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Analysis of the Effects of Amisulpride on Negative Symptoms and Cognitive Function in Patients with Schizophrenia Dependent on Benzodiazepines

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Abstract: Objective: To explore the effect of amisulpride on improving negative symptoms and cognitive function in a special group of patients with benzodiazepine-dependent schizophrenia. Methods: 100 patients with benzodiazepine-dependent schizophrenia admitted to the hospital from May 2023 to May 2024 were randomly divided into 2 groups. The control group was treated with risperidone, and the observation group was treated with amisulpride. The treatment effects of the two groups of patients were compared. Results: After 4 and 8 weeks of treatment, the negative symptom scores of the observation group were lower than those of the control group, and the difference was statistically significant ($P < 0.05$). The cognitive function scores of the patients in the observation group were higher than those of the control group, and the difference was statistically significant ($P < 0.05$). Conclusion: After treatment with amisulpride in patients with schizophrenia who are dependent on benzodiazepines, the negative symptoms and cognitive function of the patients are significantly improved, and it is worthy of recommendation.

Keywords: Amisulpride; benzodiazepines; drug dependence; schizophrenia; negative symptoms; cognitive function

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1. Introduction

Clinically, schizophrenia is a relatively common and serious mental illness. Its main characteristic is that individuals have persistent and obvious abnormalities in many aspects such as thinking, emotion, behavior, and perception[1]. The prevalence of schizophrenia has shown an increasing trend year by year in recent years[2]. Regarding the treatment of schizophrenia, benzodiazepine (BZD) drugs are widely used in clinical psychiatry and neurology because of their fast onset and obvious sedative effect. They inhibit the central nervous system, produce a sedative effect, and play a certain role in alleviating the condition of schizophrenia. However, relevant clinical studies have shown that long-term use of BZD drugs can produce significant dependence, making it difficult to discontinue the drugs and seriously damaging the patient's physical and mental health[3]. Risperidone and amisulpride are widely used in clinical applications, and both have certain advantages in the treatment of schizophrenia. Giving risperidone to patients during treatment can effectively improve the patient's positive symptoms (delusions, unfounded suspicion, etc.) and negative symptoms (reduced speech, slow reaction, loss

of social interest, etc.). However, when risperidone is used, it will affect the patient's endocrine and metabolic functions, causing metabolic abnormalities, weight gain, etc. The antipsychotic effect of amisulpride is relatively significant, and its unique mechanism of action enables it to exert a significant blocking effect at different dosages[4]. To this end, this study explores the therapeutic effect of amisulpride, and the specific reports are as follows.

2. Materials and methods

2.1. Research objects

Randomly divided 100 benzodiazepine-dependent schizophrenia patients admitted to the hospital from May 2023 to May 2024 into 2 groups. The control group included 23 males and 27 females, aged 24-55 (32.34 ± 3.64) years old; the number of years of taking BZD drugs was 1-5 (3.02 ± 0.06) years. There were 24 males and 26 females in the observation group, aged 23-55 (33.01 ± 3.96) years old; the number of years of taking BZD drugs ranged from 1-6 (3.12 ± 0.16) years. The two groups were compared ($P > 0.05$) and were comparable.

Inclusion criteria: (1) patients can express their needs and feelings; (2) can cooperate with the treatment plan in this study; (3) have comprehensive information; (4) have taken BZD drugs for at least 1 year, and have become dependent and have obvious withdrawal syndromes such as insomnia, anxiety, and depersonalization after stopping the drug. Exclusion criteria: (1) Suicidal behavior; (2) Partial data missing; (3) Patients with severe liver and kidney function impairment; (4) Contraindications to study drugs; (5) Mental retardation.

2.2. Treatment methods

Both the control group and the observation group stopped using BZD drugs for half a month before the start of the study.

The control group was treated with risperidone tablets [Novartis (Bangladesh) Limited, registration number H20171054, specification: 1 mg]. The first dose was 1 mg each time, twice a day. The target therapeutic dose was safely and effectively adjusted according to the patient's tolerance. Within 1 to 2 weeks after treatment, the drug dosage was increased to 3~6 mg each time, twice a day.

The observation group took amisulpride tablets (Qilu Pharmaceutical Co., Ltd., National Drug Approval No. H20113230, specification: 50 mg), with an initial dose of 100 mg once a day, and then increased to 600-800 mg a day. > 400mg, taken in 2 divided doses, otherwise, taken in one go. The treatment period for both groups is 8 weeks.

2.3. Evaluation criteria

Evaluate the improvement of patients' negative symptoms before treatment, after 4 weeks and 8 weeks of treatment. The Negative Symptom Scale (SANS) is used, which mainly covers attention disorders, emotional retardation, etc. The score is 0-5 points, ranging from 0-120 points. The higher the score, the more serious the patient's symptoms on this scale are.

Before treatment and after 8 weeks of treatment, the patient's cognitive function status was evaluated using the Neuropsychological State Test (RBANS), which mainly covers aspects such as speech function, immediate memory, attention, etc. The score range is between 0-100 points, and the score is proportional to the cognitive function.

2.4. Statistical methods

SPSS 26.0 statistical software was used for data analysis. Measurement data that conformed to normal distribution (including negative symptom scores and cognitive functions) were expressed as $x \pm s$, and t test was used for comparison between groups. $P < 0.05$ means the difference is statistically significant.

3. Results

3.1. Analysis of negative symptoms

After 4 and 8 weeks of treatment, the observation group was lower than the control group, and the difference was statistically significant (P < 0.05), Table 1.

Table 1. Comparison of the improvement effects of negative symptoms between the two groups of patients ($\bar{x} \pm s$, points)

Group	n	Before treatment	Treatment 4 weeks	8 weeks of treatment
control group	50	113.43 ± 14.04	77.47 ± 7.97	66.69 ± 6.73
Observation group	50	113.54 ± 14.57	67.12 ± 6.84	60.02 ± 6.42
t		0.038	6.968	5.071
P		0.969	0.000	0.000

3.2. Cognitive function analysis

There was little difference in speech function, immediate memory, attention, and visual span between the groups before treatment (P > 0.05). After 8 weeks of treatment, the observation group was higher than the control group, and the difference was statistically significant (P < 0.05), see Table 2.

Table 2. Comparison of cognitive function between two groups of patients ($\bar{x} \pm s$, points)

Group	n	Speech function		Immediate memory		Attention		Visual span	
		before treatment	8 weeks of treatment	before treatment	8 weeks of treatment	before treatment	8 weeks of treatment	before treatment	8 weeks of treatment
control group	50	56.09 ± 5.42	72.14 ± 7.12	60.33 ± 6.04	70.73 ± 7.11	69.22 ± 6.54	82.31 ± 8.74	62.33 ± 6.46	71.06 ± 8.18
Observation group	50	56.11 ± 5.45	82.06 ± 8.17	60.36 ± 6.06	79.83 ± 7.82	69.36 ± 6.58	92.86 ± 10.27	62.35 ± 6.48	81.73 ± 9.02
t		0.018	6.473	0.025	6.088	0.107	5.532	0.015	6.196
P		0.985	0.000	0.980	0.000	0.915	0.000	0.988	0.000

4. Discussion

With the rapid development of society, the pace of life continues to accelerate and competition becomes more and more fierce, which has brought unprecedented psychological pressure to modern people. The accumulation of psychological pressure, as well as the superposition of factors from family, work and other aspects, have increased the prevalence of schizophrenia. The specific cause of schizophrenia may be related to factors such as neurodevelopment, biochemistry, and genetics. In addition, environmental factors such as stressful events and childhood trauma will increase the occurrence of schizophrenia[5]. Clinically, for the treatment of schizophrenia, the efficacy of BZD drugs has been confirmed to a certain extent, and it has achieved significant efficacy in alleviating behavioral disorders in patients with schizophrenia in the acute phase[6]. However, the treatment period for schizophrenia is usually long, which further makes the administration of BZD drugs significantly more difficult. Long-term or high-dose use can easily cause patients to become dependent on the drugs, resulting in withdrawal syndrome. Patients will experience varying degrees of anxiety, depression, insomnia and other symptoms, which in turn increases the patient's mental burden and worsens the condition. Therefore, it is necessary to explore a safer and more effective treatment method to alleviate patients' drug dependence.

Negative symptoms are more common in schizophrenia patients. Patients have symptoms such as withdrawal from others, laziness, and poor thinking, which have a great impact on the patients' social functions and reduce their quality of life. In this study, the negative symptom scores of the observation group were lower than those of the control group after 4 and 8 weeks of treatment. This shows that amisulpride, as a commonly used drug in the treatment of schizophrenia, has achieved significant results in improving patients' negative symptoms. The reason: Amisulpride mainly works by blocking D2 and D3 presynaptic receptors. At low doses, it can promote the synthesis and release of dopamine, further promote the transmission of dopamine in the brain, increase the content of 5-hydroxytryptamine, dopamine, etc. When used in the treatment of schizophrenia, it can effectively alleviate negative symptoms such as social withdrawal, emotional apathy, poor thinking, isolation, laziness and other negative symptoms in patients, and the effect is relatively significant. At high doses, it prevents excessive dopamine from binding to postsynaptic membrane receptors and reduces the excitability of neurons, thereby exerting its antipsychotic effect and achieving the effect of alleviating the symptoms of schizophrenia[7]. Amisulpride is well tolerated and safe in the treatment of schizophrenia.

Patients with schizophrenia often have difficulty concentrating, memory impairment, and thinking disorders. Severe cognitive impairment has a great impact on patients' daily life and physical and mental health. Cognitive dysfunction can worsen schizophrenia and increase the likelihood of relapse. The prognosis of patients with schizophrenia is closely related to the degree of cognitive dysfunction. After 8 weeks of treatment in this study, the cognitive function score of the observation group was lower than that of the control group, indicating that the application of amisulpride can help improve patients' cognitive function, allowing patients to return to normal life and work as soon as possible. The reason: In psychiatric treatment, amisulpride is directly used in the central nervous system, which can block dopamine D2 receptors, reduce the binding of dopamine in the postsynaptic membrane, and has a high affinity for D3 receptors. By antagonizing D3 receptors, it optimizes nerve signal transmission in the brain, further regulates and improves the emotional state and cognitive function of schizophrenia patients, thereby improving the patient's attention and memory. It is worth noting that when patients are treated with amisulpride, individualized dosage adjustments must be made based on the condition and individual differences of the patient.

In summary, amisulpride given to patients in the treatment of special patients with benzodiazepine-dependent schizophrenia can relieve patients' negative symptoms and improve their cognitive function by antagonizing dopamine D2 and D3 receptors and regulating the amount of dopamine in the frontal cortex.

Disclosure statement

The author declares no conflict of interest.

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