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靶剂量美托洛尔对老年糖尿病并慢性心衰的疗效及安全性分析

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摘要 目的:探讨靶剂量美托洛尔治疗合并糖尿病的慢性心衰患者的临床疗效及安全性。**方法:**选取 154 例老年糖尿病并慢性心衰患者,随机分为观察组与对照组,每组 77 例,观察组患者予靶剂量美托洛尔及常规治疗方案,对照组仅按常规治疗方案进行治疗,比较两组患者治疗前后 NYHA 分级、左心室收缩末期内径(LVESD)、左心室舒张末期内径(LVEDD)、左心室射血分数(LVEF)、6min 步行距离及用药安全性。**结果:**与治疗前相比,观察组与对照组两组患者 NYHA 分级、LVESD、LVEDD、LVEF、6min 步行距离均有明显改善($P < 0.05$);与对照组患者治疗后相比,观察组患者治疗后以上指标改善更加显著($P < 0.05$)。在随访的 6 个月内,观察组心脏事件发生率为 3.90%,明显低于对照组的 14.29%($P < 0.05$)。两组患者平均空腹血糖、糖化血红蛋白不存在显著性差异($P > 0.05$),观察组血脂、血糖、肝功能、肾功能等指标均未发生显著变化。**结论:**靶剂量美托洛尔治疗合并糖尿病的慢性心衰患者时,可显著改善患者的心功能及活动耐量,临床疗效好,安全性高,耐受性良好。

关键词:美托洛尔;糖尿病;慢性心衰;疗效;安全性

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Analysis of Efficacy and Safety of the Target Dose of Metoprolol in Treatment of Patients with Chronic Heart Failure and Diabetes Mellitus

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ABSTRACT Objective: To explore the clinical efficacy and safety of target dose of metoprolol in the treatment of patients with chronic heart failure and diabetes mellitus. **Methods:** 154 elderly patients with diabetes and chronic heart failure were randomly divided into observation group and control group with 77 cases in each group, the patients in the observation group were treated with the target dose of metoprolol and conventional therapy, while in the control group only received routine treatment. The indexes of NYHA classification, end diastolic diameter (LVESD), left ventricular end diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), 6min walking distance and the medication safety of both groups were compared before and after treatment. **Results:** Compared with before treatment, the indexes of NYHA grade, LVESD, LVEDD, LVEF, 6 minutes' walking distance of both groups were significantly improved ($P < 0.05$); Compared with patients in the control group after treatment, the above indexes improved more significantly in the observation group ($P < 0.05$). In the sixth month of follow-up, the incidence of cardiac events of the observation group was 3.90%, significantly lower than that in the control group (14.29%) ($P < 0.05$). The average fasting blood glucose, glycosylated hemoglobin of both groups showed no significant difference ($P > 0.05$). In the observation group, the blood glucose, blood lipid and liver function, renal function and other indexes showed no significant change. **Conclusion:** The target dose of metoprolol in treatment of patients with chronic heart failure and diabetes mellitus, can obviously improve the cardiac function and activity in patients with tolerance, has good clinical effect, high security and good tolerance.

Key words: Diabetes mellitus; Metoprolol; Chronic heart failure; Curative effect; Safety

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前言

美托洛尔为 β -受体阻断剂,临床广泛用于心绞痛、高血压、肥厚型心肌病、心律失常、主动脉夹层及甲状腺功能亢进等疾病的治疗,近年来研究表明,该药应用于心力衰竭的治疗时,可大大降低心衰患者的死亡率^[1];虽美托洛尔的 β -受体阻断作用会掩盖糖尿病患者的心悸等低血糖反应,延误低血糖反应的早

期发现与处理,但糖尿病患者服用此药的利大于弊^[2,3]。本研究旨在调查 2010 年 1 月~2012 年 12 月于我院接受靶剂量美托洛尔治疗的合并糖尿病的老年心衰患者的临床疗效及安全性,现将研究结果报道如下。

1 资料与方法

1.1 一般资料

选取 2010 年 1 月~2012 年 12 月于我院心血管内科接受治疗的合并糖尿病的老年心衰患者为研究对象。入选标准:①年龄介于 60~85 周岁之间;②按美国 NYHA 分级,心功能为

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II、III或IV级;③糖尿病为非胰岛素依赖型糖尿病(即2型糖尿病),病史 ≥ 2 年,空腹及餐后血糖均控制良好;④左心室射血分数低于40%;⑤用药依从性好;⑥对随访工作配合良好。排除标准:①合并活动性心肌炎及心衰的急性冠脉综合征患者;②患者患有肥厚性心肌病或瓣膜性心脏病,病情未得到较好控制;③合并的房室传导阻滞(2度以上)、病态窦房结综合征等心律失常未得到有效控制;④慢性阻塞性肺疾病等肺部疾病反复发作;⑤心率低于55次/min,舒张压 > 110 mmHg,收缩压 > 180 mmHg或 < 85 mmHg;⑥肝功能及肾功能严重不全;⑦既往服用美托洛尔期间曾出现药物不良反应;⑧用药依从性差,

不能配合随访工作。

按以上入选标准及排除标准,共154例患者入选本项研究。其中,男性患者98例,女性患者56例,年龄为60~84岁,平均年龄为(71.43 $\pm$ 8.67)岁。按美国NYHA分级,II级40例,III级91例,IV级23例。合并酒精性心脏病者为9例,合并高血压性心肌病者为31例,合并扩张型心肌病者为24例,合并冠心病者为78例。将154例患者随机分至观察组和对照组,各77例,两组患者在性别组成、年龄、血压、基础用药、空腹血糖、糖化血红蛋白、LDL-C等一般资料方面无显著性差异,具有可比性($P> 0.05$)。详见表1。

表1 观察组与对照组患者一般资料比较

Table 1 Comparison of the general information between the observation group and the control group

Group	Number (n)	Gender		Age	Blood pressure(mmHg)		Fasting blood-glucose (mmol/L)	Glycosylated hemoglobin (%)	LDL-C (mmol/L)
		Male	Female		Systolic pressure	Diastolic pressure			
Observation group	77	50	27	71.46 $\pm$ 7.91	137.43 $\pm$ 22.5	79.2 $\pm$ 6.91	6.55 $\pm$ 1.39	6.62	3.29 $\pm$ 0.98
Control group	77	48	29	71.35 $\pm$ 9.21	141.15 $\pm$ 19.89	80.22 $\pm$ 7.02	6.49 $\pm$ 1.32	6.53	3.44 $\pm$ 0.95

1.2 治疗方案

对照组:采用临床常规治疗方案,即阿卡波糖等降低血糖药物+螺内酯等利尿剂+单硝酸异山梨酯等扩血管药+地高辛+卡托普利等血管紧张素转化酶抑制剂。具体服药剂量根据患者的临床症状、体征、病情严重程度及肝肾功能等确定。

观察组:在对照组治疗的基础上,加用 β -受体阻断剂美托洛尔进行治疗。美托洛尔初始给药量为6.25 mg po bid,根据患者耐受情况,每两周增加一次美托洛尔服药量,直至达到靶剂量100 mg po bid或达到患者最大耐受量。

1.3 疗效及安全性观察指标

对入选研究的所有154例患者进行随访,随访时间为6个月。比较患者治疗前后NYHA分级、左心室收缩末期内径(LVESD)、左心室舒张末期内径(LVEDD)、左心室射血分数(LVEF)、6min步行距离;监测患者服药期间血脂、血糖、静息

心率、肝功能、肾功能、水肿、血压的变化情况,记录心律失常、猝死、心衰加重等心脏事件。

1.4 统计学方法

数据收集及统计采用SPSS 17.0数据统计软件,计量资料以 $\bar{x} \pm s$ 表示,采用t检验进行组间比较;计数资料以n表示,采用 χ^2 检验进行组间对比, $P< 0.05$ 为差异有统计学意义。

2 结果

2.1 观察组与对照组患者治疗前后心脏功能变化比较

与治疗前相比,观察组与对照组两组患者NYHA分级、LVESD、LVEDD、LVEF、6 min步行距离均有明显改善($P< 0.05$)。与对照组患者治疗后相比,观察组患者治疗后以上指标改善更加显著,两组间存在显著性差异($P< 0.05$)。详见表2。

表2 观察组与对照组患者治疗前后心脏功能变化比较

Table 2 Comparison of the changes of cardiac function between the observation group and the control group before and after treatment

Group	Detection time	NYHA grade	LVESD (mm)	LVEDD (mm)	LVEF (%)	Walking distance of 6min(m)
Observation group	Pre-treatment	3.22 $\pm$ 0.61	57.22 $\pm$ 6.94	69.42 $\pm$ 6.29	32.58 $\pm$ 7.73	227.32 $\pm$ 189.42
	Post-treatment	2.21 $\pm$ 0.39 Δ	45.43 $\pm$ 7.01 Δ	56.42 $\pm$ 6.32 Δ	49.42 $\pm$ 9.21 Δ	436.42 $\pm$ 201.56 Δ
	D-value of pre and post-treatment	0.92 $\pm$ 0.04 Δ	7.92 $\pm$ 0.61 Δ	10.02 $\pm$ 0.37 Δ	14.59 $\pm$ 2.12 Δ	187.43 $\pm$ 17.49 Δ
Control group	Pre-treatment	3.24 $\pm$ 0.67	58.83 $\pm$ 9.17	68.26 $\pm$ 7.43	33.25 $\pm$ 9.19	229.53 $\pm$ 190.63
	Post-treatment	2.58 $\pm$ 0.42 Δ	51.82 $\pm$ 9.22 Δ	61.53 $\pm$ 7.06 Δ	41.58 $\pm$ 8.57 Δ	347.46 $\pm$ 178.52 Δ
	D-value of pre and post-treatment	0.72 $\pm$ 0.03	3.39 $\pm$ 0.43	6.32 $\pm$ 0.17	7.94 $\pm$ 1.97	98.32 $\pm$ 14.24

Note: Compared to pre-treatment, $\Delta P< 0.05$; Compared to control group, $\Delta P< 0.05$.

2.2 观察组与对照组患者心脏事件发生率比较

在随访的6个月内,观察组未发生猝死事件,1例患者出现心性死亡,2例患者因心衰加重而再次入院治疗,心脏事件发生率为3.90%;对照组患者有2例发生猝死,3例发生心性死

亡,6例因心衰加重而再次入院治疗,心脏事件发生率为14.29%。观察组患者心脏事件发生率明显低于对照组,两组间存在显著性差异($P< 0.05$)。详见表3。

表 3 观察组与对照组患者心脏事件发生率比较

Table 3 Comparison of the rate of cardiac event between the observation group and the control group

Group	Sudden death	Cardiac death	Readmission by worsening heart failure	The incidence of cardiac events(%)
Observation group	0	1	2	3.90
Control group	2	3	6	14.29

2.3 观察组与对照组患者安全性及耐受性评估

观察组患者接受治疗期间水肿、房室传导阻滞、血脂、血糖、肝功能、肾功能等均未发生显著变化。观察组患者治疗后平均空腹血糖为 (6.43 ± 1.24) mmol/L, 糖化血红蛋白为 6.75%; 而对照组平均空腹血糖、糖化血红蛋白分别为 (6.52 ± 1.31) mmol/L, 6.62%, 两组间不存在显著性差异($P > 0.05$)。观察组随访期间共 19 例患者出现 I° 房室传导阻滞, 但均未影响美托洛尔剂量的递增, 当美托洛尔每日服药量增加至 50 mg 时, 39 例患者心率减慢至 55 次/min; 当美托洛尔每日服药量增加至 100 mg 时, 29 例患者收缩压下降为 90 mmHg, 仅 4 例患者美托洛尔每日服药量达到 200 mg; 美托洛尔每日平均服药剂量为 105.33 mg。与治疗前相比, 观察组患者治疗后血压、静息心率均有一定程度的下降, 但均未超出正常范围。

3 讨论

随着社会经济的发展, 人们生活方式的改变, 糖尿病已经成为了日常生活中的常见病, 多发病, 尤其是在老年人中, 糖尿病的发生率呈现逐年上升的趋势^[4,7]。由于糖尿病至今仍然是难以治愈的疾病, 必须依靠药物才能维持患者体内血糖水平的正常。老年糖尿病患者的用药依从性差, 血糖控制情况长期不理想。可以导致心力衰竭、糖尿病肾病、末梢神经炎、视网膜病变等并发症的发生, 严重影响患者的身体健康。其中, 心力衰竭, 简称心衰, 是因心肌收缩力降低、心输出量减少而引起的一系列临床症状和体征, 临床常表现为乏力、呼吸困难、体液潴留、呕吐、肝区胀痛等, 5 年生存率较低^[8-10]。心衰患者治疗的近期目标为改善生活质量、缓解心衰症状, 远期目标为减少心肌重塑、防止并发症的发生、降低患者再次入院率及死亡率。血糖升高可大大增加患者心衰及其他心血管事件的发生率^[11-13]。美托洛尔可通过对交感神经系统的阻断作用给合并糖尿病的慢性心衰患者带来较好的临床收益。对于未发生心力衰竭的糖尿病患者, β -受体阻断剂对心衰的发生可起到预防性的作用^[14]。研究表明, β -受体阻断剂卡维地洛可通过心肌重构的逆转及交感神经系统过激活的抑制作用降低糖尿病亚组心肌梗死患者的死亡率^[15-17]。与低剂量美托洛尔相比, 高剂量美托洛尔可更好的改善患者的心脏功能及左心室射血分数, 且不增加心脏事件等药物不良反应, 提示该药服用用于治疗合并糖尿病的慢性心衰患者时, 应尽可能达到耐受量或最大用药剂量, 以使心功能得到更大程度的改善。

本项研究表明, 观察组患者治疗后虽有血压下降及心率减慢, 但变化幅度较小, 且均未超出正常范围, 患者耐受性较好; 观察组患者治疗前后血脂、血糖、肝功能、肾功能等均未发生显著变化, 且未出现低血压休克、水肿、高度传导阻滞等严重药物不良反应, 提示靶剂量美托洛尔治疗合并糖尿病的慢性心衰患

者安全性较高^[18-22]。在本项研究中, 美托洛尔每日平均服药剂量为 105.33 mg, 距每日 200 mg 服药量相差甚远, 分析可能与老年患者房室传导功能及窦房结功能降低有关。在初始治疗及递增用药阶段, 应严密监测患者血脂、血糖、血压、肝功能及肾功能的变化, 以提高患者用药依从性, 保证临床疗效及用药安全性。

综上所述, 靶剂量美托洛尔治疗合并糖尿病的慢性心衰患者时, 可显著改善患者的 NYHA 分级、LVESD、LVEDD、LVEF 及 6min 步行距离, 降低猝死等心脏事件的发生率, 安全性高, 耐受性良好。

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