

A Comparative Study of Anxiety Disorders Treatment with Paroxetine Associated with Cranial Electrotherapy Stimulation Therapy

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Abstract

Objective: To explore the add-on effect of cranial electrotherapy stimulation therapy in the treatment of anxiety disorders.

Method: One hundred and twenty patients with anxiety disorder were randomly divided into the study group and the CES control group, each group having 60 cases. All of them were given treatment of paroxetine (Paxil) for 6 weeks. In addition, patients in the study group conducted cranial electrotherapy stimulation therapy daily in 6 weeks (42 times). The efficacy was assessed with the Hamilton anxiety scale (HAM-A) and clinical global impression scale (CGI-SI), quality of life was assessed with the World Health Organization quality of life questionnaire (WHOQOL-BREF) before and after treatment.

Result: After 6 weeks of treatment the significant efficacy rates of the study group and the control group were 76.67% and 53.33% respectively, and the differences between the two groups were statistically significant ($P < 0.05$). The scores of HAM-A and CGI-SI in both groups after treatment were significantly decreased from before treatment scores ($P < 0.05$). However, the scores of HAM-A ($P < 0.01$) and CGI-SI ($P < 0.05$) in the CES group was reduced more significantly than the control group at the 6th weekend after treatment. The score in four areas of quality of life measures were significantly improved after treatment in the two groups ($P < 0.05$). The physiological domain score in the CES study group was increased significantly over the use of paroxetine alone ($P < 0.05$).

Conclusion: Treating anxiety disorders with paroxetine associated with cranial electrotherapy stimulation therapy is better than with paroxetine by itself.

Key words: Anxiety disorder; Cranial electrotherapy stimulation therapy; Paroxetine

Cranial electrotherapy stimulation (CES) therapy is a non-invasive treatment method that is approved by the US Food and Drug Administration (FDA) and can be used for the treatment of sleep disorders, depressive disorders and anxiety disorders. It can significantly improve anxiety symptoms and has been widely used in clinical treatment.¹⁻² This study uses paroxetine alone and in combination with CES to treat anxiety disorders so as to explore the additive effect of CES in the treatment of anxiety disorders.

1. Materials and Methods

1.1 General Information

Patients aged 18~60 hospitalized in the inpatient or outpatient departments of a particular mental health center who met ICD-10 diagnostic criteria for anxiety disorders, have a primary school education or above and are willing to participate in this study were selected. Patients with serious organic diseases, drug or alcohol allergy and dependence, pregnant or lactating women, and patients with anxiety disorders secondary to other mental illness or physical diseases were excluded. In case of serious adverse reactions, complications or special physiological changes, major diseases or exacerbation of symptoms during the treatment, or when the therapeutic schedule needs to be changed the subject would need to exit the study. All subjects and guardians were asked to sign the informed consent form. 120 patients who are in line with the diagnostic criteria and willing to participate in the study were randomly divided into the study group and the control group according to the random number table, with 60 in each group. In the active CES study group, there were 24 males and 36 females ages 18 to 56 (mean 32.6 ± 9.3); disease duration 3 months to 14 years with an average of $24.8 (\pm 3.6)$ years; HAMA total score $26.0 (\pm 4.3)$ points, CGI-SI score $5.2 (\pm 0.5)$ points. And in the control group, there were 20 males and 40 females ages 21 to 55 (mean 31.1 ± 9.5); disease duration 5 months to 13 years, with an average of $4.3 (\pm 3.9)$ years; HAMA total score $25.5 (\pm 4.4)$ points, CGI-SI $5.3 (\pm 0.6)$ points. There is no statistically significant difference in the general information including age, sex and disease duration between the two groups ($P > 0.05$), and the two groups are comparable. The six week treatment was completed for all 120 cases, with no loss.

1.2. Methods

1.2.1. Patients enrolled in the study entered the 6-week treatment period after a one week washout period. Both groups were given 10 - 20 mg/d of paroxetine, with an average of 13.1 mg/d for the study group and 13.5 mg/d for the control group, and there was no statistically significant difference between the groups ($P > 0.05$). The study group was treated with paroxetine in combination with CES therapy, and the therapy device used was the Alpha-Stim SCS provided by Electromedical Products International, Inc., USA. This therapy device generates bipolar asymmetrical square waves with a frequency of 0.5 Hz, and can be adjusted to provide sustained current intensity of 10 – 500 μ A. The course of treatment is 6 weeks, 1 time / day, for a total of 42 treatments. In the first treatment, the investigators applied conductive solution to the electrodes and clipped them to the earlobes of the subjects, and then adjusted the current until the patient felt a slight tingling and/or dizziness, and then adjusted the current to a value below the reported sensory threshold. If the patient did not feel anything, the current intensity was increased until the patient felt stimulation and the current was then trimmed to a value below the sensory threshold. The patients were told to use the device consistently under certain sensory threshold in the next six weeks, and a continuous 60 minutes of treatment was conducted between 3:00 and 7:00 o'clock each day.

1.2.2. Criteria for efficacy. This study took HAM-A reductive ratio as the primary indicator for efficacy evaluation and CGI-SI as the secondary indicator for efficacy evaluation. HAM-A reductive ratio $\geq 75\%$ is clinically cured, 50% - 74% obviously improved, 25% - 49% improved, and $< 25\%$ ineffective. Significant efficacy rate = [(number of cured cases + number of obviously improved cases)/ total number] $\times 100\%$. WHO quality of life measurement table was used for assessment of quality of life. HAM-A was assessed in Weeks 0, 2, 4 and 6, and CGI-SI and WHOQOL-BREF was assessed in Weeks 0 and 6. All assessment was carried out by two psychiatric physicians at the same time, and the assessors have passed the consistency assessment.

1.3. Statistical processing

EPI-Data 3.1 was used for database creation and entry of data, and SPSS 15.0 software was used for statistical analysis of the data obtained. The measurement data was expressed as ($\bar{x} \pm s$), t-test was used for comparison, the enumeration data was tested with χ^2 , where $P < 0.05$ signifies a statistically significant difference.

2. Results

2.1. Clinical efficacy: In the CES study group, 18 cases were cured, 28 cases were obviously improved, 10 cases were improved, and 4 cases were ineffective. Therefore, the significant efficacy rate was 76.67%. In the control group, the corresponding cases were 14, 18, 16 and 12 respectively, with the significant efficacy rate 53.33%. There was statistically significant difference in the significant efficacy rate between the two groups ($\chi^2=4.62$, $P<0.05$).

2.2 Comparison of HAM-A scores after treatment: HAM-A scores of the two groups significantly decreased, both with statistically significant difference compared to those before treatment ($P<0.05$); in Week 6 of treatment, decrease in HAM-A scores of the study group was more significant than that of the control group, and the difference was statistically significant ($P<0.01$), as seen in Table 1.

Table 1. Comparison of HAM-A scores of two groups before and after treatment ($\bar{x} \pm s$) points

Group	Before treatment	Week 2	Week 4	Week 6
Study group (n=60)	25.0 ± 4.2	19.4 ± 2.5	14.8 ± 4.4	8.3 ± 3.7
Control group (n=60)	24.5 ± 4.3	19.2 ± 3.1	15.2 ± 3.8	12.4 ± 3.5
t value	0.422	0.152	-1.143	-3.654
P value	>0.05	>0.05	>0.05	<0.01

2.3. CGI-SI score results: The CGI-SI scores of the study group and the control group were 4.8 (± 0.3) points and 4.9 (± 0.7) points, with no statistically significant difference between the two groups ($t=-0.587$, $P>0.05$); in Week 6 of treatment, CGI-SI scores of the two groups both significantly decreased, both with statistically significant difference compared to those before treatment ($t=-19.536$, $P<0.05$), however the decrease in CGI-SI scores of the CES study group was more significant than that of the control group, and the difference was statistically significant ($t=-2.652$, $P<0.05$).

2.4. WHOQOL-BREF assessment results before treatment: Differences in scores of the two groups in each domain were not statistically significant ($P>0.05$). In Week 6 of treatment, scores in each domain of the quality of life measurement table of both groups all significantly increased, with statistically significant differences compared to those before treatment ($P<0.05$). In Week 6 of treatment, among WHOQOL-BREF scores, only the difference in scores in the physical domain of the two groups was statistically significant ($P<0.05$); in Week 6 of treatment, the differences in scores in psychological domain, social relations and environmental areas of the two groups were not statistically significant, as seen in Table 2.

Table 2. Comparison of WHOQOL-BREF scores of two groups before and after treatment ($\bar{x} \pm s$) points

Group	Factor	Before treatment	Week 6 of treatment
Study group (n=60)	Physical domain	9.81 ± 2.47	13.23 ± 2.83* Δ
	psychological domain	10.61 ± 1.96	13.17 ± 1.98*
	Social relations	9.93 ± 2.21	12.61 ± 2.57*
	Environmental areas	9.83 ± 1.91	12.92 ± 2.35*
Control group (n=60)	Physical domain	9.72 ± 2.64	10.31 ± 1.37*
	psychological domain	10.17 ± 2.14	13.02 ± 1.72*
	Social relations	9.27 ± 2.17	12.02 ± 2.22*
	Environmental areas	9.67 ± 2.13	11.95 ± 2.85*

*Comparisons of the same factor in the same group before and after treatment, $P<0.05$;

Δ comparison with the control group in Week 6 of treatment, $P<0.05$

3. Discussion

Currently studies have confirmed that the α band of brain waves of 8 - 12 Hz is the main activity rhythm for an adult at the quiet-wakeful state. When a person is in a relaxed state, the alpha (α) component of brain waves increases. CES can introduce microcurrent through electrodes at the head to stimulate the intracranial central nervous system so as to affect and improve abnormal brain waves and induce α waves that can stabilize emotions. It can also regulate neurotransmitters and hormones including cerebral morphia peptide, 5-hydroxytryptamine and γ -aminobutyric acid so as to reduce anxiety, depression and improve somatization disorder.³ In recent years, CES has been applied in treatment of anxiety disorders, depression and related diseases at home and abroad, and results have shown that the therapeutic effect is good.⁴⁻¹⁰ However, previous studies are often limited to the clinical improvement of CES. This study not only explores the clinical efficacy of CES in anxiety but also the assessment of the quality of life in patients before and after treatment so as to explore the advantages of CES from multiple dimensions.

The results of this study showed that after six weeks of paroxetine associated with CES, the significant efficacy rate of the CES study group was significantly higher than that of the control group. In Week 2 of treatment, HAM-A scores of the study group and control group both significantly decreased. In Week 6 of treatment, decrease in HAM-A scores and CGI-SI scores of the CES study group was more significant than that of the control group. The results showed that treatment of anxiety disorders with paroxetine in combination with CES has better efficacy, which is similar to the findings of Guo Wei et al. in China.⁸

WHOQOL-BREF score results before and after treatment showed that by adding CES, the physical domain of the patients was significantly improved, while difference in improvement in other domains was not statistically significant compared with that of the control group ($P>0.05$). It may be because the physical domain is mainly related to pain, fatigue and sleep, etc. The role of CES is to effectively improve sleep and physical symptoms so as to help patients relax physically and mentally, thus achieving good therapeutic effect.

In conclusion, this study showed that treating anxiety disorders with paroxetine associated with CES has a more significant therapeutic effect than treatment with paroxetine alone, and it can significantly improve the quality of life of patients, especially in terms of the biological field. However, the samples of this study come from a single source and the observation time is short, therefore it needs to be further demonstrated by a controlled multicenter study in future.

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