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Effect of Olanzapine Combined with Paliperidone on Improving Positive Symptoms and Social Functions in Patients with Refractory Schizophrenia

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Abstract: *Objective:* To analyze the effect of olanzapine combined with paliperidone in the treatment of refractory schizophrenia, especially its intervention value on patients' positive symptoms and social functions. *Methods:* 86 cases of refractory schizophrenia hospitalized in the psychiatry department of our hospital from January 2024 to January 2025 were collected and divided into two groups according to the random number table method. A control group (olanzapine alone) and an observation group (olanzapine combined with paliperidone sustained-release tablets) were established. The treatment courses were both 12 weeks. PANSS was used to evaluate patients' positive symptoms before treatment and at 4, 8, and 12 weeks of treatment, and PSP was used to evaluate social functions. The clinical efficacy of the two groups was compared. *Results:* After treatment, the PANSS positive symptom scores of the two groups were reduced, and the PSP scores were increased. The observation group improved better in various indicators, and the total effective rate was higher than that of the control group ($p < 0.05$). *Conclusion:* Olanzapine combined with paliperidone can effectively improve the positive symptoms and overall mental state of patients with refractory schizophrenia, promote the recovery of social functions, and is worthy of promotion.

Keywords: Refractory schizophrenia; Olanzapine; Paliperidone; Positive symptoms; Social function; Clinical efficacy

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1. Introduction

Schizophrenia is a high-incidence severe chronic mental disorder. Patients with schizophrenia may suffer from a series of core symptoms such as sensory disturbances, confused thinking and logic, indifferent emotional reactions, and continued decline in daily social interactions and living abilities [1]. Clinically, 30% to 40% of schizophrenia patients have received two or more monotherapy with sufficient amounts and courses of atypical antipsychotic drugs, but their condition still has not been effectively improved. Such patients are diagnosed as treatment-resistant schizophrenia (TRS). Conventional single drug treatment

alone has limited efficacy. Olanzapine can take effect quickly and effectively control patients' acute symptoms [2]; paliperidone has a stable and long-lasting effect and is more suitable for improving patients' remaining stubborn symptoms. However, current clinical research on the combination of two drugs in the treatment of refractory schizophrenia is insufficient [3]. Based on this, this study takes patients with refractory schizophrenia as the observation objects, sets up multiple observation time points, dynamically monitors various clinical indicators, and evaluates the effectiveness of the olanzapine combined with paliperidone medication regimen in improving patients' positive mental symptoms and social functions. It aims to provide scientific reference for clinical optimization of the disease's combined medication regimen and improve treatment effects.

2. Materials and methods

2.1. General information

According to the random number table method, 86 patients with refractory schizophrenia who were hospitalized in the psychiatric department of our hospital from January 2024 to January 2025 were divided into the control group and the observation group. There were 22 males and 21 females in the control group; their age ranged from 24 to 58 (41.26 ± 6.85) years; and the disease duration ranged from 3 to 12 (7.15 ± 2.36) years. There were 23 males and 20 females in the observation group; the age ranged from 23 to 59 (40.89 ± 7.12) years; the disease duration ranged from 3 to 13 (7.32 ± 2.41) years. Comparison of data between two groups ($p > 0.05$).

2.1.1. Inclusion criteria

(1) Positive symptoms are not relieved after adequate treatment with 2 or more atypical antipsychotics (≥ 8 weeks), and a positive PANSS baseline score is ≥ 20 points;
(2) Disease duration ≥ 3 years;
(3) Clear consciousness, complete data and good compliance.

2.1.2. Exclusion criteria

(1) Combined with severe organ and endocrine diseases;
(2) Combined with other severe mental illnesses;
(3) Allergic to the test drugs;
(4) Pregnant and lactating women.

2.2. Treatment methods

2.2.1. Control group

Treated with olanzapine tablets (Jiangsu Hansoh Pharmaceutical Group Co., Ltd., national drug approval number H20052688, specification 10 mg/tablet) alone. Take orally in the morning, initial daily dose is 5 mg. Subsequently, based on the patient's improvement level of mental symptoms and individual differences in tolerance, a phased dose increase or adjustment will be implemented. The maximum daily dose shall not exceed 20 mg, and the treatment will be continued for 12 weeks.

2.2.2. Observation group

treated with olanzapine combined with paliperidone sustained-release tablets (Xi'an Janssen Pharmaceutical Co., Ltd., national drug approval number H20080500, specification 6 mg/tablet). The dosage, route of

administration and dosage adjustment scheme of olanzapine are consistent with those in the control group; the initial dose of paliperidone is 3 mg/d, taken orally in the morning, and the dosage is adjusted appropriately based on the patient's symptom relief and drug tolerance, with a maintenance dose of 3 to 9 mg/d, and continuous treatment for 12 weeks.

2.3. Observation indicators

(1) Psychiatric symptom score

Before the start of treatment and at the 4th, 8th, and 12th weeks of treatment, the Positive and Negative Syndrome Scale (PANSS) was used to evaluate the mental symptoms of the enrolled patients. The larger the scale score, the more severe the mental symptoms.

(2) Social function score

At the same time point, the Personal and Social Performance Scale (PSP) was used to evaluate the patient's social function, with a total score of 0 to 100. The higher the score, the better the patient's social ability and self-care ability.

(3) Clinical efficacy

The PANSS score reduction rate was used to evaluate the clinical efficacy at the end of 12 weeks of treatment, with three-level standards: ① Markedly effective: the score reduction rate is ≥ 50%, and the positive symptoms are significantly relieved; ② Effective: the score reduction rate is 25% to 49%, and the psychopathological symptoms are partially improved; ③ Ineffective: the score reduction rate is < 25%, and the symptoms are not improved or worsened.

2.4. Statistical methods

SPSS 26.0 was used to process data. Measurement data are represented by ($\bar{x} \pm s$), paired *t*-test is used for intra-group comparisons, and independent samples t-test is used for comparisons between groups; count data are represented by cases (%), and χ^2 test is used. ($p < 0.05$) means the difference is statistically significant.

3. Results

3.1. Comparison of PANSS positive symptom scores between the two groups at different time points

At the three observation nodes of 4, 8, and 12 weeks of treatment, the positive symptom scores of the observation group were lower than those of the control group ($p < 0.05$). See **Table 1**.

Table 1. Comparison of PANSS positive symptom scores between the two groups at different time points ($\bar{x} \pm s$, points)

Group	n	Before treatment	Treatment 4 weeks	8 weeks of treatment	12 weeks of treatment
Control group	43	28.36 ± 3.25	24.12 ± 2.86	20.58 ± 2.41	17.25 ± 2.13
Observation group	43	28.41 ± 3.18	21.05 ± 2.53	16.32 ± 2.05	12.68 ± 1.89
t value	-	0.072	5.369	8.752	10.526
p value	-	0.943	0.000	0.000	0.000

3.2. Comparison of PSP social function scores between the two groups at different time points

The PSP score of the observation group was higher than that of the control group at each time point ($p < 0.05$). See **Table 2**.

Table 2. Comparison of PSP scores between the two groups at different time points ($\bar{x} \pm s$, points)

Group	n	Before treatment	Treatment 4 weeks	8 weeks of treatment	12 weeks of treatment
Control group	43	35.26 ± 5.32	42.35 ± 5.68	49.68 ± 6.12	56.32 ± 6.58
Observation group	43	34.98 ± 5.41	48.62 ± 6.05	58.95 ± 6.83	68.59 ± 7.26
t value	-	0.245	4.986	6.528	8.365
p value	-	0.807	0.000	0.000	0.000

3.3. Comparison of clinical efficacy between the two groups

The total effective rate of the observation group was higher than that of the control group (P<0.05). See **Table 3**.

Table 3. Comparison of clinical efficacy between two groups [n (%)]

Group	n	Effective	Valid	Invalid	Always efficient
Control group	43	23	10	10	33 (76.74)
Observation group	43	32	8	3	40 (93.02)
χ^2 value	-	-	-	-	4.440
p value	-	-	-	-	0.035

4. Discussions

The core pathological mechanism of schizophrenia is related to the abnormal metabolism of dopamine and serotonin, two neurotransmitters in the brain center. Patients with refractory schizophrenia are prone to drug tolerance problems. The effectiveness of using an antipsychotic drug alone is only 70% to 75%, and it cannot completely eliminate residual symptoms [4]. Simply increasing the dosage of the drug will easily cause various side effects, and it will be more difficult for patients to insist on taking the drug.

Olanzapine is a broad-spectrum second-generation atypical antipsychotic drug commonly used in clinical practice. It can simultaneously block D2 dopamine receptors, 5-HT2A serotonin receptors, histamine receptors and cholinergic receptors in the brain center. The drug takes effect quickly and has a very significant sedative and calming effect. Its core function is to quickly inhibit the overactive dopamine transmitter in the mesolimbic pathway of the brain [5]. However, there are obvious limitations in the clinical application of olanzapine, and its shortcomings are more prominent. If this drug is used alone for a long time, it will be difficult to completely eliminate the patient's stubborn residual positive symptoms, and it will not be able to fundamentally repair the neurological function of the prefrontal lobe of the brain [6].

Paliperidone extended-release tablets are the active metabolites of risperidone in the human body. The half-life of the drug is as long as 24 hours. After taking the drug, the blood concentration in the body is stable, with small fluctuations, and the drug effect is sustained and stable. It mainly selectively antagonizes

D2 dopamine receptors and 5-HT2A serotonin receptors, and has a more durable and stable inhibitory effect on positive symptoms that are refractory to drugs and relapse [7]. In addition, paliperidone sustained-release tablets can optimize neurotransmitter transmission in the mesocortical pathways of the brain, effectively repair damaged prefrontal lobe nerve functions, and can effectively improve social functional deficits such as social withdrawal and reluctance to communicate with others. The overall risk of adverse reactions is smaller, and it is suitable for long-term maintenance treatment of schizophrenia patients with stubborn conditions and recurring attacks [8].

When the two drugs are used together, their pharmacological effects can complement each other and synergize. Olanzapine has a fast onset of action and can quickly suppress various mental symptoms of acute attacks, stabilize mood, and control agitation; paliperidone is a long-acting stabilizing drug that can continuously improve patients' residual positive symptoms such as hallucinations and delusions in the long term, and gradually help patients return to normal social living abilities. The combination of the two drugs can not only quickly control acute symptoms, but also stabilize the condition and restore social functions in the long term. The positive symptom scores of the patients enrolled in this study before treatment were generally high, which is completely consistent with the disease characteristics of refractory schizophrenia. The indicators before treatment of the two groups of patients were basically the same, and the baseline levels were balanced and comparable. The research results are referenceable. After treatment, the positive symptoms of both groups of patients were improved to varying degrees. Among them, the positive symptom score of the observation group decreased better than that of the control group at the 4th, 8th, and 12th weeks of treatment. It shows that combined medication can improve core positive symptoms such as hallucinations, delusions, confusion, and logical disorder more quickly and more thoroughly. From the perspective of the mechanism of action, patients with refractory schizophrenia commonly have drug tolerance problems. Olanzapine alone has limited blocking effect on abnormal dopamine pathways in the brain and cannot completely eliminate residual stubborn mental symptoms. The combination of the two drugs can regulate neurotransmitters in the brain through multiple targets, dually inhibit the excessive hyperactivity of dopamine in the mesolimbic pathway, accurately control stubborn positive symptoms that cannot be cured for a long time, and effectively reduce the probability of disease recurrence.

Impairment of social functions is the core reason why patients with refractory schizophrenia are disabled and unable to live a normal life. Therefore, the goal of clinical treatment for this disease is not to simply suppress superficial mental symptoms such as hallucinations and delusions. More importantly, it is to repair the patient's damaged social functions and help the patient gradually regain his ability to live, integrate into family life, and return to a normal social environment. The results of the study showed that the PSP scores of the patients in the observation group improved more significantly, fully confirming that the combined use of two drugs has a much better effect on repairing the social functions of patients with refractory schizophrenia than a single drug. From an analysis of the mechanism of action, combined medication can improve the patient's condition in all aspects. On the one hand, it can effectively control typical positive mental symptoms such as hallucinations and delusions, correct patients' disordered thinking patterns and abnormal behaviors, so that patients can receive external information normally, carry out basic interpersonal communication, and gradually restore basic social abilities. On the other hand, the two drugs can form a good complementary synergy, each drawing on its own strengths and making up for the shortcomings of a single drug. Among them, paliperidone can effectively improve the patient's prefrontal nerve function, specifically improve the

patient's cognitive level, self-identification ability and self-care ability, making up for the shortcomings of olanzapine in improving cognitive function; while olanzapine can effectively alleviate patients' irritability, emotional loss, emotional disturbance and other problems, and stabilize the patient's emotional state. The combined use of the two has long-lasting efficacy and stable effects, providing reliable guarantee for patients' long-term recovery and return to family and society.

The efficacy data of this study show that the total clinical effectiveness of the observation group is better than that of the control group, indicating that the combination of olanzapine and paliperidone can make up for the shortcomings of single drug treatment, better control the psychiatric symptoms of patients with refractory schizophrenia, reduce the severity of symptoms, and reduce the number of cases where treatment is ineffective. Using olanzapine alone is difficult to improve the stubborn symptoms that are difficult to eliminate in some patients. Many patients' symptoms are only slightly improved or even not improved at all. The combination of the two drugs can regulate neurotransmitters from multiple targets and improve mental symptoms and social functional deficits at the same time, allowing more patients to reach the standard of obvious results, and the overall treatment effect is better.

5. Conclusion

In summary, olanzapine combined with paliperidone for refractory schizophrenia can quickly and effectively control patients' stubborn positive symptoms, reduce overall psychopathological damage, and promote the recovery of damaged social functions.

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Disclosure statement

The author declares no conflict of interest.

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