

## THE CLINICAL EFFECT OF PAROXETINE ALONE OR COMBINED WITH ALPRAZOLAM IN THE TREATMENT OF DIABETES MELLITUS WITH ANXIETY AND DEPRESSION

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### ABSTRACT

**Objective:** To evaluate the clinical effect of paroxetine alone or combined with alprazolam in the treatment of diabetes mellitus with anxiety and depression.

**Methods:** A total of 66 diabetic patients with anxiety and depression were selected from our hospital from August 2018 to August 2019. The patients were divided into a study group and control group based on the difference in treatment methods, with 33 patients in each group. The control group patients were treated with paroxetine alone, the study group patients were treated with paroxetine and alprazolam, and the clinical effect was compared between the two groups.

**Results:** There was no significant difference in FPG, 2hPG and ACTH between the two groups before treatment ( $P>0.05$ ). After the treatment, the two groups were significantly lower than before the treatment ( $P<0.05$ ); after the treatment, the reduction degree of the study group was better than that of the control group, and the difference was statistically significant ( $P<0.05$ ). The results showed that there was no significant difference between the two groups before and after treatment ( $P>0.05$ ). After treatment, there was a significant decrease in the two groups compared with before treatment, and the difference was statistically significant ( $P<0.05$ ). Moreover, after treatment, the research group showed significant improvements compared to the control group ( $P<0.05$ ). The incidence of adverse reactions was 21.21% in the study group and 36.36% in the control group.

**Conclusion:** The clinical efficacy of paroxetine alone or combined with alprazolam in the treatment of diabetes mellitus with anxiety and depression is better. After treatment, the blood glucose and endocrine level of the patients improved, anxiety and depression symptoms also improved, the incidence of adverse reactions was low, and the safety of use was high.

**Keywords:** Paroxetine, alprazolam, diabetes mellitus with anxiety and depression.

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### Introduction

Psychological factors play an important role in the occurrence, development and treatment of diabetes. Biological correlations have been found between depression and Tang biao bin. Anxiety and depression are aspects of the emotional experience that biologically stems from the thalamus. In patients with diabetes and depression, the activity of the hypothalamus pituitary adrenal axis and the level of serum cortisol are significantly increased,

and these neuroendocrine disorders can easily lead to the occurrence of pancreatic island resistance<sup>(1-3)</sup>. In addition, anxiety, depression and other adverse emotions make the treatment of patients with diabetes challenging, not only hampering blood sugar control but also increasing the risk of functional disability and complications<sup>(4-6)</sup>. Therefore, the effective treatment of diabetic patients with anxiety and depression is a common clinical issue. In this study, the effects of paroxetine alone and in combination with alprazolam were compared.

## Methods

### General information

A total of 66 diabetes patients with anxiety and depression were selected from our hospital from August 2018 to August 2019.

*All the patients met the following criteria:*

- They met the diagnostic criteria for type 2 diabetes as per the Chinese diabetes prevention and treatment guidelines<sup>(7)</sup>;
- They met the Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD) scoring indicators<sup>(8)</sup>;
- They did not have any previous history or family history of mental illness;
- They participated in the study voluntarily and signed the informed consent form.

*The exclusion criteria were as follows:*

- Patients with gangrene of the lower limbs and severe infection and patients with acute complications of diabetes.

The 66 patients were divided into a study group and a control group based on the treatment method, with 33 patients in each group. In the study group, 19 patients (57.58%) were men and 14 patients (42.42%) were women. The age range of the patients was 35–68 years and the average age was  $52.35 \pm 5.23$  years. The disease duration was 0.5–7 years with an average of  $4.23 \pm 2.55$  years. Ten patients had hypertension. The control group comprised 18 male patients (54.55%) and 15 female patients (45.45%). The patients' age range was 34–67 years, with an average age of  $52.30 \pm 5.28$  years. The disease duration was 1–7 years, with an average duration of  $4.33 \pm 2.59$  years. Eleven patients had hypertension. There was no significant difference between the two groups ( $P > 0.05$ ).

### Treatment method

The patients in the control group were treated with paroxetine alone at a dose of 10 mg/d, which could be increased to 20 mg/d in the morning after 3 days. The patients in the study group were treated with paroxetine in the same dosage and manner as those in the control group. Additionally, alprazolam was administered to the study group at a dose of 1.2 mg/d three times per day, with the dose changing to 0.8 mg/d before sleeping late. The clinical effect of the two regimens was compared after 8 weeks.

### Observation indicators

- Glucose metabolism index. Blood was collected from the elbow vein of patients in the

fasting condition from both groups before and after treatment at a volume of 5 ml. The fasting blood glucose (FPG) and postprandial blood glucose (2hPG) of the two groups was examined by the hexokinase method. In addition, the HbA1c of the two groups was measured by high performance liquid chromatography.

- Endocrine function index. The levels of serum cortisol and ACTH were measured before and after treatment via radioimmunoassay.
- Anxiety and depression. Before and after treatment, the HAMA and HMAD rating scales were used to measure anxiety and depression in the two groups of patients and evaluated by trained psychologists.
- Safety evaluation. To evaluate and compare the clinical safety of the treatments in the two groups, adverse reactions occurring during the treatment period were counted and recorded.

### Statistical analysis

SPSS 21.0 was used for statistical analysis. Measurement data with a normal distribution are expressed as mean  $\pm$  standard deviation and were assessed by t-test and one-way ANOVA. Measurement data with a non-normal distribution are expressed as median (interquartile range) and were analysed by the Mann Whitney rank sum test,  $\chi^2$  test for counting data and multivariate linear regression analysis for correlation analysis. The results are expressed as mean  $\pm$  standard deviation and median. Differences were considered statistically significant at  $P < 0.05$ .

## Results

### Comparison of glucose metabolism indexes between the two groups before and after treatment

There was no significant difference in FPG, 2hPG and ACTH between the two groups before treatment ( $P > 0.05$ ). After the treatment, the two groups had significantly lower levels of these factors than before ( $P < 0.05$ ). Additionally, after the treatment, the degree of reduction in the study group was higher than that in the control group, with the difference being statistically significant ( $P < 0.05$ ). See Table 1 below for details.

### Comparison of endocrine function indexes between the two groups before and after treatment

The results showed no significant difference between the two groups before and after treatment

( $P>0.05$ ). After the treatment, the two groups were significantly lower than before the treatment ( $P<0.05$ ); additionally, the study group showed significantly greater improvement than the control group ( $P<0.05$ ). See Table 2 below for details.

Group	Number of cases	FPG (mmol/L)		2hPG (nmol/L)		ACTH (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group	33	12.34±3.24	7.68±2.14	17.47±3.14	8.22±1.95	9.53±1.69	6.05±1.24
Control group	33	12.47±2.90	9.44±2.03	17.23±2.68	10.57±1.79	9.78±1.78	7.36±1.15
P value	-	<0.05	>0.05	<0.05	>0.05	>0.05	<0.05

**Table 1:** Comparison of glucose metabolism indexes between the two groups before and after treatment.

Group	Cortisol (nmol / L)		ACTH (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment
Study group	24.24±4.24	17.35±3.73	53.14±5.22	34.24±2.68
Control group	23.87±3.92	20.68±3.13	54.03±4.24	41.63±3.67
P value	>0.05	<0.05	>0.05	<0.05

**Table 2:** Comparison of endocrine function indexes between the two groups before and after treatment.

**Comparison of anxiety and depression between the two groups before and after treatment**

The results showed no significant difference between the two groups before and after treatment ( $P>0.05$ ). After treatment, the two groups showed significant improvement compared with the condition before treatment ( $P<0.05$ ). Additionally, the study group was significantly better than the control group after treatment ( $P<0.05$ ). See Table 3 below for details.

Group	HAMA (nmol/L)		HAMD (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment
Study group	25.75±5.53	7.83±3.62	28.63±4.48	8.63±3.23
Control group	26.33±4.13	12.96±4.65	29.06±5.22	12.69±3.75
P value	>0.05	<0.05	>0.05	<0.05

**Table 3:** Comparison of anxiety and depression between the two groups before and after treatment.

**Comparison of adverse reactions between the two groups**

The incidence of adverse reactions was 21.21% in the study group and 36.36% in the control group. See Table 4 below for details.

Group	Number of cases	Anorexia	Nausea	Dizziness	Constipation	Total
Study group	33	2	2	2	1	7 (21.21)
Control group	33	3	3	3	3	12 (36.36)
P value	-					<0.05

**Table 4:** Comparison of adverse reactions between the two groups.

**Discussion**

Diabetes mellitus is a common psychosomatic disease in the clinic. Type 2 diabetes mellitus patients often present with psychological disorders. The interaction and aggravation of diabetes, anxiety and depression gradually forms a vicious circle. In addition, patients with diabetes often have cardiovascular and cerebrovascular diseases, complications that cause insomnia, further aggravating anxiety and depression<sup>(9)</sup>. Anxiety, depression and other negative emotions are chronic psychological stress factors, and the clinical treatment of diabetes mellitus is significantly impacted in patients with these conditions as such patients may show poor clinical treatment compliance and indirectly affect the diabetes control effect. Researchers have increasingly pointed out that when treating diabetes patients with anxiety and depression, not only hypoglycaemic treatment but also interventions for anxiety and depression should be strengthened<sup>(10)</sup>. Research in China and abroad shows that the use of anti-anxiety and depression drugs can reduce the clinical symptoms of diabetes patients with anxiety and depression to a certain extent and the promote reduction and improvement of HbA1c levels<sup>(11)</sup>. In addition, treatment of anxiety and depression in diabetes patients with these conditions has been shown to alleviate negative emotions and thereby effectively improve blood sugar levels. Paroxetine is a 5-5-hydroxytryptamine reuptake inhibitor that effectively inhibits the presynaptic membrane reuptake of 5-hydroxytryptamine, leading to improvement in mood.

Paroxetine has little effect on norepinephrine and dopamine, and it can control or reduce the occurrence of cardiovascular events, minimising the incidence of clinical adverse reactions. Alprazolam is a benzodiazepine that activates  $\gamma$ -aminobutyric acid type A receptor by stimulating the benzodiazepine receptor and promotes the direct entry of chloride ions into the neurons. This enhances the depolarization threshold, resulting in the alleviation of anxiety in

patients<sup>(12-14)</sup>. The results of this study showed that there was no significant difference in HAMA and HAMD between the two groups before and after treatment ( $P>0.05$ ); the difference was statistically significant ( $P<0.05$ ). After treatment, the study group showed significant improvements compared to the control group ( $P<0.05$ ). This result shows that the effect of paroxetine alone is not as good as that of the combination of paroxetine and alprazolam, which can also effectively reduce adverse reactions in patients. In addition, the results of this study showed that there was no significant difference between the two groups with respect to FPG, 2hPG and ACTH levels before treatment ( $P>0.05$ ) but after treatment, the two groups had significantly lower levels of these factors ( $P<0.05$ ).

Additionally, after treatment, the degree of reduction in the study group was significantly better than that in the control group ( $P<0.05$ ). This result shows that the combination of paroxetine and alprazolam can not only improve anxiety and depression symptoms in patients but also effectively reduce blood sugar and HbA1c levels; moreover, the ACTH and cortisol levels of patients after clinical treatment were significantly lower than before treatment. Thus, in the treatment of diabetic patients with anxiety and depression, appropriate emotional intervention can effectively improve the level of anxiety and depression and reduce the level of cortisol, thus reducing fluctuations in blood glucose level so that patients' insulin resistance is improved and demonstrating a good therapeutic effect overall.

In conclusion, the combination of paroxetine and alprazolam is more effective than paroxetine alone in the treatment of diabetes patients with anxiety and depression. Additionally, the clinical effect of paroxetine alone or combined with alprazolam in the treatment of diabetes mellitus with anxiety and depression is better. After treatment, blood glucose and endocrine parameter levels as well as symptoms of anxiety and depression are improved in patients; additionally, the incidence of adverse reactions is low and the safety of use is high.

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