CLINICAL EFFICACY OF PAROXETINE COMBINED WITH PRAMIPEXOLE AND MADOPAR IN TREATING PARKINSON'S PATIENTS COMPLICATED WITH DEPRESSIVE DISORDER AND ITS INFLUENCE ON THEIR PROGNOSTIC QUALITY OF LIFE

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ABSTRACT

Objective: *This study was designed to explore the clinical efficacy of paroxetine combined with pramipexole and madopar in the treatment of Parkinson's patients complicated with depressive disorder and its influence on their prognostic quality of life.*

Methods: *A total of 103 Parkinson's patients complicated with depressive disorder who came to our hospital from March 2015 to July 2018 were selected. Among them, 57 patients treated with paroxetine combined with pramipexole were group A, and 56 patients treated with paroxetine combined with madopar were group B. After 12 weeks of treatment, the efficacy, living ability, dyskinesia, depressive state, treatment compliance, adverse reactions and quality of life of patients in the two groups were recorded, evaluated and compared.*

Results: *The total effective rate of group A was significantly higher than that of group B (P<0.05). After treatment, the UPDRS II score, UPDRS III score, HAMD score and MADRS score of group A were significantly lower than those before treatment, but the UPDRS II score, UPDRS III score, HAMD score and MADRS score of group A were significantly lower than those of group B (P<0.05). The treatment compliance rate of group A was significantly higher than that of group B (P<0.05), there was no significant difference in the incidence rate of adverse reactions between the two groups (P>0.05), and the life quality score of patients in group A was significantly higher than those in group B (P<0.05).*

Conclusion: *Paroxetine combined with pramipexole has better efficacy on Parkinson's disease complicated with depressive disorder than that combined with madopar, hence, it can effectively improve the depressive state and Parkinson's symptoms of patients and also has good safety, which is worthy of clinical promotion.*

Keywords: *Paroxetine, pramipexole, madopar, parkinson's disease complicated with depressive disorder, clinical efficacy, quality of life.*

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Introduction

Parkinson's disease is a common chronic degenerative central nervous system disease, mostly occurring in the elderly, with motor symptoms such as muscle tremor and bradykinesia as the main manifestations[1, 2]. Parkinson's disease develops progressively, many patients will gradually develop different degrees of disability after 3 to 8 years of onset, which has caused great pressure on the family and society[3]. Depression is also a common chronic neuropsychiatric disorder, and in recent years, there have been more and more reports of Parkinson's disease accompanied by depressive disorder. Patients with severe depressive disorder may further aggravate their motor symptoms[4]. The main cause of Parkinson's disease is the disorder of dopamine transmitter production, so the treatment for Parkinson's disease is mainly dopamine replacement therapy at present. However, due to the existence of adverse reactions and drug resistance, some Parkinson's patients complicated with depressive disorder still cannot get effective treatment[5, 6]. For Parkinson's patients complicated with depressive disorder, treatment of Parkinson's disease alone is not enough, but also treatment of depressive disorder of patients

is needed[7]. Paroxetine is a new antidepressant with good efficacy and less side effects, which is widely used as antidepressant drugs in clinical practice[8].

Pramipexole is a dopamine receptor agonist, and madopar consists of levodopa and benserazide, both of which are currently commonly used drugs in clinical treatment of Parkinson's disease[9]. In the past, many studies[10] compared the efficacy of combined use in Parkinson's disease, and achieved good results. Both dopamine receptor agonists and levodopa have poor efficacy on Parkinson's patients complicated with depressive disorder, and antidepressant drugs are often required to be used together. However, no study has been conducted to compare the efficacy of pramipexole and madopar combined with antidepressant drugs respectively in Parkinson's patients complicated with depressive disorder.Therefore, we compared the clinical efficacy of paroxetine combined with pramipexole and madopar respectively in the treatment of Parkinson's patients complicated with depressive disorder and its impact on the quality of life of patients, in order to provide a more appropriate scheme for the treatment of Parkinson's patients complicated with depressive disorder.

Materials and methods

General data

From March 2015 to July 2018, 103 patients with Parkinson's disease complicated with depressive disorder were selected, including 59 male patients and 54 female patients.

The average age of all patients was (63.26±5.19) years. Among them, 57 patients treated with paroxetine combined with pramipexole were group A, and 56 patients treated with paroxetine combined with madopar were group B.

Inclusion and exclusion criteria

Inclusion criteria were as follows:

• Patients meeting Parkinson's diagnosis and classification criteria[11], and patients with HAMD-17 score >17.

Exclusion criteria were as follows:

• Patients with severe dementia and history of essential tremor, Hoehn-Yahr grade 5, severe liver and kidney dysfunction, as well as serious cardiovascular and cerebrovascular diseases;

• Patients with a history of central nervous system diseases such as cerebral infarction and cerebral hemorrhage, patients with communication and cognitive dysfunction, and patients who did not cooperate with the experiment. All patients and their families agreed to participate in the experiment and sign an informed consent.

Therapeutic regimens

Patients in group A were treated with paroxetine combined with pramipexole.

The specific therapeutic regimens were as follows

The initial dose of pramipexole was 0.125mg/time, 3 times/d, the dose was adjusted to 0.25mg/time, 3 times/d once a week, and the dose was adjusted to 0.5mg/time, 3 times/d once a week. On this basis, paroxetine, 20mg/time, 1 time/d, was added for 12 weeks. Patients in group B were treated with paroxetine combined with madopar.

The specific therapeutic regimens were as follows

The initial dose of madopar was 125mg/time, 3 times/d. After one week of administration, the dose was adjusted according to the patients' symptom stability. When the dose was increased to 250mg/time, it was taken as the maximum maintenance dose. On this basis, paroxetine, 20mg/time, 1 time/d, was added for 12 weeks.

Observation indicators

• The efficacy of patients in the two groups was evaluated and compared, Webster Symptom Score Scale[12] was used to evaluate the efficacy. The efficacy was divided into marked effect (the UPDRS score of patients after treatment decreased by more than 70%, and the depressive symptoms significantly improved compared with those before), effect (the UPDRS score of patients after treatment decreased by 30%-70%, and the depressive state was improved), ineffectiveness (the UPDRS score of patients after treatment decreased by less than 30%, or more severe depressive symptoms appeared), and the total effective rate of treatment = (number of marked effect+effective number)/total number *100%.

• The Unified Parkinson's Disease Rating Scale (UPDRS)[13] was used to compare the living ability (UPDRS II) and dyskinesia (UPDRS III) of patients in the two groups.

• Hamilton Depression Scale (HAMD)(14) and Montgomery-Asberg Depression Rating Scale (MADRS)[15] were used to evaluate and compare the depressive state of patients in the two groups before and after 6 months of treatment.

• The treatment compliance of patients in the two groups were evaluated and compared, divided

into complete compliance, partial compliance and non-compliance. The treatment compliance rate = (number of complete compliance+number of partial compliance)/total number *100%.

• The adverse reactions of patients in the two groups during treatment were recorded and compared, and the adverse reactions included nausea, anorexia, drowsiness, constipation and dizziness.

• Quality of Life Scale (QOLIE-31)[16] was used to evaluate and compare patients' quality of life after treatment, including emotion, cognition, social relations, energy, health status and overall quality of life, with a total score of 100 points. The higher the score was, the higher the quality of life was.

Statistical methods

SPSS18.0 software (Bizinsight (Beijing) Information Technology Co., Ltd.) was used for statistical analysis of the experimental data in this study, Chi-square test was used for the counting data, and mean±standard deviation was used for the measurement data. T test was used for comparison between the two groups, GraphPad Prism 6 software was used for drawing the experimental pictures, and P<0.05 was considered to be statistical difference.

Results

Comparison of general data

There was no significant difference in gender, age, BMI and Hoehn-Yahr grading between the two groups (P>0.05), which was comparable.

Factor	Group A n=57	Group B n=56	t/χ^2	*P*
Gender			0.082	0.774
Male	29 (50.88)	30 (53.57)		
Female	28 (49.12)	26 (46.43)		
Age (years)			0.007	0.933
≤63	25 (43.86)	25 (44.64)		
>63	32 (56.14)	31 (55.36)		
BMI (kg/m^2)			0.077	0.782
≤ 22	26 (45.61)	27 (48.21)		
>22	31 (54.39)	29 (51.79)		
Hoehn-Yahr grading			0.006	0.940
Grades 1-2	35 (61.40)	34 (60.71)		
Grades 3-4	22 (38.60)	22 (39.29)		
Educational level			0.216	0.642
Below junior high school	25 (43.86)	27 (48.21)		
Junior high school and above	32 (56.14)	29 (51.79)		
Place of residence			0.012	0.911
Countryside	33 (57.89)	33 (58.93)		
City	24 (42.11)	23 (41.07)		
Creatinine (μmol/L)	69.21±5.83	70.11±5.73	0.110	0.913
Urea nitrogen (mmol/L)	6.06±1.12	6.09±1.13	0.019	0.985

Table 1: General data table n (%).

Comparison of efficacy of patients between the two groups

The number of patients in group A with markedly, effective and ineffective treatment was 28, 23 and 6 respectively, with a total effective rate of 89.47%; the number of patients in group B with markedly, effective and ineffective treatment was 21, 20 and 15 respectively, with a total effective rate of 73.21%; the total effective rate of patients in group A was significantly higher than that of patients in group B (P<0.05), as shown in Table 2.

Efficacy	Group A n=57	Group B n=56	X^2	P
Marked effect	31 (54.39)	21 (37.50)	3.242	0.072
Effect	20 (35.09)	20 (35.71)	0.005	0.945
Ineffectiveness	6 (10.53)	15 (26.79)	4.936	0.026
Total effective rate	51 (89.47)	41 (73.21)	4.936	0.026

Table 2: Comparison of efficacy of patients in the two groups.

Comparison of UPDRS scores of patients between the two groups

Before and after treatment, the UPDRS II scores of patients in group A were (17.37±2.66) and (12.02±1.24), and UPDRS III scores were (33.15±2.18) and (20.21±1.97), respectively.

Before and after treatment, the UPDRS scores of patients in group B were (17.42±2.57) and (14.11±1.19), UPDRS III scores were (32.99±2.23) and (25.05±1.92). After treatment, the UPDRS II scores and UPDRS III scores of patients in group A were significantly lower than those of patients in group B (P<0.05), as shown in Figure 1.

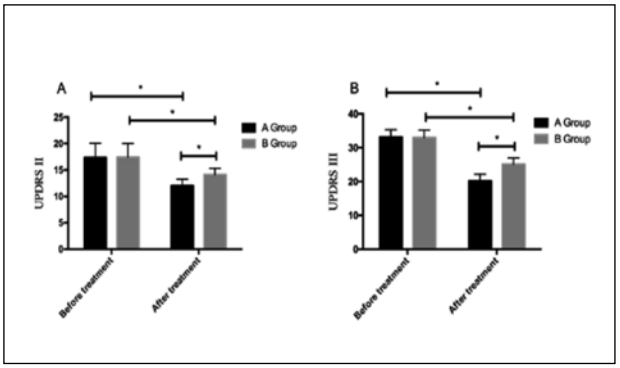

Figure 1: Comparison of UPDRS scores of patients between the two groups.

*Figure A: The UPDRS II score of patients in the two groups after treatment was significantly lower than that that before treatment, and the UPDRS II score of patients in group A after treatment was significantly lower than that of patients in group B. Figure B: The UPDRS III score of patients in the two groups after treatment was significantly lower than that before treatment (P<0.05), and the UPDRS III score of patients in group A after treatment was significantly lower than that of patients in group B. *indicated P<0.05.*

Comparison of the HAMD score and MADRS score of patients between the two groups before and after treatment

The HAMD scores of patients in group A before and after treatment were (21.34±1.24) and (9.45±0.82) respectively, the MADRS scores were (29.85±2.34) and (10.53±1.59) respectively, and the HAMD scores of patients in group B before and after treatment were (21.76±1.27) and (13.62±0.97) respectively.

The MADRS scores were (29.75±2.42) and (13.61±1.11) respectively, the HAMD score and MADRS scores of patients in the two groups after treatment were significantly lower than those before treatment (P<0.05), and the HAMD score and MADRS score of patients in group A after treatment were significantly lower than those of patients in group B (P<0.05), as shown in Figure 2.

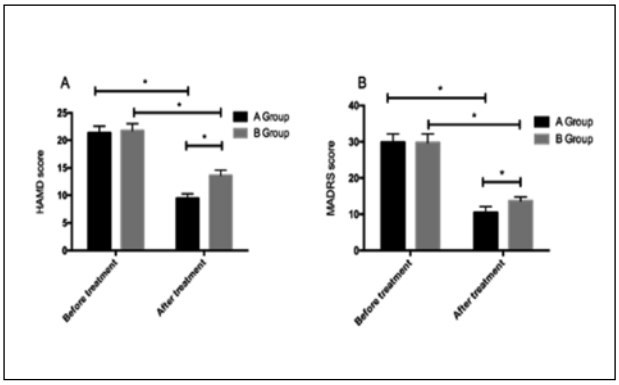

Figure 2: Comparison of the HAMD score and MADRS score of patients between the two groups before and after treatment.

*Figure A: The HAMD score of patients in the two groups after treatment was significantly lower than that before treatment, and the HAMD score of patients in group A after treatment was significantly lower than that of patients in group B. Figure B: The MADRS score of patients in the two groups after treatment was significantly lower than that before treatment (P < 0.05), and the MADRS score of patients in group A after treatment was significantly lower than that of patients in group B. *indicated P<0.05.*

Comparison of treatment compliance of patients between the two groups

The number of patients in group A who fully complied, partially complied and disobeyed during treatment was 32, 21 and 4 respectively, with a treatment compliance rate of 92.98%; the number of patients in group B who fully complied, partially complied and disobeyed during treatment was 21, 20 and 15 respectively, with a treatment compliance rate of 73.21%; the treatment compliance rate of patients in group A was significantly higher than that of patients in group B (P<0.05), as shown in Table 3.

Compliance	Group A n=57	Group B n=56	X^2	P
Complete compliance	32 (56.14)	21 (37.50)	3.941	0.047
Partial compliance	21 (36.84)	20 (35.71)	1.316	0.251
Noncompliance	4 (7.02)	15 (26.79)	0.147	0.702
Total compliance rate	53 (92.98)	41 (73.21)	0.147	0.702

Table 3: Comparison of treatment compliance of patients between the two groups.

Comparison of adverse reactions of patients between the two groups

The number of patients with nausea, anorexia, drowsiness, constipation and dizziness in group A were 2, 2, 2, 3 and 2 respectively, and the total incidence rate of adverse reactions was 22.64%; the number of patients with nausea, drowsiness, dizziness, headache, rash and loss of appetite in group B were 0, 1, 1, 1 and 1 respectively, and the total incidence rate of adverse reactions was 7.27%; the total incidence rate of adverse reactions in group B was significantly lower than that in group A, with statistically significant difference (P<0.05), as shown in Table 4.

Adverse reactions	Group A n=57	Group B n=56	X^2	P
Nausea	2 (3.51)	3 (5.36)	0.228	0.633
Anorexia	2 (3.51)	2 (3.57)	0.000	0.986
Drowsiness	2 (3.51)	1 (1.79)	0.325	0.569
Constipation	3 (5.26)	2 (3.57)	0.191	0.662
Dizziness	2 (3.51)	2 (3.57)	0.000	0.986
Incidence rate of adverse reactions	11 (19.30)	10 (17.86)	5.052	0.025

Table 4: Comparison of adverse reactions of patients between the two groups.

Comparison of patients' quality of life between the two groups before and after treatment

The life quality scores of emotion, cognition, social relations, energy, health status and overall quality of life of patients in group A before treatment were (42.15±3.24), (43.83±3.05), (43.24±3.52), (43.11±3.81) and (41.95±3.73), respectively.

The life quality scores of emotion, cognition, social relations, energy, health status and overall quality of life after treatment were (58.82±5.51), (57.93±5.63), (57.87±6.41), (58.11±6.83) and (61.74±7.39), respectively. The life quality scores of emotion, cognition, social relations, energy, health status and overall quality of life before treatment in group B were (42.65±3.71), (43.16±3.23), (42.89±3.74), (42.22±3.62) and (41.38±3.77), respectively. After treatment, the life quality scores of emotion, cognition, social relations, energy, health status and overall quality of

life were (50.33±4.49), (50.27±5.51), (50.36±5.18), (50.06±5.29) and (50.79±5.49), respectively.

There was no significant difference in the quality of life before treatment between the two groups (P>0.05). After treatment, the life quality scores of patients in the two groups were all higher than before treatment (P<0.05), and the quality of life of group A was significantly higher than that of group B (P<0.05), as shown in Table 5.

Factor	Group A n=57	Group B n=56	t	*P*
Before treatment				
Emotion	42.15±3.24	42.65±3.71	0.194	0.845
Cognition	43.83±3.05	43.16±3.23	0.045	0.964
Social relations	43.24±3.52	42.89±3.74	0.082	0.935
Energy	43.11±3.81	42.22±3.62	0.014	0.989
Health status and overall quality of life	41.95±3.73	41.38±3.77	0.053	0.958
After treatment				
Emotion	58.82±5.51	50.33±4.49	8.971	<0.001
Cognition	57.93±5.63	50.27±5.51	7.308	<0.001
Social relations	57.87±5.41	50.36±5.18	7.535	<0.001
Energy	58.11±5.83	50.06±5.29	7.683	<0.001
Health status and overall quality of life	61.74±6.39	50.79±5.49	9.763	<0.001

Table 5: Quality of life of patients in the two groups before and after treatment.

Discussion

Parkinson's disease complicated with depressive disorder is one of the common concomitant symptoms in Parkinson's patients at present, which may occur at any stage of the disease course[17]. The occurrence of Parkinson's disease complicated with depressive disorder will not only have a serious impact on the condition of patients, but also make the patients have suicidal thoughts, bringing heavy burden and trouble to families[18]. At present, the pathogenesis of depressive disorder in Parkinson's patients is still unclear, and some studies believed that this was due to the reduction of dopamine in the brain, which might also lead to depression[19].

In our study, we investigated the efficacy of two Parkinson's therapeutic drugs pramipexole and madopar combined with antidepressant paroxetine respectively on Parkinson's patients complicated with depressive disorder. First, we compared the efficacy of patients in the two groups, and the results showed that the total effective rate of patients treated with pramipexole combined with madopar was significantly higher than that of patients treated with madopar. Then, we further compared the UPDRS score of patients in the two groups, and the results revealed that whether the UPDRS II or UPDRS III score, patients in group A improved more obviously than those in the control group after treatment.

This suggested that paroxetine combined with pramipexole had better efficacy on Parkinson's disease complicated with depressive disorder than that combined with madopar. Pramipexole, as a complete dopamine receptor agonist, can highly select D3 receptor, and exert certain antidepressant effect by exciting D3 receptor[20]. However, madopar, as a compound preparation of levodopa and benserazide, can enter the central nervous system through the blood-brain barrier to supplement dopamine in the substantia nigra, thus playing a better efficacy on Parkinson, but it has no direct efficacy on depression[21].

In our study, the reason why group A has better efficacy than group B was that we suspected that this was related to the antidepressant effect of pramipexole itself. Then we compared the HAMD score and MADRS score of patients in the two groups, and the results signified that although the HAMD score and MADRS score of patients in the two groups were significantly improved after treatment compared with those before treatment, the HAMD score and MADRS score of patients in group A were significantly improved compared with those of patients in group B, which suggested that paroxetine combined with pramipexole had more significant antidepressant effect than that combined with madopar, which was consistent with our previous speculation. Paroxetine, as a new antidepressant, has the strongest selectivity for 5-HT among similar drugs, and has less influence on the uptake of norepinephrine and dopamine[22]. Previous studies[23] indicated that the combination of paroxetine and pramipexole could enhance the antidepressant effect, which was consistent with our results.

After that, we also recorded and compared the adverse reactions of patients in the two groups during treatment, and the results verified that there was no significant difference in the incidence rate of adverse reactions of patients between the two groups, which showed that the two Parkinson treatment drugs combined with paroxetine respectively both had good safety. Previous studies[24] said that pramipexole belonged to a amiphenazole derivative, which could excite striatal dopamine and maintain a stable concentration in the body, and would not increase adverse reactions while reducing stimu-

lation of striatal synaptic thick film on dopamine receptor. Madopar, however, has a very significant effect on the early treatment of Parkinson's patients with less adverse reactions, which has been proved in the past[25]. However, the long-term use of madopar would lead to gradually poor efficacy of patients and increase adverse reactions[26], and the long-term efficacy of patients was not evaluated in our study, which was also the deficiency of our study.

Finally, we compared the treatment compliance of patients in the two groups and the quality of life after 12 weeks of treatment, and the results showed that the treatment compliance of patients in group A was significantly higher than that of patients in group B, and although the quality of life of patients in the two groups was better than that before treatment, the improvement of patients in group A was more obvious, which suggested that paroxetine combined with pramipexole could have better improvement effect on the quality of life of patients than that combined with madopar. We suspected that this might be due to the higher compliance of patients in group A, or the more obvious improvement of patients' depressive state, thus reducing patients' resistance to treatment, which further enabled patients to obtain better efficacy and prognosis, thus forming a virtuous circle. However, we can only speculate on this at present.

To sum up, paroxetine combined with pramipexole has better efficacy on Parkinson's disease complicated with depressive disorder than that combined with domperidone, it can effectively improve the depressive state and Parkinson's symptoms of patients and also has good safety, which is worthy of clinical promotion. However, there are still some deficiencies in this study. For example, we did not discuss the mechanism of drug therapy in detail and our results were still arguable due to the relationship between sample size. However, we will further increase the sample size in future studies to supplement the deficiencies in this article.

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