Application of Ticlopidine Hydrochloride Combined with Butylphthalide Capsule in the Treatment of Ischemic Stroke

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Abstract
This paper analyzes the clinical study of ticlopidine hydrochloride combined with butylphthalide capsule in the treatment of ischemic stroke. The control group was treated with butylphthalide capsule, and the observation group was treated with ticlopidine hydrochloride. The nerve function, inflammatory factors and therapeutic effect of the two groups were compared and analyzed. After treatment, the levels of inflammatory factors in the two groups were decreased, and the observation group was lower than the control group; the NIHSS score and adverse reactions in the observation group were lower than the control group (P < 0.05); the effect of the observation group was significantly better than the control group (P <0.05). Ticlopidine hydrochloride combined with butylphthalide has a significant effect in the treatment of ischemic stroke. It can effectively reduce the serum inflammatory factors, improve the nerve function, without obvious adverse reactions, safe and reliable, and is worth promoting.

Key words: Ischemic stroke; Ticlopidine hydrochloride tablets; Butylphthalide capsule

1. Introduction

As a common and frequent cerebrovascular disease in clinic, the incidence of stroke has been increasing year by year in recent years, which has become an important risk factor threatening the physical and mental health and life safety of the elderly[1]. Ischemic stroke often occurs in the elderly with atherosclerosis, hypertension, rheumatic heart disease, coronary heart disease or diabetes, and smoking, drinking and other bad habits [2]. The main symptoms are headache, dizziness, vertigo, nausea, hemiplegia, weakness of limbs, incontinence of defecation, etc., which are characterized by acute onset, rapid progress and great harm [3]. If the patients are not treated effectively in time during the acute attack period, they will easily lead to disability or death. Butylphthalide and ticlopidine hydrochloride are commonly used in the clinical treatment of stroke at present, but it is found that the single drug treatment is not good, which is not conducive to the rehabilitation of patients. Based on this, this study gave the observation group ticlopidine hydrochloride combined with butylphthalide treatment, in order to explore the actual effect of the combination of drugs, to provide reference for the follow-up study, the report is as follows.
2. Materials and methods

2.1 General information

90 patients with ischemic stroke who were treated in our hospital from December 2017 to June 2018 were randomly divided into control group and observation group, 45 in each group. In the control group, there were 25 males and 20 females; the age ranged from 60 to 75 years, with an average age of (64.33 ± 4.50) years; the course of disease ranged from 1 to 4 years, with an average age of (2.62 ± 1.45) years; combined diseases included 14 cases of hypertension, 10 cases of coronary heart disease, 12 cases of hyperlipidemia and 9 cases of diabetes. In the observation group, there were 23 males and 22 females; the age was 62-74 years, the average age was (63.29 ± 4.41) years; the course of disease ranged from 1 to 4 years, with an average age of (2.62 ± 1.45) years; combined diseases included 14 cases of hypertension, 10 cases of coronary heart disease, 12 cases of hyperlipidemia and 9 cases of diabetes. In the observation group, there were 23 males and 22 females; the age was 62-74 years, the average age was (64.33 ± 4.50) years; the course of disease was 1-5 years, the average age was (3.21 ± 1.59) years; the combined diseases were 12 cases of coronary heart disease, 15 cases of hypertension, 8 cases of diabetes mellitus and 10 cases of hyperlipidemia. There was no significant difference between the two groups (P > 0.05).

2.2 Inclusion and exclusion criteria

Inclusion criteria: ①According to the Chinese guidelines for the diagnosis and treatment of acute ischemic stroke [4], the patients were diagnosed as ischemic stroke by CT, MRI and other imaging examinations; ②The patients and their families understood the basic information and signed the informed agreement; ③The patients with cerebral hemorrhage or active bleeding tendency. Exclusion criteria: ①Serious infectious diseases and malignant tumor diseases; ②History of allergy or contraindication to the drugs used in this study; ③Serious substantial organ failure; ④Mental disorders and intellectual disorders.

2.3 Method

Both groups were treated with plaque stabilization, microcirculation improvement, basic disease control, ventilator-assisted therapy, antiplatelet aggregation, etc. The control group was treated with butylphthalide capsule, which was taken orally on an empty stomach, 0.2g/time, 3 times / day, 14 days as a course of treatment. The observation group was treated with ticlopidine hydrochloride combined with butylphthalide capsule. The usage and dosage of ticlopidine hydrochloride capsule were the same as that of the control group. Ticlopidine hydrochloride tablets (produced by Sanofi in Hangzhou, national drug standard h19980186) were orally used, 0.25g/time, once a day. Before and after the treatment, 3ml of fasting venous blood was taken from the two groups in the morning, and serum samples were made by routine centrifugation. Serum high-sensitivity C-reactive protein (hs CRP) was detected by immunoturbidimetry. Tumor necrosis factor (TNF - α) and interleukin-6 (IL-6) were detected by enzyme-linked immunosorbent assay.

2.4 Observation indicators

①Before and after treatment, the levels of hs CRP, TNF - α, IL-6 and other inflammatory factors were compared between the two groups.

②Using NIHSS to evaluate the neurological deficit before and after treatment, including consciousness level, visual field, upper and lower limb activity, facial paralysis and sensation, a total of 12 items. The total score was 45 points, < 15 points were slight defect, 16-30 points were moderate defect, and > 31 points were severe defect.

③Evaluate the treatment effect of the two groups, and divide them into two groups: the clinical symptoms disappear completely, and the neurological deficit score is reduced by more than 90% compared with that before treatment; significant effect: the clinical symptoms are effectively controlled, and the neurological deficit score is reduced by more than 50% compared with that before treatment; ineffective: the clinical symptoms are not improved or aggravated compared with that before treatment, and the patients are disabled or dead. Total effective = cure + effective.

④Adverse drug reactions were recorded, including nausea, vomiting and liver dysfunction.

3. Results

3.1 Comparison of changes of inflammatory factors before and after treatment

Before treatment, the serum inflammatory factors of the two groups were detected, and there was no significant difference (P > 0.05); after treatment, each index was significantly lower than before treatment, and the observation group was lower than the control group (P < 0.05), see Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>hs-CRP (mg/L) Before</th>
<th>hs-CRP (mg/L) After</th>
<th>TNF-α (μg/L) Before</th>
<th>TNF-α (μg/L) After</th>
<th>IL-6 (μg/L) Before</th>
<th>IL-6 (μg/L) After</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Comparison of inflammatory factors between the two groups before and after treatment ( x ± s)
3.2 Comparison of NIHSS before and after treatment

Before treatment, there was no significant difference in NIHSS score between the two groups (P > 0.05); after treatment, the two groups were significantly lower than before treatment (P < 0.05), and the observation group was significantly lower than the control group (P < 0.05), as shown in Table 2.

Table 2. Comparison of NIHSS before and after treatment between the two groups ( x ± s, min)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>45</td>
<td>28.88±3.13</td>
<td>14.66±2.11</td>
<td>25.270</td>
<td>0.000</td>
</tr>
<tr>
<td>Observation group</td>
<td>45</td>
<td>28.01±3.16</td>
<td>8.22±2.04</td>
<td>35.295</td>
<td>0.000</td>
</tr>
<tr>
<td>t</td>
<td>-</td>
<td>1.312</td>
<td>14.719</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>P</td>
<td>-</td>
<td>0.192</td>
<td>0.000</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

3.3 Treatment effect comparison

The therapeutic effect of the observation group was significantly better than that of the control group (P < 0.05), as shown in Table 3.

Table 3. Comparison of therapeutic effect between the two groups [n (%)]

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Cure</th>
<th>Effective</th>
<th>Invalid</th>
<th>Total effective rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>45</td>
<td>25 (55.56)</td>
<td>12 (26.67)</td>
<td>8 (17.78)</td>
<td>37 (82.22)</td>
</tr>
<tr>
<td>Observation group</td>
<td>45</td>
<td>30 (66.67)</td>
<td>12 (26.67)</td>
<td>3 (6.67)</td>
<td>42 (93.33)</td>
</tr>
<tr>
<td>X²</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5.751</td>
</tr>
<tr>
<td>P</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.016</td>
</tr>
</tbody>
</table>

3.4 Comparison of adverse reactions

The adverse reactions in the observation group were lower than those in the control group (P < 0.05), as shown in Table 4.

Table 4. Comparison of adverse reactions between the two groups [n (%)]

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Nausea</th>
<th>Vomit</th>
<th>Abnormal liver function</th>
<th>Rash</th>
<th>Total incidence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>45</td>
<td>3 (6.67)</td>
<td>2 (4.44)</td>
<td>2 (4.44)</td>
<td>9 (20.00)</td>
<td></td>
</tr>
<tr>
<td>Observation group</td>
<td>45</td>
<td>1 (2.22)</td>
<td>0 (0)</td>
<td>1 (2.22)</td>
<td>3 (6.67)</td>
<td></td>
</tr>
<tr>
<td>X²</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9.568</td>
</tr>
<tr>
<td>P</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.000</td>
</tr>
</tbody>
</table>

4. Discussion

Clinically, there are two types of stroke, one is hemorrhagic stroke, commonly known as cerebral hemorrhage or cerebral hemorrhage, accounting for 40% of the total number of stroke. Hypertension, intracranial aneurysm or vascular malformation rupture are the main causes of hemorrhagic stroke [4]. The other is ischemic stroke, commonly known as stroke, including cerebral thrombosis and cerebral embolism. Ischemic stroke is due to the hardening and stenosis of cerebral artery itself, which gradually develops into occlusion [5]. It can also flow to the blood vessels in the brain after the thrombus in the heart part falls off, thus causing the interruption and blocking of the cerebral blood supply in this area, and the brain tissue is anoxic or necrotic. 60% of the patients are of this type of stroke. At the same time, the elderly with low immunity are more likely to have disease, and with the growth of age, the disease is often more critical, seriously affecting the quality of life of patients [6]. At present, the commonly used nerve block and antiplatelet therapy can alleviate symptoms to some extent, but the overall effect is not good, so a more safe and effective treatment is urgently needed.

Butylphthalide is one of the most frequently used drugs in the clinical treatment of stroke, which can reduce the production of mitochondrial reactive oxygen species in vascular endothelial cells, reduce the cell
damage caused by hypoxia, and maintain the normal cell function [7-8]. By relieving vasospasm, anti free radicals and improving energy metabolism, the patients' neurons can be protected and repaired. In addition, it can transform kininogen into different forms of vasodilator, thus playing the role of expanding microvasculature.

When applied to the treatment of patients with ischemic stroke, it can rapidly improve the blood supply, oxygen supply and circulation status in the ischemic area, and increase the blood flow of brain tissue in the ischemic focus area [9-10]. However, clinical investigation found that the treatment of stroke with butylphthalide alone has some limitations, which may be related to its weak inhibition of inflammatory factors. Based on this, the therapeutic effect of ticlopidine hydrochloride combined with butylphthalide in the observation group was significantly better than that in the control group (P < 0.05). Ticlopidine hydrochloride, as an antagonist, can inhibit platelet aggregation through adenosine diphosphate and inhibit the formation of lipid plaques after entering the blood. Combined use of the two drugs and complementary pharmacological mechanism can promote blood circulation, reduce nerve cell damage and improve its coagulation function, which is the main reason why NIHSS score in the observation group is lower than that in the control group (P < 0.05). In recent years, the detection of inflammatory reaction index is a common method for clinical diagnosis. Once the body has inflammatory reaction, the sensitive indexes such as hs CRP, TNF-α, IL-6 in serum will change significantly, especially when ischemia causes cerebral circulation disorder, local nerve cells die in large area, a large number of free radicals accumulate, and the metabolism rate of arachidonic acid in blood vessels and brain tissues is obviously accelerated, which results in blood The content of hs CRP in the serum increased significantly, and neuron cells died [12]. As a kind of monocyte factor, TNF-α is mainly produced by monocyte and macrophage. It can promote T cell to produce various inflammatory factors. The increase of TNF-α level in patients with ischemic stroke is mainly through promoting the release of carbon monoxide, vasoconstriction and coagulation state of the body to cause damage to brain tissue and aggravate the inflammatory response in the ischemic area [13]. This study showed that the level of inflammatory factors in the two groups before treatment was generally high, and decreased in varying degrees after treatment, and the improvement in the observation group was more significant. It was proved that the effect of ticlopidine hydrochloride combined with butylphthalide on inhibiting the level of inflammatory factors was significantly better than that of butylphthalide alone. The combination of drugs can inhibit the activities of xanthine oxidase and hypoxanthine oxidase, and increase the contents and activities of endothelial nitric oxide and antioxidant enzymes. In addition, it has a positive effect on improving the synthesis speed of prostacyclin. It can eliminate free radicals and protect neurons by reducing the synthesis of leukotriene, the inflammatory mediator. This study found that the combination of the two drugs did not increase the incidence of adverse reactions, and the safety of drug use was guaranteed.

Chen Si, Yin Wenwei, et al. [14] in the clinical study of ticlopidine hydrochloride combined with butylphthalide capsule in the treatment of ischemic stroke, pointed out that ticlopidine hydrochloride combined with butylphthalide has a significant effect on the treatment of ischemic stroke, which can effectively improve the activity of superoxide dismutase, reduce the level of serum neuron specific enolase and nitric oxide, so as to play a role in protecting neurons, and The conclusion of this study is basically the same. Xie Jiangbo, Zhang Tingting, et al. [15] divided the patients with acute ischemic cerebral infarction into two groups. The control group was treated with routine antiplatelet aggregation and lipid-lowering therapy. On the basis of routine treatment, the two groups were treated with butylphthalide and ateplase[16]. The results showed that the NIHSS scores of the two groups were significantly lower than that of the observation group before treatment, and the NIHSS scores of the observation group were significantly lower than that of the control group. The Barthel Index and the total effective rate of treatment in the control group were higher than those in the control group. Conclusion: the therapeutic effect of butylphthalide combined with ateplase on acute ischemic cerebral infarction is significant, which is of great significance to protect its neurological function. The test results of the above scholars are basically the same as the conclusions of this study, which can prove the accuracy of this study.

5. Conclusion

In conclusion, ticlopidine hydrochloride combined with butylphthalide has a significant effect in the treatment of ischemic stroke, can significantly reduce the serum inflammatory factors, improve the nerve function, no significant adverse reactions, and high safety, it is worth promoting.

References


