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Effect of perindopril on the myocardial energy consumption in patients with heart failure after myocardial infarction

Da−Peng Li[1], Dang−Hui Sun[2], Lin Wei[1], Xi−Ying Yu[1], Shi−Jin Na[1]✉

[1] *The First Hospital of Harbin City, Heilongjiang, 150010*

[2] *The First Hospital Affiliated to Harbin Medical University, 150011*

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ABSTRACT

Objective: To explore the clinical efficacy of perinodopril in the treatment of heart failure in patients after myocardial infarction and effect on the myocardial energy consumption. **Methods:** A total of 87 patients with heart failure after myocardial infarction who were admitted in our hospital from August, 2014 to October, 2015 were included in the study and divided into the routine dose group (n=43, perinodopril 4 mg/d) and high dose group (n=44, perinodopril 8 mg/d) according to the long-term oral dose. All the patients were given perinodopril, continuously for 6 months. The changes of blood pressure and serum biochemical indicators before and after treatment in the two groups were compared. The changes of cardiac function indicators and myocardial energy consumption indicators before and after treatment in the two groups were compared. 6MWT 6 months and 1 year after treatment in the two groups was calculated. **Results:** The plasma BNP and H-FABP levels, LVEDD, LVESD, MEE, and cESS after treatment in the two groups were significantly reduced when compared with before treatment, and those in the high dose group were significantly lower than those in the low dose group. LVEF and FS after treatment in the two groups were significantly increased, and those in the high dose group were significantly greater than those in the routine dose group. The seurm potassium level after treatment in the high dose group was significantly elevated when compared with before treatment, but was not significantly different from that in the routine dose group. SBP, DBP, and Scr levels after treatment in the two groups were not significantly changed. 6MWT 6 months and 1 year after treatment in the high dose group was significantly greater than that in the routine dose group. **Conclusions:** Perinodopril in a high dose can significantly reduce the plasma BNP and H-FABP levels in patients with heart failure after myocardial infarction, inhibit the ventricular remodeling, promote the recovery of systolic function, reduce the myocardial energy consumption, and will not affect the blood pressure, serum potassium, and renal function, with efficacy significantly superior to that in a low dose; moreover, it has a certain safety.

1. Introduction

Myocardial infarction is a common cardiovascular accidental disease in the clinic, with an increasing morbidity[1,2]. Perinodopril belongs to ACEI, is currently the best drug in the treatment of heart failure after myocardial infarction, can inhibit the myocardial remodeling to improve the prognosis in patients with heart failure after myocardial infarction, and extend the survival time[3,4]. However, the efficacy of perinodopril in different doses in the treatment of heart failure after myocardial infarction is different, especially have a significant difference in inhibiting the myocardial remodeling[5]. Currently, study on the effect of perinodopril in different doses on the myocardial energy consumption is less reported. The study is aimed to explore the clinical efficacy of perinodopril in the treatment of heart failure in patients after myocardial infarction and effect on the myocardial energy consumption.

✉Corresponding author: Shi-Jin Na, The First Hospital of Harbin City, Heilongjiang, 150010.
Tel: 13804521536
E-mail: lidapenghlj888@126.com
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2. Materials and methods

2.1. Clinical materials

A total of 87 patients with heart failure after myocardial infarction who were admitted in our hospital from August, 2014 to October, 2015 were included in the study and confirmed by CAG. Inclusion criteria: (1) those who were accompanied by heart failure with NYHA grading of Ⅱ-Ⅳ; (2) those whose color Doppler echocardiography showed the enlarged left ventricle and abnormal ventricular wall segment movement; (3) those whose LVEF in a rest state was less than 45%. Exclusion criteria: (1) those who had a history of cardiogenic syncope; (2) those who were allergic to perinodopril; (3) those who were accompanied by valvular heart disease and pulmonary heart disease; (4) those who had arrhythmia; (5) who were accompanied by other severe diseases. According to the long-term medication dose, the patients were divided into the routine dose group (n=43) and high dose group (n=44). In the routine dose group, 29 were male, and 14 were femlae; aged from 35 to 79 years old, with an average age of (65.3±5.6) years old; infarction sites: 17 in the anterior wall, 12 in the anteroseptal wall, 11 in the extensive anterior wall, and 3 in the inferior wall; NYHA grading: 15 at grade II, 19 at grade III, and 9 at grade IV. In the high dose group, 27 were male, and 17 were femlae; aged from 34 to 80 years old, with an average age of (67.5±6.1) years old; infarction sites: 16 in the anterior wall, 13 in the anteroseptal wall, 10 in the extensive anterior wall, and 5 in the inferior wall; NYHA grading: 14 at grade II, 22 at grade III, and 8 at grade IV. The comparison of the general materials between the two groups was comparable (P>0.05).

2.2. Methods

The patients in the two groups were given β-receptor blocker, diuretics, and other routine drugs. On the above basis, the patients in the two groups were given perindopril tert-butylamine tablet (produced by Shangyao Dongying Pharmaceutical Co. Ltd., Approval No. H20093504, 2 mg/tablet), with an initial dose of 2 mg/d. According to the patients′ own conditions, 2 mg/d was added every 1-2 week. In the routine dose group, the dose was added to the target dose of 2-4 mg/d, while in the high dose group, the dose was added to the target dose of 8-10 mg/d. During the treatment process, if hypotension and cough occurred, the original dose was maintained. After adding to the target dose, the patients in the two groups were continuously treated for 6 months.

2.3. Observation indicators

(1) The blood pressure (SBP and DBP) was recorded. The rapid fluorescence immunoassay was used to detect the plasma BNP and H-FABP levels before and after treatment in the two groups. The full automatic biochemical analyzer (7600-020 type) was used to detect the serum potassium and Scr levels. (2) The American color Doppler ultrasonic diagnostic apparatus was used to detect the left cardiac function indicators, including LVESD, LVEDD, LVEF, and FS. MEE and cESS were calculated. The formulas were listed in the following[6]

cESS=SBP (LVIDs/2)2 [LVIDs/2+PWTs)2/(LVIDs/2+PWTs/2)2+1]/[(LVIDs/2+PWTs)2-(LVIDs/2)2], MEE=cESS LVET SV 4.2 10-4. (3) 6MWT 6 months and 1 year after treatment in the two groups was recorded and compared.

2.4. Statistical analysis

SPSS 19.0 software was used for the statistical analysis. ANOVA was used for the comparison of measurement data, and t test was used. P<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of the blood pressure and biochemical indicators before and after treatment between the two groups

The plasma BNP and H-FABP after treatment in the two groups were significantly reduced when compared with before treatment, and those in the high dose group was significantly higher than those in the low dose group (P<0.01). The serum potassium level after treatment in the high dose group was significantly elevated when compared with before treatment (P<0.01), but was not significantly different from that in the routine dose group (P>0.05). SBP, DBP, and Scr levels in the two groups were not significantly changed (P>0.05) (Table 1).

Table 1.

Comparison of the blood pressure and biochemical indicators before and after treatment between the two groups.

Indicators	Routine dose group (n=43)		High dose group (n=44)	
	Before treatment	After treatment	Before treatment	After treatment
SBP	123.1±29.2	113.6±29.4	121.2±27.1	110.5±28.5
DBP	76.8±16.1	72.9±15.8	77.1±14.3	71.8±15.2
Serum potassium	4.1±0.4	4.3±0.7	4.0±0.5	4.4±0.6*
Scr	95.1±5.8	95.2±6.2	95.0±5.9	95.4±5.3
BNP	819.2±199.3	541.2±190.5*	822.5±192.3	265.4±187.7*#
H-FABP	15.3±2.2	11.2±2.5*	15.4±2.6	8.5±2.4*#

*P<0.01, when compared with before treatment; #P<0.01, when compared with the routine dose group.

Table 2.
Comparison of the cardiac function indicators before and after treatment between the two groups.

Indicators	Routine dose group (n=43)		High dose group (n=44)	
	Before treatment	After treatment	Before treatment	After treatment
LVEDD	65.3±4.2	56.3±3.9*	65.6±4.1	52.1±4.2*#
LVESD	60.2±3.6	50.1±3.4*	61.4±3.6	45.2±3.3*#
LVEF	36.2±2.2	41.2±2.7*	35.6±2.0	46.6±1.9*#
FS	19.9±3.8	23.2±3.4*	20.1±3.2	28.9±3.7*#

*P<0.01, when compared with before treatment; #P<0.01, when compared with the routine dose group.

Table 3.
Comparison of the myocardial energy consumption indicators before and after treatment between the two groups.

Indicators	Routine dose group (n=43)		High dose group (n=44)	
	Before treatment	After treatment	Before treatment	After treatment
MEE	120.1±20.5	85.6±17.5*	121.4±20.7	73.2±16.9*#
cESS	157.3±16.5	127.5±14.9*	159.6±16.3	120.3±15.4*#

*P<0.01, when compared with before treatment; #P<0.01, when compared with the routine dose group.

3.2. Comparison of the cardiac function indicators before and after treatment between the two groups

LVEDD and LVESD after treatment in the two groups were significantly reduced when compared with before treatment, and those in the high dose group were significantly lower than those in the routine dose group (P<0.01); LVEF and FS were significantly increased, and those in the high dose group were significantly greater than those in the routine dose group (P<0.01) (Table 2).

3.3. Comparison of the myocardial energy consumption indicators before and after treatment between the two groups

MEE and cESS after treatment in the two groups were significantly reduced when compared with before treatment, and those in the high dose group were significantly lower than those in the low dose group (P<0.01) (Table 3).

3.4. Comparison of 6MWT after treatment between the two groups

6MWT 6 months and 1 year after treatment in the routine dose group was (411.5±20.6) m and (455.7±21.2) m, respectively, while in the high dose group was (438.1±21.4) m and (475.6±23.4) m, respectively. 6MWT 6 months and 1 year after treatment in the high dose group was significantly greater than that in the routine dose group (P<0.01).

4.Discussion

Ventricular remodeling is an important mechanism for the occurrence and development of heart failure. It is reported that the activation of RAAS can not only cause water-sodium retention and vasoconstriction, increase the cardiac load, but also promote the ventricular remodeling; therefore, blocking of RAAS has been the key for the treatment of heart failure after myocardial infarction[7]. ACEI drugs can inhibit the cardiac RAAS and K-Ks to reach the goal of increasing the coronary blood flow volume, reducing the myocardial oxygen requirement, and improving the myocardial metabolism and cardiac function. Perindopril is a typical ACEI drug, and has been widely applied in the treatment of heart failure after myocardial infarction[8,9]. During the treatment process for patients with heart failure after myocardial infarction, ACEI drugs should be comined with other drugs. The dose of ACEI should be gradually increased, due to the long adding time and the effect of ACEI drugs on the blood pressure and renal function, the best dose of perindopril in the treatment of heart failure after myocardial infarction should be urgently explored[10].

The dose of ACEI drugs in domestic is generally low, and 4 mg/d perindopril is mostly adopted. Large-scale and long-course observational study is yet absent. Application of ACEI in a high dose in the domestic population may cause hypotension, hyperkalemia, dry cough, and other adverse reaction; therefore, clinical application of perindopril in a high dose in restricted. Perindopril can stably and slowly reduce the blood pressure, with rare occurrence of sudden blood pressure reduction. The results in the study showed that SBP and DBP after treatment in the two groups were not significantly changed; the serum potassium level after treatment in the high dose group was significantly reduced, but was not significantly different from that in the routine dose group, indicating that perindopril in a high dose will not give rise to hyperkalemia, and will not cause the serum potassium content exceeding the normal value, but clinical application should monitor the serum potassium level in a regular time in order to prevent the occurrence of hyperkalemia. Moreover, Scr level after treatment in the two groups was not significantly changed, suggesting that perindopril in a high dose will not cause renal dysfunction, and other adverse reactions. Various cytokines in the neuroendocrine and circulation tissues are involved in the left ventricular remodeling, resulting in the occurrence and development of heart failure. BNP, secreted by the ventricular muscle cells, has effects of urination, natriuresis, blood vessel expansion, and inhibition of RAAS system and sympathetic nervous system. The plasma BNP level is an important indicator for the diagnosis of heart failure and the evaluation of prognosis[11]. H-FABP is also one of the markers to reflect the myocardial damage, and is largely distributed in the myocardial tissues. Myocardial ischemia and anoxia will promote its release into the blood in quantity, resulting in the

continuous elevation of plasma H-FABP[12]. The results in the study showed that the plasma BNP and H-FABP levels after treatment in the two groups were significantly reduced, and those in the high dose group were significantly lower than those in the low dose group, suggesting that perindopril in a high dose can more significantly recover the cardiac systolic and diastolic function.

Perindopril can reduce the blood and tissue Ang II level, expand the arteriole, alleviate the water-sodium retention, inhibit the release of norepinephrine, reduce the activity of sympathetic nerve, decrease the cardiac load, lowe the activity of ACE, inhibit the degradation of bradykinin, and improve the myocardial remodeling. LVEF is the proportion of left ventricular stroke volume and end-diastolic volume. The stronger the myocardial contraction is, the greater LVEF is. LVESD and LVEDD are the effective indicators to reflect the cardiac systolic and diastolic functions, respectively. The results in the study showed that LVEDD and LVESD after treatment in the two groups were significantly reduced, and those in the high dose group were significantly lower than those in the routine dose group; LVEF and FS were significantly increased, and those in the high dose group were significantly greater than those in the routine dose group, which is consistent with the results reported by Peng et al[13]. The myocardial energy metabolism disorder is the basic pathological change in patients with heart failure after myocardial infarction. Due to the advantages of non-invasiveness, simple operation, and low cost, UCG has been the common method in studying the myocardial energy metabolism. It is reported by Wang in 2014 that[14] perindopril can reduce the myocardial energy consumption in patients with heart failure after myocardial infarction, and the change is more obvious with high dose. MEE level can reflect the myocardial biological energy consumption characteristics of different left ventricular structures in patients with hypertension.

MEE and cESS can be served as important indicators for myocardial energy consumption. The results in the study showed that MEE and cESS after treatment in the two groups were significantly reduced, and those in the high dose were significantly lower than those in the low dose group. Through regulating the neurohumoral hormones, perindopril can reduce the cardiac pre- and after load, filling pressure of left and right ventricle, and total peripheral vascular resistance, increase the cardiac output and cardiac index, enhance the local muscle blood flow and exercise tolerance, and improve the ventricular negative remodeling and long-term prognosis in patients with heart failure[15]. The results in the study showed that 6MWT 6 months and 1 year after treatment in the high dose group was significantly greater than that in the routine dose group, which is consistent with the results reported by Chang et al[16].

In conclusion, the clinical efficacy of perinodopril in different doses in the treatment of heart failure after myocardial infarction is significantly different. Perinodopril in a high dose will more significantly recover the cardiac function, reduce the myocardial energy consumption, with efficacy significantly superior to that with routine dose; meanwhile, will not cause great effect on the blood pressure, serum potassium, and renal function, and has a certain safety.

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