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Effects of lithium carbonate combined with olanzapine on glucose and lipid metabolism in the treatment of bipolar disorder and gender differences

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Abstract: To explore the effect of lithium carbonate combined with olanzapine on glucose and lipid metabolism, as well as gender differences in treating bipolar disorder (BD). 110 BD patients admitted to the Fifth People's Hospital of Luoyang from February 2022 to January 2024 were retrospectively included in the study. Patients were categorized into two groups based on treatment: the single group (lithium carbonate, n = 50) and the coalition group (lithium carbonate + olanzapine, n=60). Post-treatment, the coalition group's YMRS score was 4.67±1.34 points and BRMS score was 24.93±2.30 points, both lower than the single group's YMRS score of 7.64±1.51 points and BRMS score of 34.38±2.30 points ($P<0.05$). The coalition group's effective rate was 96.67%, significantly higher than the single group's 82.00% ($P<0.05$). Post-treatment, the coalition group had lower levels of FBG, TC, TG and LDL-C than the single group, while HDL-C was higher ($P<0.05$). Additionally, glycolipids levels in both male and female subgroups increased post-treatment compared to pre-treatment. The efficacy of lithium carbonate sustained-release tablets combined with olanzapine in the treatment of bipolar disorder (BD) is well-established. This combination therapy can effectively alleviate manic and psychiatric symptoms, enhance patients' social functioning and improve their quality of life. Furthermore, it has a minimal impact on glucose and lipid metabolism, with no observed gender differences.

Keywords: Bipolar disorder, lithium carbonate, olanzapine, glycolipid metabolism, sex difference

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INTRODUCTION

Bipolar disorder (BD), also referred to as bipolar affective disorder, is a prevalent, chronic and recurrent severe mental illness, accounting for 20% to 50% of mood disorders (Arnold *et al*., 2021). The primary clinical manifestations of this disease are hypomanic/manic and depressive episodes, which usually typically undergo a course of relapse and remission. The high rate of morbidity and mortality of BD patients during the chronic and persistent course of the disease renders it one of the primary causes of disability among young and middle-aged individuals. According to the statistics of the World Health Organization, it ranks among the top ten causes of the global disease burden (Nierenberg *et al*., 2021, Falgas-Bague *et al*., 2023). BD patients are often associated with the risks of weight gain, dyslipidemia and disorders of glucose and lipid metabolism, while obesity, dyslipidemia and diabetes are also significant risk factors for cardiovascular diseases (Kong *et al*., 2024, Qiu *et al*., 2022). The pathogenesis of BD is complex and it involves psychological, social and biological factors. Patients with long-term mental disorders and low mood, if not effectively alleviated, are prone to attacks, suicide, and other adverse behaviors, which will significantly affect the life safety of themselves and the people around them (Toledo *et al*., 2022).

Clinically, patients with BD are mostly treated with drugs. Olanzapine tablets are commonly used drugs for clinical treatment of the disease. After use, it can block dopamine receptors and 5-hydroxytryptamine 2A receptors in the brain of patients, reduce nerve excitability and thus relieve mania (Haddad *et al*., 2022, Monahan *et al*., 2022). However, there exist individual variances in the clinical efficacy of olanzapine for the treatment of BD, and some patients have poor efficacy with olanzapine alone. Even some patients often have metabolic syndrome after olanzapine treatment, such as blood glucose and lipid metabolism disorders, which seriously affect the treatment compliance of patients (Nestsiarovich *et al*., 2022). Therefore, it is necessary to combine with other drugs for adjuvant treatment. In clinical work, taking into account the changes in symptoms such as mania and depression in patients with BD, mood stabilizers combined with antipsychotic drugs are more common treatment methods.

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Lithium carbonate sustained-release tablets can promote the reuptake of norepinephrine by the presynaptic membrane, strengthen the activity of monoamine oxidase, and strongly inhibit the release of norepinephrine, improve the activity of catecholamines in the body, which can quickly relieve the mood of BD patients, stabilize the mood, and reduce manic episodes (Han *et al*., 2023, He *et al*., 2023). However, the effect of mood stabilizers such as lithium salt on lipid metabolism is not clear. Some studies suggest that the introduction of lithium salt can increase the risk of lipid metabolism (Joshi *et al*., 2019). Some studies suggest that lithium salt may promote the reduction of blood lipid and blood glucose levels (de Groot *et al*., 2019).

Given that BD patients are often accompanied by abnormal glucose and lipid metabolism and this abnormality not only affects the compliance of disease treatment, but also increases the burden of disease. Therefore, it is of great clinical value to investigate the specific impacts of lithium carbonate combined with olanzapine on glucose and lipid metabolism in the treatment of BD. Additionally, considering the potential differences in gender in the metabolism of sugar and lipids, as well as drug responses, this study also focused on the changes in sugar and lipid metabolism in male and female patients after receiving combined treatment with lithium carbonate and olanzapine. Currently, there is limited research on the effects of lithium carbonate combined with olanzapine treatment on the glycolipid metabolism in patients with BD, as well as any potential gender differences. Therefore, the aim of this study is to investigate the impact of lithium carbonate combined with olanzapine on the metabolism of sugar and lipids in patients with BD, as well as any gender differences.

MATERIALS AND METHODS

Information of participants

The retrospective study included 110 BD patients who were admitted to the Fifth People's Hospital of Luoyang from February 2022 to January 2024. Inclusion criteria: (1) Conforms to the diagnostic criteria for bipolar affective disorder (Ghaemi *et al*., 2022); (2) The patient had no communication difficulties; (3) Informed consent of the patient and his family; (4) No other treatment was received within 2 months before enrollment. (5) Complete medical records, did not quit midway. Exclusion criteria: (1) Patients with drug or alcohol dependence; (2) Consolidate patients with severe organ dysfunction (such as liver, kidney, etc.); (3) Patients with combined immune, blood system diseases or malignant tumors; (4) Patients with suicide and self-harm tendencies; (5) Patients with allergic reactions to quetiapine fumarate and sodium valproate. (6) Patients with poor treatment compliance. This study has been reviewed and approved by the Ethics Committee of our institution (Ethical number: HNK20211108).

During the design phase of this study, we carefully considered potential risks faced by patients with bipolar disorder while implementing appropriate measures to minimize these risks. Simultaneously, we focused on potential benefits associated with this research, which include providing new treatment options for individuals with bipolar disorder, improving their quality of life and advancing knowledge in related fields. We are committed to ensuring that the benefits derived from this research significantly outweigh any potential risks while delivering substantial advantages for our participants.

Patients were categorized into a single group (n=50) and a combination group (n=60) based on the distinctions in the treatment approaches they received. The two sets of baseline data maintain homogeneity (P>0.05), and are comparable (table 1).

Sample size calculation

This study was a case-control study. The sample size was calculated using the formula $n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \times 2\sigma^2}{\delta^2}$. In this case, Z1-α/2 and Z1-β were 1.96 and 1.28, respectively, σ = 2.75, δ = 1.63. According to the formula, it is calculated that $n = \frac{(1.96+1.28)^2 \times 2 \times 2.75^2}{1.63^2} \approx 60$. There were 54 subjects in each of the two groups, considering the loss of follow-up and refusal of follow-up of 5-20% and finally 60 cases in the coalition group and 50 cases in the single group, a total of at least 110 subjects were included.

Methods

Single group: The sustained-release lithium carbonate tablets (Jiangsu Enhua Pharmaceutical Co., Ltd., National Drug Approval Number H10900013, 0.3g) are administered orally at a dose of 0.6-1.5 g/day, with the dosage adjusted based on drug concentration and patient condition.

Coalition group : on the basis of Single group, combined with olanzapine tablets (Qilu Pharmaceutical Co., Ltd.), the initial dose of 10mg orally, 1 time /d, within 7 days according to the patient 's condition can be adjusted to 20 mg orally, once a day, single day medication ≤20mg. Both groups underwent treatment for 8 weeks.

Observation indicators

Young Mania Rating Scale (YMRS) (Samara *et al*., 2023) and the Brief Psychiatric Rating Scale (BPRS) (Hofmann *et al*., 2022) scores: YMRS was used to evaluate the symptoms of mania before treatment and 8 weeks after treatment, respectively. The scale consisted of 11 items, with a total score of 60. 0-5 points indicated no obvious symptoms of mania, and 6-12 points indicated mild symptoms of mania. A score of 13-19 indicates moderate manic symptoms. A score above 20 indicates severe manic symptoms; BRMS was used to evaluate the mental state of the patients pre-treatment and after 8 weeks of

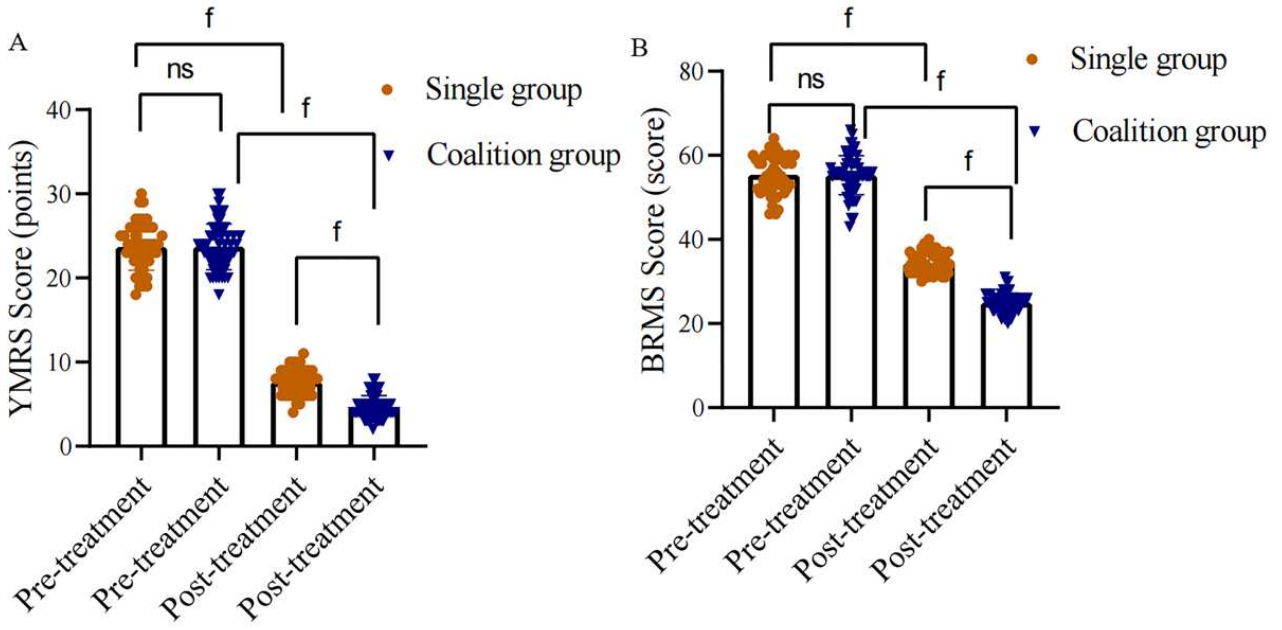

Fig. 1: Comparison of YMRS and BRMS scores between the two groups; A, comparison of YMRS scores between the single group and the coalition group; B, comparison of BRMS scores between the single group and the coalition group; $^{ns}P>0.05$; $^{f}P<0.0000001$

treatment, respectively. There were 18 items in the scale, each item scored 1-7 points and the score was positively correlated with mental symptoms.

(2) Clinical efficacy: The efficacy was evaluated based on the clinical manifestations and BRMS scores of patients. Recovery: All clinical manifestations disappeared and BRMS score decreased by 75%; Obvious effect: There was a significant improvement in the clinical manifestations of patients, with a reduction in the BRMS score ranging from 50%~75%; Effective: The clinical manifestations of the patients were improved and the BRMS score was reduced by 25%~49%; Ineffective: No improvement or exacerbation of the patient's clinical presentation, and a < 25% reduction in BRMS score. Total effective rate is calculated as the sum of recovery, obvious and effective cases divided by the total number of cases, multiplied by 100%.

(3) Glucolipid index and gender differences: Peripheral fasting venous blood was collected before treatment and 8 weeks after treatment to detect fasting blood glucose (FBG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglyceride (TG)] and the changes of each index value in male and female subgroups before and after treatment were recorded.

(4) Social function and quality of life score: Pre and post-treatment, social function was evaluated using the Scale of Social Function in Psychosis Inpatients (SSPI) (Cai *et al*., 2023), which included 12 items including daily living ability, motor and communication ability and social activity ability, with 0 to 4 points for each item and a total score of 48 points. The score is in proportion to the social function. The quality of life was assessed by means of the 36-items short form health survey (SF-36) (Cohen *et al*., 2022), which encompassed four aspects of emotional function, social function, mental health and physiological function. Each item scored 0-100 points and the total score was 400 points. The score is in proportion to the quality of life.

(5) Adverse reactions: including nausea and vomiting, lethargy, tachycardia, limb weakness, etc.

Ethical approval

This study was approved by the Fifth People's Hospital of Luoyang, reference No.HNK20211108.

STATISTICAL ANALYSIS

The project data were processed using statistical software (IBM SPSS 29.0). The measurement data confirmed by K-S test to be consistent with normal distribution were described in (mean±sd) form. Counting variables are described by [n(%)]; The above descriptions were described by t test and $\chi 2$ test. $P<0.05$ indicated that the difference was statistically significant.

RESULTS

YMRS and BRMS scores

Pre-treatment, the YMRS score and BRMS score of the coalition group were (23.70±2.71) points and (55.28±4.64) points and the YMRS score and BRMS score of the single group were (23.68±2.75) points and (55.36±4.53) points.

Table 1: Comparison of baseline data of patients

Group	Age (years)	Sex		Course of disease (d)	BMI(kg/m^2)
		Male	Female		
Coalition group (=60)	36.33±7.59	21(35.00)	39(65.00)	9.43±1.98	23.24±2.43
Single group (n=50)	35.26±7.30	18(36.00)	32(64.00)	9.18±2.21	23.43±2.34
t/χ^2	-0.750	0.012		-0.634	0.418
P	0.455	0.913		0.527	0.677

Table 2: Comparison of clinical efficacy between coalition group and single group.

Group	Cure	Obvious	Effective	Invalid	Total effective rate (%)
Coalition group (n=60)	19(31.67)	26(43.33)	13(21.67)	2(3.33)	58(96.67)
Single group (n=50)	10(20.00)	17(34.00)	14(28.00)	9(18.00)	41(82.00)
χ^2					8.328
P					0.040

Table 3: Changes of glycolipid indexes in the two groups before and after treatment.

Group	FBG (mmol/L)		TC (mmol/L)		TG (mmol/L)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Coalition group(n=60)	4.53±0.62	5.08±0.62	3.77±0.48	4.13±0.78	1.16±0.34	1.36±0.30
Single group(n=50)	4.45±0.60	5.82±0.63	3.75±0.51	4.66±0.93	1.19±0.35	1.54±0.51
t	-0.595	6.2225	-0.316	3.256	0.456	2.284
P	0.553	<0.001	0.752	0.002	0.650	0.024
Group		HDL-C (mmol/L)		LDL-C (mmol/L)		
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	
Coalition group(n=60)		1.36±0.34	1.56±0.41	2.17±0.46	2.20±0.51	
Single group(n=50)		1.37±0.31	1.36±0.35	2.15±0.44	2.46±0.79	
t		0.161	-2.815	-0.232	2.055	
P		0.873	0.006	0.817	0.042	

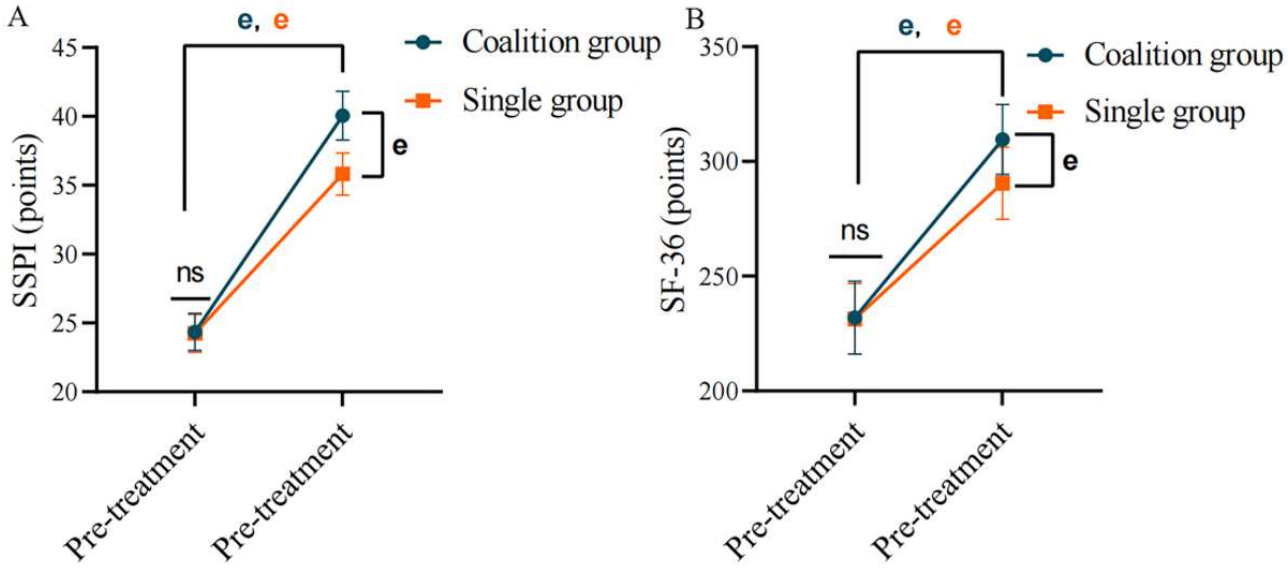

Fig. 2: Comparison of SSPI score and SF-36 score between the two groups; A, comparison of SSPI scores between the coalition group and the single group; B, comparison of SF-36 scores between the coalition group and the single group; $^{ns}P>0.05$; $^{e}P<0.000001$

Table 4: Comparison of glycolipid indexes between male and female groups pre and post-treatment

Group	FBG(mmol/L)	TC(mmol/L)	TG(mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
Coalition group					
Male(n=21)					
Pre-treatment	4.44±0.61	3.80±0.36	1.24±0.35	1.34±0.33	2.21±0.47
Post-treatment	5.05±0.70	4.21±0.67	1.44±0.23	1.61±0.49	2.09±0.50
t	3.044	2.424	2.170	2.144	-0.763
P	0.004	0.020	0.036	0.041	0.450
Female(n=39)					
Pre-treatment	4.57±0.64	3.76±0.53	1.12±0.34	1.36±0.36	2.16±0.46
Post-treatment	5.09±0.60	4.03±0.83	1.31±0.33	1.54±0.36	2.27±0.50
t	3.777	2.054	2.500	2.134	0.989
P	<0.001	0.043	0.015	0.036	0.326
Single group					
Male(n=18)					
Pre-treatment	4.56±0.77	3.90±0.50	1.24±0.36	1.42±0.27	2.18±0.38
Post-treatment	5.83±0.56	4.62±0.80	1.64±0.39	1.39±0.39	2.54±0.81
t	5.728	3.257	3.249	0.219	-1.742
P	<0.001	0.003	0.003	0.828	0.091
Female(n=32)					
Pre-treatment	4.40±0.51	3.66±0.50	1.17±0.34	1.34±0.34	2.14±0.47
Post-treatment	5.82±0.68	4.67±1.00	1.48±0.56	1.33±0.34	2.41±0.78
t	9.515	5.139	2.632	0.022	1.679
P	<0.001	<0.001	0.011	0.982	0.098

Table 5: Security comparison between the two groups

Group	Nausea and vomiting	Drowsiness	Tachycardia of heart	Limb weakness	Total incidence (%)
Coalition group (n=60)	2(3.33)	2(3.33)	1(1.67)	2(3.33)	7(11.67)
Single group (n=50)	2(4.00)	1(2.00)	1(2.00)	1(2.00)	5(10.00)
χ^2					0.343
P					0.952

The homogeneity was maintained in the comparison between the two groups (P>0.05). Post-treatment, YMRS score of (4.67±1.34) and BRMS score of (24.93±2.30) in the coalition group were lower than those in the single group (7.64±1.51) and BRMS score of (34.38±2.30) (P < 0.05). As shown in fig. 1.

Clinical effect

In terms of overall effectiveness, the coalition group demonstrated a significantly higher rate of 96.67%, as opposed to 82.00% for the single group (P<0.05) (table 2).

Changes in glycemic and lipid indexes of Coalition group and Single group

Pre-treatment, FBG, TC, TG, HDL-C and LDL-C of the two groups were homogeneous (P > 0.05). Post-treatment, the coalition group showed lower levels of FBG, TC, TG, and LDL-C compared to the single group, while HDL-C was higher (P<0.05) (table 3.

Comparison of glycolipid indexes between male and female groups before and after treatment

They were respectively categorized into male and female subgroups based on the coalition group and the single group. The results showed that FBG, TC, TG and HDL-C in the male and female subgroups of the coalition group were higher after treatment than pre-treatment (P<0.05). FBG, TC, TG in male and female subgroups in Single group were higher than before treatment (P<0.05). Pre and post-treatment, FBG, TC, TG, HDL-C and LDL-C in the male and female subgroups of both the coalition group and the single group were all homogeneous (P>0.05) (table 4).

Social functioning and quality of life scores

Pre-treatment, the SSPI score and SF-36 score of the coalition group were (24.35±1.34) and (231.90±15.90) respectively, while the SSPI score and SF-36 score of the single group were (24.24±1.38) and (231.40±15.38) respectively. The homogeneity was maintained in the comparison between the two groups (P>0.05). Post-treatment, the SSPI score of (40.05±1.77) and SF-36 score of (309.52±15.28) in the coalition group were higher than that of the single group (35.82±1.53) and SF-36 score of (290.50±15.65) (P<0.05). As shown in fig. 2.

Safety comparison between the two groups

The overall incidence of adverse reactions was 11.67% lower in the coalition group compared to the single group (P < 0.05) (table 5).

DISCUSSION

Currently, the etiology of BD remains unclear; however, it has been affirmed that depression or elevated mood, continuous decline in motivation and energy constitute the core symptoms of BD. The majority of patients will also be accompanied by varying degrees of pessimism, despondency and impulsiveness and may even harm themselves or others through words and actions, seriously endangering their own and others' life safety (Lemvigh *et al*., 2021, Cavieres *et al*., 2023).

Additionally, BD is characterized by recurrent and alternating episodes, a prolonged disease course, mixed prolongation and varying durations of intermittent attacks. During the periods of remission, patients generally exhibit relatively normal social functioning; However, some individuals may experience impairments in their social capabilities. The frequency of recurrent episodes tends to increase over time, complicating the overall clinical picture. Consequently, long-term pharmacological treatment is often necessary to maintain stability in the patient's condition. Nevertheless, it is important to consider the potential side effects associated with these medications, as they can significantly impact glucose and lipid metabolism in affected individuals (Fang *et al*., 2023).

Olanzapine tablets are among the most commonly utilized medications in the clinical management of BD. It is a typical antipsychotic drug that can release a quantitative amount of antihistamine H1 receptor, adrenergic receptor and limbic pathway D2 receptor within the body, thereby alleviating the manic symptoms of patients. Nevertheless, the efficacy of single-drug usage is limited. Long-term high-dose drug administration will increase adverse drug reactions, and the overall efficacy is relatively restricted, thus it is necessary to assist with other drugs to enhance the therapeutic effect (Kahn *et al*., 2023, Corrao *et al*., 2022). Lithium carbonate sustained-release tablets are currently the most widely employed mood stabilizer in clinical practice, which can facilitate the presynaptic membrane reuptake of norepinephrine, promote the degradation of norepinephrine within neurons, regulate catecholamines, and improve the manic manifestations of patients (Fountoulakis *et al*., 2022, Kohler-Forsberg *et al*., 2023). The results of this study indicated that post-treatment, the YMRS scores and BPRS scores of the coalition group were lower than those of the single group; In terms of overall effectiveness, the coalition group demonstrated a higher rate of 96.67%, as opposed to 82.00% for the single group ($P<0.05$). The combination of lithium carbonate sustained-release tablets and Olanzapine has been shown to effectively improve the psychiatric symptoms and manic symptoms in patients with BD. The potential mechanism underlying the efficacy of olanzapine may be attributed to its strong antagonistic effects on human neurotransmitter receptors, including 5-HT2A and dopamine receptor D2 (DRD2). Additionally, olanzapine enhances the affinity for histamine (HA) receptors and adrenergic α1 receptors (ARS-α1), thereby improving neural conduction and excitability in patients with bipolar disorder. This pharmacological action contributes to a reduction in manic symptoms and alleviates depressive episodes. Lithium carbonate sustained-release tablets exert their therapeutic effects by non-specific inhibition of glycogen synthesis kinase 3, which leads to a decrease in energy uptake by abnormal brain tissue. Furthermore, lithium promotes norepinephrine reuptake at the presynaptic membrane, enhances monoamine oxidase activity, reduces norepinephrine release and facilitates effective alleviation of various psychiatric symptoms experienced by patients. The combined administration of the two agents can synergistically diminish neural excitability in individuals with bipolar disorder while enhancing their subjective resilience to stress. Consequently, this combination therapy further improves the mental health outcomes associated with BD (He *et al*., 2023, Uwai Y and Nabekura T *et al*., 2022, Sun *et al*., 2022).

This study discovered that subsequent to treatment, the coalition group showed lower levels of FBG, TC, LDL-C and TG compared to the single group, while HDL-C was higher ($P<0.05$). It is indicated that the combination of lithium carbonate sustained-release tablets and olanzapine has a negligible impact on the lipid and glucose metabolism indices of BD. The mechanism by which olanzapine influences the glucose and lipid metabolism indices remains unclear. Some research has suggested that olanzapine can inhibit the insulin signaling pathway and interfere with the insulin sensitivity of muscles, fat and the liver. Olanzapine can also inhibit serotonin receptors and dopamine receptors, thereby influencing neuroendocrine regulation, which might lead to the elevation of blood sugar and blood lipid (Yang *et al*., 2024). It can further interfere with some crucial metabolic enzymes, such as CYP2D6, CYP3A4, and UGT1A4, thus affecting drug metabolism and liver function and subsequently resulting in hyperglycemia and hyperlipidemia (Belancic *et al*., 2024, Korosec Hudnik *et al*., 2024). During the process of drug metabolism, there is no direct evidence suggesting that lithium carbonate can inhibit sugar and lipid metabolism. In this study, the combination of lithium carbonate sustained-release tablets and olanzapine has a limited effect on the glycolipid metabolism indices of BD. It is considered that lithium carbonate tablets can facilitate the release of 5-hydroxyserotonin, significantly suppress aggressive behavior, and ameliorate mania symptoms, thereby alleviating metabolic disorders caused by antipsychotics, and thus effectively enhancing the glycolipid metabolism of patients.

Pahwa (Pahwa *et al*., 2022) found that, compared to male patients with bipolar disorder (BD), female BD patients

exhibit similar cardiovascular risk; Related studies (Tomasik *et al*., 2024, Kim *et al*., 2022) suggest that physiological fluctuations in sex hormones may render some women more susceptible to emotional instability, yet research on the mechanisms underlying this association remains limited. Investigating biological models involving estrogen, progesterone, and other steroid hormones has the potential to yield new therapeutic strategies that could alter the course of bipolar disorder in women. Lin (Lin *et al*., 2022) reported significant disturbances in glucose and lipid metabolism among patients with bipolar disorder, noting substantial gender differences in levels of TC, TG, HDL-C and LDL-C. Conversely, (Ezzaher *et al.,* 2011) argued that dysregulation of lipid metabolism in bipolar disorder patients is independent of age and gender. In this study, the two groups of patients were respectively classified into male and female subgroups. The results demonstrated that post-treatment, the FBG, TC, TG and HDL-C in both the male and female subgroups of the coalition group were higher than pre-treatment. And the FBG, TC and TG in the male and female subgroups of the single group were higher than pre-treatment ($P<0.05$). It is suggested that the sex difference might not be associated with the metabolic risk induced by the combination of lithium carbonate sustained-release tablets and olanzapine. The analysis suggests that the potential reason for the findings may be attributed to the fact that lithium carbonate sustained-release tablets are primarily used in the treatment of manic episodes, while olanzapine is classified as an antipsychotic medication. The mechanisms of action for these two drugs may not be influenced by gender; therefore, their associated metabolic side effects might also lack gender specificity. Furthermore, this study could be limited by sample size or sensitivity of statistical methods, which may hinder the detection of subtle differences between genders and consequently fail to identify any impact of gender on metabolic risk.

The results of this study revealed that post-treatment, the coalition group showed lower YMRS and BRMS scores compared to the single group. It is recommended that the combination of sustained-release lithium carbonate tablets and olanzapine tablets may enhance the cognitive function and improve the quality of life for patients with BD. Furthermore, it has been determined that this medication is safe for use. Analysis reveals that patients with BD demonstrate decreased attentional focus, as well as a significant decline in social functioning and quality of life; The combination of lithium carbonate sustained-release tablets and olanzapine exerts a synergistic effect by selectively blocking the activity of dopamine D2 receptors, inhibiting the excitability of the central nervous system, effectively suppressing the activity of serotonin receptors, stimulating the activity of post-synaptic membrane D1 receptors, and relieving the inhibitory state of norepinephrine. It can also exert a cholinergic role, promote the transport of acetylcholine in the cerebral cortex and hippocampus, and facilitate the uptake and utilization of glucose in the brain tissue, thereby improving cognitive function, social function, and quality of life. Additionally, there was no significant difference in the overall incidence of nausea, vomiting, lethargy, tachycardia, and limb weakness between the single drug group and the combination drug group during treatment. This suggests that combined drug usage does not elevate the risk of adverse reactions and is considered safe. The present study does have some limitations that should be acknowledged: (1) The sample size of this research is relatively small, and as it is an observational study, it may not fully capture the long-term effects of lithium and olanzapine on metabolic parameters. (2) Additionally, this study did not adequately consider other potential confounding variables that could influence metabolic parameters, such as patients' age, gender and body mass index. These factors might interfere with the results and lead to biased conclusions. (3) Furthermore, the observation period in this study was limited, making it difficult to assess the sustained impact of lithium and olanzapine on metabolic parameters. Therefore, we believe that future research should focus on longitudinal designs with larger sample sizes while controlling for confounding variables across multiple centers in a prospective manner to further explore these important issues.

CONCLUSION

The efficacy of lithium carbonate sustained-release tablets combined with olanzapine in the treatment of bipolar disorder (BD) is well-established. This combination therapy can effectively alleviate manic and psychiatric symptoms, enhance patients' social functioning, and improve their quality of life. Furthermore, it has a minimal impact on glucose and lipid metabolism, with no observed gender differences.

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