# 二丁酰环磷腺苷钙可增强美托洛尔对老年心力衰竭合并心律失常患者的治疗效果*

郑荷洁[1]，　胡小翠[2△]

1. 四川省人民医院 心衰中心（成都 610000）；2. 四川省人民医院 神经外科（成都 610000）

【摘要】　目的　探讨老年心力衰竭合并心律失常患者二丁酰环磷腺苷钙(dbcAMP-Ca)联合美托洛尔治疗效果及安全性。方法　选取本院2021年2月–2023年4月102例老年心力衰竭合并心律失常患者，由独立于研究外的工作人员将招募名单输入随机数据库，采用SAS9.4软件生成随机分配序列，按照1：1的比例分为试验组($n$=51)与对照组($n$=51)。对照组给予美托洛尔初始剂量6.25 mg/d，逐渐增量至目标剂量25 mg/d；试验组给予dbcAMP-Ca联合美托洛尔治疗，美托洛尔给药方式同对照组，加用dbcAMP-Ca(40 mg/次，静脉滴注，1次/d)。两组均维持治疗4周。主要结局指标为各组的临床治疗有效率(该组达到显效和有效的例数/该组总例数)，次要指标为各组的心功能、心率变异性、运动能力、血液流变学、心肌损伤指标、炎性指标及不良反应发生情况。结果　两组临床治疗有效率对比，试验组94.12%(48/51)高于对照组78.43%(40/51)，差异有统计学意义($P$<0.05)。心功能方面，试验组治疗后左心室舒张、收缩末期内径(LVEDD、LVESD)、室间隔厚度小于对照组，左心室射血分数、每搏心输出量水平高于对照组($P$<0.05)。心率变异性方面，试验组治疗后NN间期标准差/平均值标准差(SDNN、SDANN)、相邻NN差50 ms以上占总窦性心搏个数比例(PNN50%)、相邻RR间期差值均方根(RMSSD)水平高于对照组($P$<0.05)。运动能力方面，试验组治疗后6 min步行距离大于对照组($P$<0.05)。血液流变学方面，试验组治疗后血小板聚集率、纤维蛋白原、血沉、全血黏度水平低于对照组($P$<0.05)。心肌损伤指标方面，试验组治疗后血清N末端B型利钠肽原、心肌肌钙蛋白I水平低于对照组，类胰岛素生长因子 1、心肌营养素1水平高于对照组($P$<0.05)。炎性指标方面，试验组治疗后血清炎性指标白细胞介素-6、高敏C反应蛋白、肿瘤坏死因子-α水平低于对照组($P$<0.05)。治疗期间，试验组不良反应发生率(9.80%)与对照组(7.84%)相当($P$>0.05)。结论　在美托洛尔的基础上联合使用dbcAMP-Ca，可有效提高老年心力衰竭合并心律失常患者心功能，改善心率变异性，提高运动耐量，抑制机体炎性反应，用药安全性较高，治疗效果好于单用美托洛尔。

【关键词】　心力衰竭　　心律失常　　美托洛尔　　二丁酰环磷腺苷钙

**Calcium Dibutyryl Adenosine Cyclophosphate Enhances the Effect of Metoprolol in Treating Older Adults With Heart Failure Combined With Arrhythmia**　*ZHENG Hejie*[1], *HU Xiaocui*[2△]. *1. Heart Failure Center, Sichuan People's Hospital*, Chengdu 610000, China; 2. *Department of Neurosurgery, Sichuan People's Hospital*, Chengdu 610000, China

△ Corresponding author, E-mail: C601547245@163.com

【**Abstract**】　**Objective**　To explore the effect and safety of calcium dibutyryl adenosine cyclophosphate (dbcAMP-Ca) combined with metoprolol in the treatment of older adults with heart failure combined with arrhythmia. **Methods**　A total of 102 elderly patients with heart failure combined with arrhythmia were enrolled in our hospital between February 2021 and April 2023. The list of patients enrolled was entered into a random database by independent staffs not involved in the study and random assignment sequences were generated by the SAS9.4 software. Then, the 102 elderly patients were divided into a control group ($n$=51) and an experimental group ($n$=51). Patients in the control group were given metoprolol at an initial dose of 6.25 mg/d, which was gradually increased to the target dose of 25 mg/d. Patients in the experimental group were given 40 mg of dbcAMP-Ca once a day via intravenous drip in addition to the treatment given to the control group. Both groups were treated for 4 weeks. The rate of effective response to clinical treatment (the number of cases achieving significant effects and those achieving some effects divided by the total number of cases in the group) was defined as the main outcome index. Secondary indexes included cardiac function, heart rate variability, exercise ability, hemorheology, myocardial injury indexes, inflammatory indexes, and the occurrence of adverse reactions. **Results**　The rate of effective response to clinical treatment was higher in the experimental group than that in the control group (94.12% [48/51] vs. 78.43% [40/51], $P$<0.05). After treatment, the left ventricular end-diastolic and end-systolic dimensions (LVEDD and LVESD) and the interventricular septal thickness (IVS) were lower in the experimental group than those in the control group, while the left ventricular ejection fraction (LVEF) and the stroke

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volume (SV) were higher in the experimental group than those in the control group (*P*<0.05). In terms of heart rate variability after treatment, the standard deviation of all the normal-to-normal intervals/the average of all the normal-to-normal intervals (SDNN/SDANN), the percentage of NN50 in the total number of normal-to-normal intervals (PNN50%), and the root mean square of the differences between adjacent normal-to-normal intervals/root mean square differences of successive R-R intervals (RMSSD) were higher in the experimental group than those in the control group (*P*<0.05). In terms of exercise capacity after treatment, the subjects in the experimental group covered more distance in the 6-min walk test than those in the control group did (*P*<0.05). In terms of the hemorheology indexes after treatment, the levels of platelet aggregation rate (PAgT), fibrinogen (FIB), erythrocyte sedimentation rate (ESR), and whole blood viscosity (ηb) were lower in the experimental group than those in the control group (*P*<0.05). In terms of the myocardial injury indexes after treatment, the levels of serum N-terminal pro-brain natriuretic peptide (NT-pro BNP) and cardiac troponin I (cTnI) were lower in the experimental group than those in the control group, while the levels of insulin-like growth factor 1 (IGF-1) and cardiotrophin 1 (CT-1) were higher in the experimental group than those in the control group (*P*<0.05). In terms of the inflammatory indexes after treatment, the levels of interleukin-6 (IL-6), high-sensitive C-reactive protein (hs-CRP), and tumor necrosis factor-α (TNF-α) were lower in the experimental group than those in the control group (*P*<0.05). The incidence of adverse reactions in the experimental group (9.80%) and that in the control group (7.84%) were comparable (*P*>0.05). **Conclusion**　The use of dbcAMP-Ca in addition to metoprolol can effectively improve cardiac function, heart rate variability, and exercise tolerance, while inhibiting inflammatory response in elderly patients with heart failure combined with arrhythmia, with high medication safety. The combination medication shows better safety and therapeutic effects than those of metoprolol used alone.

【Key words】　Heart failure　Arrhythmia　Metoprolol　Calcium dibutyryl adenosine cyclophosphate

心力衰竭是引发心律失常发生最常见疾病类型之一,且多数属于室性心律失常[1-2]。相关数据统计结果显示[3],心力衰竭患者中,约有10% ~ 35%合并心房颤动,且发生风险随心力衰竭疾病程度加重而增高。老年群体为心力衰竭高危人群,同时由于老年患者多合并各类基础疾病,病情也相对更严重[4-5]。美托洛尔是一种β1受体阻滞药,对心脏具有高度选择性,可增加心肌电稳定性,降低心肌耗氧,改善心肌细胞损伤,提高心功能,延缓心衰进程[6]。二丁酰环磷腺苷钙(calcium dibutyryl adenosine cyclophosphate, dbcAMP-Ca)是一种新型环磷腺苷(cyclic adenosine monophosphate, cAMP)衍生物,相较于cAMP,其对细胞的渗透性更强,作用持久,可生成大量ATP,加强心肌细胞能量代谢,降低心律失常风险[7-8]。本研究将dbcAMP-Ca联合美托洛尔应用于老年心力衰竭合并心律失常患者的治疗,观察其疗效与安全性,旨在为临床疾病治疗提供参考,报告如下。

# 1　资料与方法

## 1.1　研究对象

本研究分为2组,按照统计学两样本率比较时样本含量估计公式计算:

$$n1 = n2 = \frac{P1(100-P1) + P2(100-P2)}{(P1-P2)^2} \times f(\alpha,\beta) \quad (1)$$

式(1)中*n*1和*n*2分别代表两样本所需含量;*P*1和*P*2分别为两总体率的估计值;*α*为检验水准;*β*为第二类错误的

概率。根据既往文献报道中疾病治疗有效率和临床预试验中疾病治疗有效率,取*P*1 = 95%和*P*2 = 70%,本研究采用双侧检验,取*α* = 0.05,*β* = 0.10,代入公式*n*1 = *n*2 = 43。考虑到无效结果,故将样本量进行适当扩大,最终确定每组样本量为51例。选取2021年2月–2023年4月本院102例心力衰竭合并心律失常老年患者,由独立于研究外的工作人员将招募名单输入随机数据库,采用SAS9.4软件生成随机分配序列,按照1∶1的比例分为试验组(*n* = 51)、对照组(*n* = 51)。

## 1.2　纳入与排除标准

纳入标准:①符合《中国心力衰竭诊断和治疗指南2018》中心力衰竭合并心律失常诊断[9];②年龄≥60岁;③NYHA分级为Ⅲ ~ Ⅳ级;④患者与家属知情同意。排除标准:①合并急性心肌梗死;②存在先天性心脏病、心脏瓣膜疾病、心肌病等;③既往血管外科手术史;④合并急慢性感染;⑤合并其他器质功能严重疾病或恶性肿瘤;⑥合并凝血、免疫功能疾病;⑦伴消化道出血、休克等;⑧入组前2周内使用过糖皮质激素、抗炎药物等对本研究结果造成影响的药物。

## 1.3　方法

两组均予以吸氧,并进行抗感染、强心、利尿等对症治疗。对照组给予美托洛尔(阿斯利康制药,H32025390),初始剂量6.25 mg/d,逐渐增量至目标剂量25 mg/d,若不能耐受则采用患者可耐受的最大剂量(静息状态下心率水平不低于55 min⁻¹)维持治疗。试验组给予dbcAMP-

Ca联合美托洛尔治疗，美托洛尔给药方式同对照组，加用dbcAMP-Ca（上海第一生化，H31022649），40 mg/次，溶于质量分数为5%的葡萄糖溶液，静脉滴注，1次/d。两组均维持治疗4周。本研究方案获得四川省人民医院伦理委员会批准（伦审2021年第018号）。

### 1.4　观察指标

#### 1.4.1　主要结局指标

疗效标准[10]：显效：心功能提升2级及以上或达心功能1级，室性早搏、成对室性早搏、阵发性心动过速减少分别达到70%、80%、90%及以上；有效：心功能提升1级或尚未达心功能1级，室性早搏、成对室性早搏、阵发性心动过速减少分别达到70%、80%、90%及以上；无效：尚未达到上述标准。以显效和有效的例数/总例数计算临床治疗有效率，作为主要结局指标。

#### 1.4.2　次要结局指标

①心功能：于治疗前后，通过彩色多普勒超声心动图（美国GE，Vivid E9）检测，频率设置为：1.0～4.0 MHz，患者左侧卧，屏气状态，full-volume模式下进行图像采集，检测左心室收缩、舒张末期容积（LVESV、LVEDV）、每搏心输出量（SV）、左室射血分数（LVEF）水平。②心率变异性：采用24 h动态心电图（Philips, Zymed holter 2010）记录患者治疗前后心率变异性：NN间期标准差/平均值标准差（SDNN、SDANN）、相邻NN差50 ms以上占总窦性心搏个数比例（PNN50%）、相邻RR间期差值均方根（RMSSD）。③6 min步行试验：治疗前后，所有患者均采用6 min步行实验评估活动耐量，患者于直行走廊行走6 min，记录行走距离。④血液流变学指标：治疗前后，采集患者外周空腹静脉血5 mL，测定血小板聚集率（PAgT）、纤维蛋白原（FIB）、血沉（ESR）、全血黏度（ηb）水平。⑤血清心肌损伤指标：取上述外周空腹静脉血，离心处理（3 500 r/min，10 min，离心半径12.5 cm），取血清，采用免疫荧光层析法检测N末端B型利钠肽原（NT-proBNP），采用免疫胶乳比浊法检测超敏肌钙蛋白

（cTnI），采用放射免疫法检测心肌营养素1（CT-1），采用酶联免疫吸附法检测类胰岛素生长因子1（IGF-1）。⑥炎性指标：取上述离心后的血清样本，采用酶联免疫吸附法检测高敏C反应蛋白（hs-CRP）、肿瘤坏死因子-α（TNF-α）、白细胞介素-6（IL-6）水平。⑦比较两组不良反应发生率。

### 1.5　统计学方法

采用SPSS21.0软件（IBM公司），计量资料组间比较采用独立样本$t$检验，治疗前后的比较先在同组内做差值，再采用配对样本$t$检验对差值进行组间比较；计数资料组间比较采用$\chi^2$检验，$P<0.05$为差异有统计学意义。

## 2　结　果

### 2.1　两组一般资料对比

试验组与对照组性别、年龄、病程、体质量指数（BMI）、NYHA心功能分级、病因比较差异无统计学意义（$P>0.05$）。见表1。

### 2.2　两组主要结局指标比较

试验组显效者25例，有效者23例，无效者3例；对照组显效者21例，有效者19例，无效者11例，两组有效率对比，试验组94.12%（48/51）高于对照组78.43%（40/51）（$P<0.05$）。

### 2.3　两组次要结局指标比较

#### 2.3.1　心功能指标

两组治疗前心功能水平比较差异无统计学意义（$P>0.05$）；两组治疗4周后，LVEDD、LVESD、IVS水平减小且试验组小于对照组，LVEF、SV水平升高且试验组高于对照组（$P<0.05$）。见表2。

#### 2.3.2　心率变异性

见表3。两组治疗前心率变异性指标水平比较差异无统计学意义（$P>0.05$）；两组治疗4周后，SDANN、SDNN、PNN50、RMSSD水平升高，且试验组高于对照组（$P<0.05$）。

表 1　一般资料
Table 1　General data

| Characteristics | Experimental group ($n$=51) | Control group ($n$=51) | $t/\chi^2$ | $P$ |
| --- | --- | --- | --- | --- |
| Sex (male/female)/case | 24/27 | 22/29 | 0.158 | 0.691 |
| Age/yr., $\bar{x}\pm s$ | 71.81±5.36 | 72.50±4.73 | 0.689 | 0.492 |
| Course of disease/year, $\bar{x}\pm s$ | 2.43±0.35 | 2.29±0.49 | 1.660 | 0.100 |
| BMI/(kg/m$^2$), $\bar{x}\pm s$ | 23.70±1.74 | 24.18±1.87 | 1.342 | 0.183 |
| Grading of NYHA cardiac function (grades Ⅲ/Ⅳ)/case | 28/23 | 30/21 | 0.160 | 0.689 |
| Causes of disease[*] | 13/21/6/11 | 15/19/5/12 | 0.377 | 0.945 |

[*] Hypertension/coronary heart disease/rheumatic heart disease/dilated cardiomyopathy. BMI: body mass index; NYHA: New York Heart Association.

表 2　两组心功能指标水平比较（$\bar{x} \pm s$）

**Table 2　Comparison of cardiac function indexes between the two groups ($\bar{x} \pm s$)**

| Indexes | Experimental group ($n$=51) | Control group ($n$=51) | $t$ | $P$ |
|---|---|---|---|---|
| LVEDD/mm | | | | |
| 　Before treatment | 64.35±4.08 | 63.63±4.17 | 0.881 | 0.380 |
| 　After treatment | 60.58±2.83 | 61.74±3.03 | | |
| 　Difference values | −3.77±0.51 | −1.89±0.32 | 22.299 | <0.001 |
| LVESD/mm | | | | |
| 　Before treatment | 55.75±2.95 | 56.14±3.18 | 0.642 | 0.522 |
| 　After treatment | 51.90±2.49 | 53.47±2.92 | | |
| 　Difference values | −3.85±0.46 | −2.67±0.34 | 14.732 | <0.001 |
| IVS/mm | | | | |
| 　Before treatment | 10.73±1.25 | 11.06±1.38 | 1.266 | 0.209 |
| 　After treatment | 8.71±0.85 | 9.49±0.90 | | |
| 　Difference values | −2.02±0.43 | −1.57±0.27 | 6.329 | <0.001 |
| LVEF/% | | | | |
| 　Before treatment | 41.36±3.39 | 42.27±3.56 | 1.322 | 0.189 |
| 　After treatment | 50.88±2.95 | 47.44±2.80 | | |
| 　Difference values | 9.52±1.97 | 5.17±1.04 | 13.945 | <0.001 |
| SV/(L/min) | | | | |
| 　Before treatment | 3.09±0.51 | 3.23±0.47 | 1.442 | 0.153 |
| 　After treatment | 4.50±0.74 | 4.19±0.69 | | |
| 　Difference values | 1.41±0.38 | 0.96±0.19 | 7.564 | <0.001 |

LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; IVS: interventricular septum; LVEF: left ventricular ejection fractions; SV: stroke volume.

表 3　两组心率变异性指标水平比较（$\bar{x} \pm s$）

**Table 3　Comparison of heart rate variability indexes between the two groups ($\bar{x} \pm s$)**

| Indexes | Experimental group ($n$=51) | Control group ($n$=51) | $t$ | $P$ |
|---|---|---|---|---|
| SDNN/ms | | | | |
| 　Before treatment | 94.34±13.67 | 95.25±11.90 | 0.359 | 0.721 |
| 　After treatment | 117.80±14.62 | 110.75±13.89 | | |
| 　Difference values | 23.46±3.94 | 15.50±3.17 | 11.241 | <0.001 |
| SDANN/ms | | | | |
| 　Before treatment | 100.71±10.46 | 101.49±11.15 | 0.364 | 0.716 |
| 　After treatment | 114.67±8.81 | 108.92±7.70 | | |
| 　Difference values | 13.89±2.68 | 7.52±1.95 | 13.725 | <0.001 |
| RMSSD/ms | | | | |
| 　Before treatment | 21.75±5.04 | 20.96±4.73 | 0.816 | 0.416 |
| 　After treatment | 29.95±4.36 | 27.81±3.93 | | |
| 　Difference values | 8.20±1.44 | 6.85±1.14 | 5.249 | <0.001 |
| PNN50/% | | | | |
| 　Before treatment | 3.28±0.77 | 3.52±0.80 | 1.544 | 0.126 |
| 　After treatment | 4.83±1.03 | 4.25±0.96 | | |
| 　Difference values | 1.55±0.38 | 0.73±0.22 | 13.337 | <0.001 |

SDNN: standard diviation of NN intervals; SDANN: standard deviation of sequential five-minute R-R interval means; RMSSD: root mean square of successive differences; PNN50: proportion of NN50 divided by total number of NNs.

**2.3.3　6 min步行试验结果比较**

试验组治疗前6 min步行距离为（238.66±31.52）m，治疗4周后为（350.62±22.70）m，治疗前后差值为（110.96±28.45）m；对照组治疗前6 min步行距离为（245.13±29.90）m，治疗4周后为（313.89±20.47）m，治疗前后差值为（68.76±18.49）m，两组治疗前6 min步行试验结果比较差

异无统计学意义($P > 0.05$); 两组治疗后6 min步行距离增加, 且试验组大于对照组($P < 0.05$)。

**2.3.4　血液流变学指标**

　　两组治疗前血液流变学指标比较差异无统计学意义($P > 0.05$); 两组治疗4周后, ESR、ηb、FIB、PAgT水平较治疗前降低, 且试验组低于对照组($P < 0.05$)。见表4。

**2.3.5　心肌损伤指标**

　　两组治疗前血清心肌损伤指标水平比较差异无统计学意义($P > 0.05$); 两组治疗4周后, 血清NT-proBNP、

cTnI水平降低且试验组低于对照组, IGF-1、CT-1水平升高且试验组高于对照组($P < 0.05$)。见表5。

**2.3.6　炎性指标**

　　两组治疗前血清炎性指标水平比较差异无统计学意义($P > 0.05$); 治疗4周后, 两组血清hs-CRP、TNF-α、IL-6水平降低, 且试验组低于对照组($P < 0.05$)。见表6。

**2.3.7　两组不良反应发生情况比较**

　　治疗期间, 试验组发生轻微胃肠道反应2例, 嗜睡1例, 皮疹1例, 窦性心动过缓1例, 不良反应发生率为

**表 4　两组血液流变学比较($\bar{x} \pm s$)**

**Table 4　Comparison of hemorheology findings between the two groups ($\bar{x} \pm s$)**

| Indexes | Experimental group ($n=51$) | Control group ($n=51$) | $t$ | $P$ |
|---|---|---|---|---|
| ESR/(mm/h) | | | | |
| 　Before treatment | 16.16±3.23 | 17.08±2.95 | 1.502 | 0.136 |
| 　After treatment | 11.44±1.70 | 14.15±2.77 | | |
| 　Difference values | −4.72±0.95 | −2.93±0.52 | 11.803 | <0.001 |
| ηb/(mP·s) | | | | |
| 　Before treatment | 5.51±0.48 | 5.60±0.56 | 0.871 | 0.386 |
| 　After treatment | 4.69±0.72 | 5.14±0.60 | | |
| 　Difference values | −0.86±0.20 | −0.46±0.11 | 12.515 | <0.001 |
| FIB/(g/L) | | | | |
| 　Before treatment | 9.36±1.28 | 8.95±1.31 | 1.599 | 0.113 |
| 　After treatment | 5.24±0.67 | 6.03±0.82 | | |
| 　Difference values | −4.12±0.81 | −2.92±0.54 | 8.803 | <0.001 |
| PAgT/% | | | | |
| 　Before treatment | 45.19±5.77 | 46.02±6.18 | 0.702 | 0.485 |
| 　After treatment | 33.73±4.54 | 37.18±5.49 | | |
| 　Difference values | −11.46±1.53 | −8.84±1.27 | 9.410 | <0.001 |

ESR: erythrocyte sedimentation rate; ηb: whole blood viscosity; FIB: fibrinogen; PAgT: platelet aggregation test.

**表 5　两组心肌损伤指标水平比较($\bar{x} \pm s$)**

**Table 5　Comparison of the results for myocardial injury indexes between the two groups ($\bar{x} \pm s$)**

| Indexes | Experimental group ($n=51$) | Control group ($n=51$) | $t$ | $P$ |
|---|---|---|---|---|
| NT-proBNP/(pg/mL) | | | | |
| 　Before treatment | 4 385.77±908.28 | 4 406.13±881.55 | 0.115 | 0.909 |
| 　After treatment | 1 914.35±468.73 | 2 452.71±506.02 | | |
| 　Difference values | −2 471.42±314.85 | −1 953.42±226.90 | 9.532 | <0.001 |
| cTnI/(μg/L) | | | | |
| 　Before treatment | 6.24±1.49 | 5.93±1.31 | 1.116 | 0.267 |
| 　After treatment | 1.93±0.28 | 2.21±0.31 | | |
| 　Difference values | −4.31±0.89 | −3.72±0.63 | 3.864 | <0.001 |
| IGF-1/(ng/mL) | | | | |
| 　Before treatment | 108.14±13.91 | 111.01±11.85 | 1.122 | 0.265 |
| 　After treatment | 131.46±14.73 | 123.53±10.80 | | |
| 　Difference values | 23.32±5.27 | 12.52±2.86 | 12.863 | <0.001 |
| CT-1/(ng/L) | | | | |
| 　Before treatment | 148.75±17.11 | 146.92±15.46 | 0.567 | 0.572 |
| 　After treatment | 198.63±16.26 | 188.40±13.47 | | |
| 　Difference values | 49.88±11.48 | 41.48±10.62 | 3.836 | <0.001 |

NT-proBNP: N-terminal pro-B-type natriuretic peptide; cTnI: cardiac troponin I; IGF-1: insulin-like growth factor 1; CT-1: cardiotrophin-1.

表6 两组炎性指标水平比较($\bar{x} \pm s$)

Table 6 Comparison of the results for inflammatory indexes between the two groups ($\bar{x} \pm s$)

| Indexes | Experimental group ($n$=51) | Control group ($n$=51) | $t$ | $P$ |
|---|---|---|---|---|
| IL-6/(pg/mL) | | | | |
| Before treatment | 39.37±8.59 | 41.48±10.06 | 1.139 | 0.257 |
| After treatment | 13.60±2.88 | 18.96±4.51 | | |
| Difference values | −25.77±2.93 | −22.52±3.02 | 5.516 | <0.001 |
| hs-CRP/(mg/L) | | | | |
| Before treatment | 15.85±3.11 | 16.02±2.96 | 0.283 | 0.778 |
| After treatment | 7.06±1.76 | 10.28±2.05 | | |
| Difference values | −8.52±1.24 | −5.74±1.06 | 12.170 | <0.001 |
| TNF-α/(ng/L) | | | | |
| Before treatment | 21.66±4.41 | 20.89±4.77 | 0.846 | 0.399 |
| After treatment | 5.77±1.03 | 8.06±1.88 | | |
| Difference values | −15.89±2.37 | −12.83±2.04 | 6.988 | <0.001 |

IL-6: interleukin-6; hs-CRP: hypersensitive C-reactive protein; TNF-α: tumor necrosis factor-α.

9.80%; 对照组发生轻微胃肠道反应1例, 眩晕1例, 窦性心动过缓1例, Ⅰ度房室传导阻滞1例, 不良反应发生率为7.84%, 两组不良反应率比较($P$> 0.05)。

## 3 讨论

慢性心力衰竭患者心功能严重下降, 交感神经激活, 去甲肾上腺素异常高表达, 导致心电活动紊乱, 心肌处于代偿状态, 易发心律失常[11]。合并心律失常的心力衰竭患者是致命性心脏事件的高危人群, 频发和复杂性室性心律失常心衰患者每年死亡率约15%, 且其中50%为心律失常导致的猝死[12]。美托洛尔为临床常用β-受体阻滞剂, 可阻断内源性儿茶酚胺过度刺激, 改善交感神经系统对心脏的支持作用, 改善其顺应性, 降低心肌耗氧, 减轻心肌细胞Ca²⁺超负荷[13]。dbcAMP-Ca具有血管扩张作用, 可减轻心肌缺血症状, 治疗心力衰竭疗效确切, dbcAMP-Ca可促进酶活性激活, 增加ATP生成, 加强心肌活力, 改善微循环, 提高心脏泵血功能[14-15]。

本研究中, 试验组治疗有效率高于对照组, 提示dbcAMP-Ca联合美托洛尔治疗老年心力衰竭合并心律失常效果优于单纯美托洛尔, 美托洛尔可通过醛固酮-血管紧张素-肾素系统抑制达到疾病治疗目的; dbcAMP-Ca可改善心肌细胞代谢, 扩张血管平滑肌, 减轻心脏收缩后负荷, 二者分别通过不同的作用机制改善患者疾病状态, 联合用药发挥协同作用, 进一步提高临床疗效[16-17]。超声心动图为心脏结构与功能评估首选方法, 对明确临床心力衰竭程度, 指导临床疾病治疗具有重要价值[18]。LIU等[19]研究提出将dbcAMP-Ca应用于临床冠心病心衰治疗, 治疗后试验组LVEF、SV水平增加, 认为dbcAMP-Ca可改善

患者左心室泵功能。本研究中, 两组治疗后LVEF、SV水平升高, LVEDD、LVESD、IVS水平降低, 说明两组治疗后患者心功能均有一定程度的改善, 且dbcAMP-Ca联合美托洛尔用药心功能改善效果更佳。dbcAMP-Ca可在一定程度上改善机体心肌能量代谢, 加强心肌收缩, 提高心排血量水平; 增加细胞内cAMP浓度, 发挥正性肌力作用; 松弛血管平滑肌, 降低血管阻力, 减轻心脏负荷, 从而有效提升患者心功能[20-21]。动态心电图心率变异性检测可有效评估机体心脏交感与迷走神经张力, 反映心率变化, 其中SDNN反映心率变异性总体情况; SDANN反映交感神经张力; PNN50、RMSSD则可评估副交感神经张力[22]。既往研究显示[23], 心力衰竭合并心律失常患者心肌损伤影响自主神经功能, 导致交感神经张力增加, SDNN、SDANN、RMSSD、PNN50水平降低, 且张力增加越明显其下降幅度也随之增加。本研究中, 治疗后试验组上述心率变异性指标改善优于对照组, dbcAMP-Ca的应用有利于心脏窦房细胞功能修复, 在一定程度上推迟心律失常的潜伏期, 缩短其持续时间, 改善心率变异性指标[24]。6 min步行试验可评估患者运动耐力, 本研究显示治疗后试验组6 min步行距离大于对照组, 表明dbcAMP-Ca、美托洛尔二者联合用药更能改善患者运动耐量。

血液流变学可反映血液成分变化导致的血液流动性、凝滞性改变, 血液黏度增加时则血液流动性变差, 心力衰竭合并心律失常患者易出现体循环血栓栓塞, 严重时可导致心源性猝死和脑卒中等一系列不良后果[25-26]。本研究中, 两组治疗后ESR、ηb、FIB、PAgT水平均出现不同程度的降低, 且试验组在血液流变学改善方面相较于对照组具有明显优势, dbc AMP-Ca可阻断Ca²⁺与血管平

滑肌结合, 抑制血小板聚集, 减轻血管阻力; dbcAMP-Ca可通过cAMP依赖蛋白激酶使肌球蛋白轻链激酶发生磷酸化, 抑制肌球蛋白、肌动蛋白结合, 发挥血小板功能调节作用, 抑制血小板激活[27]。心力衰竭状态下, 压力负荷增加, 心肌细胞受到牵引, 可导致血液NT-pro BNP高表达; 心肌损伤时cTnT释放入血, 血液中cTnT水平明显增高; CT-1可促进心肌细胞生长; IGF-1则是一种单链多肽, 对心脏射血功能、心输出量具有重要影响[28]。本研究中, 治疗后, 试验组NT-pro BNP、cTnI水平低于对照组, IGF-1、CT-1水平高于对照组, 进一步表明dbcAMP-Ca、美托洛尔联合用药可减轻心力衰竭合并心律失常患者心肌损伤, 提高心功能, dbcAMP-Ca可发挥心肌保护作用, 增加心肌供养, 改善冠状动脉循环[29]。炎性反应是心力衰竭疾病发生发展阶段中的重要影响因素, 本研究中试验组治疗后IL-6、IL-1β、TNF-α水平低于对照组, 提示dbcAMP-Ca联合美托洛尔的应用可降低老年心力衰竭合并心律失常患者机体炎性因子水平, 抑制机体炎性反应, dbcAMP-Ca注射后, 外源性cAMP激活蛋白激酶, 提高血液cAMP含量, 减轻机体炎症反应[30]。比较两组不良反应发生率差异无统计学意义, 在美托洛尔的基础上联合使用dbc AMP-Ca未导致患者不良反应风险增加, 联合用药具有较高的安全性。

综上所述, dbcAMP-Ca联合美托洛尔可有效提高老年心力衰竭合并心律失常患者心功能, 改善心率变异性, 有利于心室重塑, 提高运动耐量, 抑制机体炎性反应, 用药安全性较高。

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<h2 style="text-align:center">参 考 文 献</h2>

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