Clinical efficacy of oxycontin combined with gabapentin on neuropathic cancer pain and its effect on immune function

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Abstract: Objective: To investigate the clinical efficacy of oxycontin combined with gabapentin on neuropathic cancer pain (NCP) and its effect on immune function. Methods: A retrospective analysis was conducted using clinical data from 50 patients with NCP. The patients were divided into research group (RG) and control group (CG), with 25 patients in each group. Patients in both groups received oxycontin tablets for analgesic treatment; besides, those in the RG were also administered with gabapentin. Changes in cancer pain and quality of life, adverse reactions, and indicators of immune function before and after treatment were determined. Results: After medication, pain scores in both groups were decreased compared with pre-treatment scores (P<0.001); the decrease in the RG, however, was more significant than that in the CG (P<0.001). Similar results were also observed for Karnofsky Performance Status (KPS) scores before and after treatment in both groups (P<0.001), and the mean KPS score in the RG was lower than that in the CG (P<0.001). Meanwhile, total remission rate in the RG was increased compared with the CG (P<0.001). After medication, patients in the RG experienced fewer adverse reactions than those in the CG (P<0.05). After medication, immune functions in both groups were ameliorated compared with those before medication (P<0.05). However, increases in the RG were higher than those in the CG (P<0.001). Conclusion: The combination of oxycontin and gabapentin may exert a synergistic effect, with higher efficiency in pain relief than oxycontin alone. Moreover, combination of medication also decreased the incidence of adverse reactions and improved quality of life and immune function better than oxycontin alone. This strategy is worthy of promoting in clinical practice.

Keywords: Oxycontin, gabapentin, NCP, clinical efficacy, immune functions

Introduction

Neuropathic cancer pain (NCP) is the most common pain in cancer patients, and is usually concomitant with traumatic cancer pain [1]. It has been reported that nearly one-third of cancer patients suffer from moderate or severe pain, in which the incidence of NCP is approximately 33%. NCP has long been regarded as a problem in clinical studies of cancer treatment, with approximately 13% of cancer patients unable to achieve positive control, of which NCP patients account for 53% [2]. In addition to the complicated pathogenesis of NCP, tumor growth can directly compress and/or infiltrate nerves, thereby leading to pain [3]. During growth, carcinoma cells may induce excessive release of cytokines, including prostaglandin and tumor necrosis factor α, which initiate signal transduction of peripheral neuropathic pain, and trigger the sense of pain [4]. During cancer treatment, patients are also susceptible to NCP. Chemotherapeutics, such as cisplatin or paclitaxel, may induce chemotherapy-related peripheral nerve lesions [5, 6]. Although these complications may be controlled, the resultant irreversible tissue and nerve injuries may exacerbate the symptoms of cancer pain [7].

Clinical treatment of cancer pain, with a lower remission rate, has become the focus clinical
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research, and strategies developed for NCP are primarily performed using methods that are not specific for NCP. Neuropathic pain is sensitive to some opioids used in clinical practice; however, for the nociceptive pain often reported by NCP patients, opioid medications remain the most effective treatment for NCP [8]. NCP can only be controlled by high doses of opioid medication; this, however, makes patients more vulnerable to severe adverse reactions, further aggravating pain and decreasing patient compliance to treatment [9]. Thus, analgesic drugs are recommended for NCP patients treated with opioids.

Oxycontin, a novel opioid used in the treatment of cancer pain, can bind to the opioid receptors to curb the release of nerve transmitters, thereby achieving an analgesic effect, with high bioavailability and long action time [10]. However, oxycontin in cancer patients usually causes a series of adverse reactions, including constipation, nausea and/or vomiting and, in some severe cases, bronchial spasm and mental disorders [11]. Gabapentin, a novel anti-seizure drug, can alleviate pain by inhibiting nerve function and antagonizing calcium channels in the central nervous system, and has been widely applied in clinical practice [12].

However, there are few clinical studies on the combination of oxycontin and gabapentin in the treatment of NCP, thus resulting in a lack of accurate evaluation of efficacy and safety. Previous studies have reported that patients with neuropathic pain have poor immune function [13]. Thus, in the present study, we combined oxycontin and gabapentin medication in NCP patients to observe the effect of this strategy on clinical efficacy and immune function, aiming to provide a reference for the clinical treatment of NCP.

Materials and methods

General data

A retrospective analysis was conducted using clinical data from 50 NCP patients admitted to our hospital for treatment from July 2016 to March 2018. These patients were divided into the research group (RG) and the control group (CG) (n=25 each). The RG included 16 males and 9 females aged 30 to 71 years, with the mean age of 51.9±10.7 years. Diagnoses in this group included lung cancer (n=7), breast cancer (n=5), colorectal cancer (n=4), cervical cancer (n=2), esophageal cancer (n=1), and liver cancer (n=6). The CG included 18 males and 7 females aged 32 to 73 years, with the mean age of 52.4±12.3 years. Diagnoses included lung cancer (n=9), breast cancer (n=6), colorectal cancer (n=3), cervical cancer (n=4), esophageal cancer (n=1), and liver cancer (n=2).

Inclusion and exclusion criteria

This study was approved by the Ethics Committee of the Kashgar Prefecture Second People’s Hospital, and all subjects provided informed written consent. Patients who fulfilled the following criteria were included in the present study: cancer diagnosis confirmed by laboratory examination and pathological examination [14]; Neuropathic Pain Questionnaire (DN4) ≥ 4 points; pain caused by nerves compressed by a tumor(s); and those with tumor infiltration treated with chemotherapy. Clinical symptoms included shooting, knife-like or stabbing pain, and burning or lightning pain, with numbness or paresthesia. Included patients had pain for more than 3 months with a numerical rating scale (NRS) [1] score ≥ 4 before receiving analgesic treatment, an expected survival > 3 months, and all relevant clinical data were complete.

Patients with any of the following characteristics were excluded from the present study: complications resulting from insufficiency in the heart or lung; severe liver or kidney dysfunction; connective tissue disease; endocrine metabolic disease; central nervous system disease; hematopoietic failure or immune disorder(s); coma; intellectual disabilities or family history of mental disorders; chemotherapy or radiotherapy to the pain site within 2 weeks; or intolerance to the drugs investigated (i.e., oxycontin and/or gabapentin).

Treatment methods

Control group: Oxycontin tablets (Beijing Mundipharma Co., Ltd.; Lot No.: J20140125; China) were taken orally at an initial dose of 10 mg, twice per day. Twelve hours later, the dose was gradually increased to 40 mg for 4 weeks, considering the condition of the patient.

Research group: In addition to oxycontin tablets, patients in the RG received oral adminis-
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Pain was evaluated using an NRS, scored from 0 to 10: mild pain with cough, turnover, or pain during deep breaths (1 to 3 points); moderate pain with pain at rest affecting sleep (4 to 6 points); severe pain with disturbance, frequent turnover, sleeplessness, sweating, or intolerable pains (7 to 10 points).

A quality of life (QOL) scale [15] was used to assess the QOL of patients using 12 indicators to evaluate the effects of cancer pain on emotions, ambulation, sleep, social activities, and the regular activities of daily life. The highest possible score was 60 points, with scoring as follows: extremely poor QOL (<20 points); poor QOL (21 to 30 points); generally good QOL (31 to 40 points); improved QOL (41 to 50 points); and excellent QOL (51 to 60 points).

A Karnofsky Performance Status (KPS) scale [16] was applied to evaluate physical condition as follows: no discomfort or symptoms (100 points); mild symptoms, but not affecting the activities of daily life (90 points); moderate symptoms that may affect the regular activities of daily life (80 points); not able to maintain regular activities but possessed the self-care ability (70 points); need occasional help (60 points); required special care (40 points); required medical care, without any self-care ability for the activities of daily living (30 points); required treatment for severe condition (20 points); critical disease (10 points); and death (0 point).

The clinical remission rate against cancer pain in patients was also evaluated [17] according to the following criteria: complete remission (CR) for patients with no pain; partial remission (PR) for patients with significant improvement in pain after medication, QOL, and sleep; mild remission (MR) for patients with slight alleviation in pain but still with acute pain affecting sleep; no remission (NR) for patients without any alleviation after medication. The total remission rate (TRR) was calculated according to the following formula: TRR = (CR + PR)/total × 100%.

In addition, patients in both groups were monitored for the toxic reactions or side effects of drugs, including nausea, vomiting, constipation, dizziness, and insomnia.

A flow cytometer (FACSCalibur, Becton-Dickinson, USA) was used to determine the proportions of CD3⁺, CD4⁺, CD4⁺/CD8⁺ ratio, and natural killer (NK) cells with CD3-FITC/CD (16+56)-PE monoclonal antibody, CD4FITC, CD8PE, and the isotype controls, hemolysin and fluorescent microspheres for calibration (Becton-Dickinson, USA). Briefly, 2 to 3 mL of fasting venous blood was drawn from patients and transferred to vacuum anticoagulant tubes, in which 50 μL of anti-coagulated blood was sufficiently mixed with 30 μL of CD3-FITC/CD (16+56)-PE monoclonal antibodies, CD4FITC and CD8PE antibodies. The mixture was then placed in the dark for staining for 15 min, followed by incubation with 1 mL of ACK lysis buffer in the dark for an additional 10 min. The mixture was then centrifuged at 2000 rpm for 5 min, and the supernatant was discarded, while the pellet was then mixed with 1 mL of dilution with gentle shaking. Again, the mixture was centrifuged at 2000 rpm for 5 min, with the supernatant being discarded. After that, samples were stored in the dark, and after sufficient mixing, subjected to flow cytometry within 4 h.

Statistical methods

SPSS version 19.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analysis. Measurement data are expressed as mean ± standard deviation (mean ± SD). The t test or pairwise t test was adopted for intergroup comparison or the intragroup comparison before and after treatment. The Chi-squared test was used to compare data between the two groups; P<0.05 was considered to be statistically significant.
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Before and after treatment, patients in the RG demonstrated KPS scores of 59.08±8.63 and 84.43±6.16, respectively, while those in the CG demonstrated KPS scores of 60.01±9.48 and 74.63±10.93, respectively. There were no differences in KPS scores between two groups before treatment (P > 0.05). However, after treatment, the KPS scores of patients in both groups increased significantly in comparison with the scores before treatment (t=11.950, P<0.001; t=5.052, P<0.001), and patients in the RG exhibited significantly higher KPS scores than those in the CG (t=3.906, P<0.001) (Figure 3).

Oxycontin combined with gabapentin can reduce NRS scores

Before and after treatment, patients in the RG demonstrated NRS scores of 6.43±1.38 and 2.13±0.87, respectively, while those in the CG scored 6.55±1.73 and 3.37±0.68, respectively. There were no statistical differences in NRS scores between the two groups before treatment (P > 0.05). However, after treatment, the NRS scores of patients in both groups decreased significantly compared with those before treatment (t=13.180, P<0.001; t=8.554, P<0.001), and patients in the RG exhibited significantly lower NRS scores than those in the CG (t=5.615, P<0.001) (Figure 1).

Oxycontin combined with gabapentin can improve QOL scores

Before and after treatment, patients in the RG demonstrated QOL scores of 26.67±4.47 and 42.68±6.09, respectively, while those in the CG demonstrated QOL scores of 26.81±3.51 and 35.81±5.92, respectively. There were no statistical differences between the groups in QOL scores before treatment (P > 0.05). However, after treatment, the QOL scores of patients in both groups increased significantly compared with those before treatment (t=10.600, P<0.001; t=6.538, P<0.001), and patients in the RG demonstrated higher QOL scores than those in the CG (t=4.044, P<0.001) (Figure 2).

Oxycontin combined with gabapentin can improve KPS scores

Before and after treatment, patients in the RG demonstrated KPS scores of 59.08±8.63 and 84.43±6.16, respectively, while those in the CG demonstrated KPS scores of 60.01±9.48 and 74.63±10.93, respectively. There were no differences in KPS scores between the two groups before treatment (P > 0.05). However, after treatment, the KPS scores of patients in both groups increased significantly in comparison with the scores before treatment (t=11.950, P<0.001; t=5.052, P<0.001), and patients in the RG exhibited significantly higher KPS scores than those in the CG (t=3.906, P<0.001) (Figure 3).

Oxycontin combined with gabapentin can better alleviate pain after treatment

After treatment, there were 13 patients in the RG with CR (52.00%), 8 with PR (32.00%), 2 with MR (8.00%) and 2 with NR (8.00%). In the CG, there were 8 patients with CR (32.00%), 5 with PR (32.00%), 6 with MR (24.00%), and 5

### Table 1. General information of the research and the control groups [n (%)]/(x ± SD)

<table>
<thead>
<tr>
<th>Category</th>
<th>Research group (n=25)</th>
<th>Control group (n=25)</th>
<th>t/x²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (64.00)</td>
<td>18 (72.00)</td>
<td>0.368</td>
<td>0.544</td>
</tr>
<tr>
<td>Female</td>
<td>9 (36.00)</td>
<td>7 (28.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>51.9±10.7</td>
<td>52.4±12.3</td>
<td>0.153</td>
<td>0.879</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>54.7±13.5</td>
<td>55.8±11.9</td>
<td>0.306</td>
<td>0.761</td>
</tr>
<tr>
<td>Pain duration (months)</td>
<td>15.8±7.6</td>
<td>16.9±8.1</td>
<td>0.495</td>
<td>0.623</td>
</tr>
<tr>
<td>Type of cancer</td>
<td></td>
<td></td>
<td>1.412</td>
<td>0.235</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>7 (28.00)</td>
<td>9 (36.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>5 (20.00)</td>
<td>6 (24.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>4 (16.00)</td>
<td>3 (12.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>2 (8.00)</td>
<td>4 (16.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>1 (4.00)</td>
<td>1 (4.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver cancer</td>
<td>6 (24.00)</td>
<td>2 (8.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Place of residence</td>
<td></td>
<td></td>
<td>0.397</td>
<td>0.529</td>
</tr>
<tr>
<td>City</td>
<td>19 (76.00)</td>
<td>17 (68.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>6 (24.00)</td>
<td>8 (32.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of smoking</td>
<td></td>
<td></td>
<td>0.095</td>
<td>0.758</td>
</tr>
<tr>
<td>Yes</td>
<td>7 (28.00)</td>
<td>8 (32.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>18 (72.00)</td>
<td>17 (68.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinking history</td>
<td></td>
<td></td>
<td>0.333</td>
<td>0.564</td>
</tr>
<tr>
<td>Yes</td>
<td>9 (36.00)</td>
<td>11 (44.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>16 (64.00)</td>
<td>14 (56.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glu (mmol/L)</td>
<td>5.91±0.53</td>
<td>6.05±0.67</td>
<td>0.819</td>
<td>0.417</td>
</tr>
</tbody>
</table>

Results

General data

Comparisons of general data, including sex, age, weight, pain duration, cancer type, residence, smoking history, alcohol history, and blood glucose levels between the two groups demonstrated no statistically significant differences (P > 0.05) (Table 1).

Oxycontin combined with gabapentin can reduce NRS scores

Before and after treatment, patients in the RG demonstrated NRS scores of 6.43±1.38 and 2.13±0.87, respectively, while those in the CG scored 6.55±1.73 and 3.37±0.68, respectively. There were no statistical differences in NRS scores between the two groups before treatment (P > 0.05). However, after treatment, the NRS scores of patients in both groups decreased significantly compared with those before treatment (t=13.180, P<0.001; t=8.554, P<0.001), and patients in the RG exhibited significantly lower NRS scores than those in the CG (t=5.615, P<0.001) (Figure 1).

Oxycontin combined with gabapentin can improve QOL scores

Before and after treatment, patients in the RG demonstrated QOL scores of 26.67±4.47 and 42.68±6.09, respectively, while those in the CG demonstrated QOL scores of 26.81±3.51 and 35.81±5.92, respectively. There were no statistical differences between the groups in QOL scores before treatment (P > 0.05). However, after treatment, the QOL scores of patients in both groups increased significantly compared with those before treatment (t=10.600, P<0.001; t=6.538, P<0.001), and patients in the RG demonstrated higher QOL scores than those in the CG (t=4.044, P<0.001) (Figure 2).

Oxycontin combined with gabapentin can improve KPS scores

Before and after treatment, patients in the RG demonstrated KPS scores of 59.08±8.63 and 84.43±6.16, respectively, while those in the CG demonstrated KPS scores of 60.01±9.48 and 74.63±10.93, respectively. There were no differences in KPS scores between the two groups before treatment (P > 0.05). However, after treatment, the KPS scores of patients in both groups increased significantly in comparison with the scores before treatment (t=11.950, P<0.001; t=5.052, P<0.001), and patients in the RG exhibited significantly higher KPS scores than those in the CG (t=3.906, P<0.001) (Figure 3).

Oxycontin combined with gabapentin can better alleviate pain after treatment

After treatment, there were 13 patients in the RG with CR (52.00%), 8 with PR (32.00%), 2 with MR (8.00%) and 2 with NR (8.00%). In the CG, there were 8 patients with CR (32.00%), 5 with PR (32.00%), 6 with MR (24.00%), and 5
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With NR (20.00%). Thus, after treatment, the TRR of patients in the RG was higher than that in the CG ($\chi^2 = 5.882$, $P = 0.015$) (Table 2).

Oxycontin combined with gabapentin can decrease incidence of adverse reactions

After treatment, there were 2 cases of vomiting (8.00%), 3 cases of constipation (12.00%), and 3 cases of dizziness or insomnia (32.00%) in the RG. In the CG, there were 8 cases of vomiting (32.00%), 9 cases of constipation (36.00%), and 5 cases of dizziness or insomnia (20.00%).

Thus, the incidence of nausea, vomiting and constipation of patients in the RG was higher than that in the CG ($\chi^2 = 4.500$, $P = 0.034$; $\chi^2 = 3.947$, $P = 0.047$) (Table 3).

Oxycontin combined with gabapentin can ameliorate the immune function

Comparisons of the proportions of CD3⁺, CD4⁺, CD4⁺/CD8⁺ and NK cells between the two groups before treatment revealed no statistically significant differences ($P > 0.05$). After treatment, acute increases were identified in
Oxycontin combined with gabapentin on pain relief

Table 2. Comparison of pain relief between the research and the control groups [n (%)]

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>CR (52.00)</th>
<th>PR (32.00)</th>
<th>MR (8.00)</th>
<th>NR (8.00)</th>
<th>TRR (84.00)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research group</td>
<td>25</td>
<td>13</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>Control group</td>
<td>25</td>
<td>8</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>13</td>
</tr>
</tbody>
</table>

\( \chi^2 = 5.882 \; \; \; P = 0.015 \)

Table 3. Adverse reactions of the research and the control groups [n (%)]

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Feel sick and vomit (8.00)</th>
<th>Constipation (12.00)</th>
<th>Dizziness, lethargy (12.00)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research group</td>
<td>25</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Control group</td>
<td>25</td>
<td>8</td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>

\( \chi^2 = 4.500 \; \; \; P = 0.034 \)

Discussion

NCP is a common clinical symptom in patients with malignant tumors, most of whom also suffer from negative emotions, including anxiety and depression, which further exacerbate pain [18]. Medication, as the preferred choice of NCP treatment, can alleviate pain and improve QOL, which is conducive to the implementation of chemotherapy or radiotherapy against tumors [17]. Currently, patients with NCP are treated with opioid receptor agonist and antidepressive drugs, which usually result in a series of adverse reactions in a series of adverse reactions [19], severely affecting the survival of NCP patients. Thus, research on NCP medication is of significance for clinical practice.

Opioids are first-line drugs in the clinical treatment of moderate or severe cancer pain, and oxycontin, a type of opioid receptor agonist, acts primarily on smooth muscle or the central nervous system as oxycodone (the major component) by inhibiting the release of neurotransmitters, and has demonstrated promising efficacy in alleviating physical, neuropathic, or organ pain [20]. Oxycontin is clinically characterized by rapid onset and high bioavailability. Previous studies have reported that oral administration of oxycontin has a binding rate of 45% with plasma proteins and a bioavailability of 87% [21], but does not generate toxic metabolites [22]. Nevertheless, oxycontin can induce a series of adverse reactions, including nausea, vomiting, dizziness, and insomnia, and in some severe cases, patients may develop mental disorders or become faint [23]. Gabapentin is a derivative of γ-aminobutyric acid and a novel anti-seizure drug, which was initially used to treat spasms; however, it has gradually been developed as a first-line drug for the treatment of chronic pain [24]. The mechanism by which gabapentin alleviates neuropathic pain has not been fully elucidated. Current opinion is that gabapentin can bind to NMDA receptors to block their activity, thereby alleviating pain. Moreover, gabapentin can improve the efficiency of the γ-aminobutyric acid receptor, and with its ability to pass through the blood brain barrier, generate an inhibitory effect on nerves, thereby exerting sedative and analgesic effects [25]. Gabapentin can also reduce the permeability of nerve cell membranes for proteins in the calcium channel to block signal transduction through neurotransmitters and decrease excitability, which can suppress over-excitation and abnormal discharge of neurons [26]. Previous studies have reported that combination of gabapentin and opioids can increase serum gabapentin levels, thereby enhancing its efficacy [27]. In light of these features, we combined oxycontin and gabapentin for the treatment of NCP. Our results showed that NRS scores were significantly decreased after medication compared with pre-medication scores in both RG and CG. Conversely, however, QOL and KPS scores were increased. After treatment, the NRS score in the RG was significantly lower than that in the CG, while QOL and KPS scores...
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Table 4. Comparison of changes in immune indicators before and after treatment in the research and the control groups (x ± SD)

<table>
<thead>
<tr>
<th>Index</th>
<th>Research group (n=25)</th>
<th>Control group (n=25)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD3⁺ (%)</td>
<td>57.48±5.94</td>
<td>73.92±5.61</td>
<td>10.060</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4⁺ (%)</td>
<td>24.73±3.12</td>
<td>47.16±4.58</td>
<td>20.240</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4⁺/CD8⁺ (%)</td>
<td>1.09±0.28</td>
<td>1.87±0.31</td>
<td>9.336</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NK (%)</td>
<td>16.58±5.41</td>
<td>27.54±6.83</td>
<td>6.289</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: *P<0.001 compared with the control group after treatment.

A reduction in adverse reactions. Moreover, with pain control, patients' QOL was also improved significantly.

Subsets of T lymphocytes, including CD3⁺, CD4⁺, the CD4⁺/CD8⁺ ratio, and NK cell proportions, can reflect the level of immunity [28]. Previous studies have demonstrated that cancer pain is a strong stress trigger and is responsible for reduced levels of immunity. Although effective analgesic treatment can alleviate impaired immunity in patients, once they have gained effective remission of cancer pain, patients may also benefit from the improvement in immunity [29]. Results of this study indicated that after medication, immune function in the two groups was significantly improved compared with that before medication, with significantly increased CD3⁺, CD4⁺, CD4⁺/CD8⁺ and NK cells. The RG increased more significantly than the CG. Thus, we inferred that combination of oxycontin and gabapentin improved immunity in NCP patients, which may contribute to the eradication of immunosuppression due to the reduced secretion of stress mediators and stress responses caused by cancer pain following analgesic treatment.

NCP is quite complicated in classification and pathogenesis. The insufficient sample size fail-
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...ed to help in classification or elucidate the mechanism of action of NCP in this study, which can be considered as a limitation of the study. In future studies, we will expand the sample size and prolong the duration of study, so as to investigate the classification and mechanisms of NCP and further verify the results of this study.

In conclusion, combination of oxycontin and gabapentin may exert a synergistic effect, with more significant efficiency in pain alleviation than the use of oxycontin alone. Combination of medications may also reduce the incidence of adverse reactions, and improve QOL and immune function, which is superior to the use of oxycontin alone. Thus, it is worthy of promoting this strategy in clinical practice.

Disclosure of conflict of interest

None.

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