Diagnostic Brain Medicine

CLINICAL RESEAPCH

Clinical Efficacy of Quetiapine-assisted Brintellix in the Treatment of TRD Patients and the Effect on Nerve Factor and Cognitive Function

Min Shi

Zhejiang Rehabilitation Medical Centre, The Third Hospital of Zhejiang University of Chinese Medicine

Keywords

Quetiapine fumarate tablets, Brintellix, Treatment resistant depression, Nerve factor, Cognitive function

Correspondence

Min Shi, Zhejiang Rehabilitation Medical Centre, The Third Hospital of Zhejiang University of Traditional Chinese Medicine, 2828 Bin Sheng Road, Binjiang District, Hangzhou, Zhejiang Province.

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Abstract

Objective This work explored the clinical efficacy of treatment of quetiapine fumarate tablets combined with vortioxetine hydrobromide tablets (brintellix) in patients with treatment resistant depression (TRD), and the effect of cognitive function and nerve factor. **Methods** A total of 116 TRD patients in our hospital from Aug. 2018 to Aug. 2020 were selected and divided into control group (n=58) and study group (n=58) by the random number table method. Control group and study group were treated with brintellix and quetiapine fumarate tablets combined with brintellix, respectively. The clinical efficacy, nerve factor, montreal cognitive assessment scale (MOCA) score, hamilton depression scale (HAMD) score and occurrence of adverse reactions of two groups were compared before and after treatment. **Results** The total effective rate was obviously lower in control group than that in study group (P<0.05). The levels of myelin basic protein (MBP), neuron-specific enolase (NSE) and HAMD score of both groups were obviously decreased after treatment relative to before treatment (P<0.05), and those in control group after treatment were obviously increased in comparison with those in study group after treatment (P<0.05). The level of brain derived neurotrophic factor (BDNF) and MOCA score were obviously increased after treatment in contrast with before treatment (P<0.05), and those of control group after treatment were obviously declined in comparison with those of study group after treatment (P<0.05). There was no significant difference in the incidence rate of adverse reactions between control group and study group (χ^2=0.048, P=0.826). **Conclusion** Quetiapine fumarate tablets combined with brintellix had significant efficacy in the treatment of TRD patients, and it could improve nerve factor level and nerve function, alleviate the degree of depression and raise cognitive function of patients.

Introduction

As a mental disorder, depression is clinically

characterized by low spirits, loss of interest in things and retardation of thought [1, 2]. Treatment resistant depression (TRD) is a depression without clinical symptom improvement after treatment of two different kinds of antidepressants with sufficient dose and sufficient course, which results in serious negative impact on life quality and mental health of patients [3]. Hence, therapeutic approaches with good curative effect and powerful antidepressant activity on mitigating clinical symptoms have an important significance for ameliorating quality of life of patients. A former study found that application of drug combination in the clinical treatment for TRD patients achieved good antidepressant effect [4]. Quetiapine fumarate tablets are a mood stabilizer fulfilling the sedative function through blocking 5-hydroxytryptamine (5-HT) and dopamine (DA) receptors in the nerve center [5]. Vortioxetine hydrobromide tablets (brintellix), a strong 5-HT reuptake inhibitor as well as a 5-HT1A receptor agonist, possess antidepressant and anxiolytic effects. The present research observed the clinical efficacy of quetiapine fumarate tablets combined with brintellix in the treatment for patients with TRD and its influence on never factor and cognitive function.

Data and methods

Clinical data

A total of 116 TRD patients in our hospital from Aug. 2018 to Aug. 2020 were selected and divided into control group (n=58) and study group (n=58) by the random number table method. The general information of each case comprising sex, age and course of disease was collected from patient records. Control group: sex, 21 males and 37 females; age, 25-58 years; average age, (41.51±8.85) years; course of disease, 1-75 months; average course of disease, (39.34±5.25) months. Study group: sex, 23 males and 35 females; age, 23-54 years; average age, (42.23±7.22) years; course of disease, 1-81 months; average course of disease, (37.84±5.67) months. There was no significant difference in general information between two groups (P>0.05). This study was approved by the Ethics Committee of in our hospital. All patients were willing to participate and signed informed consent.

Inclusion and exclusion criteria

Inclusion criteria

Patients met the diagnostic criteria of TRD in *Classification and Diagnostic Criteria of Mental Disorders in China* [6] without suicidal tendency.

Exclusion criteria

Patients were accompanied by central nervous system diseases, manic depression, other mental diseases, malignant tumors, immune diseases or allergic to brintellix or quetiapine fumarate tablets.

Methods

Control group

Control group received oral brintellix (Vortioxetine Hydrobromide Tablets, 10 mg*14 tablets; registration certificate number H20170383, H.Lundbeck A/S, Denmark) treatment with an initial dosage of 0.01 g/d which was increased to 0.02 g/d after 10 days. The treatment lasted for 8 weeks.

Study group

On the basis of the treatment in control group, study group was additionally treated with oral quetiapine fumarate tablets (25 mg*20 tablets; country medicine accurate character J20171029, registration certificate number H20160664, AstraZeneca UK limited, UK) with an initial dosage of 0. 1 g/d which was increased to 0. 2 g/d after 10 days. The treatment lasted for 8 weeks.

Outcome measures

1. Clinical efficacy: the clinical efficacy was evaluated according to the therapeutic effect standards in *Classification and Diagnostic Criteria of Mental Disorders in China* [7]. Markedly effective: clinical symptoms of patients basically disappeared; hamilton depression scale (HAMD) score reduced no less than 75%. Effective: clinical symptoms of patients partially disappeared; HAMD score reduced no less than 50%. Ineffective: clinical symptoms of patients did not

change obviously or even deteriorated; HAMD score reduced no more than 50%. The total effective rate = (markedly effective cases+ effective cases)/total cases ×100%.

2. Nerve factor: Before and after treatment, the fasting venous blood (3 mL for each) of patients was taken and enzyme linked immunosorbent assay (ELISA) was used to detect myelin basic protein (MBP), neuron-specific enolase (NSE) and brain derived neurotrophic factor (BDNF) levels.

3. Montreal cognitive assessment scale (MOCA) score: the cognitive function of patients was assessed by MOCA [8]. The scale had 11 items with a total score of 30 and score > 26 indicated a normal cognitive function.

4. HAMD score: HAMD was adopted for depression evaluation [9]. The scale had 17 items with a total scale of 0-53. Severe depression: 24-53; mild or moderate depression: 17-24; no depression: 0-7.

5. Adverse reaction: the adverse reactions containing nausea, dry mouth, constipation, dizziness and palpitation were observed.

Statistical analysis

Statistical analysis was operated by SPSS 20.0 (IBM, Armonk, NY, USA). The enumeration data was compared through χ^2 test whereas measurement data performed as the means ± standard deviation were contrasted using Student's *t* test. A statistically significant difference was accepted when $P<0.05$.

Results

Clinical efficacy

There existed marked difference in clinical efficacy between two groups, as the total effective rate of control group was appreciably lower than that of study group (Table 1, $P<0.05$).

Table 1 Clinical efficacy of patients [n (%)]

Group	n	Cured	Markedly effective	Effective	Ineffective	Total effective rate
Control	58	11 (18.97)	13 (22.41)	16 (27.59)	18 (31.03)	40 (68.97)
Study	58	19 (32.76)	17 (29.31)	15 (25.86)	7 (12.07)	51 (87.93)
χ^2						6.170
P						0.013

Nerve factor level

Before treatment, levels of MBP, NSE and BDNF did not differ notably between two groups (Table 2, $P>0.05$). After treatment, both groups reduced MBP and NSE levels relative to before treatment (Table 2, $P<0.05$), with MBP and NSE levels in control group higher than those in study group (Table 2, $P<0.05$), while BDNF level of two groups after treatment was higher than before treatment (Table 2, $P<0.05$) and control group declined BDNF level in comparison with study group (Table 2, $P<0.05$).

Table 2 Nerve factor level of patients ($\bar{x}\pm s$, μg/L)

Group	n	MBP		NSE		BDNF	
		Before	After	Before	After	Before	After
Control	58	11.73±1.95	8.18±1.08*	20.68±3.27	16.08±2.4*	22.74±3.54	37.24±4.31*
Study	58	11.27±1.62	5.94±0.74*	20.02±2.88	13.28±1.8*	23.03±2.58	41.45±4.96*

t	1.382	13.030	1.154	6.945	0.504	4.879
P	0.170	0.000	0.251	0.000	0.615	0.000

Compared with before treatment, **P*<0.05

Cognitive function and depression score

No obvious difference in scores of MOCA and HAMD was viewed between two groups before treatment (Table 3, *P*>0.05), whereas after treatment MOCA score was increased in two groups while HAMD score is decreased in contrast with before treatment (Table 3, *P*<0.05), as MOCA score after treatment of control group was lower than that of study group (Table 3, *P*<0.05) and HAMD score after treatment of control group was higher than that of study group (Table 3, *P*<0.05).

Table 3 Cognitive function and depression score of patients ($\bar{x}$±s , point)

Group	n	MOCA		HAMD	
		Before	After	Before	After
Control	58	18.42±1.32	26.35±1.79*	21.63±3.12	12.33±1.7*
Study	58	18.64±1.02	28.12±1.07*	22.02±2.75	8.42±1.33*
t		1.004	6.464	0.714	13.401
P		0.317	0.006	0.477	0.000

Compared with before treatment,**P*<0.05

Adverse reaction occurrence

As shown in Table 4, the incidence of adverse reactions was not significantly different between two groups (χ^2=0.048, *P*=0.826).

Table 4 Adverse reaction occurrence of patients [n (%)]

Group	n	Nausea	Dry mouth,	Constipation	Dizziness	Palpitation	Incidence of adverse reactions
Control	58	5 (8.62)	3 (5.17)	1 (1.72)	2 (3.45)	3 (5.17)	14 (24.14)
Study	58	3 (5.17)	3 (5.17)	2 (3.45)	1 (1.72)	4 (6.70)	13 (22.41)
χ^2							0.048
P							0.826

Discussion

In recent years, with the improved living standards and accelerated pace of life, the number of population suffering from depression is gradually increasing. Depression patients with long-term low spirits appear inferiority complex, feel hopeless about the future, or even become pessimistic, harm themselves and commit suicide, which brings heavy mental pressure and economic burden to patients and their families. Thus, for patients with depression, especially TRD, selecting treatment strategies which can reduce the rates of self-mutilation and suicide to the maximum

for depression amelioration is helpful for patients' recovery. Currently, clinical treatment methods for TRD patients are composed of dosage increase, drug change and combination therapy [10]. This study utilized brintellix alone and quetiapine fumarate tablets combined with brintellix to treat patients with TRD, the consequences of which exhibited that the total effective rate in study group was significantly higher than that in control group, implicating the better therapeutic effect of quetiapine fumarate tablets combined with brintellix.

Researches have demonstrated that the occurrence of depression connects with disturbance of neurotransmitter secretion caused by hippocampal nerve injury [11]. Nerve factor level can reflect the degree of nerve injury to a certain extent: MBP is a strong alkaline membrane protein synthesized by oligodendrocytes and schwann cells, whose level is able to suggest severity of nerve function damage; NSE is an acid protease [12]; BDNF, a neurotrophic factor generated by target cells, play a positive role in neuron nutrition, protection and repair [13]. In our work, both groups appreciably improved MBP, NSE and BDNF levels after treatment when contrasted with before treatment, with the degree of improvement after treatment in study group was dramatically higher than that of control group. Those findings implied that quetiapine fumarate tablets combined with brintellix achieved a marked therapeutic effect in the treatment of TRD patients, which could mitigate nerve injury and ameliorate nerve factor level. Brintellix can bind to G protein-related receptors to activate 5-HT1A receptors and elevate the release of neurotransmitters such as 5-HT and DA, thereby declining damage of neurons. Besides, quetiapine fumarate tablets is able to promote neural precursor cell proliferation in the hippocampus, facilitate neuronal regeneration and improve neuronal function so as to down-regulate levels of MBP and NSE while up-regulate BDNF level.

Cognitive function refers to the comprehensive ability that the brain identifies, integrates and processes information to solve problems and finish goals [14]. However, owing to long-term low spirits, patients with TRD are unable to normally think and judge, which affects their cognitive function: MOCA score is a pivotal index reflecting cognitive function; HAMD score can exactly reflect the degree of depression in time. This study viewed that scores of MOCA and HAMD in two groups after treatment obviously improved when contrasted with those before treatment, in which study group performed better than control group, revealing that patients with TRD ameliorated cognitive function and depression after treatment and quetiapine fumarate tablets combined with brintellix treatment had the more remarkable therapeutic effect. Brintellix suppresses 5-HT reuptake of presynaptic membrane and up-regulates 5-HT level in synaptic cleft so as to enhance neurotransmission function of 5-HT and improve cognitive function; quetiapine fumarate tablets can bind to receptors of 5-HT and DA, selectively activate mesolimbic system and nerve cells in the prefrontal region, advance release of transmitters including DA and NE in the prefrontal region and ameliorate cognitive function. Moreover, there was no significant difference in incidence of adverse reactions between two groups, suggesting a certain safety of quetiapine fumarate tablets combined with brintellix in the treatment for TRD patients.

All in all, quetiapine fumarate tablets combined with brintellix had the more significant efficacy in the treatment of TRD patients, and it could improve nerve factor level and nerve function, raise cognitive function and alleviate depression of patients.

Declaration of conflict-of-interest

The authors declare no conflict-of –interest.

References

[1] Qian Z, Feng L, Zhang G, et al. Research progress on agomelatine in the treatment for depression [J]. China Pharmacy,2019,30(17):2435-2440.

[2] Ruberto VL, Jha MK, Murrough JW. Pharmacological Treatments for Patients with Treatment-Resistant Depression[J]. Pharmaceuticals (Basel). 2020, 13(6):116.

[3] Zhi Z, Wang Y, Zhang T, et al. Effect of Jieyu Pill Combined with Citalopram on NE, 5-HT, BDNF

Level and social function in patients with refractory depression [J]. Journal of International Psychiatry,2019,46(04):672-674.

[4] Xi Z, Zhu F, Shi X, et al. Discussion on drug therapy for treatment resistant depression from pharmacological mechanism [J]. Journal of International Psychiatry,2018,45(03):409-412.

[5] Fang L, Fan Y, Zhang Y, et al. The effect of quetiapine fumarate and magnesium valproate sustained release tablets combined with lithium carbonate in patients with manic attack of bipolar disorder [J]. Journal of International Psychiatry,2019,46(01):81-83+95.

[6] Cui G, Ke Q, Zhang P, et al. Clinical Observation of Mirtazapine Combined with Citalopram in the Treatment of Sleep Disorder of De-pressive Patients [J]. China Pharmacy,2017,28(05):670-673.

[7] Jing C, Ling D. Effects of paroxetine combined with exercise behavior intervention on the treatment of depression and the level of γ-aminobutyric acid [J]. International Journal of Laboratory Medicine,2020,41(20):2485-2488.

[8] Wen Z, Xu X, Zeng Y, et al. Comparison of the cognitive impairment in late-life depressive patients with different degree of depression [J]. Journal of Clinical Psychiatry,2020,30(01):12-14.

[9] Hai Y, Fan F, Chen X, et al. Clinical Observation of Jieyu Pill Combined with Mirtazapine in Treating Refractory Depression [J]. World Chinese Medicine,2020,15(10):1454-1457.

[10] Ke X, Li X, Fang J, et al. Clinical research progress on vagus nerve stimulation in the treatment of treatment resistance depression [J]. Journal of International Psychiatry,2020,47(02):236-239.

[11] Hui W, Wang Z, Lin M, et al. Adcance in neurotrophin abnormality on pathogenesis of depression [J]. Chinese Pharmacological Bulletin,2020,36(10):1333-1337.

[12] Yan L, Liu Z, Chen L, et al. Influence of Paroxetine Combined with High Frequency Repetitive Transcranial Magnetic Stimulation on Cognitive Functions, MBP and NSE of Elderly Patients with Treatment-refractory Depression [J]. Journal of International Psychiatry,2017,44(01):12-15.

[13] Ji L, Yang J, Liu A. The therapeutic effect of duloxetine and venlafaxine in thetreatment of elderly depression and its influence on serum brain-derived neurotrophic factor, 5-hydroxytryptamine and norepinephrine [J]. Chinese Journal of Gerontology,2018,38(24):6012-6014.

[14] Wen C. Relationship between anxiety-depression emotions and cognitive impairment in patients with anxiety disorder [J]. China Modern Doctor,2018,56(36):93-95.