Efecto de la simvastatina combinada con aspirina sobre la microangiopatía renal diabética y su influencia en el entorno interno de los pacientes

Effect of Simvastatin combined with Aspirin on Diabetic Renal Microangiopathy and Influence on Patients’ Internal Environment

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Resumen
Investigar el efecto de la simvastatina combinada con aspirina sobre la microangiopatía renal diabética y sus efectos sobre la P-selectina, TNF-α, hs-CRP, IL-1β e ICAM. Índice de lípidos en sangre observado, factores inflamatorios, enfermedad coronaria, hipertensión, infarto agudo de miocardio. Los niveles de lípidos en sangre del grupo de tratamiento combinado disminuyeron antes y después del tratamiento (P<0,05). La disminución de lípidos en sangre en el grupo de tratamiento combinado fue significativamente mayor que la del grupo de control (ambos P<0,05). Los niveles de P-selectina, TNF-α, hs-CRP, IL-1β e ICAM del grupo de tratamiento de combinación disminuyeron antes y después del tratamiento (todos P<0,05). P-selectina y TNF- después del tratamiento en el grupo de combinación. La disminución de los niveles de α, hs-CRP, IL-1β e ICAM fue significativamente mayor que la del grupo de control (P<0,05). La incidencia de enfermedad coronaria e hipertensión en el grupo de tratamiento combinado fue mucho menor que la del grupo de control ($\chi^2=4.853, 6.346, P<0.05$). El efecto de control y el grado de control de lípidos en sangre, P-selectina, TNF-α, hs-CRP, IL-1β, ICAM y las complicaciones en el grupo de tratamiento tratado con simvastatina y aspirina son mejores que los del tratamiento simple.

Palabras clave: Simvastatina; Microangiopatía renal; Diabetes; Aspirina

Abstract
To investigate the effect of simvastatin combined with aspirin on diabetic renal microangiopathy and its effects on P-selectin, TNF-α, hs-CRP, IL-1β and ICAM. Observed blood lipid index, inflammatory factors, coronary heart disease, hypertension, acute myocardial infarction. The blood lipid levels of the combined treatment group decreased before and after treatment (P<0.05). The decrease of blood lipids in the combined treatment group was significantly higher than that of the control group (both P<0.05). The combination treatment group P-selectin, TNF-α, hs-CRP, IL-1β, and ICAM levels were decreased before and after treatment (all P<0.05). P-selectin and TNF- after treatment in the combination group. The decrease of α, hs-CRP, IL-1β and ICAM levels was significantly higher than that of the control group (P<0.05). The incidence of coronary heart disease and hypertension in the combined treatment group was much less than that of the control group ($\chi^2=4.853, 6.346, P<0.05$). The control effect and control degree of blood lipid, P-selectin, TNF-α, hs-CRP, IL-1β, ICAM and complications in the treatment group treated with simvastatin and aspirin are better than those of simple treatment.

Key words: Simvastatin; Renal microangiopathy; Diabetes; Aspirin

1. Introduction

Diabetes patients often have abnormal blood sugar and blood lipid levels [1], and have certain effects on their internal organs, so they have a great negative effect on patients’ living standards and work quality. After a large number of clinical observations and animal experiments, the main pathological and physiological basis of diabetic nephropathy is caused by the abnormal glucose metabolism in the patient's body, which leads to the destruction of the intact morphology of the vascular endothelium [2,3]. It is generally believed that the extracellular matrix components in the body of diabetic renal microangiopathy are massively accumulated, resulting in the hardening of the patient's glomerulus [4]. Aspirin has a lower effect on platelet aggregation and adhesion in diabetic patients, and therefore has a certain effect on the treatment of atherosclerosis caused by
diabetes [5]. Because diabetes is accompanied by elevated lipid levels and related inflammatory factors during the formation and development [6], statin drugs with lipid-lowering drugs are selected for treatment. The statins not only have the effect of lowering lipids but also the patient's atherosclerotic plaque has a certain stabilizing effect, which has a certain preventive effect on adverse events in patients. This article studies the treatment of simvastatin combined with aspirin. The results of the study are reported below.

2. Materials and Methods

2.1 General Information

Patients who were admitted to our hospital from February 2018 to October 2019 were retrospectively divided into two groups (55 patients in each group). The male-female ratio of the control group was 30:25, the average age was (56.3±81.6) years old; the male-female ratio of the observation group was 29:26, and the average age was (55.9±80.8) years old. Inclusion criteria: (1) meet the diagnostic criteria for diabetic renal microangiopathy [7]; (2) no major critical illness occurred within 3 months before treatment; (3) the selected patients have stopped in the first two weeks of the trial Drugs that affect the outcome are used; (4) Compliance is strong and informed consent is signed. Exclusion criteria: (1) patients with diabetic renal microangiopathy who did not follow the doctor's advice; (2) infectious diseases, diseases on the blood system; (3) blood glucose could not return to normal levels. There were no significant differences in the general data of the course and condition of the selected patients with diabetic renal microangiopathy (P>0.05). This experiment was approved by the Medical Ethics Association.

2.2 Method

2.2.1 Treatment methods

The selected patients were treated with basic treatment. Firstly, the patient's bad eating habits and lifestyle were corrected, and the conventional hypoglycemic drugs were used. The specific drug was metformin hydrochloride tablets (National Medicine Standard H22021486, Jilin Jichun Pharmaceutical Co., Ltd.) combined with Xiaohe Pills (National Medicine Zhunzi Z44020045, Guangzhou Baiyunshan Zhongyi Pharmaceutical Co., Ltd.), the use of metformin hydrochloride tablets is 1 tablet / 1 time, 3 times / 1d, the use of Xiaohe pills is oral, once 5-10 pills, 2-3 a day Second, use warm water to send clothes before meals. Then, the two groups of patients were treated separately. The control group used 100 mg of aspirin per day (Jilin Henghe Pharmaceutical Co., Ltd.); the observation group of the combined treatment was based on the control group, taking 20 g of Yixin before going to bed every day. (simvastatin, Beijing Wansheng Pharmaceutical Co., Ltd.). During the period, the two groups of patients should be examined regularly, mainly to test the liver function and coagulation function of the two groups of patients.

2.2.2 Detection method

For the detection of blood biochemical indicators, the enzyme biooxidation analyzer was used for enzyme oxidation detection, and the inflammatory factors in serum were detected by EIISA method [8]. After the blood was drawn, the two groups of patients were given urine for 24 hours, and then the urine collected by each patient was mixed separately, and then the samples were immunized to try to detect UAER [9].

2.3 Observation Index

(1) Blood lipid index. Including TC, TG, LDL-C, HDL-C levels. (2) Inflammation indicators. Including UAER, P-selectin, TNF-α, hs-CRP, IL-1β, ICAM levels. (3) Comparison of adverse events, including coronary heart disease, hypertension, and acute myocardial infarction.

2.4 Statistical Processing

The data was processed by the statistical software SPSS22.0. The count data was represented by (n, %), and the line $X^2$ test; the measurement data was represented by $(\overline{X} \pm s )$, and the line test was performed. $P < 0.05$ was considered statistically significant.

3. Results

3.1 Blood Lipid Index

The blood lipid index of the combined treatment group decreased before and after treatment (all $P<0.05$), and the decrease of blood lipids in the combined treatment group was significantly higher than that of the control group (both $P<0.05$). See Table 1 for details.

Table 1. Comparison of Blood Lipids before and after Treatment in Both Groups ($\overline{x} \pm s ,\text{mmol/L}$)

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Before</th>
<th>TG</th>
<th>LDL-C</th>
<th>HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>5.43±0.52</td>
<td>2.15±0.39</td>
<td>3.74±0.92</td>
<td>0.99±0.40</td>
</tr>
</tbody>
</table>
shows that <0.001 14.122 a <0.001 3.621 <0.001 0.45 5.49)
a 13.046 a <0.001 <0.001 0.055 18.344 0.001 greater <0.001 0.833 in 3.70 3.281 119.07 5.12 and 0.001 0.125 9.94 in b of factors the 18.99 0.82 173.62 0.387 178.08 of combined 1.00 the treatment 173.62 0.387 178.08 of combined 1.00 the treatment 173.62 0.387 178.08 of combined 1.00 the treatment 173.62 0.387 178.08 of combined 1.00 the treatment 173.62 0.387 178.08 of combined

Note: \( \text{t}, \text{P} \) shows the comparison test value in the group; \( \text{t}, \text{P} \) shows the comparison test value between the groups before treatment; \( \text{t}, \text{P} \) shows the comparison test value between the groups after treatment.

3.2 Inflammatory Index

The inflammatory factors of the combination group before and after treatment decreased \((P<0.05)\). The decrease of inflammatory factor levels in the combined treatment group was significantly higher than that of the control group \((P<0.05)\). See Table 2 for details.

Table 2. Comparison of Inflammatory Factor Levels between the Two Groups \((\bar{x} \pm s)\)

<table>
<thead>
<tr>
<th>Grouping</th>
<th>UAER (µg/min)</th>
<th>P-Selectin (µg/L)</th>
<th>TNF-α (µg/L)</th>
<th>hs-CRP (mg/L)</th>
<th>IL-1β (µg/L)</th>
<th>ICAM (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>238.53±28.32</td>
<td>18.99±1.59</td>
<td>24.73±2.75</td>
<td>10.62±1.48</td>
<td>0.74±0.18</td>
<td>172.45±14.12</td>
</tr>
<tr>
<td>After treatment</td>
<td>140.05±45.75</td>
<td>12.94±1.64</td>
<td>18.20±2.01</td>
<td>5.12±0.99</td>
<td>0.45±0.12</td>
<td>119.07±9.53</td>
</tr>
<tr>
<td>After treatment</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Before treatment</td>
<td>238.61±28.29</td>
<td>19.01±1.80</td>
<td>23.81±2.80</td>
<td>10.7±1.59</td>
<td>0.68±0.21</td>
<td>173.62±14.23</td>
</tr>
<tr>
<td>After treatment</td>
<td>178.08±28.01</td>
<td>17.82±1.60</td>
<td>20.10±2.10</td>
<td>9.94±1.49</td>
<td>0.56±0.16</td>
<td>164.26±13.11</td>
</tr>
<tr>
<td>( \text{t} ) value</td>
<td>10.312</td>
<td>3.351</td>
<td>7.189</td>
<td>2.366</td>
<td>3.083</td>
<td>3.281</td>
</tr>
<tr>
<td>( \text{P} ) value</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.02</td>
<td>0.003</td>
<td>0.001</td>
</tr>
<tr>
<td>( \text{t} ) value</td>
<td>0.013</td>
<td>0.055</td>
<td>1.553</td>
<td>0.244</td>
<td>1.432</td>
<td>0.387</td>
</tr>
<tr>
<td>( \text{P} ) value</td>
<td>0.989</td>
<td>0.956</td>
<td>0.124</td>
<td>0.808</td>
<td>0.156</td>
<td>0.700</td>
</tr>
<tr>
<td>( \text{t} ) value</td>
<td>4.748</td>
<td>14.122</td>
<td>4.327</td>
<td>17.695</td>
<td>3.621</td>
<td>18.344</td>
</tr>
<tr>
<td>( \text{P} ) value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: \( \text{t}, \text{P} \) shows the comparison test value in the group; \( \text{t}, \text{P} \) shows the comparison test value between the groups before treatment; \( \text{t}, \text{P} \) shows the comparison test value between the groups after treatment.

3.3 Comparison of Adverse Events

The combined treatment group had a much greater incidence of coronary heart disease and hypertension during the treatment period than the control group. See Table 3 for details.

Table 3. Comparison of Adverse Events between the Two Groups \([n, \%]\)

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Coronary heart disease</th>
<th>Hypertension</th>
<th>Acute myocardial infarction</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group ((n=55))</td>
<td>1(1.82)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>1(1.82)</td>
</tr>
<tr>
<td>Control group ((n=55))</td>
<td>7(12.73)</td>
<td>6(10.91)</td>
<td>1(1.82)</td>
<td>14(25.45)</td>
</tr>
<tr>
<td>( \text{X}^2 ) value</td>
<td>4.853</td>
<td>6.346</td>
<td>1.009</td>
<td>13.046</td>
</tr>
<tr>
<td>( \text{P} ) value</td>
<td>0.028</td>
<td>0.012</td>
<td>0.315</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
4. Discussion

The occurrence of diabetes is the result of a combination of multiple environmental factors and internal factors [10]. With the increasing number of diabetic patients in China, the research on diabetes has become more and more intensive, leading to various clinical symptoms of diabetes patients mainly due to abnormal blood vessels in patients, with the treatment of patients for a long period of time and the use of drugs. The single type and dose will lead to an increase in the incidence of complications as the treatment time increases [11]. In the research mechanism of diabetic renal microangiopathy, most scholars tend to have inflammatory theory [12]; the most important feature of patients with diabetic renal microangiopathy is that UAER in urine is higher than normal, and there are studies on UAER and Correlation studies of inflammatory factors found that UAER and inflammatory factors have a certain positive correlation [13], that is, the UAER content in the body will increase its inflammatory factors to a certain extent. The inflammatory factors associated with diabetic renal microangiopathy are mainly serum P-selectin, TNF-α, hs-CRP, IL-1β, ICAM. P-selectin is a protein mainly located on the vascular endothelial cells in the body. In normal people, the body weight is relatively low [14]; but when the body's histamine, thrombin, and Ca2+ increase, P-selectin will increase in the plasma membrane, and P-selectin also participates in the inflammatory reaction. A representative of molecules [15]. The insulin secretion system in the body of diabetic patients is often in an abnormal state, and TNF-α has an increased expression of insulin resistance in diabetic patients. In addition, TNF-α acts on insulin receptors in diabetic patients. This causes an increase in insulin resistance in patients [16]. hs-CRP and IL-1β are cytokines that cause inflammatory stimulation of liver cell synthesis in the body [17].

In this study, the treatment of simvastatin plus aspirin and the simple use of aspirin in the control of UAER and blood lipids related indicators TC, TG, LDL-C, HDL-C were significantly better than the simple Aspirin treatment (both P < 0.05). In the present study, the observation group using the combination therapy showed a significant reduction in the expression level of inflammatory factors. The main factors affecting diabetic renal microvascular disease are complications during continuous treatment, and serious complications can directly lead to death. The overall incidence of adverse events using combination therapy in this study was 1.82%, while the overall incidence of treatment with aspirin alone was as high as 25.45%, with a significant difference (P < 0.05). Aspirin is used in diabetic patients to significantly improve the patient's hypercoagulable state. However, studies on the long-term effects of aspirin on diabetic patients have found that some patients develop resistance reactions when using aspirin, which greatly reduces aspirin. Therapeutic effect [18]; Studies have shown that simvastatin has a significant lipid-lowering effect, and also has a certain effect on the protection of kidney function, mainly because simvastatin has significant effects on anti-inflammatory and anti-oxidation, and inflammation and oxidation Directly leading to damage to kidney function [19].

5. Conclusion

In summary, the combined treatment group has better control effect and control degree on blood lipids, inflammatory factors P-selectin, TNF-α, hs-CRP, IL-1β, ICAM and complications than aspirin alone. treatment.

References


