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Effects of donepezil on emotion, cognitive function, and inflammatory factors in patients with Hashimoto's thyroiditis

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ABSTRACT

Objective: To investigate the impact of donepezil on emotional responses, cognitive function, and inflammatory factors in patients with Hashimoto's thyroiditis (HT).

Methods: A total of 109 patients with Hashimoto's thyroiditis treated in the Department of Endocrinology at Huangshan Shoukang Hospital between February 2021 and May 2024 were selected for this study. The patients were randomly divided into a treatment group (n = 54) and a control group (n = 55) using a random number table. The treatment group was administered donepezil hydrochloride tablets and vitamin C tablets orally in the morning on an empty stomach, while the control group received only vitamin C tablets under the same conditions. Both groups followed this regimen for three months. Outcomes were assessed using the Mini-Mental State Examination (MMSE), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), thyroid hormone levels, and inflammatory markers.

Results: There were no statistically significant differences in thyroid hormone levels (T3, T4, TSH) or thyroid antibodies (TGAb, TPOAb) between the two groups before or after treatment ($P > 0.05$). Prior to treatment, MMSE, SAS, and SDS scores were comparable between the groups ($P > 0.05$). After treatment, MMSE scores in the treatment group were significantly higher, while SAS and SDS scores were significantly lower compared to the control group ($P < 0.05$). Additionally, no baseline differences in inflammatory factors were observed ($P > 0.05$), but after treatment, serum levels of IL-6, IL-4, IL-1β, and TNF-α were significantly lower in the treatment group compared to the control group ($P < 0.05$).

Conclusion: Donepezil can improve cognitive function and emotional responses in patients with Hashimoto's thyroiditis, which may be related to the downregulation of key inflammatory factors.

Introduction

Hashimoto's thyroiditis (HT) is a common autoimmune thyroid disease, characterized by elevated levels of thyroid peroxidase antibodies (TPOAb) and anti-thyroglobulin antibodies (TGAb). It has an insidious onset and is accompanied by persistent lymphocytic infiltration into thyroid tissue and subsequent tissue destruction, making it one of the primary causes of hypothyroidism.[1,2] During the prolonged course of the disease, due to fluctuations in thyroid hormone levels and abnormalities in the immune system, patients with HT often experience mood problems, including emotional instability, anxiety, and depression, as well as cognitive impairments like memory loss and difficulty concentrating.[3] These issues severely impact the patients' work capacity and daily life, which impose a significant burden on society and families. Currently, there are no effective interventions for cognitive and emotional disorders caused by HT. Donepezil, a cholinesterase inhibitor, is widely used in the treatment of cognitive disorders, such as Alzheimer's disease. It inhibits acetylcholinesterase activity to reduce the breakdown of acetylcholine, thereby increasing acetylcholine concentration in the synaptic cleft and improving neurotransmission efficiency.[4,5] Recent studies have suggested the potential role of cholinesterase inhibitors for alleviating anxiety and depression, but the underlying mechanism remains unclear.[6] In this study, a total of 109 euthyroid patients with HT were selected to investigate the effects of donepezil treatment on cognitive function, emotional responses, and the potential mechanisms involved. The results of the study are reported below.

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Subjects and methods

Subjects

A total of 109 euthyroid patients with HT treated in the Department of Endocrinology at Huangshan Shoukang Hospital from February 2021 to May 2024 were selected for the study. The patients were randomly divided into a treatment group (n = 54) and a control group (n = 55) using a random number table. In the control group, there were 13 males and 42 females, aged 21–55 years, with a mean age of 42.57 ± 10.26 years and a disease duration ranging from 10 to 44 months, with a mean of 21.57 ± 4.25 months. In the treatment group, there were 8 males and 46 females, aged 22–54 years, with a mean age of 42.01 ± 10.11 years and a disease duration ranging from 10 to 45 months, with a mean of 21.68 ± 4.78 months. There were no significant differences between the two groups in baseline characteristics ($P > 0.05$).

Inclusion and exclusion criteria

Inclusion criteria: (1) Hashimoto's thyroiditis meeting the diagnostic criteria outlined in Internal Medicine (9th Edition):[7] thyroid enlargement with firm texture; positive serum TGAb and/or TPOAb; diffuse changes in the gland observed via ultrasound; and fine-needle aspiration biopsy under ultrasound guidance showing diffuse lymphocytic and plasma cell infiltration in the thyroid, with the formation of lymphoid follicles and fibrous tissue proliferation. Diagnosis is confirmed when the patient meets criteria 1–3 and/or criterion 4; (2) normal thyroid function; (3) in the past year, no history of antithyroid treatment or thyroid hormone replacement therapy, and no history of glucocorticoid or other relevant medication use; (4) signed informed consent; (5) mild to moderate anxiety, with a Self-Rating Anxiety Scale (SAS) score of $50 \leq SAS < 70$; with or without mild to moderate depression, defined as a Self-Rating Depression Scale (SDS) score of $53 \leq SDS < 72$; mild cognitive impairment, defined as a Mini-Mental State Examination (MMSE) score of $21 \leq MMSE < 27$.

Exclusion criteria: (1) coexisting thyroid diseases (hyperthyroidism, hypothyroidism, thyroid malignancies, subacute thyroiditis, etc.); (2) history of thyroid dysfunction; (3) coexisting other autoimmune diseases; (4) pregnancy or lactation; (5) severe hepatic, renal, or cardiac insufficiency; (6) coexisting malignant tumors, cardiovascular and cerebrovascular diseases, neurodegenerative diseases, psychiatric disorders, or endocrine diseases; (7) allergy to medications used in this study; (8) coexisting acute or chronic infectious diseases, or occurrence of such infections during the medication period.

This study was approved by the Medical Ethics Committee of Huangshan Shoukang Hospital (Approval No. 2023-LC-14).

Therapeutic regimen

Both groups received general treatment, including a low-iodine diet, regular lifestyle habits, and emotional adjustment. Patients in the treatment group were administered with donepezil hydrochloride tablets (Zhejiang Huahai, specification: 5 mg/tablet, batch number: 2101147) combined with vitamin C tablets (Sichuan Yike, specification: 0. 1 g/tablet, batch number: 201217), both taken orally on an empty stomach in the morning. The dosage of donepezil hydrochloride was 5 mg/day. The control group was only given vitamin C tablets (same specification as above), taken orally on an empty stomach in the morning at a dose of 0.1 g/day. Both groups adhered to the prescribed medication regimen for three months, with regular follow-ups.

Biochemical indicators and scales

(1) Thyroid hormones and autoantibodies measurement: For both groups of patients, 5 ml of fasting venous blood was collected in the morning before and after treatment. Using electrochemiluminescence immunoassay, levels of triiodothyronine (T3), thyroxine (T4), thyroid peroxidase antibody (TPOAb), thyroglobulin antibody (TGAb), and thyroid-stimulating hormone (TSH) were measured. The measurements were performed using a Roche ECL2010 electrochemiluminescence analyzer and corresponding kits.
(2) Inflammatory factors measurement: Fasting venous blood (5 ml) was collected before and after treatment in both groups, and centrifuged to obtain serum. Enzyme-linked immunosorbent assay (ELISA) was used to measure the levels of interleukin-6 (IL-6), interleukin-4 (IL-4), interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α). The kits used for the assays were from Shanghai Jingkang Bioengineering Co., Ltd., and the measurements were performed using a BIO-RAD Microplate Reader (Model 550, USA).
(3) MMSE Scale: The MMSE scale assesses time orientation, place orientation, delayed recall, immediate recall, attention, calculation ability, language, and visuospatial ability, totaling 30 questions. Each correct answer scores 1 point, while "don't know" or incorrect answers score 0. The total score ranges from 0 to 30, with higher scores indicating more normal cognitive function.
(4) SAS Scale: The SAS scale consists of 15 items scored positively and 5 items scored in reverse. The total score of the 20 items is multiplied by 1.25, and the integer part is taken to obtain the standard score. A higher score indicates a stronger tendency towards anxiety.
(5) SDS Scale: The SDS scale consists of 10 items scored positively and 10 items scored in reverse. The total score of the 20 items is multiplied by 1.25, and the integer part is taken to obtain the standard score. A higher score indicates more pronounced depressive emotions.

Statistical analysis

Statistical analysis was performed using the SPSS software (version: 26.0). Measurement data conforming to a normal distribution were presented as mean ± standard deviation (mean ± SD). Intergroup comparisons were conducted using the independent sample *t*-test, and paired t-tests were used for comparisons before and after treatment. A significance level of $\alpha = 0.05$ was set, and differences were considered statistically significant when $P < 0.05$.

Results

Comparison of thyroid function between the two groups before and after treatment

As shown in Table 1, No statistically significant differences in T3, T4, TSH, TGAb, and TPOAb levels were observed between the two groups before treatment ($P > 0.05$). After treatment, there were still no statistically significant differences in these thyroid function indicators between the two groups ($P > 0.05$).

Differences in MMSE, SAS, and SDS scores between the two groups before and after treatment

Before treatment, there were no statistically significant differences in MMSE, SAS, and SDS scores between the two groups ($P > 0.05$). In the control group, scores did not change significantly before and after

Table 1
Comparison of thyroid hormone indicators between the two groups before and after treatment.

Group	T3 (nmol/l)		t value	P value	T4 (nmol/l)		t value	P value	TSH (mIU/l)		t value	P value	TGAb (U/ml)		t value	P value	TPOAb (U/ml)		t value	P value
	Before	After			Before	After			Before	After			Before	After			Before	After		
Control (n = 55)	1.84 ± 0.26	1.74 ± 0.51	1.296	0.198	109.81 ± 21.47	114.92 ± 26.06	1.122	0.264	2.26 ± 1.10	2.27 ± 1.05	0.049	0.961	227.51 ± 72.12	208.36 ± 61.59	1.498	0.137	802.34 ± 266.03	772.31 ± 257.31	0.602	0.549
Treatment (n = 54)	1.76 ± 0.38	1.73 ± 0.34	0.432	0.666	104.11 ± 26.35	105.21 ± 27.54	1.716	0.089	2.19 ± 1.13	2.25 ± 1.04	0.287	0.775	228.43 ± 75.38	205.31 ± 78.33	1.563	0.121	807.02 ± 267.26	770.46 ± 252.17	0.731	0.466
t value	1.285	0.120			1.239	1.891			0.328	0.100			0.065	0.226			0.092	0.038		
P value	0.202	0.905			0.218	0.061			0.744	0.921			0.948	0.822			0.927	0.970		

Note:
T3: triiodothyronine; T4: thyroxine; TGAb: thyroglobulin antibody; TPOAb: thyroid peroxidase Antibody; data for thyroid hormone indicator levels are presented as mean ± SD.

treatment ($P > 0.05$). However, in the treatment group, MMSE scores increased significantly after treatment ($P < 0.05$), while SDS and SAS scores decreased significantly ($P < 0.05$). After treatment, the treatment group had significantly higher MMSE scores and lower SAS and SDS scores compared to the control group ($P < 0.05$), as shown in Table 2.

Comparison of inflammatory cytokine levels between the two groups before and after treatment

The baseline levels of IL-6, IL-4, IL-1β, and TNF-α were similar between the two groups before treatment ($P > 0.05$). In the control group, these inflammatory cytokine levels did not change significantly before and after treatment ($P > 0.05$). In contrast, in the treatment group, levels of IL-6, IL-4, IL-1β, and TNF-α were significantly lower after treatment compared to before ($P < 0.05$). Additionally, post-treatment levels of these four cytokines in the treatment group were significantly lower than those in the control group ($P < 0.05$). These results were shown in Table 3.

Discussion

Hashimoto's thyroiditis is a chronic autoimmune thyroid disease characterized by chronic inflammation of the thyroid tissue and hypothyroidism.[8] In addition to its effects on the thyroid, HT can negatively impact the central nervous system and contributes to cognitive and emotional disturbances, although the underlying mechanisms remain unclear. It is suggested that these effects may be related to the influence of thyroid hormones or thyroid antibodies on neurons in the brain. Studies have found that patients with HT frequently experience cognitive impairments, such as anxiety, decreased cognitive function, lack of concentration, and memory loss, which significantly affect their learning, daily life, and overall health.[9,10] In severe cases, HT patients suffer from insomnia and palpitations. These emotional and cognitive disturbances have a wide-ranging impact on the physical health and emotional well-being, underscoring the importance of timely diagnosis and treatment.[11] However, there are currently no effective clinical interventions specifically targeting the cognitive and emotional disturbances associated with HT.

Donepezil is a cholinesterase inhibitor primarily used to improve cognitive impairment in patients with Alzheimer's disease. Multiple recent studies suggest that donepezil can significantly improve daily symptoms and behaviors, and it has also shown potential in alleviating anxiety and depressive symptoms, but its exact mechanisms remain unclear.[12] Donepezil increases the concentration of acetylcholine (ACh) in the synaptic cleft by inhibiting cholinesterase activity. According to the cholinergic hypothesis, activation of central cholinergic receptors can increase the release of neurotransmitters such as glutamate, gamma-aminobutyric acid (GABA), dopamine, and serotonin, which in turn helps regulate mood.[13] In addition to the involvement of donepezil in modulating the release and balance of various neurotransmitters, donepezil might enhance neural plasticity to alleviate anxiety and depressive symptoms. Studies have shown that donepezil can promote synaptic connectivity and communication between neurons, thereby strengthening the functionality of neural networks.[14] Bai Fengfeng et al. demonstrated that the addition of donepezil hydrochloride to conventional antidepressant therapy has a synergistic effect on the alleviation of depressive symptoms, which significantly improves treatment-resistant geriatric depressive disorder and cognitive function.[15]

Currently, there is growing research interest in the relationship between central nervous system (CNS) inflammation and cognitive and emotional disorders. Neuroinflammation refers to inflammatory responses occurring within the central nervous system. Glial cells, including microglia and astrocytes, play key roles in regulating neuroinflammation.[16] Under pathological conditions, glial cells become activated and release inflammatory mediators to modulate neuronal

Table 2
MMSE, SAS, and SDS scores before and after treatment between the two groups.

Group	MMSE score		SAS score		SDS score	
	Before	After	Before	After	Before	After
Control (n = 55)	25.56 ± 2.38	25.82 ± 2.45	57.54 ± 8.69	56.68 ± 8.23	54.17 ± 8.25	53.12 ± 9.64
Treatment (n = 54)	25.17 ± 2.26	27.44 ± 2.03[a]	58.16 ± 9.21	47.25 ± 7.83[a]	55.23 ± 8.17	45.26 ± 8.59[a]
t value	1.197	3.755	0.362	6.127	0.674	4.491
P value	0.234	0.000	0.718	0.000	0.502	0.000

Note:
MMSE: Mini-Mental State Examination; SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale; MMSE, SAS, and SDS scores are presented as mean ± SD; [a] indicates $P < 0.05$ compared with the condition before treatment.

Table 3
Comparison of inflammatory factor levels between the two groups before and after treatment.

Group	IL-6 (pg/ml)		IL-4 (pg/ml)		IL-1β (pg/ml)		TNF-α (pg/ml)	
	Before	After	Before	After	Before	After	Before	After
Control (n = 55)	3.36 ± 0.71	3.55 ± 0.64	70.02 ± 11.04	71.34 ± 9.27	60.21 ± 13.41	62.06 ± 15.95	105.43 ± 12.73	112.66 ± 18.74
Treatment (n = 54)	3.22 ± 0.78	2.82 ± 0.73[a]	71.53 ± 16.41	54.21 ± 11.47[a]	55.70 ± 14.48	46.42 ± 11.80[a]	107.54 ± 15.32	97.81 ± 10.46[a]
t value	0.980	5.554	0.565	8.798	1.688	5.811	0.783	5.095
P value	0.329	0.000	0.574	0.000	0.094	0.000	0.436	0.000

Note:
IL-6: interleukin-6; IL-4: interleukin-4; IL-1β: interleukin-1 beta; TNF-α: tumor necrosis factor-alpha; data for inflammatory factor levels are expressed as mean ± SD; [a] indicates $P < 0.05$ compared with the condition before treatment.

function and participate in repair processes, thereby influencing the progression and outcomes of neuroinflammation. A previous animal study demonstrated that in HT mice, microglial activation in the brain was increased. Microglia, the resident immune cells of the CNS, released pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α, which further exacerbated the inflammatory response and were associated with anxiety- and depression-like behaviors in the HT mice.[17] Furthermore, emerging evidence suggests that HT-related cognitive impairments are associated with damage of astrocytes.[18] Neuroinflammation can result in neuronal damage and disrupt neurotransmitter balance, leading to the development of emotional disorders such as anxiety and depression. Studies have also shown that in HT patients, there is an increased presence of inflammatory cells and cytokines within the thyroid tissue, which may enter the bloodstream, cross the blood-brain barrier, and trigger neuroinflammatory responses within the CNS.[19,20]

In HT patient, abnormally elevated thyroid antibodies not only lead to thyroid dysfunction but also affect various aspects of the body, such as hypometabolic syndrome, skin changes, gastrointestinal abnormalities, emotional and cognitive disturbances, immune system alteration, cardiovascular diseases, and a decline in quality of life. Our results indicate that there were no statistically significant differences in T3, T4, TSH, TGAb, and TPOAb levels between the two groups before and after treatment ($P > 0.05$). However, a slight decrease in TGAb and TPOAb levels was observed in both groups, with a more pronounced reduction in the treatment group, though the results were not statistically significant. This may be attributed to the small sample size in this study.

Additionally, this study showed that after treatment, the MMSE scores in the treatment group were significantly higher than those in the control group, while SAS and SDS scores were significantly lower ($P < 0.05$). This suggests that donepezil treatment can effectively improve depression and anxiety in patients, alleviate thyroid-specific antibody imbalances to some extent, and enhance cognitive function and quality of life. Furthermore, there were no significant differences in inflammatory factor levels between the two groups before treatment ($P > 0.05$). After treatment, serum IL-6, IL-4, IL-1β, and TNF-α levels in the treatment group were significantly lower than in the control group ($P < 0.05$), indicating that donepezil significantly reduced serum inflammatory cytokine levels. This suggests that donepezil may exert its therapeutic effects on cognitive and emotional disorders in HT patients by inhibiting the release of peripheral inflammatory cytokines such as TNF-α and IL-6, thereby modulating neuroinflammatory responses and preventing systemic inflammation or inflammation-mediated pathophysiological reactions.

The small sample size is a limitation of this study. Besides, our study is a single-center study, there may be selection bias in case recruitment. To further validate the findings of this study, we will increase the sample size in future research.

Conclusion

The donepezil significantly improves emotional disorders and enhances cognitive function in HT patients, potentially through the downregulation of serum inflammatory cytokines. The findings of this study provide a new therapeutic approach for addressing cognitive and emotional disorders in patients with HT. However, it should be noted that the exact mechanism by which donepezil improves anxiety and depressive symptoms remains unclear, and further research is needed to explore this aspect in greater detail.

Declarations

Not applicable.

Authors' contributions

Chengwu Wang: Conceptualization, Methodology, Software. Xuelian Jiang: Data curation, Writing- Original draft preparation. Xiumei Sun: Visualization, Investigation. Defa Zhu: Supervision. Wenlu Guo: Software, Validation. Fen Wang: Writing- Reviewing and Editing.

Ethics approval and consent to participate

The study received approval from the medical ethics committee of Huangshan Shoukang Hospital (2023-LC-14).

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Declarations of Competing interests

The authors declare that they have no competing interests.

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Authors' other information

Not applicable.

References

1. Xu SJ, Qi S, Shang JW, et al. Distribution of clinical symptoms and syndrome in enthyroid Hashimoto thyroiditis patients (Chinese). *China Med Herald.* 2022;19(29):134–138. https://doi.org/10.20047/j.issn1673-7210.2022.29.31
2. Zhang X, Lian S, Zhang Y, et al. Efficacy and safety of donepezil for mild cognitive impairment: a systematic review and meta-analysis(Chinese). *Clin Neurol Neurosurg.* 2022;213(42):107134.
3. Chen Y, Li SS, Wang WY, et al. A randomized controlled study:qingying powder in improving depression,anxiety and antibody disorder in patients with hashimoto thyroiditis complicated with subclinical hypothyroidism (Chinese). *Tianjin J Tradit Chinese Med.* 2024;41(1):24–28. https://doi.org/10.11656/j.issn.1672-1519.2024.01.06
4. Berthier ML, Edelkraut L, López-González FJ, et al. Donepezil alone and combined with intensive language-action therapy on depression and apathy in chronic post-stroke aphasia: a feasibility study. *Brain Lang.* 2023;236:105205. https://doi.org/10.1016/j.bandl.2022.105205
5. Huang MC, Weng ZC, Lin CY. Efficacy of different doses donepezil combined with memantine in the treatment of Alzheimer's disease:a comparative study (Chinese). *Guangxi Med J.* 2023;45(3):257–261. https://doi.org/10.11675/j.issn.0253-4304.2023.03.01
6. Wang P, Jin Y, Mei R, et al. Effect of Shenghui Yizhi decoction combined with donepezil hydrochloride on behavioral and psychological symptoms of patients with mild to moderate Alzheimer's disease (Chinese). *Chinese J Basic Med Tradit Chinese Med.* 2024;30(3):495–499.
7. Ge JB, Xu YJ, Wang C. *Internal Medicine.* Ninth Edition Beijing: People's Medical Publishing House; 2018:692–694.
8. Liu XY, Peng J, Xia ZY. Eight methods of Fuzheng Xiaoying for treating Hashimoto's thyroiditis (Chinese). *Chinese J Clin Healthcare.* 2020;23(5):717–720. https://doi.org/10.3969/J.issn.1672-6790.2019.05.035
9. Tao YT, Wu JM. Effects of Donepezil hydrochloride regulating lncRNA GAS5 on cognitive dysfunction and inflammatory response in vascular dementia mice (Chinese). *Chinese J Integr Med Cardio/Cerebrovasc Dis.* 2024;22(7):1247–1251. https://doi.org/10.12102/j.issn.1672-1349.2024.07.014
10. Byers AL, Yaffe K. Depression and risk of developing dementia(Chinese). *Nat Rev Neurol.* 2021;7(6):323–331.
11. Wang Y, Sun J, He MM, et al. Analysis of the relationship between serum ENO1Ab level and mild cognitive impairment in Hashimoto's thy-roiditis patients with normal thyroid function (Chinese). *Chinese J N Clin Med.* 2023;16(9):946–950. https://doi.org/10.3969/j.issn.1674-3806.2023.09.14
12. Chen DY, Liao HJ, Yan HR, et al. Study on the effect of Yi'naokang capsules combined with donepezil hydrochloride tablets on patients with post-stroke cognitive impairment (Chinese). *Tradit Chinese Drug Res Clin Pharmacol.* 2023;34(12):1793–1798. https://doi.org/10.19378/j.issn.1003-9783.2023.12.017
13. Wang AA, Li WJ, Huang WQ, et al. Clinical research of qingling granule combined with donepezil hydrochloride in the treatment of cognitive dysfunction after stroke (Chinese). *Anhui Med Pharma J.* 2022;26(12):2524–2528. https://doi.org/10.3969/j.issn.1009-6469.2022.12.042
14. Nagahara AH, Tuszynski MH. Potential therapeutic uses of BDNF in neurological and psychiatric disorders. *Nat Rev Drug Discov.* 2011;10(3):209–219. https://doi.org/10.1038/nrd3366
15. Bai FF, Li T, Li XZ, et al. Efficacy and safety of Donepezil hydrochloride in the treatment of refractory senile depressive disorder (Chinese). *Pract Geriatr.* 2020;34(12):1292–1294. https://doi.org/10.3969/j.issn.1003-9198.2020.12.021
16. Wang N, Sun Y, Yang H, et al. Hashimoto's thyroiditis induces hippocampus-dependent cognitive alterations by impairing astrocytes in euthyroid mice. *Thyroid.* 2021;31(3):482–493. https://doi.org/10.1089/thy.2020.0139
17. Cai YJ, Wang F, Chen ZX, et al. Hashimoto's thyroiditis induces neuroinflammation and emotional alterations in euthyroid mice. *J Neuroinflammation.* 2018;15(1):299. https://doi.org/10.1186/s12974-018-1341-z
18. Hu XJ, Zhang AG, Zhang L, et al. Difference and correlation analysis of serum inflammatory factors in patients with and without psychotic symptoms with major depressive episode (Chinese). *Anhui Med J.* 2021;42(12):1381–1383. https://doi.org/10.3969/j.issn.1000-0399.2021.12.011
19. Wang ZG, Yang F, Wang XB, et al. Study on curative effect and mechanism of using donepezil assisted with Bushen Tianjing Yisui decoction in the treatment of Alzheimer's disease (Chinese). *J Sichuan Tradit Chinese Med.* 2022;40(5):172–175.
20. Wang ZG, Chen YX, Yin CP, et al. Research progress on the effect of inflammation on perioperative neurocognitive disorders (Chinese). *J of Clin Anesthesiol.* 2023;39(2):189–192. https://doi.org/10.12089/jca.2023.02.016