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Original Article

Effects on social functioning and metabolism in the patients with first-episode schizophrenia: aipiprazole vs risperidone

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Abstract: Objective: To investigate the influence of aripiprazole and risperidone on metabolic indicators and social functions in the first-episode schizophrenia. Methods: 47 patients treated with aripiprazole as group A and 46 patients treated with risperidone as group B were enrolled. The clinical efficacy, positive and negative symptom scale (PANSS), personal and social performance scale (PSP), levels of insulin, ghrelin, adiponectin, leptin, and body mass index (BMI) in two groups were investigated pre- and post-treatment. Results: The general psychopathological scores, negative symptom scores, and the total PANSS scores following treatment in group A were lower than those in B ($P<0.05$). Group A and B exhibited notable distinction in the total effective rate (TER) of treatment ($P>0.05$). The PSP scores of two groups increased following treatment ($P<0.05$); however, no notable distinction in PSP scores between two groups were found ($P>0.05$). In group A, the levels of insulin and adiponectin were not significantly different from those before treatment ($P>0.05$); the levels of ghrelin after treatment were lower than those before treatment, and the levels of leptin were higher than those before treatment ($P<0.05$). In group B, insulin and leptin levels were higher than those before treatment, and adiponectin levels were lower than those before treatment ($P<0.05$). The differences in levels of insulin, ghrelin, adiponectin, and leptin exhibited obvious distinction between two groups ($P<0.05$). Two groups showed no obvious distinction in BMI prior to treatment ($P>0.05$). However, the increase of BMI in group A following treatment was dramatically lower than that in B ($P<0.05$). Conclusion: Aripiprazole and risperidone have similar clinical effects in patients with first-episode schizophrenia, and both can effectively improve social functioning. Aripiprazole regulated ghrelin and leptin levels, and has no effect on BMI, while risperidone has effect on all indexes examined in this study.

Keywords: First-episode, schizophrenia, aripiprazole, risperidone, metabolism, social function

Introduction

Schizophrenia is a kind of serious mental disturbance which can cause hallucinations, delusions, and terribly disordered thoughts and behaviors [1]. The causative factor of it is still unknown, but scholars believe that genetics, brain chemistry and environment were implicated in disorder progression [2]. Schizophrenia can cause terrible problems which endanger people' life, including suicide, anxiety, obsessive-compulsive disorder (OCD), and alcohol, etc. if not treated timely.

Currently, the treatment of schizophrenia includes the non-drug therapy and drug therapy, while antipsychotic agents are the mainstay of the drug therapy [3]. Chlorpromazine and haloperidol are two kinds of classic antipsychotics, but these medicines were liable to bring about side effects, including adverse reactions, cardiovascular adverse reactions, extrapyramidal symptoms, and excessive sedation, which adversely influence patients' life quality [4, 5]. Atypical antipsychotics refer to antipsychotics that are less liable than conventional antipsychotics to result in certain side effects. They could not only block dopamine D2 receptors, but also improve the negative and positive symptoms of patients with schizophrenia, and patients' cognitive function was not affected. Atypical antipsychotics have mostly substituted conventional agents as first-line therapy in treating schizophrenia [6, 7]. Ziprasidone, aripiprazole, quetiapine, olanzapine, and risperidone are most-prescribed atypical

antipsychotic drugs. Compared with traditional ones, these drugs exhibited higher safety and security [8].

Clinical studies performed in patients with schizophrenia usually focused on alleviating and controlling psychiatric symptoms, and the latest views deem that we should not only effectively relieve the patient's mental symptoms, but also avoid metabolic syndrome, weight gain, and the ability of social functioning should be improved [9, 10]. This study mainly explores the effects of aripiprazole and risperidone on metabolic-related indicators and social functioning in the treatment of first-episode of schizophrenia.

Materials and methods

Baseline data

93 patients with first- episode schizophrenia were evaluated retrospectively and classified to two groups according the treatment method. 47 patients treated with aripiprazole were enrolled as group A, including 30 males and 17 females. 46 patients treated with risperidone were included in group B, including 29 males and 17 females. Inclusion criteria was patients who signed informed consent; met diagnostic criteria for schizophrenia outlined in Chinese Classification of Mental Disorders Version 3 [11]; total PANSS scores ≥60; without history of antipsychotics treatment.

Exclusion criteria was patients with family history of diabetes; suicide attempt; serious aggressive behavior; abnormal electrocardiogram; pregnant; history of drug abuse; psychoactive substances misuse; combined with other serious physical diseases. The study has been approved by medical ethics committee in our hospital.

Methods

Patients in group A were given aripiprazole orally disintegrating tablets (cat.No: H20060521, Chengdu Kanghong Pharmaceutical Group Co., Ltd. Specification: 5 mg × 20 tablets/box), the daily dosage was 0-30 mg/d for 24 weeks.

Patients in group B were administrated with risperidone oral tablet (cat. No: H20061072, Beijing Tianheng Pharmaceutical Research Institute Nanyang Tianheng Pharmaceutical Factory, Specification: 1 mg × 20 tablets/box), daily dosage was 2-6 mg/d for 24 weeks.

Outcome measurement

PANSS score [12]: PANSS scores in two groups pre- and post-treatment was assessed. The PANSS yields a total average symptom score, based on 30 items, of which there were 16 general pathological items, 7 negative items, and 7 positive items. The patient is mentally assessed by a specially trained psychiatrist. The lower score indicated the better mental symptoms. The scale's Cronbach's alpha coefficient is 0.988.

Efficacy evaluation criteria [13]: The clinical efficacy of the two groups was evaluated regarding percentage of PANSS reduction. ≥75%, 50%-74%, 30%-49%, and <30% PANSS reduction were set as cured, markedly effective, effective, and ineffective, with total effective = cured + markedly effective + effective.

PSP scores [14]: The social functions of two groups were evaluated using the PSP, which determines 4 aspects of personal and social behaviors (socially useful activities, personal and social connections, self-care, interference and aggression behaviors) and provides a score between 1 and 100. Scores ≤ 30 indicates low social functioning, and the patient requires close monitoring and active support, 31-70 manifests disabilities of various degrees, and 70 to 100 is indicative of mild difficulties or better than adequate functioning. The scale's Cronbach's alpha coefficient is 0.922.

Metabolic indicators: 5 mL morning fasting elbow venous blood in the two groups was collected before and after treatment, centrifuged at 3000 r/min for 5-10 min. ELISA (enzyme-linked immunosorbent assay, Hebei Changtian Pharmaceutical Co., Ltd.) was used to measure levels of insulin, ghrelin, adiponectin, and leptin in two groups. All operations strictly conformed to kit instructions.

BMI [15]: BMI was calculated before and after two gorups, BMI = weight(kg)/[height(m)]^2.

Statistical analysis

SPSS 22.0 was the statistical analysis tool. Measurement data were expressed as mean ± standard deviation. Data that met the normal

Table 1. Baseline data [n(%)] /($\bar{x}$ ± sd)

Data		A (n=47)	B (n=46)	t/X^2	*P*
Gender	Male	30 (63.83)	29 (63.04)	0.006	0.937
	Female	17 (36.17)	17 (36.96)		
Age (year)		23.15 ± 1.08	23.19 ± 1.05	0.181	0.857
Course of diease (month)		7.15 ± 0.29	7.19 ± 0.23	0.736	0.464
Duration of education (year)		7.05 ± 0.28	7.03 ± 0.21	0.389	0.698

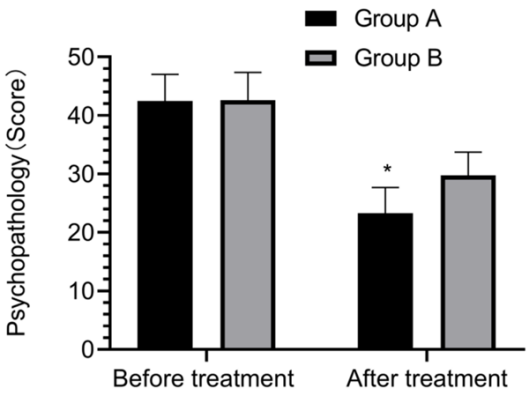

Figure 1. Comparison of general psychopathological scores pre- and post-treatment in two groups. General psychopathological scores prior to treatment in group A and B were not significantly different, *P*>0.05. General psychopathological scores in group A were lower than those in B, *P*<0.05. *indicates vs. group B, *P*<0.05.

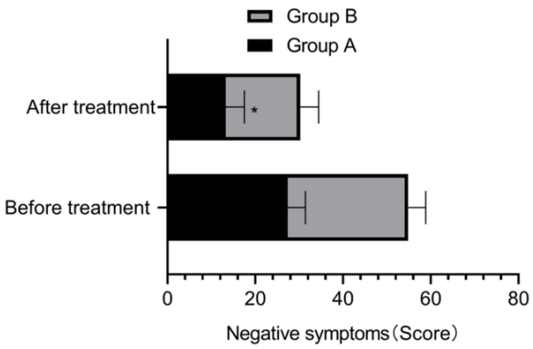

Figure 2. Distinction in negative symptom scores in two groups pre- and post-treatment. The two groups displayed no difference in negative symptom scores before treatment, but exhibited difference following treatment, *P*<0.05.

distribution was tested by independent sample t test. Otherwise, it was examined using Mann-Whitney U test. Enumeration data was expressed as [n(%)], and compared by paired t test. Comparison between groups was performed with X^2 test. *P*<0.05 indicated statistical significance.

Results

Baseline data comparison

Group A: 30 males (63.83%), 17 female (36.17%), age (19-32) years, course of 1-11 months; Group B: 29 males (63.04%), and 17 females (36.96%), age (20-33) years, course of 2-12 months. There was no statistical significance in terms of baseline data such as gender, age, course of disease and years of education in two groups (*P*>0.05) (**Table 1**).

PANSS scores comparison

The general psychopathological scores in group A and B prior to treatment were 39.25 ± 5.52 and 39.28 ± 5.49, and exhibited no obvious distinction (*P*>0.05). The general psychopathological score after treatment in group A was 20.12 ± 2.18, which was lower than 26.96 ± 6.12 of group B (*P*<0.05) (**Figure 1**).

The negative symptom scores before treatment in group A and B were 24.58 ± 3.28 and 24.62 ± 3.25, and exhibited no obvious distinction (*P*>0.05). The negative symptom score following treatment in group A was 10.25 ± 0.28, which was lower than 13.99 ± 0.23 of group B (*P*<0.05) (**Figure 2**).

The positive symptom scores before treatment in group A and B were 25.69 ± 4.18 and 25.72 ± 4.15. The positive symptom scores after treatment in group A and B were 11.25 ± 0.42 and 11.29 ± 0.45, and exhibited no obvious distinction (*P*>0.05) (**Figure 3**).

The total PANSS scores before treatment in group A and B were 91.78 ± 7.25 and 91.82 ± 7.23, with no significant difference (*P*>0.05). PANSS score in group A was 42.12. ± 5.28 following treatment, which was lower than 52.58 ± 5.38 of group B (*P*<0.05) (**Figure 4**).

Distinction in clinical effects of two groups

In group A, 25, 10, 6, and 6 patients were cured, dramatically effective, effective, and ineffective, respectively. The TER was 87.23%. In group B, 23, 11 and 11, 6 and 6 patients were cured, significantly, effective, and ineffective. The TER was 86.96%. No obvious distinction in TER existed (*P*>0.05) (**Table 2**).

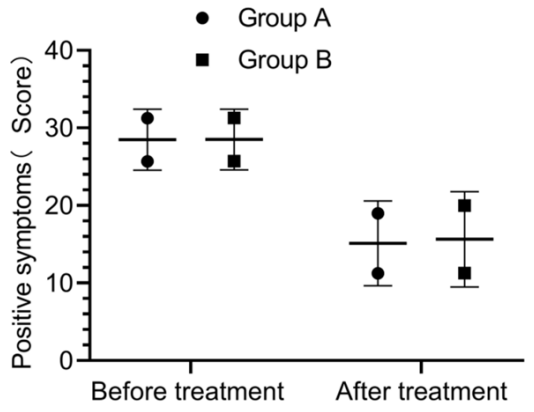

Figure 3. Distinction in positive symptom scores in two groups pre- and post-treatment. The two groups displayed no distinction during pre- and post-treatment, *P*>0.05.

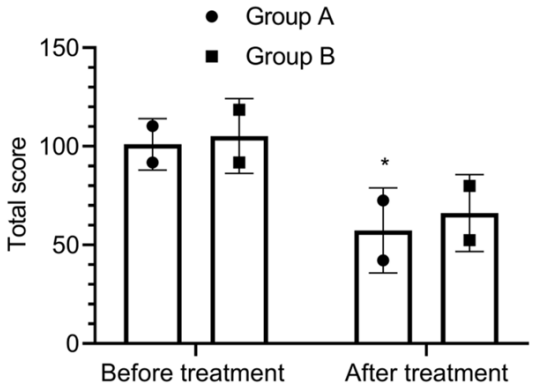

Figure 4. Distinction in total PANSS scores in two groups pre- and post-treatment. The two groups displayed no distinction in total PANSS scores pre- and post-treatment *P*>0.05; *indicates vs. group B, *P*<0.05.

Distinction in PSP scores of two groups

PSP scores of two groups before treatment exhibited no obvious distinction (*P*>0.05). Compared with scores before treatment, the PSP scores were increased after treatment in two groups, and exhibited obvious distinction (*P*< 0.05). No obvious distinction existed in PSP scores between two groups after treatment (*P*>0.05) (**Table 3**).

Distinction in metabolic indicators of two groups

The levels of insulin, ghrelin, adiponectin, leptin before treatment between two groups exhibited no obvious distinction (*P*>0.05). No obvious distinction existed in insulin and adiponectin levels in group A pre- and post-treatment (*P*>0.05). Ghrelin level following treatment in group A was lower than that before treatment, and leptin level exhibited the opposite result (*P*<0.05). Ghrelin level in group B after treatment was not significantly different from that prior to treatment (*P*>0.05). Following treatment, the insulin and leptin levels in group B were higher than those prior to treatment, and the level of adiponectin was lower than that prior to treatment (*P*<0.05). A statistically significant difference existed in the levels of insulin, ghrelin, adiponectin, and leptin following treatment between two groups (*P*<0.05) (**Table 4**).

Distinction in BMI of two groups

BMI prior to treatment between two groups exhibited no obvious distinction (*P*>0.05). BMI before and after treatment in group A exhibited no obvious distinction (*P*>0.05). BMI in group B after treatment was dramatically greater than that prior to treatment (*P*<0.05). The increase of BMI in group B after treatment was dramatically greater than that in A (*P*<0.05) (**Table 5**).

Discussion

Schizophrenia is a highly diagnosed psychiatric disease. Clinically, it is necessary not only to alleviate and control the patient's mental symptoms, but also to improve the social and metabolic functions of patients [16, 17]. In this study, aripiprazole and risperidone were used to treat patients with schizophrenia. Compared with before treatment, the general psychopathological score, negative symptom score, positive symptom score, and total PANSS scores after treatment were decreased (P< 0.05), suggesting that aripiprazole and risperidone can effectively improve the clinical symptoms of patients with schizophrenia.

Except for the positive symptom score, the general psychopathological score, negative symptom score, and the total PANSS scores were lower in group A than in B (P<0.05), suggesting that aripiprazole excelled in improving patients' emotional symptoms and negative symptoms in comparison with risperidone. The reason may be that Aripiprazole is not only a serotonin and dopamine system stabilizer, but also a presynaptic autonomous receptor agonist [18]. In

Table 2. Comparison of clinical efficacy [n(%)]

Grouping	cases	Cured	Markedly effective	Effective	ineffective	Effective rate
A	47	25 (53.19)	10 (21.28)	6 (12.77)	6 (12.77)	41 (87.23)
B	46	23 (50.00)	11 (23.91)	6 (13.04)	6 (13.04)	40 (86.96)
X^2						0.002
P						0.968

Table 3. Comparison of PSP scores between ($\bar{x}$ ± sd)

Grouping	Before treatment	After treatment
A (n=47)	45.52 ± 5.29	75.56 ± 6.18
B (n=46)	45.59 ± 5.23	75.15 ± 6.13
t	0.064	0.321
P	0.949	0.749

the model of DA hyperfunction, aripiprazole displayed strong antagonistic activity, while in the model of dopamine hypofunction, the drug also showed a strong excitatory effect, so the drug could stabilize the dopamine system [19]. At the same time, the drug is also a the serotonin 1A receptor agonist, which has been shown to be effective in improving negative symptoms, cognitive impairment, depression and anxiety in patients with schizophrenia [20].

Increasingly, scholars adopted PSP scores to assess schizophrenia patients' social functions [21]. Studies have shown that 30-70% of patients with schizophrenia can be effectively relieved of sychiatric symptoms after treatment, but their social functioning did not change too much. [22]. There is a close correlation between psychiatric symptoms and schizophrenia patients' social functions. After the patients' psychiatric symptoms are relieved, it is beneficial to ameliorate life quality and social functions [23]. This study showed that compared with those before treatment, the PSP scores of the two groups were increased after treatment, and exhibited obvious difference ($P<0.05$); however, no obvious difference existed between two groups after treatment ($P>0.05$), suggesting that aripiprazole and risperidone can effectively improve social functions of patients with schizophrenia, thus providing the possibility for patients to return to society as soon as possible. This may be because both aripiprazole and risperidone can increase the release of dopamine transmitters in the brain area. The release of dopamine transmitters depends on the early response genes, and fos is one of the common ones. After the action, it will increase the expression of fos gene. After a large amount of fos protein is generated, it will play an important role in the subsequent signal transduction pathway, promote the increase of synaptic release of dopamine, improve the prefrontal correlative function, and reduce mental symptoms, thus improving quality of life and social functions.

Studies have shown that using antipsychotic drugs for a long time can result in weight gain, and there is a close correlation between changes in ghrelin, insulin, adiponectin, and leptin levels and obesity [24]. Leptin is a kind of hormone produced by adipocytes which assumes a key part in regulation of food intake, energy consumption, and neuroendocrine function. By acting on the metabolic regulation center of the hypothalamus, it controls appetite, thereby inhibiting fat synthesis, reducing energy intake, increasing consumption, suppressing insulin secretion, and ultimately energy balance is effectively regulated [25]. Adiponectin is a protein hormone that is secreted from adipose tissue. Clinical studies have shown that there is a close correlation between adiponectin and diabetic vascular disease, atherosclerosis, insulin resistance, type 2 diabetes, and obesity [26]. Ghrelin is an endogenous ligand for the growth hormone secretagogue receptor, which increases appetite and stimulates the release of growth hormone [27]. Insulin is a hormone closely related to substance metabolism and could inhibit lipolysis [28].

The study displayed that no obvious difference existed in the levels of insulin, adiponectin, and BMI in group A following treatment relative to that prior to treatment ($P>0.05$). Ghrelin level after treatment in group A was lower than that prior to treatment, and leptin level exhibited opposite result ($P<0.05$), indicating that aripiprazole mainly affected the concentrations of ghrelin and leptin, and had little effect on insu-

Table 4. Comparison of metabolic indicator ($\bar{x}$ ± sd)

Group	Insulin (uIU/ml)		Ghrelin(ng/ml)		Adiponectin (ug/ml)		Leptin (ng/ml)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
A (n=47)	6.72 ± 0.28	6.65 ± 0.15*	4.15 ± 0.52	3.12 ± 0.22#,*	7.85 ± 0.69	7.69 ± 0.52*	3.96 ± 0.28	5.96 ± 0.25#,*
B (n=46)	6.78 ± 0.25	7.89 ± 2.36#	4.18 ± 0.49	4.19 ± 0.42	7.88 ± 0.63	6.15 ± 0.46#	3.99 ± 0.26	7.99 ± 0.29#
t	1.089	3.595	0.286	15.437	0.219	15.115	0.535	36.181
P	0.279	0.001	0.775	0.000	0.727	0.000	0.594	0.000

Note: #indicates comparison with that before treatment, $P<0.05$; *indicates comparison with group B, $P<0.05$.

Table 5. Comparison of BMI before and after treatment ($\bar{x}$ ± sd, kg/m^2)

Group	Before treatment	After treatment
A (n=47)	64.12 ± 5.12	65.02 ± 5.13*
B (n=46)	64.18 ± 5.23	68.89 ± 6.68#
t	0.056	3.138
P	0.956	0.002

Note: #indicates comparison with that before treatment, $P<0.05$; *indicates comparison with group B, $P<0.05$.

lin and adiponectin levels, and it will not increase the patient's weight after administration. This was consistent with the study of Moroder [29], which is speculated that aripiprazole may regulate leptin concentration through ghrelin, and the combined effect of the two will not increase patients' weight. After treatment, there was no significant difference in ghrelin level in group B as compared with that before treatment. Insulin, leptin and BMI levels in group B after treatment were higher than those prior to treatment, and adiponectin levels were lower than those prior to treatment ($P<0.05$), suggesting that risperidone affected insulin, leptin, adiponectin levels, and BMI, but had little effect on ghrelin level. Mechanistically, atypical antipsychotics can reduce the sensitivity of the central nervous system to leptin signal, reduce adiponectin concentration, and promote appetite and weight gain. In addition, weight gain will activate the ob gene and promote the continuous secretion of leptin. Sustained increase in plasma leptin levels may change the function or quantity of leptin receptors, reduce the biological effects of leptin, leading to leptin resistance and eventually produce insulin resistance. It will also promote weight gain, and in severe cases, it can even cause metabolic syndrome.

In summary, aripiprazole and risperidone have similar clinical effects when treating first-episode schizophrenia, and both can effectively improve the social functioning of patients. Aripiprazole could regulate ghrelin and leptin levels and has no effect on BMI while risperidone has an effect on levels of insulin, leptin, adiponectin, and BMI.

However, due to the limited sample size in the study, the results obtained are not sufficiently representative, which needs to be further explored by expanding the sample size in the future.

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Disclosure of conflict of interest

None.

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