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Exploring the pathogenesis of cancer pain from the perspective of traditional Chinese medicine

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Abstract: The management of cancer pain is crucial during cancer treatment, as many patients endure both physiological and psychological suffering. Cancer pain research has primarily focused on the etiology, pathogenesis, and treatment principles, but significant breakthroughs remain elusive. Cancer pain is a prominent issue in clinical practice, and effective pain control is essential for improving the quality of life for cancer patients. Traditional Chinese Medicine (TCM) approaches cancer pain by emphasizing its holistic view and individualized treatment, with a particular focus on the relationship between the tumor and pain. This article explores the epidemiology, etiology, and TCM understanding of cancer pain, aiming to provide valuable insights into the pathogenesis of cancer pain and its clinical treatment.

Keywords: Cancer Pain, Pathogenesis, Theory, Innovation.

1. Introduction

Cancer pain is pain caused by tumors, cancer-related lesions, and anti-cancer treatments. It primarily manifests in patients with advanced-stage cancer. According to modern medical research, cancer pain results from various factors, such as the direct infiltration of tumors, compression of surrounding nerve tissues, changes in local pH levels, release of pain-inducing substances, and cytokine release [1]. In recent years, due to changing demographics, the incidence of cancer has been steadily rising. Cancer pain significantly impacts patients' behavior, diet, sleep, and psychological well-being, profoundly affecting the quality of life of cancer patients.

Currently, modern medicine has not fully elucidated the pathogenesis of cancer pain. Pain control is mainly based on anti-tumor therapies, with a focus on pain relief, radiotherapy, and bone protection. The World Health Organization promotes the "four-step analgesic ladder," which builds upon the three-step treatment by introducing pain intervention in the fourth step. The fourth-step treatment includes regional blockade techniques, patient-controlled epidural analgesia (PCEA), nerve injury blockade techniques, and implantable drug delivery systems [2]. Although these treatments have achieved certain efficacy, cancer pain remains inadequately controlled, often resulting in significant side effects, addiction risks, and the potential for recurrence after discontinuation.

Traditional Chinese Medicine (TCM) possesses certain advantages and fewer side effects in the treatment of cancer pain. TCM can raise pain thresholds and mitigate adverse reactions to stimuli while providing pain relief. Moreover, Chinese herbal medicine can delay and alleviate pain by regulating

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emotions. Patients with malignant tumors often experience unstable emotions, including anxiety, irritability, fear, and tension, which can lead to the early onset or exacerbation of pain. Furthermore, many Chinese herbal medicines can promote blood circulation, improve tissue oxygen perfusion, prevent hypercoagulability, and reduce tumor-related thrombosis. Therefore, the pathological and physiological basis of TCM treatment for cancer pain may be associated with improving tissue oxygenation [3]. This article intends to explore the etiology and pathogenesis of cancer pain, with the aim of benefiting its clinical application.

2. Epidemiology and Etiology of Cancer Pain

According to estimates from the World Health Organization (WHO), approximately 3.5 to 4 million cancer patients worldwide suffer from pain every day, with 50% experiencing moderate to severe pain, and 30% enduring unbearable severe pain [4]. Statistics indicate that globally, there are 10 million new cancer cases each year, with 6 million cancer-related deaths. Of these, 51.1% of cancer patients experience varying degrees of pain after receiving treatment, and 70% of late-stage cancer patients predominantly exhibit painful symptoms [5-6]. The National Comprehensive Cancer Network (NCCN) guidelines in the United States state that in newly diagnosed patients, the incidence rate of cancer pain is as high as one in four, while in advanced-stage patients, the prevalence of cancer pain reaches three in four [7].

According to the latest 2017 cancer report in China, there are approximately 4.29 million new cancer cases each year, equating to around 10,000 new cancer diagnoses daily, or approximately seven cases per minute. Assuming an average life expectancy of 85 years in China, the cumulative risk of developing cancer for each individual is 36%. On a global scale, China accounts for approximately 22% of new cancer cases and 27% of cancer-related deaths. The five most common cancers in men are lung cancer, stomach cancer, esophageal cancer, liver cancer, and colorectal cancer, which together comprise two-thirds of all cancer cases. Among women, the most prevalent cancers are breast cancer, lung cancer, stomach cancer, colorectal cancer, and esophageal cancer, making up 60% of all cancer cases. Breast cancer accounts for 15% of female cancer cases [8].

In September 2018, the prestigious journal "CA: A Cancer Journal for Clinicians" published its latest global cancer statistics report (impact factor: 244.585), which compiled cancer incidence and mortality rates for 36 types of cancer in 185 countries. According to the report, there were an estimated 18.1 million new cancer cases and 9.6 million cancer-related deaths globally in 2018 [9]. The 2019 American Cancer Society report revealed that approximately 17 million people were diagnosed with cancer in 2018, with 9.5 million succumbing to the disease. As the global population continues to grow and age, the burden of cancer is projected to increase further, with an estimated 27.5 million new cases and 16.3 million deaths from cancer by 2040 [10].

Pain in the early stages of cancer is often subtle and tends to become more pronounced in the middle and late stages. Rapid tumor growth and increased volume can exert pressure on surrounding blood vessels and nerve tissues, leading to persistent pain symptoms. The degree of pain associated with tumors is influenced by factors such as their location, growth pattern, and rate of growth. In the middle and late stages, cancer pain can become refractory [11].

Pain related to cancer treatment can include pain-inducing peripheral neuropathy caused by chemotherapy drugs such as vincristine, platinum agents, bortezomib, and others. Radiation-related nerve damage encompasses conditions like radiation brachial plexopathy and radiation-induced pelvic pain syndrome. Post-mastectomy pain syndrome, amputations, and thoracotomy surgery can also lead to pain in cancer patients. Additionally, cancer patients may experience non-cancer-related pain, such as postoperative pain from peripheral neuropathy or diseases unrelated to cancer, such as in diabetic patients. Therefore, a series of examinations may be necessary to rule out the possibility of cancer in these cases.

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3. Traditional Chinese Medicine Understanding of Cancer Pain Pathogenesis

The recognition of tumors in Traditional Chinese Medicine (TCM) has a history spanning thousands of years. Evidence of tumors can be found as far back as 3500 years ago in oracle bone scripts from the Yin and Shang Dynasties. The "Zhou Li Tian Guan" from the Zhou Dynasty contains records on the principles of treating "swellings and ulcers," which includes tumors. TCM views pain as a self-aware symptom of various diseases, and this includes cancer pain.

In ancient classical texts, there is no specific and systematic documentation of cancer. The "Sheng Ji Zong Lu" mentions, "Lumps that are benign stay stagnant." While it does not explicitly refer to cancer, it provides an understanding of tumors. The term "cancer" first appeared in the book "Wei Ji Bao Shu" by Song Dong Xuan Ju Shi [12]. In the "Ling Shu: Jing Mai" section, it is documented that gastric cancer can lead to symptoms such as abdominal distension, gastric pain, and vomiting [13]. Chao Yuan Fang's "Zhu Bing Yuan Hou Lun" discusses the symptoms and pathogenesis of liver cancer, which are more complex [14]. These ancient Chinese medical texts provide a foundation for the modern medical exploration of cancer pain etiology and mechanisms.

In Chinese medicine, pain caused by cancer is referred to as "cancer pain." It occurs when malignant toxins invade meridians or when tumors obstruct the flow of qi and blood in a specific part of the body [15]. It is often associated with various pathological conditions such as stagnation, masses, calculi, addiction, mammary nodules, carbuncles, phlegm obstruction, and the resulting qi and blood deficiency. Cancer pain is the result of the accumulation of various pathogenic factors over an extended period, and it is rarely caused by a single mechanism.

3.1. Pain Arises from Obstruction and Insufficiency

In the "Su Wen: Ju Tong Lun," it is mentioned that "pain is closure and lack of openness," and there is also the saying "pulse cries for blood, blood pain is due to blood." The "Zheng Zhi Yao Jue" states, "When there is pain, there is obstruction; when there is openness, there is no pain." The "Yi Zong Jin Jian" from the Qing Dynasty states, "In cases of injury and damage, pain arises from blood deficiency." Modern medical practitioners have further proposed the concept that "openness leads to comfort, and abundance leads to pain."

Cancer pain falls within the scope of "pain syndromes" in Chinese medicine. From the perspective of TCM's understanding of pain mechanisms, pain can be classified into two major categories: "pain due to obstruction" and "pain due to insufficiency." "Pain due to obstruction" occurs when the flow of qi and blood in the body's meridians is hindered, leading to various types of pain. "Pain due to insufficiency" arises from a deficiency of qi and blood, leading to impairment of the organs, meridians, and blood vessels, resulting in pain [16]. The "Su Wen: Ju Tong Lun" states, "When the pulse cries for blood, blood pain is due to blood." In the context of cancer-related pain, prolonged exposure to the cancer consumes qi and blood, leading to qi and blood deficiency and subsequent pain. Prominent TCM practitioner Liu Shengwei from Guangdong differentiates cancer pain into four categories: solid pain, deficient pain, cold pain, and hot pain. He believes that "stagnation of qi and blood leads to obstruction and pain, while deficiency of qi and yang leads to pain" [17].

Modern medicine suggests that pain can lead to the release of endogenous pain-inducing substances, vasodilation, increased local blood stasis, and exacerbation of pain. Cancer pain patients often experience circulatory disorders, especially microcirculatory issues. Therefore, TCM often employs principles of promoting blood circulation, removing blood stasis, tonifying qi, and activating blood as treatment strategies, along with personalized adjustments based on specific patterns. The mechanisms of action for the analgesic effects of promoting blood circulation and removing blood stasis may include the direct or indirect dilation of coronary and peripheral blood vessels, increased blood flow, relief of smooth muscle spasms, and reduced platelet aggregation. Additionally, it can improve tissue oxygenation and directly inhibit tumor growth [18]. Research by Du Yeqin and others has analyzed compound formulas for oral Chinese medicine treatment of cancer-related pain published in domestic medical journals from 1995 to 2009. They suggest that the principles for treating cancer pain with Chinese medicine are based on the concept of "lack of abundance leads to suffering, abundance leads to

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comfort." Treatment strategies include nourishing, supplementing, promoting blood circulation, and resolving phlegm and stasis based on symptom differentiation [19].

However, Liu Zhaokun believes that in the later stages of cancer, yang deficiency and pathogenic factors are more pronounced, leading to contraction and constriction causing pain. In emergency cases, the focus is on pain relief and replenishing qi, with the use of herbs such as Paeonia and Glycyrrhiza. Modern experimental research has confirmed that such herbs possess central analgesic, reflex inhibition, sedative, and peripheral nerve inhibition functions, which can relax and relieve constriction, achieving analgesic effects [20].

3.2. Phlegm, Stasis, and Deficiency

In TCM, there is an ancient saying that "many diseases are caused by phlegm," and "strange diseases are often attributed to phlegm." Dan Xi says, "Most blockages in the upper, middle, and lower parts of the body are often due to phlegm." The accumulation of phlegm dampness is the fundamental characteristic of cancer masses. Dampness is considered an evil yin substance that is heavy, turbid, and viscous, leading to the aggregation of phlegm. Phlegm dampness can lead to the stagnation of cancer toxins, obstruction of qi circulation, poor blood flow, and subsequently, pain. As stated in the "Dan Xi Xin Fa," "Phlegm accumulates due to stagnation of qi, and once it accumulates, it obstructs the pathways, leading to pain." It mentions that phlegm and stasis mutually affect each other and result in fixed and unrelenting pain. The pain associated with phlegm and dampness often presents with a pattern of pain that is severe in the morning and worsens in the evening [21].

The "Ling Shu: Bai Bing Shi Sheng Pian" states, "When pathogens gather, there must be a deficiency of qi." Li Zhongzi's "Yi Zong Bi Du: Ji Ju" states, "The condition of accumulation arises due to insufficiency of righteous qi, followed by the occupation of pathogenic qi." A deficiency of righteous qi and a favorable environment for the growth of malignant tumors create the pathological basis for the concept of "pain arises when there is no comfort." Furthermore, cancer toxins further deplete the body's righteous qi, leading to further dysfunction of internal organs and meridians, resulting in the production of pathological substances such as phlegm and blood stasis. These secondary pathological substances and the deficiency of righteous qi coexist and mutually reinforce each other, creating a vicious cycle that makes cancer pain difficult to treat [22]. Zhou Zhenxiang suggests that the main mechanism behind cancer pain is the lack of circulation of qi and blood, meridian blockage, and organ dysfunction [23]. Modern pharmacological research has shown that various phlegm-resolving and blood-activating herbs like Hericium erinaceus, Bulbus Fritillariae Thunbergii, Momordica grosvenori, Aristolochia mollissima, Boswellia carterii, Commiphora myrrha, Persica, Panax notoginseng, and Rubia cordifolia have significant analgesic, immunoregulatory, and anti-tumor cell growth effects [24].

3.3. Cold, Phlegm, Stasis, and Toxins

In Traditional Chinese Medicine (TCM), the understanding of cold pathogenic factors dates back to ancient texts such as the "Huang Di Nei Jing." The "Su Wen: Ju Tong Lun" states, "Pain is often caused by the predominance of cold, and pain can occur due to cold." The "Jing Yue Quan Shu" notes, "Pain symptoms caused by cold are ten times more common than those caused by heat, which is only one or two out of ten." From this, it can be inferred that cold pathogenic factors tend to contract and easily lead to stagnation. Stagnation can result in qi stagnation and counterflow of qi, which in turn can lead to poor local circulation of qi and blood. This can give rise to pain, the production of phlegm, and the formation of blood stasis. The presence of phlegm and stasis can further disrupt the flow of meridians, intensifying the pain. Zheng Wu, Yang Jinkun, and others [25] believe that the development of tumors is closely related to cold pathogenic factors. "Internal cold" and "yang deficiency leading to cold congealing" are important factors in the occurrence and development of tumors. Yang deficiency and cold congealing play essential roles in the pathological mechanisms.

He Xinhui et al. [26] conducted a statistical analysis of 1206 entries from historical medical literature on the differentiation and treatment of "wangjia" (abdominal masses) and accumulation syndrome. The results showed that ancient physicians considered yang deficiency to be the main etiological and

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pathological factor in wangjia and accumulation syndrome and often used warming methods in treatment. The pathological nature of cancer pain generally falls under the category of deficiency within excess. Most cancer pain is due to deficiency leading to the development of excess, resulting in localized excess within the context of overall deficiency. In late-stage cancer patients, there is often a deficiency of yang qi. Yang deficiency leads to the continuous generation of internal cold, and as cold primarily causes contraction and condensation, it can lead to the formation of phlegm and blood stasis, contributing to severe pain. Zhang Bo et al. [27] propose the use of the TCM approach of "pain—harmony—warming." By renewing and regulating through harmonization and warmth, they aim to improve the patient's constitution, enhance immune function, and boost the body's antibody production.

3.4. Stasis, Phlegm, Deficiency, and Toxins Combined with Cold Congealing, Flow of Phlegm Toxins

In TCM, it is believed that the entire process of cancer toxin formation is closely related to pathogenic factors. The "Zhong Cang Jing" contains records that state, "Ulcer pain and malignant sores are both due to the accumulation of toxins in the five viscera and six bowels, which do not flow freely, leading to the blockage of qi and wei." This indicates that under the influence of internal and external pathogenic factors, the human body not only experiences stagnation of qi, blood, and body fluids but also the appearance of "toxins." These toxins accumulate in the body over time, eventually leading to the development of cancer. "Toxins" include two categories: one is the accumulation of pathogenic factors over time, such as dampness toxins formed from the accumulation of dampness pathogenic factors, blood toxins formed from prolonged blood stasis, and cold toxins and heat toxins. The second category refers to cancer toxins. Cancer toxins are a unique and highly pathogenic substance, and they are the main cause of cancer development. Diseases with strong pathogenicity are characterized by severe conditions that are difficult to treat, marked by deficiency of qi and blood stasis. The strong adherence between pathogenic factors and cancer toxins leads to more severe and challenging-to-treat cancer pain [28].

Wang Wenping et al. [29] proposed a hypothetical basis for the pathogenesis of "phlegm toxins flowing" in the context of tumor metastasis. They suggest that tumors, as well as post-tumor surgery, can lead to deficiency of righteous qi, internal generation of phlegm and dampness, and the intertwining of phlegm and residual toxins. This combination of phlegm and toxins flows through the meridians and organs, obstructing the flow of qi and blood. This, in turn, leads to the formation of blood stasis and the subsequent development of metastasis. Phlegm and toxins flow to the liver, forming "liver accumulation," to the lungs, forming "lung accumulation," and to the meridians, forming "lymphadenopathy." The spleen is the source of phlegm production, and the lungs store phlegm. In cases of lung-spleen qi deficiency, the generation of internal phlegm, the intertwining of phlegm and toxins, and the flow of phlegm and toxins through the vessels can result in the formation of blood stasis when qi and blood are obstructed, leading to pain [29].

3.5. Cancer Toxin Accumulation, Phlegm and Stasis Mutual Entanglement, Meridian Obstruction

Liu Dan et al. [30] proposed that cancer pain is primarily caused by weakened vital qi and invasion of external pathogenic factors. The mutual entanglement of phlegm and stasis, resulting in the formation of "toxins" and "stasis," leading to meridian blockages, is the fundamental pathological mechanism underlying cancer pain. The internal accumulation of cancer toxins is a crucial factor in the development of cancer pain, and the mutual entanglement of phlegm and stasis is a significant pathological factor. Cancer toxin accumulation within the body is pivotal in the pathogenesis of cancer pain. The presence of internal accumulation of cancer toxins, coupled with factors such as external pathogenic factors (Liu Dan et al. [30] mention the Six Pernicious Influences), dietary imbalance, weakened spleen and stomach, and emotional disturbances, allows these factors to exert their influence on the body over an extended period. This leads to dysfunction of the organs, resulting in the production of phlegm, blood stasis, and meridian blockages. When cancer toxins accumulate in the body for an extended period, they can give rise to the formation of tumors. Cancerous growth occurs when tangible pathogenic factors, qi stagnation

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blocking blood circulation, or direct invasion of cancer toxins into the meridians all contribute to severe and persistent cancer pain.

Renowned traditional Chinese medicine expert Zhou Zhongying introduced the concept of "cancer toxin theory." According to this theory, cancer toxins are specific pathogenic factors responsible for the development of cancer. While cancer cells may be the visible manifestation of cancer toxins, cancer toxins are not synonymous with cancer cells, nor are they the masses formed by cancer cells. Long-term exposure to carcinogens within the body may induce the internal generation of cancer toxins, but the carcinogens themselves are not cancer toxins [31]. Instead, it is the abnormal metabolism of body fluids, impaired circulation of bodily fluids, and blood circulation disorders, exceeding the body's compensatory capacity, that can lead to the accumulation of toxins. Professor Wu Mianhua pointed out in 2008 that cancer pain is primarily caused by the Six Pernicious Influences, emotional disturbances, dietary imbalances, and weakened vital qi. He emphasized the importance of cancer toxin accumulation, mutual entanglement of phlegm and stasis, and meridian blockage as the fundamental pathological mechanisms underlying cancer pain [12].

3.6. Systemic Deficiency and Local Blockage

The prerequisite for the formation of cancer toxins is the deficiency of vital qi. Dysfunction of the organs leads to inadequate nourishment of the overall qi and blood in the body. Multiple pathogenic factors take advantage of this deficiency to infiltrate the body. When vital qi is deficient and qi stagnation, phlegm condensation, blood stasis, and dampness pathogenic factors accumulate, it results in the formation of cancer toxins. The occurrence of cancer toxins disrupts the local circulation of qi and blood, which further damages vital qi. Therefore, cancer patients are essentially deficient in both qi and blood. In the context of tumors, this manifests as the accumulation of cancer toxins, blood stasis, phlegm, and turbidity. Due to the insufficiency of vital qi to resolve the cancerous growth, the pathogenic factors thrive. As the pathogenic factors grow stronger, the deficiency becomes more pronounced, creating a vicious cycle that leads to increasingly severe cancer pain. Consequently, advanced cancer patients often exhibit signs such as muscle wasting, emaciation, dull complexion, lackluster eyes, and a significant loss of body weight. Vital qi is depleted, and the pain becomes excruciating, making it difficult to alleviate. Excessive pathogenic factors dominate in this scenario.

Modern medicine classifies cancer as a chronic, wasting disease with a long course. This aligns with the traditional Chinese medicine perspective that chronic illnesses are often characterized by deficiencies. Vital qi deficiency plays a continuous role in the development of cancer, particularly in advanced stages. Qi and blood deficiency leads to aching discomfort in cancer patients, and studies have shown that tonifying herbs like Western ginseng, astragalus, codonopsis, atractylodes, yam, adenophora root, ophiopogon root, wolfberry fruit, and glossy privet fruit can directly inhibit the growth of tumor cells. These herbs can also enhance the immune system, boost NK cell activity, promote interferon production, and possess strong analgesic and anti-inflammatory effects, benefiting cancer patients with compromised immune function. For patients with deficiency-induced cancer pain, formulas like Ba Zhen Tang and Ren Shen Yang Rong Tang, which strengthen the body and dispel pathogenic factors, can be administered to nourish the deficiency, resolve stasis, relieve pain, and prevent further spread [32].

According to a study, anti-inflammatory and analgesic Chinese herbal formulas [33] may have superoxide dismutase-like activity. Malignant tumors can lead to an increase in reactive oxygen species such as oxygen radicals and hydrogen peroxide, which the body attempts to eliminate, resulting in a decrease in superoxide dismutase [34]. Elevated levels of oxygen radicals can elicit responses in cellular membranes, especially nerve endings, leading to structural damage and cell death, resulting in pain. This suggests that reducing the production of oxygen radicals or blocking the damage caused by oxygen radicals may be beneficial for cancer pain [33].

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3.7. Stagnation of Pathogenic Factors and Deficiency of Vital Qi

The ancient text "Lan Shi Mi Cang" states, "Adjust the balance of yin and yang; supplement deficiencies and reduce excess." This deficiency manifests as a sign of weakness, as seen in deficient spleen yang accompanied by cold congelation or weakened kidney qi accompanied by general frailty. However, the presence of qi stagnation, blood stasis, phlegm congelation, and damp accumulation is collectively referred to as pathogenic toxins. When cancer patients experience pain symptoms, they often have visible tumors. Hence, there is a cause-and-effect relationship between the two. The pathological mechanisms of tumor formation are similar to those of pain, involving factors such as qi stagnation, blood stasis, phlegm congelation, dampness accumulation, and deficiency of vital qi [11].

Modern research has shown that traditional Chinese medicine's concept of "vital qi" functions similarly to the modern medical immune system. Nurturing vital qi can enhance CD4+ cells, CD8+ cells, NK cell cytotoxicity, monocyte and macrophage phagocytosis, and the activity of biological factors like interferon (IFN) and tumor necrosis factor (TNF). Therefore, based on cancer pathology and staging, it can be differentiated as stage I or T≧2 (N0M0), when the patient's immune function is still good, and the entire immune system functions in harmony. In stage II or T≧2 (N1M1), it can be differentiated as a deficiency syndrome. During this stage, local inflammation responses are strong, but tissue damage is severe, immune regulation is impaired, tumor-specific immunity is reduced, and the immune system is compromised due to cancer cell metastasis or infiltration. Thus, treatment during this stage should focus on boosting vital qi [35].

The method of "nourishing the body to stop pain" aims to address the pathology of cancer pain, where the deficiency of vital qi leads to suffering. It mainly employs qi-tonifying and blood-nourishing herbs to adjust the body's immune function and inhibit tumor growth indirectly, ultimately alleviating pain. Yang Shuming used modified Tao Hua Tang for the treatment of advanced cancer pain, believing that the combined use of multiple herbs could restore vital qi, enhance immune function, suppress cancer cell proliferation, and relieve pain, ultimately leading to a state where "the absence of pain results in self-recovery" [36]. Zhao Ximin used the formula "Xiao Ai San He Fu Yuan Tang" to treat cancer pain. The primary herbs, Codonopsis pilosula and Astragalus membranaceus, are used to boost immunity and enhance anticancer effects. The combination of various herbs in the formula synergistically achieves pain relief [37].

Liang Qijun [38] employed the "strengthening vital qi and clearing toxins" approach to treat malignant tumors. "Strengthening vital qi" is the main method for supporting the body in cancer treatment. Si Jun Zi Tang is used to strengthen middle qi. "Clearing toxins" is the primary method for eliminating pathogenic factors in cancer treatment. Ban Zhi Lian and Bai Hua She She Cao are the fundamental herbs in this category. Emphasizing the strengthening of vital qi and clearing of toxins can help delay cancer pain in cancer patients.

3.8. Deficiency of Vital Qi and Exuberance of Pathogenic Factors, Internal and External Factors Converging

The ancient text "Jin Gui Gou Xuan Liu Yu" states, "Stagnation refers to the gathering and accumulation that cannot be vented. What should ascend cannot ascend; what should descend cannot descend; what should change cannot change." "Yi Xue Zheng Zhuan · Yu Zheng" explains, "Dan Xi said: When qi and blood are in harmony, no illnesses occur; but if there is stagnation, various illnesses will arise. There are six types: qi stagnation, damp stagnation, heat stagnation, phlegm stagnation, blood stagnation, and food stagnation." Prolonged exposure to psychological stress or sudden severe emotional trauma, beyond the body's normal physiological regulatory range, disrupts the normal circulation of qi and blood in the body. Emotional disturbances, qi stagnation, and the additional factors of dietary irregularities can result in qi stagnation, blood stasis, the formation of phlegm, and eventually the generation of cancer toxins, leading to various cancer pains over time [15]. Therefore, when vital qi is deficient, combined with external pathogenic factors like the Six Pernicious Influences, emotional disturbances, qi stagnation, and dietary irregularities, as well as internal factors like emotional imbalances, compromised vital qi, and weakened

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organ functions, pathogenic factors accumulate, and vital qi diminishes, forming a state of "internal and external factors converging."

The liver plays a crucial role in the smooth flow of qi throughout the body, promoting blood and fluid circulation. When liver function is normal, qi circulation remains unobstructed, and the balance of qi and blood is maintained. Meridians remain unblocked, and the functions of organs and tissues are harmonious. Pain does not occur under these circumstances. However, when liver function is compromised due to emotional trauma or invasion by external pathogenic factors, the smooth flow of qi is disrupted. This disruption prevents the movement of fluids, leading to their accumulation and the formation of phlegm. Since "qi leads the blood," stagnation of qi disrupts the circulation of blood, causing blood stasis. The presence of phlegm, stasis, and other pathological substances obstructs meridians, and prolonged meridian blockages can lead to various cancer pains. Therefore, during the treatment of cancer pain, it is essential to focus on regulating liver qi to facilitate the overall circulation of qi in the body and harmonize the circulation of qi and blood, as mentioned in "Liu Yuan Zheng Ji Da Lun," which states, "Wood governs stagnation" [39].

In modern times, the renowned traditional Chinese medicine practitioner Gu Nailong [40] believes that insufficient vital qi is the internal cause of tumor development, while pathogenic qi is the key external factor. Common external pathogenic factors include exposure to the Six Pernicious Influences and toxic pathogenic factors. Common internal factors include emotional disturbances, excessive physical or mental strain, which can damage the spleen and stomach, leading to organ deficiency. The cunningly induced cancer factors alter the conditions, interact with internal factors, and, in combination with external pathogenic factors, lead to a situation where the body's qi is deficient, blood is depleted, qi stagnates, blood stasis occurs, phlegm congeals, toxins accumulate, and tumors form.

4. Conclusion

Cancer pain poses a significant clinical challenge, and its effective treatment is crucial for improving the quality of life of cancer patients. Cancer pain is a complex symptom with multifaceted mechanisms, often involving a combination of deficiency and excess patterns, resulting in a presentation known as "mixed deficiency and excess." Traditional Chinese medicine (TCM) offers a unique perspective on the pathogenesis of cancer pain, leveraging its holistic view and pattern-based diagnosis and treatment. TCM places great emphasis on understanding the interconnectedness between the patient's cancer and their pain, aiming to address the root causes while alleviating and managing pain.

Cancer pain, as the primary symptom in patients with advanced-stage cancer, places individuals in a state of extreme physical and psychological distress. The sudden diagnosis of cancer and the fear of death impose significant psychological stress, leading to fear, depression, insomnia, and increased sensitivity to pain. Therefore, emotional counseling for cancer pain patients can often have unexpected positive effects, making treatment more systematic and comprehensive.

In recent years, as clinical research has advanced, TCM has demonstrated increasingly significant roles in comprehensive cancer treatment. TCM not only helps alleviate symptoms and stabilize tumor tissues but also improves the quality of life and extends survival time for cancer patients [41]. To achieve breakthroughs in cancer pain treatment using TCM, it is essential to adhere to the foundational theories of pattern-based diagnosis and treatment. By clarifying the etiology and pathogenesis of cancer pain and fully utilizing the distinctive features of TCM, standardized treatment protocols for cancer pain in TCM can be established. This paves the way for new approaches and insights into cancer pain prevention using TCM, highlighting the inherent charm of TCM culture.

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