Curative effects of enalapril combined with folic acid tablets on hypertension and its mechanism

Li-Hong Zhang*

Department of Internal Medicine, Chinese Tibetology Research Center, Beijing Tibetan and Ethnic Medicine Hospital, Beijing 100029, China

1. Introduction

H type hypertension refers to essential hypertension with high homocysteine. Some studies have indicated that in our country, this type of hypertension accounted for 75% high blood pressure patients. High homocysteine and hypertension are independent risk factors for cardiovascular disease[1,2], which seriously threatens the health and life of patients. Enalapril is clinically common used antihypertensive drugs, folic acid can reduce the serum homocysteine levels[3]. In this study, we aim to further explore the effects of two drugs combination on the body's blood pressure and related factors. Reports as follows.

2. Materials and methods

2.1. General information

A total of 92 cases of H type hypertension patients were average randomly divided into the observation group and control group, the control group was treated with enalapril maleate tablets for treatment, the observation group in the control group based on the combined use of folic acid tablets for treatment, compared two groups of serum homocysteine cysteine (Hcy), inflammatory factor and vascular endothelial injury related indicators of change. Results: The effective rate of the observation group was 60.9%, the control group was 60.9%, the difference was not statistically significant; the two groups Hcy, CPR, B12, TNF-α, MMP-9, NO and ET-1 were significantly better than before treatment, the difference was statistically significant, but there were significant differences between the observation group and the control group. Conclusion: For the H type hypertension patients and enalapril maleate tablets in the treatment can be a certain extent, it can improve the patients' blood pressure, reduce Hcy levels, improve endothelial function, alleviate the inflammatory reaction, if combined with a dose of folic acid, the clinical curative effect is better, the H type hypertension patients with the treatment of the ideal method.
average (98.1±7.6) mmHg; The two groups had no significant difference in sex ratio, age, course of disease and blood pressure level (P>0.05) and were comparable.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) patients with essential hypertension, systolic blood pressure between 140-180 mmHg and diastolic blood pressure between 90-110 mmHg; (2) Hcy level >15 μmol/L; (3) all patients signed the informed consent and willing to actively cooperate with medical personnel to carry out related clinics.

Exclusion criteria: (1) patients with secondary hypertension; (2) with heart, brain, kidney and other important organ disease; (3) voluntary withdrawal of the treatment; (4) the clinical drug allergy.

2.3. Treatment method

Both two group patients were given routine nursing measures, the control group was given enalapril maleate tablets and the observation group was given oral folic acid tablets on the basis of the control group. The control group was given oral enalapril maleate tablets (10 mg, Shanghai Modern Pharmaceutical Co., Ltd.) in the morning around 8:00 with 10 mg/time/d; The observation group was given oral folic acid tablets (5 mg, Beijing Silian Pharmaceutical Co., Ltd.) on the basis of the control group in the morning around 8:00 with 5 mg/time/d; After 8 weeks treatment, the levels of serum homocysteine, inflammatory factors and vascular endothelial injury were detected.

2.4. Detection indexes

Serum homocysteine (Hcy), inflammatory factors and vascular endothelial injury related indexes of the patients were detected before and after treatment. Serum homocysteine (Hcy), folic acid and vitamin B12 levels were detected by electrochemical luminescence method; Inflammatory related factors including tumor necrosis factor alpha (TNF-alpha), C-reactive protein (CRP) and matrix metalloproteinase-9 (MMP-9), they were detected by ELISA. Vascular endothelial injury related indexes including vascular endothelium (ET-1) and nitric oxide (NO), NO was measured by double antibody sandwich ELISA and ET-1 was detected by Solid phase sandwich ELISA. The specific testing method was in strict accordance with the relevant operation instructions.

2.5. Curative effect standards

Efficacy evaluation criteria referred to the "new drug clinical research standards" that established in 1993, the judgment of the effect of reducing blood pressure is markedly effective, effective and invalid if diastolic blood pressure fall 10 mmHg above, reach the normal range, or fall 20 mmHg above are judged to be markedly effective; If diastolic blood pressure decreased less than 10 mmHg, but in normal range, or decreased in 10-20 mmHg, and if the patients were systolic hypertension, systolic pressure decreased greater than 30 mmHg are judged to be effective; If the blood pressure fall after treatment but did not reach the effective criteria are judged to be invalid. Have efficiency = (markedly effective + effective)/total number 100%.

2.6. Statistical treatments

All data were analyzed by SPSS19.0. The count data were tested by Chi square test and the measurement data were expressed by (mean±SD), the t test was used, P<0.05 was considered the difference to be statistically significant.

3. Results

3.1. Comparison the clinical efficacy of the two groups

After treatment, the observation group was markedly effective in 14 cases, effective in 18 cases, and the efficiency rate was 69.5%; the control group was markedly effective in 12 cases, effective in 16 cases, and the efficiency rate was 60.9%; There was no significant difference in the clinical treatment of the two groups (P>0.05).

3.2. Comparison the levels of Hcy, folic acid and vitamin B12 of two groups before and after treatment

Before treatment, there was no significant difference in the levels of Hcy, folic acid and vitamin B12 between the two groups (P>0.05); After treatment, the levels of Hcy, folic acid and vitamin B12 in the observation group were (8.95±1.32) μmol/L, (21.05±3.58) μg/L, and (463.13±67.58) pg/mL, which were significantly better than (16.03±1.67) μmol/L, (13.51±2.14) μg/L and (311.52±61.06) pg/mL of the control group, the difference was statistically significant (P<0.05); After treatment, both two groups’ indicators were significantly better than before treatment and the difference was statistically significant (P<0.05). See table 1.

3.3. Comparison the level of serum inflammatory factors of the two groups before and after treatment

Before treatment, there was no significant difference in the levels of serum inflammatory factors CPR, TNF-α and MMP-9 between the two groups (P>0.05); After treatment, the levels of CPR, TNF-α and MMP-9 in the observation group were (18.27±1.96) mg/L, (50.13±9.18) μg/L and (15.93±2.45) μg/L, which were significantly better than (27.18±2.03) mg/L, (79.05±10.16) μg/L and (31.65±5.67) μg/L of the control group, the difference was statistically significant (P<0.05); After treatment, both two groups’ indicators were significantly better than before treatment and the difference was statistically significant (P<0.05). See table 2.
Table 1.
Comparison the levels of Hcy, folic acid and vitamin B12 of the two groups before and after treatment (n=46).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>Hcy (μmol/L)</th>
<th>Folic acid (μg/L)</th>
<th>Vitamin B12 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>21.0±1.32</td>
<td>7.7±0.83</td>
<td>240.15±37.03</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>8.95±1.32</td>
<td>21.05±3.58</td>
<td>463.13±67.38</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>20.96±3.05</td>
<td>7.69±0.78</td>
<td>239.87±36.52</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>16.03±1.67</td>
<td>13.51±2.14</td>
<td>311.52±61.06</td>
</tr>
</tbody>
</table>

Ps: Compared with the control group, P<0.05; Compared with before treatment,*P<0.05.

Table 2.
Comparison the level of serum inflammatory factors of the two groups before and after treatment (n=46).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>CPR (mg/L)</th>
<th>TNF-α (μg/L)</th>
<th>MMP-9 (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>39.01±5.31</td>
<td>107.12±15.18</td>
<td>54.61±8.45</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>18.27±1.96</td>
<td>50.13±9.18</td>
<td>15.93±2.45</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>38.95±5.22</td>
<td>106.94±14.97</td>
<td>53.97±8.15</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>27.18±2.03</td>
<td>79.05±10.16</td>
<td>31.6±5.67</td>
</tr>
</tbody>
</table>

Ps: Compared with the control group, P<0.05; Compared with before treatment,*P<0.05.

3.4. Comparison of vascular endothelial injury of two groups before and after treatment

Before treatment, there was no significant difference in the levels of NO and ET-1 between the two groups (P>0.05); After treatment, the levels of NO and ET-1 in the observation group were (78.12±13.05) μmol/L and (53.36±9.61) ng/L, which were significantly better than (57.26±9.17) μmol/L and (69.73±10.34) ng/L of the control group, the difference was statistically significant (P<0.05); After treatment, both two groups’ indicators were significantly better than before treatment and the difference was statistically significant (P<0.05). See table 3.

Table 3.
Comparison of vascular endothelial injury of two groups before and after treatment (n=46).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>NO (μmol/L)</th>
<th>ET-1 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>46.13±8.61</td>
<td>97.01±17.53</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>78.12±13.05</td>
<td>53.36±9.61</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>38.95±5.22</td>
<td>96.89±17.12</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>57.26±9.17</td>
<td>69.73±10.34</td>
</tr>
</tbody>
</table>

Ps: Compared with the control group, P<0.05; Compared with before treatment,*P<0.05.

4. Discussions

The main reason that H type hypertension occurred is the methionine metabolism disorder caused by the insufficient vitamin, folic acid intake, it’s also closely related to genetic and methionine diet intake. In our country, guidelines for prevention and treatment of hypertension has pointed out that the elevated blood pressure caused stroke was 1.5 times that of westerners and high Hcy occurrence rate was very high[4,5]. The mainly clinical manifestations of H type hypertension are the increased blood pressure and Hcy[6,7].

The two often cause many indicators changes such as inflammatory factors, vascular endothelial injury, and so on. Therefore, through the detection and observation of these indicators, we can provide support and basis for diagnosis and clinical medication of the disease.

Serum homocysteine (Hcy) is an intermediate product, which is produced by the body in the process of methionine synthesis. The increase of serum Hcy level has many negative effects on the vascular system and it is an independent risk factor for the occurrence of atherosclerosis[8,9]. The related research shows that more than 75% essential hypertension patients with high Hcy level, so we need to detect and observe the index to detect and observe the severity of the disease[10,11]. High Hcy may cause some damage to vascular endothelial cells, the main damage is to trigger inflammation, activation of endoplasmic reticulum and oxidative stress reaction, the level of in vivo thrombin, adenosine two phosphate and 5-serotonin will be abnormal after vascular endothelial cell damage, thereby affecting the balance and stability of the system, leading to the enhanced vascular endothelin (ET-1) secretion, vascular smooth muscle proliferation and the significant reduction of NO secretion, making the level of ET/NO abnormal and eventually make the normal vascular wall structure to change, further affect the vascular smooth muscle, platelet and coagulation factors which lead to the increase of atherosclerosis[12,13]. Oxidation reaction can occur in Hcy metabolism, the increase of oxygen free radial will further aggravate the vascular endothelial damage, increase the degree of platelet aggregation, causing the change of inflammatory factors level. CRP and TNF-α are important factors which can reflect the level of inflammation in the body. MMP-9 belongs to the matrix metalloproteinase (MMP) family. Its main function is to degrade and reshape the dynamic balance of the extracellular matrix, and it plays an important role in the pathogenesis of cardiovascular disease[14,15]. Therefore, through the detection of Hcy, inflammatory factors, and the level of NO and ET, can response the clinical treatment effect.
Current clinical treatment of H type hypertension is mainly to lower blood pressure and Hcy level. Enalapril is a kind of ACEI drugs, it lowers blood pressure mainly by renin-angiotensin-aldoosterone system and mainly used for the primary hypertension and renal vascular hypertension treatment. Folic acid can promotes the process of homocysteine methyl oxidation and effectively reduce Hcy levels[16]. In this study, the observation group was given enalapril combined with folic acid treatment while the control group was only given enalapril. The effective rate was 69.5% and 60.9% in observation and control group. There was no significant difference between the two groups ($P>0.05$), both two groups had the same clinical therapeutic significance in lowering blood pressure; However, after treatment, two groups Hcy, folic acid, vitamin B12, CPR, TNF-α, MMP-9, NO and ET-1 were significantly better than before treatment, the difference was statistically significant ($P<0.05$), which indicated that giving a certain dose of folic acid, can not only reduce the level of serum homocysteine, but also improve the inflammatory factor and vascular endothelial injury.

In summary, enalapril can improve the patients’ blood pressure, reduce the level of Hcy, improve endothelial function, and further ease the inflammatory reaction. Enalapril combined with folic acid has better clinical efficacy and it is an ideal treatment method for H type hypertension.

References

[1] Lai CQ, Parnell LD, Troen AM. MAT1A variants are associated with hypertension, stroke, and markers of DNA damage and are modulated by plasma vitamin B-6 and folate. *Am J Clin Nutr* 2010; 91(5): 1377-1386.