Effect Evaluation of Madopar Combined with Pramipexole in the Treatment of Parkinson’s Patients

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Abstract: Objective: To analyze the clinical efficacy of Madopar combined with pramipexole in the treatment of Parkinson’s disease. Methods: This study was conducted from January 2021 to January 2023. This study involved 80 patients who were divided into two groups using a computerized randomization. The control group received pramipexole and the experimental group received both madopar and pramipexole. The treatment outcomes of these two groups were compared and analyzed. Results: The efficacy of the treatment received in the experimental group was 95.00%, which was higher than that of the control group (77.50%), whereas the total adverse reaction rate of the experimental group was 12.50%, which was lower than that of the control group, 35.00%; the difference was significant (P < 0.05). There was no difference in the levels of tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), C-reactive protein (CRP), miR-124, miR-137, and Unified Parkinson’s Disease Rating Scale (UPDRS) total score (UPDRS II, UPDRS III, and UPDRS IV scores) between the control group and the experimental group (P > 0.05). After treatment, these indicators were significantly improved in the experimental group compared to the control group. Conclusion: Madopar combined with pramipexole in the treatment of Parkinson’s is both effective and safe. It delays the progression of the disease and has broad application prospects. Keywords: Madopar; Pramipexole; Parkinson’s disease

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1. Introduction

Parkinson’s disease is manifested by resting tremor, muscle rigidity, etc., accompanied by mood disorders, sleep disorders, etc., and causes great harm to patients [1]. Parkinson’s disease is a chronic disease with a high disability rate. The occurrence of the disease is closely related to the degeneration of substantia nigra and the appearance of Lewy bodies. Pramipexole is a commonly used drug for the treatment of Parkinson’s disease, which can stimulate dopamine receptors [2]. This study mainly analyzes the clinical efficacy of Madopar combined with pramipexole in the treatment of Parkinson’s disease.
2. Clinical data and methods

2.1. Clinical data

This study was conducted from January 2021 to January 2023. This study involved 80 patients who were divided into two groups using a computerized randomization. Inclusion criteria: (i) Patients who meet the diagnostic criteria for Parkinson’s disease based on the International Movement Disorder Society (MDS)\(^3\), (ii) patients who signed and informed consent along with their families, (iii) patients with good compliance. Exclusion criteria: (i) patients with contraindications to the drugs used in the study, (ii) patients with heart, liver, or kidney diseases, (iii) patients with systemic infectious diseases, (iv) patients with motor and cognitive impairments caused by other reasons. There were 21 male and 19 female patients respectively, aged between 48 and 80 years old, with an average of 64.00 ± 4.87 years, and the course of disease was between 0.5 and 1 year, with an average of 0.75 ± 0.07 years. In the experimental group, there were 23 male and 17 female patients, aged between 50 and 85 years old, with an average of 67.50 ± 4.91 years, and the course of disease was between 0.5 and 1.5 years, with an average of 0.00 ± 0.10 years. The above information was entered into statistical software for comparison, and the results showed no significant difference \((P > 0.05)\).

2.2. Methods

Patients in the control group were given pramipexole: 250 mg orally each time, 3 times a day. The duration of treatment was two months.

Patients in the combined group were given Madopar on the basis of the single group: the initial dose of Madopar was 0.0625 mg, taken 3 times a day, and the dosage was gradually increased, with the highest daily dose being > 250 mg. The duration of treatment was two months.

2.3. Evaluation of efficacy and evaluation index

The evaluation of efficacy\(^4\) was performed based on established criteria from the Movement Disorder Society (MDS). (1) Significantly effective: substantial improvement in motor function and muscle tension, enabling the patient to effectively perform general work and activities. (2) Effective: improvement in motor function and muscle tension, although the patient remains unable to perform general work and activities effectively. (3) Ineffective: suggesting only slight improvement in motor function and muscle tension or even worsening of these parameters.

Evaluation indicators: (1) Detection of inflammatory cytokines by enzyme-linked immunosorbent assay, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), C-reactive protein (CRP). In addition, venous blood was drawn in a fasting state, and microribonucleic acid-124 (miR-124) and microribonucleic acid-137 (miR-137) were detected by PT-PCR technology. (2) The incidence of adverse reactions was compared between the two groups. (3) The Unified Parkinson’s Disease Rating Scale (UPDRS)\(^5\) was used to evaluate the symptoms of the disease. The scale comprised a total of 42 items, encompassing assessments of activities of daily living (UPDRS II), exercise capacity (UPDRS III), and complications (UPDRS IV), with 4, 27, and 11 items, respectively. For items 40–42, scores ranged from 0 to 1 point, while the remaining items were scored on a scale of 0 to 4 points. Higher scores on the scale corresponded to a more severe symptom status.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 22.0. Independent sample t-tests were employed for analyzing measurement data, presented as mean ± standard deviation, while count data were assessed using the \(\chi^2\) test and
expressed as percentages (%). A significance level of $P < 0.05$ was used to denote statistical significance.

### 3. Results

#### 3.1. Comparison of the total effective rate of treatment in different groups of patients

Compared with the total efficacy of 77.50% in the control group, the efficacy of the experimental group was 95.00%, which was significant higher ($P < 0.05$), as shown in Table 1.

**Table 1.** Comparison of the total effective rate of treatment in different groups of patients ($n$[%])

<table>
<thead>
<tr>
<th>Group</th>
<th>Very effective</th>
<th>Effective</th>
<th>Ineffective</th>
<th>Total effective rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>11 (25.50)</td>
<td>20 (50.00)</td>
<td>9 (22.50)</td>
<td>31 (77.50)</td>
</tr>
<tr>
<td>Experimental group</td>
<td>24 (60.00)</td>
<td>12 (35.00)</td>
<td>2 (5.00)</td>
<td>38 (95.00)</td>
</tr>
</tbody>
</table>

$\chi^2$ 5.164  
$P < 0.05$

#### 3.2. Levels of cytokines, miR-124 and miR-137

There was no difference in the levels of TNF-α, IL-6, CRP, miR-124, and miR-137 between the control group and the combination group ($P > 0.05$). After treatment, the levels of TNF-α, IL-6, CRP, miR-124, and miR-137 were significantly lower than those of the control group ($P < 0.05$), as shown in Table 2.

**Table 2.** Comparison of cytokines, miR-124 and miR-137 levels in different groups of patients (mean ± standard deviation)

<table>
<thead>
<tr>
<th>Group</th>
<th>TNF-α (ug/L) Before treatment</th>
<th>After treatment</th>
<th>IL-6 (pg/L) Before treatment</th>
<th>After treatment</th>
<th>CRP (umol/L) Before treatment</th>
<th>After treatment</th>
<th>miR-124 Before treatment</th>
<th>After treatment</th>
<th>miR-137 Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>3.72 ± 0.93</td>
<td>3.04 ± 0.88</td>
<td>7.63 ± 1.71</td>
<td>6.75 ± 1.37</td>
<td>1.35 ± 0.54</td>
<td>1.16 ± 0.47</td>
<td>0.64 ± 0.11</td>
<td>0.70 ± 0.14</td>
<td>2.81 ± 0.77</td>
<td>1.89 ± 0.60</td>
</tr>
<tr>
<td>Experimental group</td>
<td>3.73 ± 0.95</td>
<td>2.20 ± 0.61</td>
<td>7.60 ± 1.68</td>
<td>4.51 ± 1.06</td>
<td>1.34 ± 0.52</td>
<td>0.83 ± 0.22</td>
<td>0.63 ± 0.10</td>
<td>0.88 ± 0.23</td>
<td>2.80 ± 0.76</td>
<td>1.34 ± 0.55</td>
</tr>
</tbody>
</table>

$t$ 0.048  
$P > 0.05$

$\chi^2$ 5.164  
$P < 0.05$

#### 3.3. Rate of adverse reactions

The experimental group had a significantly lower adverse reaction rate of 12.50% compared to the control group (35.00%), with $P < 0.05$, as shown in Table 3.

**Table 3.** Comparison of adverse reactions in different groups of patients ($n$ [%])

<table>
<thead>
<tr>
<th>Group</th>
<th>Constipation</th>
<th>Insomnia</th>
<th>Orthostatic hypotension</th>
<th>Headache</th>
<th>Drowsiness</th>
<th>Vomit</th>
<th>Total adverse reaction rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>4 (10.00)</td>
<td>2 (5.00)</td>
<td>1 (2.50)</td>
<td>2 (5.00)</td>
<td>2 (5.00)</td>
<td>3 (7.50)</td>
<td>14 (35.00)</td>
</tr>
<tr>
<td>Experimental group</td>
<td>2 (5.00)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>1 (2.50)</td>
<td>1 (2.50)</td>
<td>1 (2.50)</td>
<td>5 (12.50)</td>
</tr>
</tbody>
</table>

$\chi^2$ 5.591  
$P < 0.05$

#### 3.4. Clinical symptoms

Before treatment, there were no significant differences in the UPDRS total score, UPDRS II, UPDRS III, UPDRS IV scores between the control group and experimental ($P > 0.05$). However, after treatment, the scores of the
experimental group were significantly higher than the control group \((P < 0.05)\), as shown in Table 4.

Table 4. Comparison of clinical symptom status scores of patients in different groups \((\bar{x} \pm s, \text{false, points})\)

<table>
<thead>
<tr>
<th>Group</th>
<th>UPDRS total score</th>
<th>UPDRS II</th>
<th>UPDRS III</th>
<th>UPDRS IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>Control group</td>
<td>62.71 ± 5.67</td>
<td>40.46 ± 4.26</td>
<td>8.47 ± 1.00</td>
<td>5.49 ± 0.88</td>
</tr>
<tr>
<td>Experimental group</td>
<td>62.74 ± 5.69</td>
<td>28.51 ± 2.98</td>
<td>8.50 ± 1.03</td>
<td>3.63 ± 0.54</td>
</tr>
<tr>
<td>(t)</td>
<td>0.024</td>
<td>14.538</td>
<td>0.132</td>
<td>11.394</td>
</tr>
<tr>
<td>(P)</td>
<td>&gt; 0.05</td>
<td>&lt; 0.05</td>
<td>&gt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

4. Discussion

There has been an increasing trend in the incidence of Parkinson’s disease in China. Although China’s medical technology has greatly improved, Parkinson’s still cannot be completely cured. Therefore, the goal of treatment of this disease is mainly to relieve the symptoms and to reduce the impact of poor mobility and pain \([8]\). Studies have shown that inflammatory response can increase the incidence of Parkinson’s Disease. This increased risk is associated not only with inflammatory responses within the central nervous system but also with inflammation occurring in peripheral organs and vascular endothelium, all of which can contribute to the onset and progression of Parkinson’s disease \([9]\).

Madopar is the drug of choice for the treatment of Parkinson’s disease. It is a complex of benserazide and levodopa. Levodopamine is the prerequisite for dopamine, and it will generate dopamine after the action of related enzymes \([10]\). Benserazide is a peripheral dopa dehydrogenase inhibitor, which can inhibit the deacidification reaction of levodopa outside the brain, thereby increasing the concentration of dopamine in the brain. However, with the development of the disease, the required dosage of Madopar will also increase, thereby increasing the risk of adverse reactions \([11,12]\). Pramipexole is a dopamine receptor agonist that has high receptor selectivity. Activation of dopamine receptors enhances the neuroprotective actions of dopamine neurons, suppresses the production and release of reactive oxygen species, and effectively mitigates the degeneration and necrosis of dopamine neurons. This mechanism can slow down the progression of Parkinson’s disease and enhance treatment outcomes. The combination of Madopar and pramipexole has an increase efficacy. It can not only relieve the disease as soon as possible, but also improve cognitive ability and mental state. Although two drugs are being used, the rate of adverse reactions will not increase, suggesting good drug safety \([13]\). This is because pramipexole can reduce the release of dopamine and protect the structure of neurons. When used together with Madopar, it can increase the concentration of dopamine in the brain, which is beneficial to the restoration of extrapyramidal system function. In addition, pramipexole is a non-ergot dopamine agonist, which can activate striatal dopaminergic D2 receptors, and improve the symptoms of Parkinson’s Disease.

miR-124 can protect dopaminergic neurons, and miR-137 can target dopamine receptors, and play an important role in the process of dopaminergic neuron proliferation and decline \([14]\). After the combined application of Madopar and Pramipexole, the miR-124 level and miR-137 in Parkinson’s patients were significantly improved. Pramipexole has D2 receptor selectivity, and its pharmacological effects are relatively special. It has a high affinity for the D3 receptor subtype in the D2 receptor family and can protect dopaminergic neurons and improve levels of miR-124 and miR-137. In Parkinson’s disease, inflammatory factors play an important role throughout the pathogenesis, such as IL-6, TNF-α, etc. As the disease progresses, the levels of
inflammatory factors also increase continuously, promoting the regeneration of dopamine neurons. This study found that the levels of inflammatory factors in patients with Parkinson’s disease significantly decreased after the combined drug treatment. It was found that the combined drug can effectively relieve the inflammatory response, resist oxidative stress, and protect the brain nerve function. In addition, the clinical symptom status scores of Parkinson’s patients were also significantly improved after the combined treatment. The loss of dopaminergic nerves in patients with Parkinson’s disease will damage the dorsal nucleus of the vagus nerve and other parts, thereby causing non-motor symptoms. Pramipexole can be quickly absorbed after entering the body, has a high bioavailability, and is metabolized by the kidneys. Pramipexole can directly activate postsynaptic dopamine receptors in the absence of dopamine, thereby achieving the effect of improving clinical symptoms. Most importantly, pramipexole has a long half-life and can continuously stimulate dopamine receptors. The combination of drugs is not only more effective, but it also reduces the occurrence of adverse reactions. This is because after pramipexole enters the body, very little of it is absorbed in the stomach, and most of it is absorbed in the small intestine. Therefore, the consumption of the drug will not have any effect on the food in the stomach. After the body absorbs it, it can be dispersed throughout the body, especially in the lacrimal glands, kidneys, and salivary glands. Pramipexole can protect nerves, stimulate dopamine receptors, affect the number of neuronal discharges, prevent cell apoptosis, and protect cranial nerves. Therefore, this combination of medications is highly safe.

**5. Conclusion**

In conclusion, Madopar combined with pramipexole in the treatment of Parkinson’s is highly effective and safe, and it delays the progression of the disease and has broad application prospects.

**Disclosure statement**

The authors declare no conflict of interest.

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