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Original Article

Clinical effects of relaxation training combined with paracetamol and tramadol hydrochloride tablets on patients with chronic pain

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Abstract: Objective: This study was designed to investigate the effect of relaxation training combined with Paracetamol and Tramadol Hydrochloride Tablets in the treatment of chronic pain from the aspects of pain relief, anxiety and depression, quality of life and adverse reactions. Methods: A total of 94 patients with chronic pain admitted to our hospital from January 2018 to December 2019 were selected and divided into the study group (SG, n=47) and the control group (CG, n=47) by a random number table. Paracetamol and Tramadol Hydrochloride Tablets were given to all patients included, and relaxation training was additionally provided to the patients in the SG. The two groups were compared for the pain relief, scores of anxiety and depression, quality of life and adverse reactions. Results: (1) After treatment, the pain relief and incidence of adverse reactions were 95.74% and 19.15% in the SG; 74.47% and 44.68% in the OG (P<0.05). (2) The scores of anxiety and depression at 2 weeks and 4 weeks after treatment were significantly lower in the SG (P<0.05), but at 1 week after treatment, the SG demonstrated a significantly higher score of depression (P<0.05). Both groups achieved significant decreases in the scores of anxiety and depression at 1 week, 2 weeks and 4 weeks after treatment (P<0.05); (3) There was no significant difference in quality of life in both groups before treatment (P>0.05). After treatment, the scores for physical role (PR), physical function (PF), cognitive function (CF), emotional function (EF), role function (RF) and total score of quality of life were significantly increased in both groups (P<0.05), and the SG achieved higher scores than the CG (P<0.05). Conclusion: The combination of relaxation training and Paracetamol and Tramadol Hydrochloride can effectively relieve pain, anxiety and depression, reduce adverse reactions, and have a positive effect on improving the quality of life of patients.

Keywords: Relaxation training, paracetamol and tramadol hydrochloride tablets, chronic pain, pain relief, anxiety and depression, quality of life, adverse reactions

Introduction

Pain can be defined as an emotional and subjective feeling caused by underlying or existing tissue damage. It is a common complaint in clinic. As the main symptom of distal injury, chronic pain lasts for more than one month and is accompanied by drowsiness, anorexia, sleep disorders and other neurological dysfunctions, which can lead to reduced immunity, body dysfunction, and a variety of other complications, seriously impacting the quality of life of patients. The incidence of chronic pain is high, about 10%-20%. As a form of discomfort, patients may be accompanied by anxiety, depression and other adverse conditions [1, 2]. It has been reported that about 10.6%-57.4% of patients with chronic pain may experience anxiety, and about 17.9%-92.4% may experience depression [3, 4]. Therefore, it is of great significance to improve the discomfort of chronic pain to relieve the unhealthy emotions such as anxiety and depression.

There are many drugs for the treatment of chronic pain, including Paracetamol and Tramadol Hydrochloride Tablets, an artificially synthetic compound with long-lasting effects of central analgesics [5]. However, drug treatment may cause some complications, which may affect the therapeutic effect. Studies have shown that the combination of drug treatment and nursing intervention can effectively reduce the incidence of adverse reactions. In relaxation training, music and language are used to directly stimulate the cerebral cortex of

patients, and draw their attention to sound, movement, breathing, and imagination, so that they would no longer pay attention to the pain and emotion, thus improving the quality of life [6, 7]. Relaxation training includes abdominal breathing, progressive muscle relaxation and meditation. Patients breathe along with the rise and fall of diaphragm, relax the muscles freely, and achieve the therapeutic effect through meditation [8].

Some studies have shown that relaxation training could effectively relieve unhealthy emotions of patients with coronary disease or diabetes and improve the quality of life. However, there are fewer studies on the combination of drugs and relaxation training in chronic pain. In the presents study, relaxation training was combined with Paracetamol and Tramadol Hydrochloride to treat patients with chronic pain and analyze its effects on pain relief, scores of anxiety and depression, quality of life and adverse reactions, in order to find more reasonable therapies and interventions.

Materials and methods

General materials

A total of 94 patients with chronic pain admitted to our hospital from January 2018 to December 2019 were selected. Inclusion criteria: patients who experienced pain for more than a month and yielded a VAS score at or above 3 points were included in this study. The study has been approved by the Medical Ethics Committee of our hospital. Written informed consent was signed and provided by the patients. Exclusion criteria: some patients were excluded due to severe liver and kidney dysfunction, malignant tumor or neurological diseases, mental disorder that seriously impaired communications, and a history of use of sleep improvement or sedative drugs. Patients were assigned treatment by use of a random number table; with 25 males and 22 females aged 26-65 years, with the average age of (45.79±10.54) years included into the SG, while 27 males and 20 females aged 27-68 years, with the average age of (45.62±10.58) years were included into the CG. The course of disease was 2-22 (average 12.72±4.81) months in the SG, and 4-23 (average 12.29±4.52) months in the CG. No statistical difference was observed between the two groups in terms of gender, age and course of disease (P>0.05).

Methods

After hospitalization, all patients were given diets rich in vitamins and proteins, and low in carbohydrates, fat and salt. They were closely monitored for vital signs such as heart rate and blood pressure, and were required to get sufficient sleep as well as proper movement, *etc*. ① Patients in the CG were administered with Paracetamol and Tramadol Hydrochloride Tablets (Manufacturer: Xi'an Janssen Pharmaceuticals Co., Ltd., GYZZ H20050676) for consecutive 5 d at the dose of 2 tablets each time, and 3 times a day. ② In addition to the same medication treatment, patients in the SG also received relaxation training. Through one-on-one lecturing and explanation, patients preliminarily mastered relaxation training and practiced with the "portable relaxation pillow" under the guidance of a professional psychological therapist in the context of music. The training was scheduled twice a day for about 45 min. During training, patients practiced abdominal respiration by lifting and lowering the diaphragm slowly, deeply, gently, and evenly. In the progressive muscle relaxation and mediation training, patients laid down or sat comfortably and quietly with both eyes slightly closed. The instructor guided them to relax and mediate with guided imagery until the correct procedures of relaxation training were thoroughly mastered.

Observation indices

① The two groups were compared for pain relief 4 weeks after treatment. The results included complete relief, marked relief, moderate relief, mild relief and failure. The total relief = (total number of cases - failed cases)/total number of cases × 100%. The pain relief was judged according to the following criteria: complete relief: no pain; marked relief: percentage of pain relief above 75%; moderate relief: percentage of pain relief around 50%; mild relief: percentage of pain relief around 25%; failure: no improvement. ② The two groups were compared for the scores of anxiety and depression measured by the HAD scale of the hospital before, at 1 week, 2 weeks and 4 weeks after treatment. Higher scores indicate more severe cases. ③ The two groups were compared for the scores of quality of life before and after treatment by the SF-36 which consists of physical role (PR), physical function (PF), cognitive function (CF), emotional function (EF), role function (RF) and total score of quality of life.

Table 1. Comparison between the two groups for the pain relief after treatment (*n,* %)

Group	n	Complete relief	Marked relief	Moderate relief	Mild relief	Failed	Total
SG	47	12 (25.53)	26 (55.32)	4 (8.51)	3 (6.38)	2 (4.26)	45 (95.74)
CG	47	8 (17.02)	18 (38.30)	5 (10.64)	4 (8.51)	12 (25.53)	35 (74.47)
χ^2		1.016	2.735	0.123	0.154	8.393	8.393
P		0.313	0.098	0.726	0.694	0.004	0.004

Table 2. Comparison between the two groups for the scores of anxiety and depression before and after treatment ($\overline{x}\pm s$)

Index	Group	Before treatment	1 week after treatment	2 weeks after treatment	4 weeks after treatment
Score of anxiety	SG (47)	12.21±0.53	11.45±0.54$^{\Delta}$	9.98±0.52$^{*,\Delta}$	9.29±0.49$^{*,\Delta}$
	CG (47)	12.37±0.47	11.63±0.61$^{\Delta}$	11.31±0.58$^{\Delta}$	11.27±0.48$^{\Delta}$
F		$F_{\text{time point}}$=711.282, $F_{\text{interaction}}$=174.858, $F_{\text{intergroup}}$=98.185			
P		$P_{\text{time point}}$=0.000<0.001, $P_{\text{interaction}}$=0.000<0.001, $P_{\text{intergroup}}$=0.000<0.001			
Score of depression	SG (47)	11.35±0.68	10.24±0.72$^{*,\Delta}$	9.26±0.71$^{*,\Delta}$	7.99±0.72$^{*,\Delta}$
	CG (47)	11.13±0.67	9.79±0.73$^{\Delta}$	9.74±0.71$^{\Delta}$	9.98±0.75$^{\Delta}$
F		$F_{\text{time point}}$=281.696, $F_{\text{interaction}}$=121.305, $F_{\text{intergroup}}$=13.430			
P		$P_{\text{time point}}$=0.000<0.001, $P_{\text{interaction}}$=0.000<0.001, $P_{\text{intergroup}}$=0.002<0.05			

Note: *indicates P<0.05 as compared with the CG; $^{\Delta}$indicates P<0.05 as compared with the observations before treatment.

Higher scores correspond to better quality of life. ④ The two groups were compared for adverse reactions, including nausea, vomiting, dizziness, abdominal distension and constipation.

Statistical analysis

Statistical analysis was performed with SPSS 22.0. In case of nominal data expressed as [n (%)], the comparison studies were carried out through independent-samples X^2 test; in case of numerical data normally distributed and expressed as Mean ± Standard Deviation, intergroup comparison studies were carried out through independent-samples T test, and intragroup comparison studies through the paired t test. Indices at different time points were tested by Repeated Measures ANOVA, and post hoc test was performed with LSD-t test. For all statistical comparisons, significance was defined as *P*<0.05.

Results

Pain relief

The number of patients in each relief group for; complete, marked, moderate, mild relief or failed were 12 (25.53%), 26 (55.32%), 4 (8.51%), 3 (6.38%) and 2 (4.26%) respectively in the SG; and 8 (17.02%), 18 (38.30%), 5 (10.64%), 4 (8.51%) and 12 (25.53%) respectively in the CG. The total relief rate was 95.74% in the SG and 74.47% in the CG (*P*<0.05, **Table 1**).

Scores of anxiety and depression

The scores of anxiety and depression were significantly lower in the SG at 2 and 4 weeks after treatment (*P*<0.05), but the SG yielded a higher score of depression at 1 week after treatment (*P*<0.05). Both groups attained a marked decrease in the scores of anxiety and depression at 1 week, 2 weeks and 4 weeks after treatment (*P*<0.05, **Table 2**, **Figures 1** and **2**).

Score of quality of life

There was no statistical difference in quality of life in the two groups before treatment (*P*>0.05). While after treatment, the scores of PR, PF, CF, EF, and RF, and the total score of quality of life were increased in both groups (*P*<0.05), and the SG achieved higher scores (*P*<0.05, **Table 3**).

Adverse reactions

In the SG, there were 4 (8.51%) cases of nausea, 1 (2.13%) case of vomiting, 2 (4.26%)

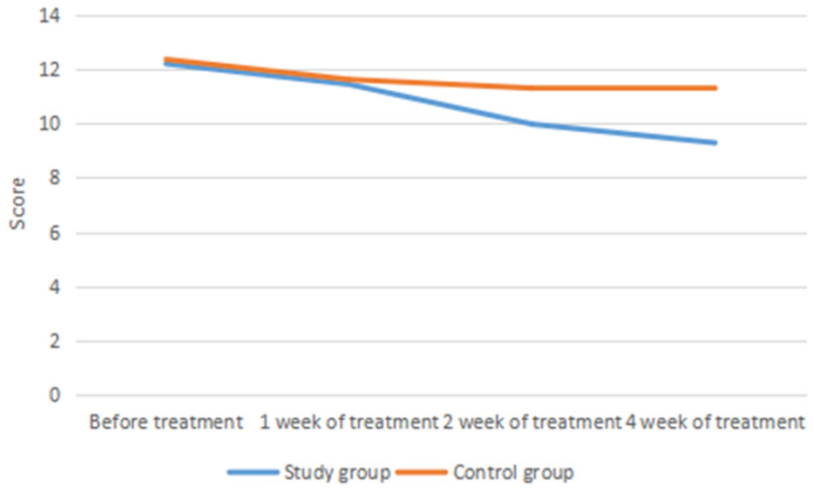

Figure 1. Changes in the Scores of Anxiety. The picture shows that at 2 and 4 weeks after treatment, the score of anxiety was lower in the SG (P<0.05). Both groups achieved significant reduction in the score of anxiety at 1 week, 2 weeks and 4 weeks after treatment (P<0.05).

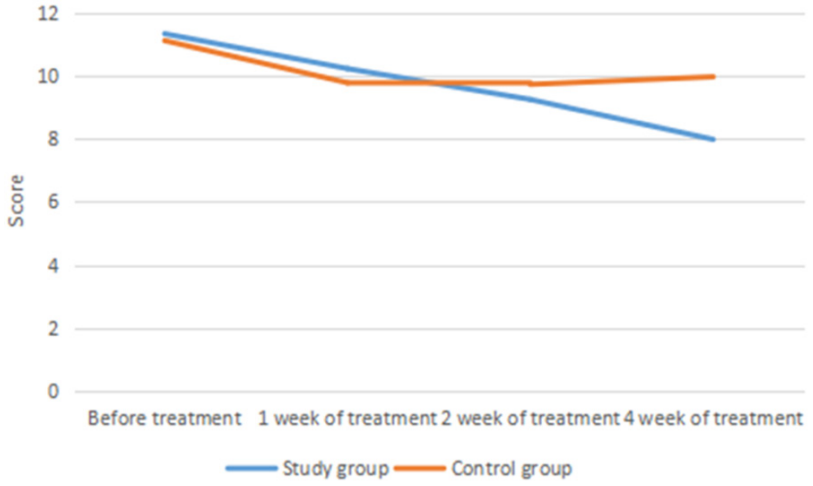

Figure 2. Changes in the scores of depression. The score of depression was lower in the SG at 2 and 4 weeks after treatment (P<0.05), but higher at 1 week after treatment (P<0.05). Both groups achieved significant reduction in the score of depression at 1 week, 2 weeks and 4 weeks after treatment (P<0.05).

cases of dizziness, 1 (2.13%) case of abdominal distension and 1 (2.13%) of constipation; while the cases of these adverse reactions in the CG were 8 (17.02%), 3 (6.38%), 4 (8.51%), 3 (6.38%) and 3 (6.38%), respectively. The total incidence of adverse reactions was 19.15% in the SG and 44.68% in the CG (*P*<0.05, **Table 4**).

Discussion

Chronic pain refers to physical pain lasting for more than one month. With the increasing incidence, chronic pain has a serious impact on the physical and mental health of patients [9-11]. Pain is a subjective feeling accounting for emotional reaction, especially anxiety and depression. Patients with chronic pain will suffer from anxiety, depression and other emotions due to the pain itself, while adverse emotional changes and pain share the biological channels, neurotransmitter systms, and conduction channels. As our body is stimulated, the limbic area of the brain will regulate emotions which change significantly as the conduction of pain perception is from the hypothalamus to the second parietotemporal region and limbic lobe of the brain [12-14]. Therefore, anxiety and depression interact and coexist with body pain.

Paracetamol and Tramadol Hydrochloride Tablet is a compound consisting of acetyl aminophenol and Tramadol. Tramadol is a mild opioid analgesic that is effective in patients with moderate and severe pain with low habituation and respiratory depression [15, 16]; while acetyl aminophenol is a classical analgesic and COX inhibitor that works better in patients with moderate and mild pains, but may cause hepatotoxicity at high doses [17]. Paracetamol and Tramadol Hydrochloride Tablets combine the pharmacokinetics and mechanisms of both drugs to achieve better analgesic effect [18]. Relaxation training alleviates patients from anxiety, depression and pains by mental and physical relaxation and reduces the excitement of sympathetic nervous system, so as to improve the quality of life [6, 19, 20].

Table 3. Comparison between the two groups for the incidence of adverse reactions (n, %)

Group	n	Nausea	Vomiting	Dizziness	Abdominal distension	Constipation	Total adverse reactions
SG	47	4 (8.51)	1 (2.13)	2 (4.26)	1 (2.13)	1 (2.13)	9 (19.15)
CG	47	8 (17.02)	3 (6.38)	4 (8.51)	3 (6.38)	3 (6.38)	21 (44.68)
χ^2		1.528	1.044	0.712	1.044	1.044	7.05
P		0.216	0.307	0.399	0.307	0.307	0.008

Table 4. Comparison between the two groups for the quality of life before and after treatment ($\bar{x}\pm s$)

Group	Time point	RP	PF	CF	EF	RF	Total quality of life
SG (47)	Before treatment	53.05±3.86	60.15±3.91	61.55±3.85	63.38±3.4	59.42±4.92	54.47±4.82
	After treatment	72.44±4.55*	80.51±4.39*	73.37±6.96*	82.38±3.96*	72.86±4.32*	71.85±5.06*
	T	22.279	23.743	10.188	24.957	14.073	17.05
	P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
CG (47)	Before treatment	53.49±3.01	60.32±2.42	61.79±3.87	64.14±3.59	59.66±4.91	55.12±3.31
	After treatment	60.37±4.09	66.41±4.17	65.57±7.46	71.33±2.96	62.99±4.64	61.26±4.15
	T	9.288	8.66	3.084	10.594	3.379	7.93
	P	<0.001	<0.001	0.003	<0.001	0.001	<0.001

Note: *indicates P<0.05 as compared with the CG after treatment.

In this study, the total relief rate was 95.74% in the SG and 74.47% in the CG. The SG obtained much lower scores of anxiety and depression at 2 and 4 weeks after treatment, but the score for anxiety was higher at 1 week after treatment. The scores of anxiety and depression were decreased in both groups at 1 week, 2 weeks and 4 weeks after treatment, indicating that the combination of relaxation training and Paracetamol and Tramadol Hydrochloride Tablets can effectively relieve pain, anxiety and depression. The possible reasons may be that the combination of the two drugs could relax patients physically and mentally to improve emotions, as the unhealthy emotions and pain interacted and co-existed; the pain would be relatively improved with the improvement of emotions [21, 22].

Studies have shown that higher pain intensity indicates poor quality of life. Chronic pain will have a negative impact on the lives of the patients and their families [23, 24]. In this study, quality of life of the patients was evaluated, and both groups achieved elevation in the scores of PR, PF, CF, EF and RF, and total score of quality of life, which was more significant in the SG. The results supported the positive effect of the treatment combination on the quality of life. Adverse reactions, such as nausea, vomiting, dizziness, abdominal distension, and constipation, were inevitable, but at a mild level with treatment of Paracetamol and Tramadol Hydrochloride Tablets. According to the study, the total incidence of adverse reactions was 19.15% in the SG, and 44.68% in the CG, indicating that the addition of relaxation training on the basis of drug treatment could effectively reduce the drug-related adverse reactions.

In conclusion, anxiety and depression are generally considered to act on and coexist with pain, affecting the therapeutic and analgesic effects. Therefore, the clinical treatment of patients with chronic pain should give consideration to anxiety and depression, and take targeted measures accordingly to relax patients physically and mentally, and improve the therapeutic effects. In this study, relaxation training was combined with Paracetamol and Tramadol Hydrochloride Tablets in the treatment of chronic pain, demonstrating that it has advantages of reducing pains, anxiety, depression and adverse reactions.

In summary, relaxation training combined with Paracetamol and Tramadol Hydrochloride Tablets can effectively relieve pain, anxiety and depression of patients and reduce the occurrence of adverse reactions, which is of positive significance for the improvement of their

quality of life. However, the study samples in this paper are relatively small and the intervention time is relatively short, so the long-term treatment effect for patients with chronic pain is not clear. In the future, studies with larger sample sizes and longer relaxation training should be conducted, thus providing a reference for the long-term efficacy.

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Disclosure of conflict of interest

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