重组人脑利钠肽;阿托伐他汀;急性心梗后心衰;心肌肌钙蛋白;肌红蛋白;肌酸激酶同工酶

中图分类号:R542.22 **文献标识码:**A **文章编号:**1673-6273(2019)19-3776-04

Clinical efficacy of Intravenous rh-bnp Combined with Atorvastatin in the Treatment of Heart Failure after Acute Myocardial Infarction and Its Effect on the Serum Levels of cTn-I, Myo and CK-MB*

YUAN Xiao-hong¹, LI Peng^{2Δ}, HU Yan-chao¹, LI Yu-wei³, LIU Jun-hui²

(1 Department of Clinical Laboratory, Second Affiliated Hospital, Xi'an Jiaotong University, Xi'an, Shaanxi, 710004, China;

2 Department of Clinical Laboratory, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, China;

3 Northwest Women and Children's Hospital Genetic Center, Xi'an, Shaanxi, 710061, China)

ABSTRACT Objective: To study Clinical efficacy of Intravenous rh-bnp Combined with Atorvastatin in the Treatment of Heart Failure after Acute Myocardial Infarction and Its Effect on the Serum Levels of Myocardial troponin (cardiac troponin, cTn-I), Myoglobin (Myoglobin, Myo), creatine kinase isoenzyme (CK-MB). **Methods:** 72 patients with heart failure after acute myocardial infarction admitted to our hospital from February 2017 to January 2019 were selected, were divided into observation group 38 cases and control group 34 cases according to random number table method. The control group was treated with atorvastatin, and rh-bnp was added to the observation group on the basis of the control group to observe and compare the clinical efficacy of the two groups, the changes of serum ctn-i, Myo and ck-mb levels before and after treatment, and the occurrence of adverse reactions after treatment. **Results:** After treatment, the total effective rate of the observation group was significantly higher than that of the control group ($P<0.05$), and the serum levels of ctn-i, Myo and ck-mb were significantly lower than those of the control group [(0.23 ± 0.10) vs (0.16 ± 0.08), (27.54 ± 3.86) vs (21.62 ± 2.54), (70.82 ± 9.25) vs (61.28 ± 8.33)]($P<0.05$). The overall incidence of adverse reactions after treatment in the observation group was 7.89%, significantly lower than that in the control group (26.47%, $P<0.05$). **Conclusion:** Compared with atorvastatin alone, intravenous rh-bnp combined with atorvastatin in the treatment of heart failure after acute myocardial infarction can significantly improve the clinical efficacy and safety, and effectively reduce serum levels of ctn-i, Myo and ck-mb.

Key words: Intravenous; Recombinant human brain natriuretic peptide; Atorvastatin; Heart failure after acute myocardial infarction; Cardiac troponin; Myoglobin; Creatine kinase isoenzyme

Chinese Library Classification(CLC): R542.22 **Document code:** A

Article ID: 1673-6273(2019)19-3776-04

前言

急性心肌梗死是因冠状动脉缺血缺氧导致的心肌坏死,患

* 基金项目:陕西省自然科学基金项目(20131623)

作者简介:袁晓红(1966-),女,汉族,大专,主管检验师,主要从事临床检验

Δ 通讯作者:李鹏(1965-),男,硕士,副主任技师,主要从事临床检验,电话:13991890553, E-mail: huaerseem@163.com

(收稿日期:2019-05-07 接受日期:2019-05-31)

者普遍出现突发性的胸骨疼痛,严重者可并发休克,具有发病快、发病率高、病死率高的特点^[1-3]。心力衰竭为急性心肌梗死最常见且较为严重的一种并发症,约占急性心肌梗死总发病率的20%-40%,其发病时间不定,一般主要集中在起病最初的几个小时内,偶数日后也有发生。目前临床治疗急性心肌梗死的药物较多,虽然可在一定程度上缓解患者病情,但对于患者心功能指标以及不良反应影响不大,整体治疗效果不理想^[4]。既往研究表明^[5]静脉注射 rh-BNP 联合阿托伐他汀治疗急性心梗后心衰具有较好的疗效。

研究显示血清 cTn-I、Myo 及 CK-MB 在急性心梗伴心衰的发生发展中具有重要作用^[6,7],急性心梗伴心衰患者血清 cTn-I、Myo 及 CK-MB 水平在发病期迅速升高,且随着病情越严重其水平越高。但目前临床对于 rh-BNP 联合阿托伐他汀治疗心梗后心衰对患者血清 cTn-I、Myo 及 CK-MB 水平的影响较为罕见。本研究主要探讨了静脉注射 rh-BNP 联合阿托伐他汀治疗急性心梗后心衰的临床疗效及对患者血清 cTn-I、Myo、CK-MB 水平的影响。

1 资料与方法

1.1 一般资料

选择我院 2017 年 2 月~2019 年 1 月收治的 72 例急性心梗后心衰患者,纳入标准:①符合心力衰竭的诊断标准同时经冠状动脉造影确诊为急性心肌梗死^[8];②患者已经家属知情并签署知情同意书。排除标准:①对本研究药物具有过敏史;②伴有严重肝肾功能不良者;③伴有重度传染病者;④伴有恶性肿瘤者。将符合上述标准的患者随机分为两组,对照组 34 例,包括男 20 例,女 14 例;年龄 42~71 岁,平均(51.62±10.65)岁,伴有糖尿病 15 例,高血压 19 例;观察组 38 例,男 23 例,女 15 例,年龄 40~73 岁,平均(52.34±11.74)岁,伴有糖尿病 26 例,高血压 16 例。两组一般资料比较无统计学差异($P>0.05$),具有可

比性。

1.2 方法

两组均行吸氧、扩张血管、利尿、抗感染等基础治疗。对照组另口服阿托伐他汀(厂家:广东百利制药有限公司,规格:10 mg,批号:J20120050),剂量为 20 mg·d⁻¹,晚间顿服,每天一次。观察组在对照组基础上联合静脉注射 rh-BNP(成都诺迪康生物制药有限公司,规格:0.5 mg;500 u,国药准字 S20050033),首先以 1.5 μg/kg 静脉冲击后,再以 0.0075 μg/kg/min 的速度持续静脉滴注,维持 24~72 小时,总剂量为 3.0 mg。两组均治疗 7 天,而后评价疗效。

1.3 观察指标

观察两组患者的临床疗效,比较治疗前后患者血清 cTn-I、Myo、CK-MB 水平的变化以及不良反应的发生情况。

临床疗效评价标准参照相关文献进行:痊愈:患者经检查后临床症状完全消退;显效:患者经检查症状及体征得到明显改善;无效:经检查患者临床体征无任何改善甚至加重。

收集两组治疗前后清晨空腹静脉血 5 mL,经离心处理后,取血清置于 -20℃ 环境中保存,便于待检。血清 cTn-I 水平采用双位点酶免法检测,血清 Myo 水平采用免疫荧光层析法检测,血清 CK-MB 水平采用酶抑制法检测。

1.4 统计学分析

使用 SPSS19.0 软件包对数据进行分析,计量资料比较使用独立样本 t 检验,计数资料比较 χ^2 检验比较,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

观察组治疗后总有效率为 92.11%,对照组为 73.53%,显著高于对照组,两组比较差异显著($P<0.05$),见表 1。

表 1 两组临床疗效的比较[(例)%]

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

Groups	n	Heal	Significant Effect	Invalid	Total effective rate
Control group	34	13(38.24)	12(35.29)	9(26.47)	25(73.53)
Observation group	38	20(52.64)	15(39.47)	3(7.89)	35(92.11) ^a

Note: Compared with the control group, ^a $P<0.05$.

2.2 两组治疗前后血清 cTn-I、Myo、CK-MB 水平的比较($\bar{x} \pm s$)

治疗前,两组血清 cTn-I、Myo、CK-MB 水平比较无统计学差异($P>0.05$);治疗后,两组血清 cTn-I、Myo、CK-MB 水平均

较治疗前明显下降,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 cTn-I、Myo、CK-MB 水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the serum levels of cTn-I, Myo and CK-MB between the two groups before and after treatment ($\bar{x} \pm s$)

Groups	n	cTn-I(μg/L)		CK-MB(U/L)		Myo(μg/L)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Control group	34	1.36±0.59	0.23±0.10 ^b	33.75±4.57	27.54±3.86 ^b	160.25±22.89	70.82±9.25 ^b
Observation group	38	1.41±0.62	0.16±0.08 ^{ab}	33.95±5.64	21.62±2.54 ^{ab}	157.34±21.24	61.28±8.33 ^{ab}

Note: Compared with the control group, ^a $P<0.05$; Compared with the same group before treatment, ^b $P<0.05$.

2.3 两组不良反应发生情况的比较

对照组(26.47%, $P < 0.05$), 见表 3。

治疗后, 观察组不良反应总发生率为 7.89%, 明显低于对

表 3 两组患者不良反应的发生情况比较[(例)%]
Table 3 The adverse reactions of the two groups were compared [(n)%]

Groups	n	Intestines and stomach discomfort	Have a headache	Muscle pain	The total incidence of
Control group	34	4(11.76)	2(5.88)	3(8.83)	9(26.47)
Observation group	38	1(2.63)	1(2.63)	1(2.63)	3(7.89) ^a

Note: Compared with the control group, ^a $P < 0.05$.

3 讨论

急性心肌梗死是常见的临床疾病, 由于持续性的缺血缺氧所致, 可并发休克、心力衰竭等, 已成为现在临床医学研究的重要问题之一^[9,10]。近年来, 因人们生活节奏的加快, 人口老龄化加剧, 急性心肌梗死的发病率呈上升趋势, 急性心肌梗死伴心力衰竭的发生率也相应随之增加^[11]。急性心梗后心衰多数表现为绵软无力、心率增快、腹胀、水肿、恶心、呼吸困难等症状。如何有效减轻患者心脏前后负荷、缓解患者临床症状, 为临床治疗急性心梗后心衰的关键。

研究表明^[12]在行吸氧、扩张血管、利尿、抗感染等基础治疗下, 急性心肌梗死伴心力衰竭虽然有一定的疗效, 但临床疗效并不显著, 患者血清 cTn-I、Myo、CK-MB 水平以及治疗后的不良反应未达到理想效果, 加入静脉注射 rh-BNP 联合阿托伐他汀相对于常规下治疗心梗后心衰临床效果更为显著。现目前使用 rh-BNP 治疗心力衰竭具有一定的安全性及可靠性^[13,14], 其机制可能是增加了患者冠状动脉血管直径及血流量, 使循环阻力降低, 从而将血液充分灌注到缺血组织^[15]; 在机体中能够有效的维持水盐代谢, 参与调节水容量, 有效抑制急性心肌梗死范围进一步扩大; 此外 rh-BNP 能够通过抑制生长因子活性从而抑制心肌成纤维细胞的增殖及分化, 使心室重构有效得到缓解, 是一种保护心功能的重要因素, 由于 rh-BNP 在心室合成, 其合成和分泌的剂量能更加受到心室所受压力的调节, 所以对于心功能的保护更准确快速。阿托伐他汀可增强低密度脂蛋白的分解、代谢, 减少胆固醇合成, 降低血浆中胆固醇、脂蛋白水平, 降血脂作用得到明显体现^[16,17]; 另外还有松弛血管平滑肌、抗氧化应激、抗血管炎症反证的效果, 降低非致死性心肌梗死的风险、降低致死性和非致死性卒中的风险、降低血管重建术的风险、降低因心力衰竭而住院的风险等, 从而达到保护心血管的目的。

相关文献显示^[18]血清 cTn-I、Myo、CK-MB 与急性心梗后心衰密切相关。另大量研究显示^[19], 在急性心肌梗死伴心力衰竭等心中, 血清 cTn-I、Myo、CK-MB 水平明显升高, 且患者病情越严重则水平越高, 另有研究发现^[20], 一旦患者心肌缺血缺氧状态在有效改善后, 会增加血流的灌注, 从而使其水平会降低^[21]。CK-MB 大部分分布于心肌组织中, 可用于评估梗死范围、再梗死可 1 能及溶栓效果, CK-MB 会在心肌梗塞发生后 4-6 小时上升, 24 小时达到最高点, 3 天内恢复正常^[22,23]。cTn-I 由肌钙蛋白-原肌凝蛋白络合物组成, 是一种心肌特有的抗

原, 在机体的心肌以及骨骼肌中大量存在^[24]。有研究证实^[25,26], cTn-I 在急性心肌梗死症状出现后 12 h, 对危险分层最为适宜。Myo 是肌细胞中的氧结合蛋白, 是由一个血红素辅基和一条珠蛋白多肽链组成, 也是早期急性心肌梗死最灵敏的指标^[27]。由此可见, 血清中有关标志物的动态变化对于隐藏性急性心肌梗死早期、快速、准确诊断具有特殊价值^[28]。本研究显示在常规治疗的基础上加入静脉注射 rh-BNP 联合阿托伐他汀观察, 血清 cTn-I、Myo、CK-MB 水平改善程度相对常规治疗效果显著, 对心肌缺血缺氧具有更为显著的改善效果, 缓解了心肌损伤的程度, 同时临床疗效相对以前上升了将近 20 个百分点, 相比之前有了显著的效果, 治疗后, 观察组不良反总发生率也从 26.47% 降到了 7.89%, 得到了明显的改善, 这与文献研究结果保持一致^[29,30]。

综上所述, 与单用阿托伐他汀治疗相比, 静脉注射 rh-BNP 联合阿托伐他汀治疗急性心梗后心衰可显著提高临床疗效和安全性, 有效减低血清 cTn-I、Myo、CK-MB 水平。

参考文献(References)

- [1] Lee C, Cui Y, Song J, et al. Effects of familial hypercholesterolemia-associated genes on the phenotype of premature myocardial infarction [J]. *Lipids Health Dis*, 2019, 18(1): 95
- [2] George B, Misumida N, Ziada KM. Revascularization Strategies for Non-ST-Elevation Myocardial Infarction [J]. *Curr Cardiol Rep*, 2019, 21(5): 39
- [3] Otto CM. Heartbeat: Primary care delays in heart failure diagnosis[J]. *Heart*, 2019, 105(9): 661-662
- [4] Zachura M, Wilczek K, Janion M, et al. Long-term outcomes in men and women with ST-segment elevation myocardial infarction and incomplete reperfusion after a primary percutaneous coronary intervention: a 2-year follow-up[J]. *Coron Artery Dis*, 2019, 30(3): 171-176
- [5] Duan P, Tan J, Miao Y, et al. Potential role of exosomes in the pathophysiology, diagnosis, and treatment of hypoxic diseases [J]. *Am J Transl Res*, 2019, 11(3): 1184-1201
- [6] Zarei B, Mousavi M, Mehdizadeh S, et al. Early Effects of Atorvastatin on Vitamin D and Parathyroid Hormone Serum Levels Following Acute Myocardial Infarction[J]. *J Res Pharm Pract*, 2019, 8(1): 7-12
- [7] Toso A, Leoncini M, De Servi S. Statins and myocardial infarction: from secondary 'prevention' to early 'treatment' [J]. *J Cardiovasc Med (Hagerstown)*, 2019, 20(4): 220-222
- [8] Walthall H PhD, RN, Floegel T PhD, et al. Patients experience of fatigue in advanced heart failure[J]. *Contemp Nurse*, 2019, 9: 1-23
- [9] Ayan M, Alshebani Y, Tantoush H, et al. Acute myocardial infarction in a young man with large left ventricular thrombus and the antiphos-

- pholipid syndrome [J]. Proc (Bayl Univ Med Cent), 2018, 32(1): 110-112
- [10] George B, Misumida N, Ziada KM. Revascularization Strategies for Non-ST-Elevation Myocardial Infarction[J]. Curr Cardiol Rep, 2019, 21(5): 39
- [11] Fu Y, Liu X, Zhang F, et al. Bortezomib-inducible long non-coding RNA myocardial infarction associated transcript is an oncogene in multiple myeloma that suppresses miR-29b [J]. Cell Death Dis, 2019, 10(4): 319
- [12] Schwemer TF, Deutscher N, Diermann N, et al. Effect of ranolazine on plasma arginine derivatives and urinary isoprostane 8-iso-PGF2 α in patients with myocardial infarction in the randomized RIMINI-Trial [J]. Sci Rep, 2019, 9(1): 5708
- [13] Yu L, Shi X, Han C, et al. A rapid reporter assay for recombinant human brain natriuretic peptide (rhBNP) by GloSensor technology[J]. J Pharm Anal, 2018, 8(5): 297-301
- [14] Zhang C, Pan S, Aisha A, et al. Recombinant human brain natriuretic peptide regulates PI3K/AKT/mTOR pathway through lncRNA EGOT to attenuate hypoxia-induced injury in H9c2 cardiomyocytes [J]. Biochem Biophys Res Commun, 2018, 503(3): 1186-1193
- [15] Li X, Peng H, Wu J, et al. Brain Natriuretic Peptide-Regulated Expression of Inflammatory Cytokines in Lipopolysaccharide (LPS)-Activated Macrophages via NF- κ B and Mitogen Activated Protein Kinase (MAPK) Pathways[J]. Med Sci Monit, 2018, 24: 3119-3126
- [16] Ali I, Alharbi OML, ALOthman ZA, et al. Preparation of a carboxymethylcellulose-iron composite for uptake of atorvastatin in water[J]. Int J Biol Macromol, 2019, 132: 244-253
- [17] Zarganes-Tzitzikas T, Neochoritis CG, Dömling A. Atorvastatin (Lipitor) by MCR[J]. ACS Med Chem Lett, 2019, 10(3): 389-392
- [18] Chowdhury UK, Sheil A, Kapoor PM, et al. Short-term prognostic value of perioperative coronary sinus-derived-serum cardiac troponin-I, creatine kinase-MB, lactate, pyruvate, and lactate-pyruvate ratio in adult patients undergoing open heart surgery [J]. Ann Card Anaesth, 2016, 19(3): 439-453
- [19] Pletsch-Borba L, Grafetstätter M, Hüsing A. Biomarkers of vascular injury in relation to myocardial infarction risk: A population-based study[J]. Sci Rep, 2019, 9(1): 3004
- [20] Çetin E. Pretreatment with β -glucan attenuates isoprenaline-induced myocardial injury in rats[J]. Exp Physiol, 2019, 104(4): 505-513
- [21] Lee C, Cui Y, Song J, et al. Effects of familial hypercholesterolemia-associated genes on the phenotype of premature myocardial infarction[J]. Lipids Health Dis, 2019, 18(1): 95
- [22] Zhou Y, Liu L, Gao C, et al. Puerarin pre-conditioning on the expression levels of CK-MB, cTnI and inflammatory factors in patients undergoing cardiac valve replacement [J]. Exp Ther Med, 2019, 17(4): 2598-2602
- [23] He RQ, Xiong DD, Ma J, et al. The Clinicopathological Significance and Correlative Signaling Pathways of an Autophagy-Related Gene, Ambra1, in Breast Cancer: a Study of 25 Microarray RNA-Seq Datasets and in-House Gene Silencing [J]. Cell Physiol Biochem, 2018, 51(3): 1027-1040
- [24] Zhang Y, Luo Y, Nijiatijiang G, et al. Correlations of Changes in Brain Natriuretic Peptide (BNP) and Cardiac Troponin I (cTnI) with Levels of C-Reactive Protein (CRP) and TNF- α in Pediatric Patients with Sepsis[J]. Med Sci Monit, 2019, 25: 2561-2566
- [25] Clerico A, Ripoli A, Masotti S, et al. Evaluation of 99th percentile and reference change values of a high-sensitivity cTnI method: A multicenter study[J]. Clin Chim Acta, 2019, 493: 156-161
- [26] Yan J, Yang Q, Li W, et al. Two desired epitopes of cTnI benefit for preparation of standardized monoclonal antibodies[J]. Chirality, 2019, 31(4): 321-327
- [27] Chen S, Zhuang Z, Yin P, et al. Changes in growth performance, haematological parameters, hepatopancreas histopathology and antioxidant status of pacific white shrimp (Litopenaeus vannamei) fed oxidized fish oil: Regulation by dietary myo-inositol[J]. Fish Shellfish Immunol, 2019, 88: 53-64
- [28] Takahashi M. Role of NLRP3 Inflammasome in Cardiac Inflammation and Remodeling after Myocardial Infarction[J]. Biol Pharm Bull, 2019, 42(4): 518-523
- [29] Safdar B. Clues to Diagnose Myocardial Infarction in the Young: No Longer a Needle in the Haystack [J]. J Am Coll Cardiol, 2019, 73(5): 585-588
- [30] Yandrapalli S, Nabors C, Goyal A, et al. Modifiable Risk Factors in Young Adults With First Myocardial Infarction[J]. J Am Coll Cardiol, 2019, 73(5): 573-584