The effect of rosuvastatin on cardiogenic cerebral infarction

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Abstract: Objective: To investigate the effect of rosuvastatin on cardiogenic cerebral infarction and its related effects on patients’ neurological function, lipid levels, inflammatory factor levels, and oxidative stress status. Methods: 300 patients with cardiogenic cerebral infarction were recruited as the study cohort and randomly divided into an observation group and a control group. Routine treatment, including urinary kallikrein injections and bayaspirin tablets were given to the patients in the control group for one month. Rosuvastatin was given once a day in addition to the treatment the control group received to the patients in the observation group, also for one month. The two groups’ treatment efficacies were compared. Also, the two groups’ NIHSS and mRS scores, lipid and inflammatory factor levels, and their oxidative stress statuses were also compared. Results: The total effective rate in the observation group was significantly higher than it was in the control group (74.0% vs 84.7%, P=0.023). The NIHSS and mRS scores in the observation group were significantly lower than they were in the control group (all P<0.001). Compared with their levels after the treatment in the control group, the cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) levels in the observation group were significantly decreased and the high-density lipoprotein cholesterol (HDL-C) was significantly increased (all P<0.001). Moreover, after the treatment, the inflammatory factors, such as the tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP) levels, and the oxidative stress status, such as the oxidatively modified low density lipoprotein (ox-LDL) levels, were significantly lower than they were in the control group, but the superoxide dimutase (SOD) levels were significantly higher. Conclusions: Rosuvastatin remarkably improves the treatment efficacy and neurological function in cardiogenic cerebral infarction patients, and is associated with the improvement of the lipid levels, the inflammatory response, and the oxidative stress status.

Keywords: Cardiogenic cerebral infarction, rosuvastatin, blood lipids, inflammation, oxidative stress

Introduction

Cerebral infarction is a common, clinical, neurological systemic disease characterized by its acute onset, its severity, and its major complications. Most patients have varying degrees of limb or language dysfunction, leading to hemiplegia and the inability to take care of themselves, seriously affecting their quality of life and bringing a heavy burden to their families [1, 2]. It is reported that cardiogenic cerebral infarction makes up the highest incidence of this disease, accounting for 60%-75% [3, 4]. Cardiogenic cerebral infarction is defined as cordis mural thrombus breaking off to the cerebral arteries and blocking the cerebrovascular system, resulting in ischemia and anoxia of the corresponding brain tissue and neurological dysfunction [5, 6]. Many studies report that oxidative stress and the inflammation response play important roles in the progression of cardiogenic cerebral infarction [7, 8]. One epidemiological survey indicated that the incidence of cardiogenic cerebral infarction is increasing yearly [9]. Therefore, targeted prevention and intervention measures should be taken to reduce mortality from cerebral infarction.

At present, there are many drugs used clinically to treat cardiogenic cerebral infarction. Antiplatelet drugs are the most common and can effectively prevent platelet aggregation and help avoid thrombosis. However, antiplatelet drugs alone often have a poor overall efficacy.
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Previous studies also described the ongoing controversy about the effect of antiplatelet drugs combined with statins on cardiogenic cerebral infarction [11]. Rosuvastatin is a member of the statin family. Studies on rosuvastatin show lipid lowering action, antioxidative stress action, an anti-inflammatory effect, and the up-regulation of endothelial nitric oxide [12]. However, studies on rosuvastatin’s effects on the recovery of neurological function in patients with cardiogenic cerebral infarction are rarely reported at home or abroad [13]. In this context, this study was performed to investigate whether rosuvastatin treatment is associated with a better curative effect for patients with cardiogenic cerebral infarction and its mechanisms. The results of this study will provide the guidance and an experimental foundation for the clinical treatment of cardiogenic cerebral infarction.

Materials and methods

Subjects

300 patients with cardiogenic cerebral infarction admitted to the first department of Neurology of Tangshan People’s Hospital from January 2017 to May 2020 were recruited as the study cohort. The cohort was randomly divided into an observation group (n=150) and a control group (n=150). During their routine treatment, the patients in the control group were administered 0.15 PNA unit of urinary kalilikrein injection (ivgtt. qd) (Guangdong TECHPOOL Bio-Pharma Co., Ltd., China. No. H2005-2064. Specification: 0.15 PNA unit/bottle) and 100 mg of Bayaspirin (po. qd) (Bayer AG, Germany, no. J20130078. Specification: 100 mg/Tablet). In addition to the treatment administered to the control group, the patients in the observation group were also administered 10 mg of rosuvastatin (po. qn) (AstraZeneca, Co. Ltd. USA. No. H20203224. Specification: 10 mg/Tablet). The treatment was continued for one month.

The inclusion criteria: Patients whose cardiogenic cerebral infarction was diagnosed for the first time according to the results of their clinical manifestations, imaging examinations, and echocardiography [14] Patients who were admitted to the hospital within 72 h after onset. Patients over 18-years old. Patients who had complete clinical data, who cooperated with the medication treatment, and who came to their follow up visits.

The exclusion criteria: patients also suffering from myocardial infarction, heart failure, malignant tumors, severe liver or kidney dysfunction, cerebral hemorrhage, and intracranial occupative lesions. Female patients who were pregnant or lactating. Patients who were allergic to the drugs used in this study. Patients who lacked clinical data or who could not cooperate with this research.

The implementation of this study was reviewed by the Ethics Committee of Tangshan People’s Hospital, and informed consent was provided by all patients participating in this study.

Observed indexes

Comparison of treatment effect between two groups: the criteria for the assessment of the treatment efficacy were as follows: Cured: all the symptoms and signs disappeared, the muscle strength is normal, and in everyday life the patients could completely live on their own. Effective: all the symptoms and signs were significantly improved, and the muscle strength showed a remarkable recovery. In daily life the patients could basically live on their own. Invalid: The conditions showed no change between before and after the treatment. There was no improvement in muscle strength. The patients were not able to live on their own in everyday life. The formula for the total effective rate was as follows: formula: Total effective rate = Number of (effective cases + cured cases)/Total number of patients × 100%.

Comparison of the neurological function between two groups: the National Institutes of Health Stroke Scale (NIHSS) [15] and the modified Rankin Scale (mRS) [16] were applied to evaluate the neurological function. The NIHSS score is based on 11 items, including gaze, consciousness level, visual field, facial paralysis, upper limb movement, lower limb movement, limb freeing movement, language, sensation, dysarthria, and neglect. The total possible score is 42 points. Higher scores indicate more serious neurological function damage. The mRS score ranges from 0 to 5 points according to the disability rating scale. 0 points indicates completely asymptomatic. 5 points indicates severe disability. The higher scores indicate poorer neurological function.
Table 1. Comparison of the general information in the two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Experimental group (n=150)</th>
<th>Control group (n=150)</th>
<th>T/χ² value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female (cases)</td>
<td>113/37</td>
<td>115/35</td>
<td>0.073</td>
<td>0.787</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.9±0.6</td>
<td>22.0±0.7</td>
<td>1.328</td>
<td>0.185</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.3±4.6</td>
<td>54.7±5.1</td>
<td>0.713</td>
<td>0.476</td>
</tr>
<tr>
<td>Time from onset to treatment (hours)</td>
<td>8.3±0.7</td>
<td>8.4±0.8</td>
<td>1.152</td>
<td>0.250</td>
</tr>
<tr>
<td>Hyperlipemia (cases)</td>
<td>67</td>
<td>73</td>
<td>0.482</td>
<td>0.488</td>
</tr>
<tr>
<td>Diabetes (cases)</td>
<td>59</td>
<td>53</td>
<td>0.513</td>
<td>0.474</td>
</tr>
<tr>
<td>Coronary heart disease (cases)</td>
<td>46</td>
<td>42</td>
<td>0.257</td>
<td>0.612</td>
</tr>
<tr>
<td>Hypertension (cases)</td>
<td>78</td>
<td>83</td>
<td>0.335</td>
<td>0.563</td>
</tr>
<tr>
<td>History of smoke</td>
<td>36</td>
<td>40</td>
<td>0.282</td>
<td>0.595</td>
</tr>
<tr>
<td>Location of cerebral infarction (cases)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nucleus basalis</td>
<td>57</td>
<td>55</td>
<td>1.156</td>
<td>0.764</td>
</tr>
<tr>
<td>Brainstem</td>
<td>18</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebellum</td>
<td>40</td>
<td>44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobes</td>
<td>35</td>
<td>38</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comparison of the lipid indexes, the inflammatory factors, and the oxidative stress statuses: 5 mL of fasting blood was drawn from the patients' median cubital veins and placed in anticoagulation tubes. Then, the serum was separated using centrifugation at 3000 r/min for 15 min and kept at -20°C. The lipid indexes, such as total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), were examined using an automatic biochemical analyzer (Model 7600, Hitachi, Japan). The tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP) levels were measured using ELISA assays according to the manufacturer’s protocols (Sigma, USA). The oxidatively modified low density lipoprotein (ox-LDL) and superoxide dimutase (SOD) concentrations were also examined using ELISA Kits (Sigma, USA) according to the manufacturer’s instructions.

Statistical analysis

All data were analyzed using SPSS statistical software version 23.0. The enumeration data were expressed as number/percentage (n/%). The comparisons between two groups were done using chi-square tests. The measurement data were expressed as the mean ± standard deviation (mean ± SD). Paired t-tests were used for the comparisons between before and after the treatment, and independent sample t-tests were used for the comparisons between two groups. P<0.05 indicated that a difference was statistically significant.

Results

Comparison of the general information

As seen in Table 1, there were no significant differences in terms of gender, BMI, age, the time from onset to treatment, underlying diseases, or the location of cerebral infarction between the two groups, so they were comparable (P>0.05).

Comparison of the treatment effects

As seen in Table 2, the total effective rate in the observation group was 84.7%, which was significantly higher than the rate in the control group (74.0%), and the difference was significant (P=0.023).

Comparison of the blood lipid levels

As seen in Table 3, before the treatment there was no significant difference in terms of the
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Comparison of the NIHSS and mRS scores

As shown in (Figure 1), there were no significant differences in the NIHSS and mRS scores before the treatment in the two groups. The NIHSS and mRS scores after the treatment in the two groups were significantly decreased compared with the scores before the treatment (all \( P<0.001 \)). The NIHSS and mRS scores after the treatment in the observation group were significantly lower than the corresponding scores in the control group (all \( P<0.001 \)).

Comparison of the inflammatory factor levels

As shown in (Figure 2), there was no significant difference in the inflammatory factor levels before the treatment in the two groups. The TNF-\( \alpha \) and CRP levels after the treatment in the two groups were significantly reduced compared with the levels before the treatment (all \( P<0.001 \)). The TNF-\( \alpha \) and CRP levels after the treatment in the observation group were significantly lower than the corresponding levels in the control group (all \( P<0.001 \)).

Comparison of the SOD and ox-LDL levels

As seen in (Figure 3), no differences were seen in the SOD or ox-LDL levels before the treatment in the two groups. Compared with their levels before the treatment in the two groups, the SOD levels after the treatment were signifi-

Table 3. Comparison of the blood lipid levels in the two groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>TC (mmol/L)</th>
<th>TG (mmol/L)</th>
<th>LDL-C (mmol/L)</th>
<th>HDL-C (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>5.6( \pm )0.8</td>
<td>1.6( \pm )0.4</td>
<td>3.5( \pm )0.7</td>
<td>0.9( \pm )0.2</td>
</tr>
<tr>
<td></td>
<td>After the treatment</td>
<td>5.3( \pm )0.5</td>
<td>1.4( \pm )0.3</td>
<td>3.3( \pm )0.5</td>
<td>1.0( \pm )0.3</td>
</tr>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>5.5( \pm )0.7</td>
<td>1.5( \pm )0.3</td>
<td>3.4( \pm )0.6</td>
<td>0.8( \pm )0.2</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>4.6( \pm )0.3***###</td>
<td>1.2( \pm )0.2###</td>
<td>2.8( \pm )0.4###</td>
<td>1.2( \pm )0.4###</td>
</tr>
</tbody>
</table>

Note: Compared with before the treatment in the same group, ***\( P<0.001 \); Compared with after the treatment in the control group, ###\( P<0.001 \).
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The NIHSS and mRS scores can reflect the recovery of neurological function. And it was reported that the NIHSS and mRS scores are commonly used in clinics [22]. This study showed that the NIHSS and mRS scores after the treatment in the observation group were significantly lower than they were in the control group, suggesting that rosuvastatin can significantly improve the neurological functions in patients with cardiogenic cerebral infarction. Other studies also revealed that statins were beneficial for patients with cerebral infarction [23]. As we can see, rosuvastatin helps to relieve the symptoms of patients with cardiogenic cerebral infarction and promotes the recovery of their neurological functions.

The blood lipid levels are a considerable factor affecting the hemorheology indexes. It was reported that an increase in the blood lipid levels can enhance the erythrocyte aggregation and blood viscosity, which could aggravate the condition [24]. Other studies showed that statins are associated with reduced LDL-C levels and a decreased risk of cerebral infarction [25]. Our results showed that the TC, TG, and LDL-C levels after the treatment in the observation group were significantly lower than they were in the control group, but the HDL-C level was significantly increased in the observation group, which suggests that rosuvastatin can reduce the TC, TG, and LDL-C levels and increase the HDL-C level. Some studies also showed that the use of statins in acute cerebral infarction correlates with good clinical outcomes [26]. This study further confirmed the clinical benefits of rosuvastatin in patients with cardiogenic cerebral infarction.

In addition, the inflammatory factors and oxidative stress play important roles in the progression of cerebral infarction. It was reported that a significant increase in the pro-inflammatory cytokine and oxidative stress levels were observed in the peripheral blood of patients with cerebral infarction [27]. Some studies showed that there was a positive correlation between the severity of cerebral infarction and the severity of the inflammatory response and the

![Figure 3. Comparison of the oxidative stress statuses in the two groups. (A) SOD level; (B) ox-LDL level. Compared with before the treatment in the same group, ***P<0.001; Compared with after the treatment in the control group, ###P<0.001. Note: SOD: Superoxide dimutase; ox-LDL: Oxidatively modified low density lipoprotein.](image-url)
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oxidative stress status [28]. An improvement of the inflammatory response and oxidative stress statuses in patients with cerebral infarction may be able to relieve the impairment induced by cerebral infarction. In this study, the results showed that the TNF-α and CRP levels and the ox-LDL levels after the treatment in the observation group were significantly lower than they were in the control group, but the SOD levels after the treatment in the observation group were significantly higher. These results indicated that rosuvastatin can remarkably inhibit the inflammatory response and the oxidative stress status and that patients with cardiogenic cerebral infarction can benefit from rosuvastatin administration. This finding is similar to the results reported by previous researchers [29, 30].

In conclusion, the oral administration of rosuvastatin can significantly improve the treatment effect in patients with cardiogenic cerebral infarction and can enhance their neurological function recovery. This may be associated with the improvement of the patients’ lipid levels, inflammatory factor levels, and oxidative stress statuses. However, there are some limitations to this study, such as it being a single center study, its small sample size, and the absence of any long-term follow-up results, and so on. In the future, a large sample size, and a multi-center randomized controlled prospective study should be performed to further confirm the long-term effect of the different doses of rosuvastatin on patients with cardiogenic cerebral infarction.

Disclosure of conflict of interest

None.

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