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# 曲美他嗪对扩张型心肌病患者的临床疗效

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[摘　要] **目的**　探讨曲美他嗪对扩张型心肌病(DCM)慢性心力衰竭(CHF)的临床疗效。**方法**　40 例扩张型心肌病伴中、重度心力衰竭患者。随机分为两组,对照组 19 例,常规使用洋地黄、利尿药、血管紧张肽转换酶抑制药、β-受体阻滞药等药物治疗。治疗组 21 例,在对照组常规治疗基础上,加用曲美他嗪 20 mg ,po,tid,均 8 周为 1 个疗程。观察曲美他嗪治疗前及治疗 8 周后,对心功能分级、左心室射血分数(LVEF)、左室舒张末期内径(LVDd)及脑钠肽(BNP)的影响。**结果**　治疗组临床心功能分级明显改善,总有效率 90.5%,对照组为 52.6%。治疗组 LVEF 值显著提高、LVDd 显著减小,BNP 水平明显升高,而血压、心率则无影响。**结论**　曲美他嗪能明显改善扩张型心肌病患者的心功能。

[关键词]　曲美他嗪;心肌病,扩张型;心功能;脑钠肽

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## The Clinical Therapeutic Effectiveness of Trimetazidine in the Treatment of Patients with Dilated Cardiomyopathy

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**ABSTRACT**　**Objective**　To probe into the clinical therapeutic effectiveness of trimetazidine in the treatment of dilated cardiomyopathy (DCM) associated with moderate to severe chronic congestive heart failure (CHF).　**Methods**　40 patients with DCM associated with moderate to severe chronic congestive heart failure were randomly divided into 2 groups: the control group

($n$ = 19) and the trial group($n$ = 21). Patients of the control group were routinely treated with digitalis, diuretics, converting enzyme inhibitor, β-receptor blocker etc.. On the basis of the routine treatment, patients of the trial group were given each additionally 20 mg of trimetazidine PO, t. i. d.. The course of treatment lasted 8 weeks. The grade of cardiac function, left ventricular ejection fraction (LVEF), left ventricular end-distolic diameter (LVDd) and the serum level of brain natriuretic peptide(BNP) were determined before and after the 8 week treatment in patients of both groups. **Results** The grade of cardiac function in patients of the trial group was greatly improved after the trimetazidine treatment. The overall effective rate in patients of the trial group was 90.5% while that in those of the control group was 52.6% ($P$ < 0.05). In patients of the trial group, the LVEF was dramatically increased, the LVDd greatly reduced, and the serum level of BNP significantly elevated after the treatment. However, the blood pressure and heart rate showed no apparent changes in patients treated with trimetazidine. **Conclusion** Trimetazidine was shown to have good therapeutic effects in the treatment of patients with DCM associated with congestive heart failure.

**KEY WORDS** Trimetazidine; Dilated cardiomyopathy; Cardiac function; Brain natriuretic peptide

慢性心力衰竭(chronic heart failure, CHF)是扩张型心肌病(dilated cardiomyopathy, DCM)的主要死亡原因之一。脑钠肽(brain natriuretic peptide, BNP)是心脏分泌的一种神经激素,研究表明,血 BNP 水平与心力衰竭严重程度呈正相关,可用于心力衰竭的诊断、预后评估[1]。2004 年 6 月 ~2005 年 12 月,笔者通过观察曲美他嗪(TMZ)对扩张型心肌病患者心功能和 BNP 的作用,以探讨能量代谢对心力衰竭预后的影响。

## 1 资料与方法

**1.1** *临床资料* 本院在我科住院的扩张心肌病患者 40 例,年龄 26 ~72 岁,平均(60.2 ±12.2)岁,男 23 例,女 17 例,心功能分级按 NYHA 心功能分级标准,其中心功能Ⅲ级 12 例, Ⅳ 级 28 例。所有患者均经询问病史、体格检查、心脏超声、胸部 X 线片、心电图等检查明确诊断,扩张型心肌病的诊断标准按照 1995 年 WHO/ISFC 工作组关于心肌病的定义和分类标准[2],并排除下列并发症:①明显肾功能障碍;②低血压[血压≤90/60 mmHg (1 mmHg = 0.133 kPa)]、休克;③严重心律失常;④严重电解质紊乱未纠正者;⑤严重感染者。所有患者均按随机化原则分为两组,治疗组 21 例,对照组 19 例。治疗组心功能Ⅲ 级 6 例,Ⅳ级 15 例;对照组心功能Ⅲ级 6 例,Ⅳ级 13 例。

**1.2** *治疗方法* 治疗期间两组均常规使用洋地黄、利尿药、转换酶抑制药、β-受体阻滞药等药物治疗。治疗组加用曲美他嗪(法国雅施达制药有限公司提供,批准文号:国药准字 J20030132)20 mg ,po,tid。8 周为 1 个疗程。

**1.3** *观察指标* 对所有患者每天均有专人进行心功能分级评价,测量心率(HR)、血压(BP),观察不良反应,并在治疗前后进行血尿常规,肝、肾功能,BNP 水平及心电图、心脏超声检查。

**1.4** *超声心动图检查* 应用美国 GE 公司生产的 GE VIVID 7 超声心动图诊断仪,探头频率为 2.5 MHz。患者取左侧卧位,平静呼吸。以左室腱索水平为标准测量区,测量左室舒张末期内径(LVDd)和左室收缩末期内径(LVDs),求得左室舒张末期容积(EDV)和左室收缩末期容积(ESV),根据公式左心室射血分数(LVEF) = (EDV - ESV)/EDV。测量 2 次,取平均植。LVEF≤45% 为左室功能不全。

**1.5** *BNP 测定* 患者在治疗前后分别采取清晨空腹静脉血 2 mL,采血前避免高盐饮食,置于 EDTA 抗凝和含抑肽酶试管中,立即离心 10 min,取血浆放入 -70 ℃冰箱保存待测。采用酶联免疫吸附测定法(ELISA)测定 BNP 浓度,试剂为美国 Phoenix 公司生产的人的 BNP 32 EIA 试剂盒,严格按照说明书操作。

**1.6** *疗效判定标准* 治疗组 8 周后心功能改善Ⅱ级或以上者为显效,心功能改善Ⅰ级为有效,心功能无变化或恶化为无效。总有效率(%) = (显效例数 + 有效例数)/总例数 ×100%。

**1.7** *统计学方法* 计量资料以均数 ± 标准差表示,等级资料采用 Ridit 检验,计量资料采用 $t$ 检验, $P$ < 0.05为差异有显著性。

## 2 结果

**2.1** *临床疗效比较* 两组临床疗效比较见表 1。结果显示治疗组心功能改善的显效率、有效率和总有效率均显著高于对照组。

**表 1 两组患者治疗后临床疗效**

| 组别 | 例数 | 显效 | | 有效 | | 无效 | | 有效率/% |
|---|---|---|---|---|---|---|---|---|
| | | 例 | % | 例 | % | 例 | % | |
| 治疗组 | 21 | 11 | 52.4 | 8 | 38.1 | 2 | 9.5 | 90.5 |
| 对照组 | 19 | 6 | 31.6 | 4 | 21.0 | 9 | 47.4 | 52.6 |

**2.2** *心率、血压和心脏超声指标的比较* 两组患者治疗后心率均有明显减慢,但两组间比较差异无显著性,

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心脏射血分数差异有显著性,且治疗组射血分数明显高于对照组,左室舒张末期内径治疗组则明显小于对照组。见表2。

**2.3** BNP 的变化　治疗组和对照组患者治疗后血脑钠肽水平均较治疗前有显著提高,且治疗后脑钠肽水平治疗组也显著高于对照组。提示 TMZ 不仅可以提高心力衰竭患者 NHAY 心功能分级,并且可以升高血浆 BNP 水平。见表2。

**表2　两组患者治疗前后心率、血压和超声心电图指标的变化**　　$\bar{x} \pm s$

| 组别与时间 | 心率/(次·min$^{-1}$) | 收缩压/mmHg | 舒张压/mmHg | LVEF/% | LVDd/mm | BNP/(ng·L$^{-1}$) |
|---|---|---|---|---|---|---|
| 治疗组 | | | | | | |
| 治疗前 | 102.9 ± 21.70 | 119.4 ± 17.57 | 72.4 ± 10.3 | 37 ± 6 | 64.80 ± 5.55 | 280 ± 85 |
| 治疗后 | 84.0 ± 17.72$^{*1}$ | 112.6 ± 10.35 | 70.5 ± 6.4 | 56 ± 12$^{*1*2}$ | 53.49 ± 6.09$^{*1*3}$ | 120 ± 34$^{*1*3}$ |
| 对照组 | | | | | | |
| 治疗前 | 103.0 ± 22.6 | 122.0 ± 16.5 | 75.9 ± 9.7 | 35 ± 6 | 65.90 ± 6.12 | 245 ± 80 |
| 治疗后 | 83.2 ± 16.8$^{*1}$ | 114.5 ± 12.2 | 71.9 ± 7.1 | 45 ± 12$^{*1}$ | 60.87 ± 4.91$^{*1}$ | 190 ± 50$^{*4}$ |

与治疗前比较,$^{*1}P<0.01$,$^{*4}P<0.05$;与对照组比较,$^{*2}P<0.05$,$^{*3}P<0.01$

**2.4** 不良反应　治疗组未发现与药物有关的不良反应,也未出现中途停药退出者。

## 3　讨论

近年来由于建立以改善神经-内分泌功能为基础的心力衰竭治疗模式,使得 CHF 的病死率不断下降。但 CHF 的患病率仍持续增长,CHF 患者的预后及生活质量仍有待进一步改善。随着对 CHF 分子生物学机制的认识,已了解到 CHF 的发生发展除神经、内分泌激活外,心室的重构和心肌的纤维化起着非常重要的作用。DCM 时心肌重量、心室容量的增加和心室形态的改变,使单位重量的心肌毛细血管数目减少,氧的弥散间距增大,产生相对心肌低氧,从而使糖酵解及脂肪代谢增强。文献报道脂肪酸作为心肌能量来源不如葡萄糖有效,产生等量三磷腺苷(ATP)需要多消耗 10% 的氧[3],且游离脂肪酸浓度的升高,可以抑制线粒体氧化过程和 $Na^+$-$K^+$-ATP 酶,心肌细胞膜 $Na^+$-$K^+$-ATP 酶及肌质网 $Ga^{2+}$-ATP 酶活性也受抑制,影响 ATP 水解能力及肌质网对 $Ca^{2+}$ 的摄取,导致细胞内酸中毒、钙超载,从而影响心肌细胞的结构和功能。曲美他嗪主要通过抑制线粒体酶长链 3-酮酰辅酶 A 硫解酶(KAT),从而使心肌代谢远离脂肪酸的 β-氧化,转向糖的氧化代谢,提高产生 ATP 的效率,同时还能阻滞细胞内钙超载和细胞内酸中毒[4],以满足缺血、低氧心肌的需要,并提高心肌的功能。马琦林等[5]研究结果提示:随着心力衰竭的加重,超氧化物歧化酶(SOD)活性越低,而丙二醛(MDA)含量则越高。FABIANI 等[6]对 CABG 患者的研究显示,术前口服和体外循环中加入 $10^{-6}$ mol·$L^{-1}$ 的 TMZ 患者术后 20 min 冠状静脉窦 MDA 明显下降。BELARDINELLI 等[7]报道曲美他嗪可显著提高缺血性心肌病患者左室射血分数和运动时最大氧摄入量,而对心率和血压无影响。

BNP 是一种神经激素,属于利钠肽家族中的一员,由 32 个氨基酸组成,主要由心室肌细胞合成和分泌,反映心室压力和容量负荷的变化。BNP 具有利尿、利钠、降血压和松弛平滑肌的功能,与心房利钠肽(atrial natriuretic peptide ,ANP)一样,BNP 通过对肾脏和全身血管的作用参与体内水盐代谢的调节,在肾脏,BNP 直接作用于肾小球和髓质内的集合管,从而抑制肾素的释放和醛甾酮的分泌,增加尿钠和尿液的排泌,同时不改变血压、肾小球滤过率和肾血流量。BNP 与左室功能障碍的程度密切相关。LEE 等[8]观察了 98 例 CHF 患者发现 BNP 水平较 LVEF 与 NYHA 分级相关性更强;对其中 41 例正规治疗 6 ~ 12 个月后结果显示在 BNP 水平降低的患者,NYHA 分级提高,而在 BNP 水平不变的患者,NYHA 分级亦不变。YU 等[9]的观察表明 BNP 水平是 12 个月内心源性死亡的良好预测指标,其准确性高于年龄、性别、LVEF、心脏病病因和 NYHA 分级。

本研究显示曲美他嗪不仅可显著改善扩张型心肌病伴心力衰竭患者的心功能,提高 LVEF 值,减少左室舒张末期内经,而且显著提高血 BNP 水平,但对血压、心率则无影响,提示曲美他嗪可以通过优化心肌的能量代谢,从而改善心肌的功能,降低心力衰竭患者病死率,提高患者的生活质量,为心力衰竭的治疗开辟了新途径,值得临床推广应用。

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# 葛根素注射液与复方丹参注射液治疗不稳定型心绞痛的疗效比较

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[摘要] **目的** 比较葛根素注射液与复方丹参注射液治疗不稳定型心绞痛的疗效。**方法** 98 例不稳定型心绞痛患者随机分为治疗组 50 例和对照组 48 例。两组患者均常规口服缓释硝酸异山梨酯(消心痛)、肠溶阿司匹林及硝苯地平。心绞痛发作时舌下含服硝酸甘油。治疗组加用葛根素注射液 10 mL,对照组加用复方丹参注射液 40 mL,加入 5% 葡萄糖注射液 500 mL,静脉滴注,qd。两组均连续应用 14 d。观察临床症状、心电图变化及血液流变学变化指标。**结果** 治疗组与对照组临床疗效总有效率分别为 96.0% 及 81.2%,差异有显著性($P<0.05$);治疗组在治疗后低切全血黏度明显降低($P<0.05$),红细胞变形性显著增高,红细胞比容、红细胞聚集指数和血小板聚集率均显著下降,治疗前后比较差异有极显著性($P<0.01$)。对低切全血黏度的下降和红细胞变形性升高幅度,治疗组显著高于对照组($P<0.01$)。对红细胞比容,红细胞聚集指数和血小板聚集率的下降作用,治疗组优于对照组($P<0.05$)。**结论** 葛根素注射液治疗不稳定型心绞痛疗效优于复方丹参注射液。

[关键词] 葛根素注射液;丹参注射液,复方;心绞痛,不稳定型
[中图分类号] R286;R541.4 [文献标识码] A [文章编号] 1004-0781(2007)04-0375-03

# A Comparison between the Therapeutic Effects of Puerarin Injection and Compound *Radix Salviae Miltiorrhizae* Injection in the Treatment of Unstable Angina Pectoris

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**ABSTRACT** **Objective** To compare the therapeutic effects of puerarin injection and compound *Radix Salviae Miltiorrhizae* injection in the treatment of unstable angina pectoris(UAP). **Methods** Ninety-eight patients with unstable angina pectoris were randomly divided into two groups: the trial group ($n=50$) and control group ($n=48$). Patients of both group were treated routinely with isosorbide dinitrate, enteric-soluble aspirin and nifedipine. Nitroglycerin to be sucked sublingually were administered during episodes of angina pectoris. On the basis of these conventional measures, patients of the trial group were given each 10 mL of puerarin injection added to 500 mL of 5% glucose solution administered by IV instillation q. d., while those of the control group were given each 40 mL of compound *Radix Salviae Miltiorrhizae* injection added to 500 mL of 5% glucose solution administered by IV instillation q. d. as well. The course of treatment in both groups lasted 14 days. Clinical symptoms, changes in electrocardiogram and parameters of hemorrheology were kept under observation before and after the treatment. **Results** The overall effective rates in patients of the trial group and control group were 96.0% and 81.2%, respectively, the difference being significant($P<0.05$). The low shear value of the whole blood viscosity was sharply decreased ($P<0.05$), the erythrocyte deformability was apparently increased, while the hematocrit, erythrocyte aggregation index and platelet aggregation rate were markedly decreased in patients of the trial group. Differences between these parameters before and