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Acupuncture for Moderate to Severe Cancer-Related Pain: A Review of Clinical Research Progress

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Abstract: *This article aims to review the clinical research outcomes of acupuncture for the treatment of moderate to severe cancer-related pain over the past decade. By searching and reviewing clinical research literature on acupuncture for moderate to severe cancer-related pain from 2014 to 2024, this paper organizes and summarizes the progress in clinical research over the last 10 years. In the treatment of moderate to severe cancer-related pain, acupuncture therapies are diverse, including traditional acupuncture, electroacupuncture, acupoint injection, and comprehensive treatments. When combined with one or more acupuncture therapies, the clinical analgesic effects are generally superior to those of simple three-step drug therapy alone. Additionally, acupuncture can reduce the use of analgesic medications and their side effects, prolong the duration of pain relief, and help patients improve their quality of life. It has the advantages of being safe, economical, easy to operate, and easily disseminated, and holds good application value in clinical practice.*

Keywords: *Acupuncture,Moxibustion, Moderate to Severe, Cancer-Related Pain, Research Progress*

1. Introduction

Malignant tumors continue to be a formidable challenge in the medical field. The pain caused by tumors themselves or by their compression of surrounding tissues is more intense than general pain, making it difficult for patients to bear and often leading to significant psychological stress that undermines their confidence in recovery. Moreover, after undergoing multiple courses of radiotherapy and chemotherapy, many patients experience a marked decrease in physical tolerance, with the torment and fear associated with cancer-related pain sometimes surpassing that of the cancer itself. According to statistical data from the International Agency for Research on Cancer [1], the number of new cancer cases worldwide reached 19.3 million in 2020, with an expected increase to over 28 million by 2040. The World Cancer Report 2020 indicates that in many countries, cancer has become the leading cause of death among residents, with an estimated annual growth rate of 50% in global new cancer cases, increasing from 18 million in 2018 to 28 million by 2040 [2]. Pain, as the most common and severe symptom affecting cancer patients, severely impacts the daily life and quality of life of oncology patients and interferes with the progress and effectiveness of anti-tumor treatments. Data show that the incidence of pain in newly diagnosed cancer patients is around 25%, which can rise to 60%-80% in advanced stages of cancer [3]. Furthermore, a study [4] found that approximately 40% of cancer patients worldwide suffer from cancer-related pain, with 38% of these patients experiencing moderate to severe pain.

In clinical practice, the management of cancer pain primarily follows the "three-step" analgesic ladder recommended by the World Health Organization [5], utilizing opioids or nonsteroidal anti-inflammatory drugs (NSAIDs) to alleviate cancer-related pain. Long-term use of opioid drugs can lead to adverse reactions such as vomiting, dizziness, constipation, and addiction. When employing the three-step analgesic ladder for pain management, the side effects of analgesics, drug resistance, and issues of addiction are difficult to effectively address, leading to a gradual decrease in the efficacy of drug-based pain relief over time. With the increase in cancer pain cases, reports of deaths due to opioid misuse are also on the rise [6]. Consequently, 70% of patients with moderate to severe cancer pain still do not receive adequate pain relief [7]. Compared to traditional analgesic drug therapies, acupuncture for moderate to severe cancer pain not only has good pain-relieving effects but also offers advantages such

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as safety, ease of operation, minimal adverse reactions, and no dependency or addiction, making the clinical research on acupuncture for moderate to severe cancer pain in China develop rapidly. This review summarizes the progress in clinical research on acupuncture for moderate to severe cancer pain, aiming to provide a reference for clinical application.

2. General Acupuncture Therapy

2.1. General Acupuncture Needling Therapy

Zheng Kai et al.[8] selected 45 patients with lung cancer and associated cancer pain. The control group was treated according to the WHO three-step pain treatment plan, while the observation group received acupuncture at points Kongzui (LU6), Fengmen (GV4), Shousanli (LI10), Hegu (LI4), Ashi points, and Feishu (BL13). After treatment, the observation group had lower VAS scores and adverse reaction incidence rates, and better pain relief and quality of life improvement ($P<0.05$). Yang Fengying[9] selected 120 patients with cancer pain. The control group was treated with morphine slow-release tablets, while the observation group was treated with acupuncture plus anti-inflammatory and analgesic suppositories. The main acupoints for body acupuncture were Zusanli (ST36), Yanglingquan (GB34), Yanglingquan(ST34), Sanyinjiao (SP6), Juegu (GB32), and Taichong (LR3). For lung cancer pain, additional points Kongzui (LU6) and Neiguan (PC6) were used; for breast cancer pain, additional points Tianzong (SI11) and Shanzhong (CV17) were used; for gastric cancer pain, additional points Liangmen (ST21), Zhongwan (CV12), and Neiguan (PC6) were used; for liver cancer pain, additional points Yanglingquan (GB34) and Zhongdu (LR2) were used. The results showed that the adverse reaction rate in the treatment group was 8.3%, compared to 25% in the control group ($P<0.05$); the pain relief efficacy was 96.6% in the treatment group and 73.3% in the control group ($P<0.01$). Hui Jianrong et al.[10] divided 80 cancer pain patients into a control group treated according to the WHO three-step pain treatment guidelines, and a treatment group that additionally received acupuncture at Hegu (LI4), Dazhui (GV14), Dazhu (BL11), Yanglingquan (GB34), Taichong (LR3), and Ashi points. After treatment, both groups showed a decrease in NRS[11] scores compared to before treatment, with the treatment group scoring lower than the control group ($P<0.05$). The analgesic onset time in the treatment group was shorter than in the control group, and the duration of pain relief was longer in the treatment group ($P<0.05$). The total effective rate of pain relief in the treatment group was 82.5%, compared to 57.5% in the control group, with a statistically significant difference between the two groups ($P<0.05$). The equivalent morphine consumption during the entire treatment course in the treatment group was lower than in the control group ($P<0.05$). The incidence of adverse reactions such as nausea, vomiting, fatigue, constipation, and dizziness in the treatment group was significantly lower than in the control group ($P<0.05$). This indicates that the combination of general analgesic therapy with acupuncture can enhance the analgesic effect, while reducing the adverse reactions and dosage of analgesic drugs, thus also reducing the potential for abuse of painkillers.

2.2. Electroacupuncture

Lu Xiaoting[12] randomly divided 80 patients diagnosed with malignant tumors and associated cancer pain into an experimental group and a control group. The experimental group received three-step pain relief treatment, while the observation group, in addition to this, selected Ashi points, corresponding spinal segment back-shu points of the pain area, Hegu (LI4), Zusanli (ST36), and Sanyinjiao (SP6) for electroacupuncture treatment. The results showed that the observation group could reduce the amount of analgesic medication used by patients, achieve analgesic effects more quickly, and reduce the number of breakthrough pain episodes, which was statistically significant ($P<0.05$), and could also improve patients' quality of life and reduce the probability of adverse reactions ($P<0.05$). Wang Can[13] selected 80 patients with cancer pain and divided them into a control group treated with hydromorphone and an observation group treated with hydromorphone combined with electroacupuncture. The results showed that the total effective rate of pain relief in the observation group was 90.0%, significantly higher than the control group's 70.0%; the adverse reaction rate in the observation group was 15.0%, significantly lower than the control group's 35.0%, with both differences being statistically significant ($P <0.05$); moreover, the number of breakthrough pain episodes, NRS[11], and KPS[14] scores in the observation group were all better than in the control group ($P <0.05$). This indicates that electroacupuncture combined with analgesic drug treatment for cancer pain can effectively alleviate patients' pain perception, control the dosage of analgesic drugs, and reduce the probability of adverse reactions.

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2.3. Auricular Acupuncture

Xuan Jing[15] randomly divided 80 patients with moderate to severe pain due to liver cancer into a control group treated with sustained-release morphine sulfate tablets and an observation group that additionally received auricular acupuncture treatment. The results showed that the total effective rate of the observation group was 87.50%, which was superior to the control group's total effective rate of 80.00%, with a statistically significant difference (P<0.05). Hou Xiao[16] used auricular acupuncture to treat breast cancer patients in the recovery period with Liver Qi stagnation. The control group received endocrine therapy plus XiaoYaoSan treatment, while the observation group added auricular acupuncture treatment (liver, stomach, heart, shenmen, subcortex, endocrine, and sympathetic). The final scores on the FACT-B questionnaire and the additional attention section scores were higher in the observation group than in the control group, with a statistically significant difference (P<0.05). This indicates that combined auricular acupuncture treatment can better improve patients' pain and various aspects of living conditions, helping patients return to society and family.

2.4. Ophthalmic Acupuncture

Zhao Shuge et al.[17] divided 60 patients with cancer pain into a control group that took oral oxycodone and an observation group that, in addition to this, received ophthalmic acupuncture therapy. According to the principles of ophthalmic acupuncture point selection[18], different acupoints were chosen for treatment based on the type of cancer and the syndrome differentiation of the patients' organs. The results showed that the total effective rate of the observation group was 90.00%, significantly higher than the control group's 63.33%, with a statistically significant difference (P<0.05). The decrease in NRS scores and the increase in QOL scores in the observation group were more pronounced than in the control group (P<0.01). This indicates that the combination of ophthalmic acupuncture and oxycodone hydrochloride for pain relief is more effective and can improve patients' sleep, appetite, psychological stress, and overall quality of life, providing a new clinical treatment approach for cancer patients to alleviate pain.

2.5. Moxibustion

Sun Ting et al.[19] divided 60 patients with cancer pain into a control group treated with oral administration of oxycodone and a treatment group that, in addition to this, received moxibustion therapy at Ashi points. The results showed that the total pain relief rate in the treatment group was 90.33%, significantly higher than the control group's 73.33% (P<0.05). The treatment group also had higher pain relief duration and QOL scores than the control group (P<0.05), fewer breakthrough pain episodes, and lower levels of TNF-αand IL-6 compared to the control group (P<0.05). TNF-αcan mediate heat-sensitive responses related to cancer pain, and IL-6 mediates pain behavior through neurons [19]. This clinical study indicates that moxibustion can effectively alleviate cancer pain in patients and reduce the total amount of related cancer pain mediators in the blood, providing evidence for the support of moxibustion in relieving cancer pain with observable clinical indicators.

3. Special Acupuncture Therapies

3.1. Auricular Point Pressing Therapy

Chen Run et al.[20] divided 100 patients with cancer pain into a control group treated with sustained-release oxycodone hydrochloride tablets and an observation group that, in addition to oral oxycodone, selected auricular points such as stomach, liver, spleen, cardia, sympathetic, shenmen, and subcortex for auricular point pressing therapy with Vaccaria seeds, and additional points were added according to different concurrent symptoms. The results showed that the effective rate of the observation group was 80%, significantly higher than the control group's 60% (P<0.05). After treatment, the PPI[21] scores of the observation group were lower than those of the control group (P<0.05); the KPS scores were higher than those of the control group (P<0.05), and the incidence of adverse reactions (nausea/vomiting 7%, dizziness 4%, somnolence 2%, urinary retention 3%, constipation 6%) and the number of clinical breakthrough pain episodes in the observation group were significantly lower than those in the control group (nausea/vomiting 18%, dizziness 10%, somnolence 7%, urinary retention 6%, constipation 16%), with statistically significant differences (P<0.05). This indicates that the combination of analgesic drugs and auricular point pressing therapy can significantly

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improve clinical analgesic efficacy and significantly reduce the side effects brought about by the use of analgesic drugs, improving patients' quality of life and reducing the potential for drug abuse.

Wang Ling et al.[22] divided 96 patients with advanced bone malignancies and moderate to severe pain into a control group treated with morphine and an observation group treated with auricular point pressing therapy. The results showed that the total effective rate of the observation group was 84.38%, higher than the control group's 59.38%, with a statistically significant difference ($P<0.05$); the negative emotion scores and NRS scores of the observation group were lower than those of the control group($P<0.05$)[22] .

3.2. Acupoint Embedding Therapy

Wei Yougang et al.[23] randomly divided 60 patients with moderate cancer pain due to lung cancer into a control group treated with oral controlled-release oxycodone hydrochloride tablets and an observation group that received acupoint embedding therapy at points Feishu (BL13), Shenshu (BL23), Danzhong (CV17), Zusanli (ST36), and Ashi points. The results showed that the KPS score of the observation group was better than that of the control group; the pain relief rate for moderate pain in the observation group was 88.9%, for severe pain was 75%, and the reduction in breakthrough pain episodes was 30%, all higher than the control group's rates of 68.8%, 71.4%, and 20%, respectively; moreover, the incidence of adverse reactions and the usage of controlled-release oxycodone hydrochloride tablets in the observation group were both better than in the control group, with statistically significant differences ($P<0.05$). This indicates that acupoint embedding can significantly alleviate patients' pain and reduce the dosage of analgesic drugs, helping to improve the quality of life for patients.

3.3. Wrist- Ankle Needle Therapy

Zhang Yingzun[24] randomly divided 68 patients with cancer pain into a control group treated with strong opioids according to the three-step analgesic ladder and an observation group that received wrist-ankle needle therapy in addition to this. The results showed that the total effective rate of the observation group was 96%, which was superior to the control group's 86% ($P<0.05$), with a statistically significant difference; both groups showed an increase in KPS scores ($P>0.05$), but the PHQ-9 scores in the observation group were significantly lower than in the control group ($P<0.05$), indicating that wrist-ankle needle therapy combined with opioid drugs can better alleviate patients' anxious and tense mental states, improve patients' living conditions, and reduce the probability of adverse events occurring[24]. Wang Lingling et al.[25] randomly divided 80 patients with pain due to primary liver cancer into an observation group and a control group. The control group was treated with "three-step" analgesia using hydrochloride buccal or morphine, and the observation group received wrist-ankle needle therapy in addition to this. The results showed that the pain relief rate in the observation group was 62.5%, and the incidence of adverse reactions was 17.5%, significantly lower than the control group's rates of 40.0% and 37.5% ($P<0.05$); moreover, the reduction in pain intensity scores in the observation group after treatment was more significant than in the control group ($P<0.05$), indicating that wrist-ankle needle therapy combined with drug therapy for cancer pain has significant clinical efficacy and brings considerable benefits to patients.

3.4. Fire Needle Therapy

Zhang Yutian et al.[26] randomly divided 200 patients with cancer pain due to bone metastasis into a control group treated with sustained-release oxycodone hydrochloride tablets and an observation group treated with fire needle therapy, and evaluated the pain relief effects according to CR/PR/MR/NR[27]. The results showed that the pain relief effects in the observation group were CR 36%, PR 50%, MR 9%, NR 5%, all higher than the control group's CR 24%, PR 32%, MR 35%, NR 9%, with statistically significant differences ($P<0.05$), and the KPS scores and the total incidence of adverse reactions in the observation group were lower than in the control group ($P<0.05$). After treatment, the expression levels of stress response factors (adrenaline, noradrenaline, cortisol) in the observation group were lower than in the control group ($P<0.05$). This clinical study indicates that fire needle therapy can enhance the analgesic effect and reduce the release levels of stress response factors in the human body, providing better and longer-lasting relief for patients' discomfort.

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3.5. Acupoint Injection

Guo Huili et al.[28] divided 100 patients with advanced cancer and associated cancer pain into a control group and an experimental group. The control group was treated with conventional morphine sustained-release tablets, and the experimental group, in addition to this, used a compound Danshen injection for acupoint injection at bilateral Ququan (LR8), Feishu (BL13), and Xinshu (BL15). The results showed that the total effective rate of the experimental group was 88%, higher than the control group's 70%, with a statistically significant difference ($P<0.05$). After four weeks of treatment, the total effective rate of the control group was 70%, and that of the observation group was 88%. At the same time, the incidence of gastrointestinal and central nervous system adverse reactions in the experimental group was lower than in the control group, indicating that the combination of acupoint injection and opioid analgesia has a shorter onset time, better analgesic effect, and lower incidence of adverse reactions.

3.6. Acupoint Plaster Therapy

Fan Xianglou et al.[29] divided 86 patients with moderate to severe cancer pain into a control group treated with oral hydrocodone, and an experimental group that received the same medication along with acupoint plaster therapy based on the type of cancer and concurrent symptoms. The results showed that the total effective rate of pain relief in the experimental group was 95.35%, with an adverse reaction incidence rate of 6.98%, significantly better than the control group's 79.07% and 27.91%, respectively, with statistically significant differences ($P<0.05$). Both groups' SAS and SDS scores were lower than before treatment ($P<0.05$). This indicates that acupoint plaster therapy, as a simple medical procedure, can effectively help patients alleviate pain symptoms and reduce the occurrence of side effects such as constipation, dizziness, and sleep disturbances, while also reducing patients' anxious or fearful psychological states.

3.7. Transcutaneous Electrical Nerve Stimulation (TENS)

Wang Hong[30] divided 60 patients with non-small cell lung cancer and bone metastasis into an experimental group and a control group, both of which were given a low dose of hydrocodone. The experimental group, in addition to this, used TENS[31] for the treatment of cancer pain. The results showed that after 28 days of treatment, the experimental group had significantly lower analgesic drug usage and breakthrough pain episodes compared to the control group ($P<0.05$). The patients in the experimental group had better BPI scores and overall quality of life than the control group ($P<0.05$), and overall mental state, daily activity ability, social interaction, psychological stress, and anxiety levels improved better than in the experimental group ($P<0.05$).

4. Combined Therapies

Combined therapies refer to the simultaneous use of two or more traditional Chinese medicine (TCM) pain relief methods, with or without the use of conventional three-step analgesic drugs. Relevant research indicates that the efficiency of integrated Chinese and Western medicine in treating cancer pain can reach over 90%[32]. Wu Miaomiao et al.[33] randomly divided 60 patients with moderate cancer pain into a control group treated with oral sustained-release tablets of tramadol hydrochloride and a treatment group that, in addition to taking tramadol hydrochloride, received combined electroacupuncture and acupoint embedding therapy. The results showed that the NRS, KPS, and QOL[34] scores of the treatment group were superior to those of the control group, with statistically significant differences ($P<0.05$). The total effective rate of the treatment group was 86.67%, higher than the control group's total effective rate of 63.33%, and there was a significant difference in the total effective rate between the two groups after treatment, which was statistically significant ($P<0.05$). Moreover, the incidence of gastrointestinal side effects such as constipation, nausea, and vomiting caused by opioid drugs in the observation group was low, the quality of life of patients was significantly improved, and there was an improvement in the state of anxiety and behavior.

Li Hongyu et al.[35] randomly divided 64 patients with moderate pain due to lung cancer into a control group treated with acupoint plaster therapy and auricular acupuncture, and an experimental group that, in addition to this, used electronic moxibustion devices for intervention. The results showed that the PFS-R scale[36] and VAS scores of the experimental group were lower than those of the control group ($P <0.05$); the WHOQOL-BREF[35] scale scores of the observation group were higher than

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those of the control group (P <0.05).

Wu Ji et al.[37] divided 120 patients with cancer pain into a control group treated with three-step analgesic drugs and a treatment group treated with a combination of basic three-step analgesic drugs and acupuncture combined with auricular therapy. The results showed that the proportion of patients in the treatment group who experienced a decrease in analgesic drug side effects was 34.48%, and the proportion of patients who reduced or stepped down the use of analgesic drugs was 58.62%, both significantly higher than the control group's 21.43% and 17.86%, respectively, which was statistically significant (P<0.05). The VAS and ZPS[38] scores before and after treatment in the treatment group were significantly lower than those in the control group (P<0.05); the differences in CD3+, CD4+, and CD4+/CD8+ levels were statistically significant, with the treatment group showing a better improvement than the control group (P<0.05).

5. Discussion and outlook

Despite the general progress in global medical standards and public health, the number of new cancer cases continues to rise annually. Cancer-related pain is the most common comorbidity in cancer patients, often accompanying them throughout the entire course of the disease, and even until death. An effective analgesic plan can help alleviate both the pain symptoms and psychological stress in patients, enhance their confidence in fighting cancer, and prevent the misuse of analgesic drugs. Acupuncture therapy, with its defined boundaries, safety, economy, and ease of promotion, plays a role in unblocking meridians, activating blood circulation, balancing yin and yang[39]. Additionally, acupuncture has been recognized internationally for its efficacy and safety, further supporting its broader application in clinical settings. The combination of acupuncture with other traditional Chinese medicine pain relief methods, such as moxibustion, has also demonstrated significant benefits in managing cancer pain, including improved immune function and reduced reliance on analgesic medications. These findings underscore the importance of integrating traditional acupuncture methods into the modern cancer pain management paradigm to achieve better patient outcomes.

By reviewing the literature from the past decade, the vast majority of clinical studies have concluded that compared with the conventional single application of the three-step analgesic ladder therapy, the combination of acupuncture treatment can prolong the onset time of analgesia, achieve better pain-relieving effects, and to a greater extent help patients reduce the pain brought about by cancer. At the same time, it can effectively reduce the use of analgesic drugs and their adverse reactions, thereby improving the quality of life for patients, preventing the misuse of analgesic drugs, and helping patients alleviate anxiety or fear, and enhancing their confidence in fighting cancer. Therefore, acupuncture is considered to have a high clinical application value in the treatment of moderate to severe cancer-related pain and is worth promoting in clinical practice.

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