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To Explore the Application Value of Paroxetine Hydrochloride Combined with Low-dose Atypical Antipsychotic Drugs in the Treatment of Elderly Patients with Depression

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Abstract: *Objective:* To explore the application value of paroxetine hydrochloride combined with low-dose atypical antipsychotics (olanzapine is selected) in the treatment of elderly patients with depression. *Methods:* 70 elderly patients with depression who were treated in our hospital from January 2022 to December 2023 were selected and divided into two groups using the random number table method, with 35 cases in each group. The single medication group was treated only with paroxetine hydrochloride, while the combined medication group was treated with paroxetine hydrochloride combined with low-dose olanzapine. The therapeutic effects of the two groups were compared. *Results:* The post-treatment depression scale (HAMD) score of the combined medication group was lower than that of the single medication group, the total effective rate of treatment was higher than that of the single medication group, and the incidence of adverse reactions was lower than that of the single medication group ($p < 0.05$). *Conclusion:* Paroxetine hydrochloride combined with low-dose atypical antipsychotics in the treatment of elderly patients with depression can effectively improve depressive symptoms and improve treatment effects, and is highly safe and has important clinical application value.

Keywords: Paroxetine hydrochloride; Low-dose atypical antipsychotics; Geriatric depression; Therapeutic effect; Adverse reactions

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1. Introduction

Geriatric depression is a common mental disorder among the elderly. Patients often show symptoms such as depression, loss of interest, and sleep disorders. These symptoms not only seriously affect the quality of life, but may also increase adverse consequences such as cognitive decline and suicide risk. The physiological functions of elderly patients decline, the activity of liver metabolic enzymes decreases, and the function of the cytochrome P450 enzyme system will weaken. This causes the drug metabolism in the body to slow down and drug accumulation is prone to occur, which in turn makes the safety of drugs used in the treatment of elderly depression facing higher challenges. Currently, most clinical treatments for geriatric depression are based on selective serotonin reuptake inhibitors. Paroxetine hydrochloride is one of the commonly used drugs. It exerts a therapeutic effect by inhibiting the reuptake of serotonin in the presynaptic membrane.

However, when using this drug alone, some patients have difficulty coping with the complex pathogenesis of geriatric depression due to a single neurotransmitter regulatory pathway. Not only is the treatment effect poor, but they are also prone to adverse reactions such as drowsiness and dry mouth [1].

Olanzapine is an atypical antipsychotic drug that can act on multi-target neurotransmitter receptors and is highly safe when used in small doses. It may have a synergistic effect when used in combination with paroxetine hydrochloride. Based on this situation, this study combined paroxetine hydrochloride with a small dose of an atypical antipsychotic drug (olanzapine) in the treatment of elderly patients with depression to observe the application value of this combined treatment plan and provide a reference for the optimization of clinical treatment plans.

2. Materials and methods

2.1. General information

70 elderly patients with depression who received treatment in our hospital from January 2022 to December 2023 were selected and divided into a single medication group and a combined medication group using the random number table method, with 35 cases in each group. In the single medication group, there were 19 and 16 male and female cases, respectively, with an age of 60 to 82 (68.52 ± 4.36) years; in the combined medication group, there were 18 and 17 male and female cases, respectively, with an age of 61 to 81 (69.03 ± 4.18) years. There was no significant difference in the general information of the two groups of patients ($p > 0.05$), indicating they were comparable.

2.1.1. Inclusion criteria

(1) Meet the diagnostic criteria for depression;
(2) Age ≥ 60 years old;
(3) Hamilton Depression Rating Scale (HAMD) score ≥ 17 points.

2.1.2. Exclusion criteria

(1) Combined with severe heart, liver, kidney and other organ failure;
(2) Have other mental diseases such as schizophrenia;
(3) Allergic to study drugs.

2.2. Method

In this study, patients were divided into single medication group and combined medication group. The single-medication group only uses paroxetine hydrochloride tablets for treatment, and the initial dose is set at 10 mg per day, taken orally. Taking into account the individual differences and drug tolerance of elderly patients, the dose was adjusted to 20 mg per day after 1 week based on the actual situation, and the entire treatment cycle lasted for 8 weeks.

The combined medication group is based on the single medication group, combined with low-dose olanzapine tablets. Among them, the usage and dosage of paroxetine hydrochloride are consistent with those of the single-medication group. The initial dose of olanzapine is 2.5 mg daily, also administered orally. If the patient does not experience any obvious adverse reactions during the medication, the dose level will be maintained and the treatment will be continued for 8 weeks.

During the treatment period in both groups, medical staff will regularly monitor the patients' vital signs and liver and kidney functions, and provide routine nursing intervention. Routine nursing intervention covers many aspects. One is health education, in which medical staff will explain the knowledge about geriatric depression in detail to patients and their families, including the causes of the disease, symptom manifestations, development process, etc., while emphasizing medication precautions, such as taking medication on time, not increasing or decreasing the dosage at will, possible adverse drug reactions and coping methods, etc.; the other is psychological counseling, paying close attention to patients.

Emotional changes: once patients are found to have negative emotions such as anxiety and irritability, they can be

alleviated through heart-to-heart talks, psychological suggestions, diversion of attention, etc.; the third is life guidance, which helps patients plan and develop regular work and rest habits, such as going to bed early and getting up early, ensuring adequate sleep, and guiding patients to establish reasonable eating habits and balanced dietary nutrition to promote the overall treatment effect.

2.3. Observation indicators

This study will compare the three core indicators of the two groups of patients, namely the HAMD score before treatment and after 8 weeks of treatment, the total effective rate of treatment, and the incidence of adverse reactions. The full HAMD score is 52 points. The higher the score, the more severe the patient's depressive symptoms are. The overall effectiveness of treatment is evaluated based on the HAMD score reduction rate. The specific judgment standard is that the score reduction rate ≥ 75% is defined as recovery, the score reduction rate between 50% and 74% is defined as significant progress, and the score reduction rate is 2 A range of 5% to 49% is defined as progress, and a reduction rate of less than 25% is defined as ineffective.

The total effective rate is calculated as (number of recovered cases + number of significantly improved cases + number of improved cases) divided by the total number of cases and then multiplied by 100%; adverse reaction types included in adverse reaction incidence statistics include drowsiness, dizziness, dry mouth, and constipation.

2.4. Statistical methods

Data were analyzed using SPSS24.0. *t*-test for measurement data; χ^2 test for count data. $p < 0.05$ represents significant difference.

3. Results

3.1. Comparison of HAMD scores between the two groups of patients before and after treatment

There was no significant difference in HAMD scores between the two groups before treatment ($p > 0.05$); after 8 weeks of treatment, the HAMD score of the combined drug group was lower than that of the single drug group ($p < 0.05$), see **Table 1**.

Table 1. Comparison of HAMD scores between the two groups of patients before and after treatment ($\bar{x} \pm s$, points)

Group	Score before treatment	Score after 8 weeks of treatment
Single medication group (35)	28.65 ± 3.24	16.82 ± 2.56
Combined medication group (35)	29.03 ± 3.15	10.54 ± 2.13
t	0.497	11.156
p	0.620	0.000

3.2. Comparison of the total effective rate of treatment between the two groups of patients

The total effective rate of treatment in the combined medication group was higher than that in the single medication group ($p < 0.05$), see **Table 2**.

Table 2. Comparison of the total effective rate of treatment between the two groups of patients [n (%)]

Group	Recovery	Significant progress	Progress	Invalid	Totally effective [n (%)]
Single medication group (35)	5 (14.29)	8 (22.86)	10 (28.57)	12 (34.28)	23 (65.71)
Combined medication group (35)	12 (34.29)	11 (31.43)	9 (25.71)	3 (8.57)	32 (91.43)
χ^2					6.873
p					0.009

3.3. Comparison of the incidence of adverse reactions between the two groups of patients

The incidence of adverse reactions in the combined medication group was lower than that in the single medication group ($p < 0.05$), see **Table 3**.

Table 3. Comparison of the incidence of adverse reactions between the two groups of patients [n (%)]

Group	Drowsiness	Dizziness	Dry mouth	Constipation	Overall incidence [n(%)]
Single medication group (35)	4 (11.43)	3 (8.57)	5 (14.29)	2 (5.71)	14 (40.00)
Combined medication group (35)	1 (2.86)	1 (2.86)	2 (5.71)	0 (0.00)	4 (11.43)
χ^2					7.479
p					0.006

4. Discussion

Elderly patients with depression have reduced ability to metabolize drugs due to decline in physiological functions, and often have multiple underlying diseases. Therefore, treatment should not only focus on improving depression symptoms, but also take into account the safety of medication. Paroxetine hydrochloride is a selective serotonin reuptake inhibitor. It can increase the concentration of serotonin in the synaptic cleft by inhibiting the reuptake of serotonin in the presynaptic membrane, thereby exerting an antidepressant effect. However, when using this drug alone, some patients may not only have unsatisfactory therapeutic effects due to insufficient neurotransmitter regulation, but may also experience various adverse reactions due to the drug's effects, affecting treatment compliance. From the perspective of drug metabolism, paroxetine hydrochloride is mainly metabolized by CYP2D6 in the cytochrome P450 enzyme system of the liver. The reduced activity of CYP2D6 enzyme in elderly patients can easily lead to accumulation of the drug in the body and increase the risk of adverse reactions. This is also one of the reasons for the higher incidence of adverse reactions in the single-medication group.

The results of this study show that after 8 weeks of treatment, the HAMD score of the combined medication group was lower than that of the single medication group. This result shows that paroxetine hydrochloride combined with low-dose olanzapine can more effectively improve the depressive symptoms of elderly patients with depression. Analyzing its mechanism of action, olanzapine, as an atypical antipsychotic, has unique multi-target action characteristics. In addition to acting on dopamine D2 receptors and 5-hydroxytryptamine 2A receptors, it can also act on 5-hydroxytryptamine 1A receptors, histamine H1 receptors, etc. Among them, the antagonism of 5-hydroxytryptamine 2A receptors can enhance the effect of paroxetine hydrochloride on the regulatory effect of the 5-hydroxytryptamine system can reduce the desensitization of 5-hydroxytryptamine receptors and prolong the antidepressant effect; the partial agonistic effect on dopamine D2 receptors can improve symptoms such as lack of motivation and anhedonia that are often associated with elderly patients with depression. However, these symptoms cannot be effectively alleviated simply by regulating the 5-hydroxytryptamine system with paroxetine hydrochloride. In addition, the agonistic effect of olanzapine on 5-hydroxytryptamine 1A receptors can further enhance the neurotransmission effect of 5-hydroxytryptamine in the synaptic cleft, and form a synergistic effect with paroxetine hydrochloride to regulate neurotransmitter balance through multiple pathways, thereby more significantly improving depressive symptoms. At the same time, the use of olanzapine in small doses can not only exert a synergistic therapeutic effect, but also avoid an increase in adverse reactions caused by excessive doses, which meets the medication safety needs of elderly patients. From a pharmacokinetic perspective, olanzapine is mainly metabolized by CYP1A2 and CYP2D6. When combined with paroxetine hydrochloride, the two have no obvious competitive inhibition on the metabolic pathway and will not cause a large amount of accumulation of one of the drugs in the body. This provides a pharmacokinetic basis for the safety of the combined drug [2].

From the perspective of the total effective rate of treatment, the total effective rate of the combined medication group was 91.43%, which was significantly higher than the 65.71% of the single medication group, which further reflects the advantages

of the combined medication regimen. There are more cases of ineffective treatment in the single medication group, mainly because some patients are insensitive to a single serotonin regulation. Such patients may have dopamine system dysfunction or other neurotransmitter disorders. Combination medication, through multi-target effects, expands the scope of treatment and allows more patients to improve their depressive symptoms. It can also be seen from the increase in the number of cases that have recovered and made significant progress that combined medication can not only improve the effectiveness, but also enhance the depth of the treatment effect. From the perspective of the mechanism of action, the onset of depression in the elderly is not caused by a single neurotransmitter disorder, but involves the imbalance of multiple neurotransmitter systems such as serotonin, dopamine, and norepinephrine. Paroxetine hydrochloride only targets the serotonin system, while olanzapine can regulate multiple systems such as dopamine and serotonin at the same time. The combination of the two can correct neurotransmitter imbalances more comprehensively, thereby improving the depth and breadth of the treatment effect [3,4].

In terms of adverse reactions, the total incidence rate in the combined medication group was 11.43%, which was lower than 40.00% in the single medication group, which is closely related to the use of low-dose olanzapine. In the single-medication group, adverse reactions such as drowsiness and dry mouth were relatively common. The main reason is that paroxetine hydrochloride has a certain effect on cholinergic receptors and histamine receptors. Although olanzapine may also affect these receptors, when used in small doses, the drug interaction is milder and may reduce the degree of adverse reactions when single medication is used by regulating neurotransmitter balance. Specifically, paroxetine hydrochloride has a slight blocking effect on cholinergic M1 receptors, resulting in reduced saliva secretion and dry mouth; its blocking effect on histamine H1 receptors can cause drowsiness. However, low-dose olanzapine has a weak effect on these receptors, and its synergistic regulatory effect on the 5-hydroxytryptamine system can reduce the dose dependence of paroxetine hydrochloride and indirectly reduce the risk of adverse reactions. At the same time, routine nursing intervention during treatment also played a supporting role. Health education provided patients with knowledge about adverse reactions, reducing anxiety caused by misunderstandings. Life guidance helped patients alleviate some adverse reactions through reasonable work and rest and diet, such as increasing water intake when dry mouth, adjusting diet when constipation, etc., further reducing the impact of adverse reactions on patients. From the safety monitoring data, there were no obvious abnormalities in the liver and kidney function indicators of the two groups of patients during treatment, indicating that the combined medication regimen did not significantly damage the liver and kidney functions of elderly patients. This is related to the smaller burden on liver metabolism when olanzapine is used in small doses, and is also in line with the special needs of elderly patients for drug safety [5,6].

In the treatment of geriatric depression, patient compliance is very critical, and adverse reactions are an important factor affecting compliance. Combination medication regimens can improve efficacy while reducing adverse reactions, making patients more willing to adhere to treatment and avoid voluntary discontinuation of medication due to poor efficacy or uncomfortable symptoms, thereby ensuring the continuity and effectiveness of treatment. In addition, elderly patients often have underlying diseases such as hypertension and diabetes, and drug interactions need to be considered when taking medications. Olanzapine and paroxetine hydrochloride, at commonly used doses, have few interactions with most medications for treating underlying diseases. For example, they have no obvious adverse interactions with commonly used antihypertensive drugs such as calcium channel blockers and antidiabetic drugs such as metformin. This also provides a safety guarantee for the application of combined drug regimens in elderly patients. From clinical practice observations, the number of medication adjustments due to adverse reactions in patients in the combined medication group was significantly less than in the single medication group, further proving the safety advantages of this regimen. In clinical practice, for the treatment of elderly patients with depression, individual differences, such as age, underlying diseases, and tolerance to drugs, etc., need to be fully considered. The combined drug regimen also needs to be adjusted according to the patient's specific conditions. For example, for patients with slightly poor liver and kidney function, the drug dose adjustment cycle can be appropriately extended and liver and kidney function indicators can be closely monitored; for patients with sleep disorders, the sedative effect of low-dose olanzapine can also help improve sleep, killing two birds with one stone. This personalized treatment approach can fully leverage the advantages of combined drug regimens while minimizing risks. Judging from the individual differences in the mechanism of drug action, different elderly patients have

different sensitivities to neurotransmitter regulation. Some patients may be more sensitive to serotonin regulation, while some patients are more sensitive to dopamine regulation. Combination drug regimens can better adapt to this individual difference through multi-target effects and improve the pertinence and effectiveness of treatment [7,8].

In summary, paroxetine hydrochloride combined with low-dose atypical antipsychotics (olanzapine) in the treatment of elderly patients with depression can effectively reduce HAMD scores and improve the overall treatment efficiency through multi-target synergistic regulation of neurotransmitter balance. The low-dose medication mode reduces the risk of adverse reactions, and the pharmacokinetic characteristics also meet the physiological needs of elderly patients, making it a safe and effective treatment option. In clinical treatment, this combination drug regimen should be actively promoted and adjusted based on the patient's individual situation to provide better treatment services for elderly patients with depression, help patients improve their depressive symptoms, improve their quality of life, and reduce the burden on their families and society.

About the author

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Disclosure statement

The author declares no conflict of interest.

References

[1] Tang C, Wang X, 2025, Analysis of the Effect of Paroxetine Hydrochloride Combined with Low-Dose Atypical Antipsychotic Drugs in the Treatment of Elderly Patients with Depression. Chinese and Foreign Medical Research, 4(9): 73–75.

[2] Zhou P, 2021, To Explore the Effect of Paroxetine Hydrochloride Combined with Low-Dose Atypical Antipsychotic Drugs in the Treatment of Geriatric Depression—Comment on "Geriatric Depression". Chinese Clinical Pharmacology and Therapeutics, 26(8): 975.

[3] Liu Y, 2021, The Application Value of Paroxetine Hydrochloride Combined with Low-Dose Atypical Antipsychotic Drugs in Elderly Patients with Depression. Modern Chinese Doctors, 59(21): 30–33.

[4] Zhang H, 2020, Study on the Effect of Paroxetine Hydrochloride Combined with Low-Dose Atypical Antipsychotic Drugs in the Treatment of Elderly Depression. Chinese Community Physicians, 36(12): 96–97.

[5] Sun P, 2020, Analysis of the Efficacy and Safety of Paroxetine Hydrochloride Combined with Atypical Antipsychotics in the Treatment of Elderly Depression. Primary Medicine Forum, 24(11): 1508–1509.

[6] Yu X, 2019, Analysis of the Efficacy of Paroxetine Combined with Low-Dose Atypical Antipsychotics on Elderly Depression. Chinese Medical Guide, 17(33): 138–139.

[7] Lei L, 2019, Clinical Controlled Study of Paroxetine Combined with Low-Dose Atypical Antipsychotics in the Treatment of Elderly Depression. Chinese Medical Guide, 17(16): 157.

[8] Cao T, 2016, Efficacy and Safety of Paroxetine Combined with Low-Dose Atypical Antipsychotics or Paroxetine Alone in the Treatment of Elderly Depression. Chinese Medical Guide, 14(23): 119.