

Review

Thoughts on the treatment of cancer pain under the guidance of traditional Chinese medicine

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Abstract

Chinese medicine diagnosis and treatment of cancer is a feature of traditional Chinese medicine in the prevention and treatment of major diseases. Cancer pain is one of the main clinical symptoms of cancer patients, especially those with advanced cancer, which seriously affects the quality of life of patients. At present, the principle of three-step analgesic ladder is mainly used in the treatment of cancer pain. However, the side effects such as constipation, nausea and vomiting caused by long-term use of analgesic drugs are often limited by patients' tolerance, meanwhile the pain is not effectively controlled. The mechanism of cancer pain is extremely complex. To fully understand the pathogenesis and syndromes of cancer pain in traditional Chinese medicine is an important basis for effectively alleviating the symptoms of cancer pain. Chinese medicine has unique advantages in treating cancer pain, such as addiction, drug resistance and side effects. Based on the etiology and pathogenesis of cancer pain, this paper discusses the application of different classifications of traditional Chinese medicine in the treatment of cancer pain.

Keywords: Cancer pain, Traditional Chinese medicine, Modern medicine

摘要

中医诊治肿瘤是当今中医防治重大疾病的一个特色。癌性疼痛是癌症患者尤其是中晚期癌症患者的主要临床症状之一,严重影响患者生存质量。目前对于癌痛的药物治疗主要采用三阶梯止痛原则,但长期使用止痛药物容易引起的便秘、恶心呕吐等副作用,故受患者耐受性的限制,而使疼痛没有得到有效控制。癌痛发生的机制极其复杂,全面了解癌痛中医的发病和证型,是进行有效缓解癌痛症状的重要基础。中药治疗癌痛具有不成瘾性、耐药性及毒副作用小等独特优势。文章从癌痛病因病机特点出发,探讨不同分类中药治疗使用规律,对恶性肿瘤引起癌痛的基本病机的再认识和治疗具有重要指导作用。

关键词: 癌痛; 中药; 现代医学

Abbreviations: TCM, traditional Chinese medicine. WHO, World Health Organization.

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Background

Cancer pain is one of the most common and difficult to control symptoms in cancer patients, especially in advanced cancer patients. It brings great pain to patients and their families, and seriously affects the quality of life of patients. According to the statistics of the World Health Organization (WHO), the proportion of cancer patients with pain in the world is 30% - 50%, and the proportion of advanced patients is 60% - 90%. In recent years, 51% - 62% of the patients have pain in different degrees, and more than 30% of the patients have moderate and severe pain. Cancer pain makes patients suffer pain, anxiety, or even lose confidence in life, and speed up the progression of the disease [1]. WHO established the WHO Cancer Pain Treatment Committee in 1982 and proposed to achieve the worldwide goal of "making cancer patients painless" by 2000. However, it is regrettable that about 30%-50% of cancer pain patients still do not get satisfactory relief [2]. Therefore, the WHO has made aggressive treatment of cancer pain one of the four priorities of the Comprehensive Cancer Programme [3]. The "three-step" therapy recommended by WHO is the main means of modern medical treatment of cancer pain. It has a certain effect on relieving cancer pain, but its clinical use is limited because of its toxic side effects, addiction dependence, and sometimes "capping effect" and other reasons. In recent years, many doctors use traditional Chinese medicine, external use, acupuncture and other methods to treat cancer pain, with less toxic side effects, safe use, long maintenance time, no addiction and dependence advantages, with practical clinical significance.

Classification of traditional Chinese medicine in treating cancer pain

Promoting blood circulation and removing blood stasis

Blood stasis pain is the most common type of cancer pain. All kinds of pathogenic effects on the body will eventually affect the operation of Qi and blood and cause pain. Ye Tianshi, a famous scholar in Qing Dynasty, once put forward the famous theory of "long-term pain entering collaterals" to the pathogenesis of pain, emphasizing the collaterals stasis causing pain. At the same time, TCM holds that blood stasis is not only one of the pathological mechanisms of cancer pain, but also the pathological product in the process of tumor lesion. Therefore, traditional Chinese medicine of promoting blood circulation and removing blood stasis is particularly important in the treatment of cancer pain. Zhang Xianbin [4] has studied 20 literatures, which shows that this kind of Chinese medicine is the most widely used in the treatment of cancer pain. Commonly used prescriptions are Tao Hong Si Wu Tang, Shi Xiao

San, Fu Yuan Huo Xue Tang, Zhuyu Tang and so on, commonly used drugs are Sanleng (*Sparganii Rhizoma*), Ezhu (*Curcumae Rhizoma*), Chishao (*Paeoniae Radix Rubra*), Danshen (*Salviae Miltiorrhizae Radix et Rhizoma*), Tubiechong (*Eupolyphaga*), Ruxiang (*Olibanum*), Moyao (*Myrrha*), Danggui (*Angelicae Sinensis Radix*), Chuanxiong (*Chuanxiong Rhizoma*), Yanhusuo (*Corydalis Rhizoma*), Sanqi (*Notoginseng Radix et Rhizoma*), Yujin (*Curcumae Radix*), Puhuang (*Typhae Pollen*) and so on. It is advisable to apply these prescriptions and Chinese herbs according to specific diseases.

Heat clearing and detoxicating

Heat-clearing and detoxifying drugs or heat-clearing and detoxifying methods are commonly used in clinic. They can relieve the symptoms caused by heat evil or fire-toxin stagnation. There is a close relationship between heat toxicity and tumors. Heat toxicity is one of the basic pathogenesis of tumors. The symptoms of malignant tumors have been described in the early literature of TCM, such as "intestinal paralysis" and "stone plague" in the *Neijing* (the Canon of Internal Medicine), "accumulation" in the *Nanjing*, and "disease plague" in the *Treatise on the Origins of Diseases*. In the course of tumor development, the expression of "heat and toxin blocking" is more common, such as breast cancer ulceration, tumor purulence, lung cancer cough phlegm yellow, fever and hematemesis. In the treatment of cancer pain, antipyretic and detoxicating drugs have the functions of eliminating swelling toxin (direct anti-cancer), clearing away evil heat (clearing cancer toxin), and treating various manifestations of tumor hyperthermia (anti-cancer, anti-bacterial, anti-virus), that is, they have the dual effects of eliminating pathogeny and adjusting the body's anti-disease ability [5]. Common Clinical Prescriptions include Huanglian Jiedu Tang, Qingwen Baidu Yin, Angelica Longyi Pills, Xian Fang Huo Ming Yin and so on. Drugs such as Baihuasheshecao (*Herba Hedyotis*), Jinyinhua (*Lonicerae Japonicae Flos*), Lianqiao (*Forsythiae Fructus*), Banzhilian (*Scutellaria barbata*), Pugongying (*Taraxaci Herba*), Luhui (*Aloe*) and so on. But in practical application, doctors should dialectically use antipyretic and detoxicating drugs and pay attention to the compatibility with other drugs according to the different parts of the tumor, the damaged viscera, the positive deficiency and evil excess, and the symptoms and manifestations.

Dispersing cold and relieving pain

Cold is Yin evil, its nature is stagnation and control pain, as the *Su Question* said: "Pain, cold is more, there is cold pain also." The reason why the body's qi, blood and body fluid can run continuously and smoothly depends on the warm promotion of the body's Yang and qi. Once the evil of yin and cold is overwhelming and Yang Qi is damaged,

the blood of meridians is blocked by cold evil, and if it is obstructed, it will be painful. Sini Tang, Yanghe Tang and Mahuang Fuzi Xixin Tang are selected as prescriptions. Commonly used drugs are Fuzi (*Aconiti Lateralis Radix Praeparata*), Ganjiang (*Zingiberis Rhizoma*), Rougui (*Cinnamomi Cassiae Cortex*), Wuzhuyu (*Evodiae Fructus*), Xiaohuixiang (*Foeniculi Fructus*), Xixin (*Asari Radix et Rhizoma*), etc. At the same time, because the cold is Yin evil, its nature convergence, easy to cause Qi stagnation, so the prescription should be compatible with the products of regulating qi to relax the Qi machine, such as Chuanlianzi (*Toosendan Fuctus*), Yanhusuo (*Corydalis Rhizoma*), Houpo (*Magnoliae Officinalis Cortex*) and so on.

Regulating qi and inducing stagnation

"Confucian family affairs" in the "melancholy, angry, Qi disharmony, accumulated over time," the argument that Qi stagnation is also one of the pathogenesis of tumor formation. Qi stagnation can cause blood stasis, qi stagnation can also make phlegm coagulate, and become a tumor for a long time. Many tumor patients will show signs of qi stagnation and qi depression. Patients with breast cancer often suffer from liver depression and breast distention. Gastric cancer, esophageal cancer patients often have pain, belching, chest swelling and stuffy, so the method of regulating qi stagnation in the treatment of some tumors is also very important. The prescriptions are Chaihu Shugan Powder, Jinling Zi Powder, Tiantaiwu Yaosan Powder, Wumo Yinzi, etc. The medicines are Chaihu (*Bupleuri Radix*), Xiangfu (*Cyperus Rhizoma*), Wuyao (*Linderae Radix*), Foshou (*Citri sarcodactylis Fructus*), Muxiang (*Aucklandiae Radix*) and so on. In the course of cancer pain treatment, according to the principle of dialectical treatment, attention should be paid to regulating Qi-Regulating mechanism, reasonable and accurate application of Qi-Regulating drugs, often receive better curative effect.

Dissipating phlegm and softening hardening

Phlegm is a pathological product of the human body. As a pathological cause, it acts on the sick body. According to TCM, many tumors are caused by phlegm coagulation, and many phlegm syndromes and masses appear in clinical manifestations. "Danxi Heart Law" said: "Phlegm as a thing, with the rise and fall of qi, everywhere," ordinary people on the body, in, under the block, mostly phlegm. If phlegm wet in the lungs, then cough purulent blood (such as lung cancer), in the esophagus is difficult to eat (such as esophageal cancer), subcutaneous channeling into a knot, phlegm nucleus (such as breast cancer, malignant lymphoma, thyroid tumor, etc.). The pain caused by phlegm turbidity varies with the location of the lesion. There are many forms, but most of them are dull pain and distending pain. Erchen Tang and Wendan Tang are commonly used in clinic. The commonly used medicines are Shancigu (*Cremastreae Pseudobulbus*;

Pleiones *Pseudobulbus*), Chenpi (*Citri Reticulatae Pericarpium*), Haizao (*Sargassum*), Muli (*Ostreae Concha*), Gualou (*Trichosanthis Fructus*), etc. Attention should be paid to the use of this kind of Chinese herbal medicine. Patients with bleeding tendency should be careful or not to prevent bleeding. And this kind of medicine is also a product of elimination. It should be paid attention to yin deficiency and fire.

Dispelling wind and dredging collaterals

Limbs, including limbs and exterior bodies, are connected with meridians and collaterals, which can defend against external pathogens and protect internal organs and tissues. Physiologically, Tongli is beneficial to human body. Under pathological conditions, meridians and collaterals are affected by pathogenic factors, obstruction of obstruction, injury of viscera and collaterals, and diseases of veins and veins can lead to the occurrence of diseases. In clinical treatment, traditional Chinese medicine for dispelling wind and dredging collaterals is suitable for obstructing meridians and joints, affecting the movement of Qi and blood, resulting in pain, weight, acid anesthesia and other symptoms in tendons and bones, joints, muscles and other places, common symptoms such as breast cancer or lung cancer bone metastasis. In addition to conventional Chinese medicine for anti-tumor treatment, such as Qianghuo (*Notopterygii Rhizoma et Radix*), Duhuo (*Angelicae Pubescentis Radix*), Weilingxian (*Clematidis Radix et Rhizoma*), Sangjisheng (*Taxilli Herba*), etc. If cancer pain enters the collaterals for a long time, constriction pain, limb constriction, mostly use insects to search wind analgesic drugs, to reach the meridian analgesia, commonly used Chuanshanjia (*Manis Squama*), Wugong (*Scolopendra*), etc. Some studies have shown that this kind of traditional Chinese medicine can dispel rheumatism and relax muscles and collaterals, but also has the effect of anti-tumor and inhibiting the proliferation of cancer cells.

Strengthening the body and strengthening the deficiency

Qi deficiency is an important factor in tumorigenesis. Tumors are chronic wasting diseases, mostly asthenia syndrome. Especially in the middle and late stages or through surgery, radiotherapy and chemotherapy, resulting in serious body consumption and injury, gas and blood failure, and even the decline of systemic function, long-term life will end. Therefore, in the treatment of tumor, the principle of "adjusting the essence and tonifying the vital qi" should run through it from beginning to end. Deficiency pain in clinical manifestations of dull pain, continuous pain, temperature is slow, must be reduced according to pain, and accompanied by a series of deficiency syndrome. Sijunzi Tang, Liujunzi Tang, Paeoniae Glycyrrhiza Tang and so on are selected as the prescriptions. The commonly used Chinese medicines are Baizhu (*Atractylodis*

Macrocephalae Rhizoma), Dangshen (*Codonopsis Radix*), Huangqi (*Astragali Radix*), Danggui (*Angelicae Sinensis Radix*). The following two points should be paid attention to in the course of tonifying: first, according to the different pathological attributes, we must adopt the treatment drugs of tonifying qi, nourishing blood, nourishing yin and warming yang; second, we should closely combine the different location of the five Zang-organs and choose the prescription to strengthen the pertinence of treatment.

Calm and soothe the nerves

Tumor is a disease that seriously endangers the health of human body and mind. There are many factors causing the disease, but psychological factors have a direct impact on the occurrence, development and curative effect of tumor. In the course of illness, patients will produce complex psychological activities, such as fear, doubt, irritability, resentment, pessimism and disappointment, these adverse psychological reactions will affect the "pain" feeling and judgment, or even painless and hallucinatory pain. Therefore, in addition to dialectical treatment according to the disease, it is necessary to add in the process of treatment, such as Zhusha Anshen Pills, Cizhu Pills and so on, commonly used drugs are Zhusha (*Cinnabaris*), Cishi (*Magnetitum*), Suanzaoren (*Ziziphi Spinosae Semen*), Yuanzhi (*Polygalae Radix*), Longgu (*Os Draconis*), etc.

Etiology and mechanism of cancer pain

Etiology and pathogenesis of traditional Chinese Medicine

The mechanism of cancer pain is that Qi stagnation, blood stasis, phlegm turbidity, cold evil and other pathogens obstruct the viscera, meridians, Qi and blood, directly or indirectly affect the physiological function of the body, resulting in Qi ascending and descending in and out of disorder, eventually blocked blood flow, blood stasis, congestion and pain. This kind of pain caused by evil facts is called "real pain", and the predecessors generalized its pathogenesis as "pain if obstructed". In addition, the tumor for a long time, Qi and blood Yin and Yang deficiency, dysfunction, viscera and meridians dystrophy, can also occur pain, this kind of pain caused by deficiency of vital energy called "deficiency pain", its pathogenesis is "no nourishment pain" [7]. In clinical practice, the pain of cancer is much more complicated.

Mechanism of modern medicine for alleviating cancer pain by traditional Chinese Medicine

Increasing the level of opioid peptides and the role of opioid like receptor agonists

Opioid peptides (beta-endorphins, enkephalin and dynorphin) are recognized as endogenous analgesic substances. They are widely distributed in hypothalamus,

brain and spinal cord. They can bind to opioid receptors and reduce the release of substance P, thus producing a strong analgesic effect. The serum levels of morphine like substance and plasma leucine in patients with cancer pain were lower than those in normal subjects. Certain Chinese medicines can increase such substances through the central nervous system and produce powerful analgesic effects. When acupuncture analgesia, the contents of these substances in the brain and cerebrospinal fluid increased (8). The analgesic effect of *Panax notoginseng* saponins can be blocked by naloxone, suggesting that it may act through these substances and is an agonist of opioid peptide receptors. NiuHongmei [9] Aitongxin nasal drops can increase the content of beta-endorphin in hypothalamus of rats, inhibit the growth of local tumor of S180 mice, prolong the survival time of tumor-bearing mice and promote the proliferation of immune organs.

Anti-inflammatory and analgesic effects

The presence of pain substances (such as PGE2) is a major cause of pain caused by tumors. Non-steroidal anti-inflammatory drugs act as analgesics by inhibiting the synthesis of pathological products such as PGE2 that invade or metastasize cancer. Most antipyretic and detoxicating Chinese herbs may achieve analgesic effect through this mechanism, such as Compound Sophora Flavescens Injection for advanced cancer patients with moderate and mild pain [10], Zhang Guangping [11] for 35 patients with severe cancer using *Sagittaria* treatment, and achieved good analgesic effect. Many pharmacological experiments of single Chinese herbal medicine show that it has both anti-inflammatory and analgesic effects, such as Cobra venom, *Panax notoginseng* saponins and so on. It can be considered that anti-inflammatory action is one of the mechanisms of analgesic effect. Because anti-inflammatory, especially the inhibition of PGE2, has great significance in relieving cancer pain. And tumor cells secrete a large number of prostaglandins, not only can directly stimulate pain receptors to produce pain, but also promote cell proliferation, and at the same time mediate the inhibition of natural killer cell activity, so that the body's immunity is low, indirectly promote tumor proliferation and development to aggravate pain [12].

Regulation of local blood circulation

Traditional Chinese medicine believes that the occurrence of pain is related to Qi, blood stasis and stagnation. Blood stasis pain is the most common in cancer pain. Qi stagnation is an important pathogenesis of cancer pain. Therefore, promoting qi and activating blood circulation to remove blood stasis is the main method to treat cancer pain. Modern medical research has shown that pain can cause the dissociation of endogenous painful substances leading to vasodilation, aggravation of local blood stasis and aggravation of pain. Patients with cancer pain often

suffer from blood circulation, especially microcirculation. Huoxue Huayu herbal medicine can improve peripheral circulation, increase local blood flow, increase blood flow rate, relieve vasospasm, reduce blood cell aggregation, and then make the nutritional imbalance and metabolic disorders caused by tissue ischemia adjusted. In addition, the traditional Chinese medicine of activating blood circulation and removing blood stasis can improve the local blood supply and oxygen content of the tumor, thereby enhancing the sensitivity of the tumor tissue to radiation and chemotherapy drugs. For example, Liu Zhanhua *et al.* [13, 14] used intravenous drip ligustrazine, Xiangdan injection and other traditional Chinese medicine to remove blood stasis and collaterals, combined with self-made Jiedu Tongluo Decoction fumigation and washing treatment of tumor patients with deep venous thrombosis of the lower extremity in 18 cases, the effective rate was 94.4%, and achieved good results. It is concluded that Ligustrazine and Xiangdan injection can dilate local microvessels, increase blood flow, release vasoactive substances from vascular endothelial cells, promote the establishment of collateral circulation and venous blood reflux.

Regulating immune function

The intensity of immune function is closely related to cancer pain, and the occurrence and development of tumors are mutually causal with the decrease of immune function. Long-term chronic pain can lead to adverse stress response, causing a series of pathophysiological changes, including changes in immune function. The results of immune indices in patients with advanced cancer pain showed that their immune function was low, analgesia could improve immune function, and the improvement of immune function could help to control cancer pain [15]. Sunagawa [16] and other animal models of chronic pain show that pain has an inhibitory effect on immunity. The immune cells themselves can also synthesize and release opioid peptides. Immune enhancers can activate the corresponding receptors on the immune cells to promote the release of opioid peptides, so as to facilitate the realization of peripheral analgesia [17]. Fuzheng Buxu analgesic is through this mechanism to regulate the body's immune function, inhibit tumor growth, and has analgesic effect. Some research results show that: Spleen-strengthening and Qi-Tonifying drugs can increase the anti-pain ability of tumor patients, and Kidney-tonifying drugs can help to control pain. For severe chest pain caused by lung cancer, the use of Yin-nourishing drugs at the same time, plus Roucongrong (*Cistanches Herba*) and other kidney tonic drugs. Good results can be obtained in clinical practice [18]. Zhou Jie [19] and other studies found that four kinds of Chinese herbs which include Nourishing yin and nourishing blood, replenishing qi, strengthening spleen, nourishing yin and promoting fluid, warming kidney and strengthening yang can activate the human immune system or mediate the

immune function of the body, inhibit the occurrence and development of tumor, improve the effect of tumor treatment.

Change the mental environment to slow down and relieve the pain

Traditional Chinese medicine holds that emotional activities are closely related to tumors, especially the irrepressibility of worrying plays an important role in the pathogenesis and development of tumors. For example, "the source of diseases" is: "Qi disease, anxiety is also born. There is something in the heart, there is a stop in the spirit, and the Qi stays in the heart, but not in the heart. "Cancer is caused by excessive worry. Spiritual stimulation can promote the occurrence and development of cancer. Emotional internal injury is not only an important pathogenic factor of tumorigenesis, but also closely related to cancer pain. Because emotional trauma leads to dysfunction of Qi and blood circulation, channel obstruction, for the occurrence and progress of cancer pain has created a pathological basis. In recent years, studies have also found that patients with fear, anxiety, irritability, despair, depression and other complex psychological activities can affect the feeling of pain. Some people have studied bone metastasis of breast cancer in women, and found that psychological factors have a more significant impact on pain than the location of tumor metastasis. The author summarized in clinical treatment found that patients who can correctly face the illness, ideological stability, cheerful mood less complain of pain, and patients with obvious emotional and psychological fluctuations often feel pain intolerable, continuous. It can be seen that mental adjustment is not only conducive to the recovery of tumor, but also can prevent or reduce the occurrence of cancer pain to a greater extent. Under the guidance of the concept of integration of body and mind, on the one hand, the patients were given dialectical treatment by taking Chinese medicine orally and applying it externally, on the other hand, special attention was paid to the psychological treatment of the patients. Through these two aspects of mutual mingling and infiltration, through physical and mental interaction effect, significantly improved the clinical efficacy. This combination of body and mind not only embodies the scientific spirit of the integration of body and mind, but also embodies the rational application of medical science and the humanistic characteristics of medicine in the treatment of malignant tumors.

The treatment of cancer pain by traditional Chinese medicine has obvious effect in clinic. In a considerable number of advanced cancer patients, analgesia by traditional Chinese medicine has played a huge role and has been widely used in clinic. Moreover, the analgesic effect of traditional Chinese medicine is persistent and slow. And it has the characteristics of non-addiction, drug resistance and little side effects. It has a far-reaching

significance in the clinical application of cancer pain and its current advantages and future development and application prospects. However, from the current research and reports, there are still many problems in the application of traditional Chinese medicine in the treatment of cancer pain, such as some of the treatment methods are largely original and rough; dosage forms are still traditional preparations, some single or external preparations have certain toxic side effects and skin allergy, poor tolerance and other phenomena. There is a lack of uniform evaluation criteria, so that the results of each study are difficult to compare with each other. These are urgent problems.

References

1. Mai TX, Wu NY, Xie CM, *et al.* Investigation on pain and social psychological status of cancer patients. *The Journal of Practical Medicine* 2008, 24:133-135.
2. Wu MH. Research status and Countermeasures of cancer pain in traditional Chinese Medicine. *Chin J Inf Tradit Chin Med* 2005,12: 105-108.
3. Zhou JC. *Practical Oncology*. Beijing, People's Health Publishing House 2003, 102-117.
4. Zhang XB, Lin HS, Hua BJ, *et al.* Literature quality evaluation of TCM External Treatment of cancer pain and regularity of prescriptions and prescriptions. *Chin J Inf Tradit Chin Med* 2009,16: 96-97.
5. Chen Y. *Essentials of TCM treatment of tumor*. Shanghai, Shanghai Science and Technology Press 2007: 74-77.
6. Kang JG, Zhang SZ, Li YH, *et al.* Experimental study on inhibition of CT-26 tumor cell growth by house lizard anti tumor components with fresh webbed. *Chin J Hosp Pharm* 2007, 27: 441-444.
7. Li PW, Li X. *Chinese medicine oncology clinical manual*. Shanghai, Shanghai Science and Technology Press 2006: 34-35.
8. Xia Y. Effect of acupuncture on central transmitter. *Acupuncture Research* 1985, 2: 81
9. Niu HM. Clinical and experimental study on cancer pain treated with AI Tong Xin nose drops. *Journal of Shandong University of Traditional Chinese Medicine* 1999, 23: 430-433.
10. Chen JQ, Tang YH, Wu XA. Curative effect of compound *Sophora flavescens* injection in treating cancer pain. *Sichuan Journal of Cancer Control* 2002, 15: 236-237.
11. Zhang GP, Chen DS, Deng M. Analgesic effect of sagittal vine on cancer pain. *Chinese Journal of Tissue Engineering Research* 2002, 6: 1785.
12. Theodove L, Mclenore, *et al* . Profiles of prostaglandin biosynthesis in normal lung and tissue from lung cancer patients. *Cancer Res* 1998, 48: 3140.
13. Liu ZH, Lu Y, Chen RS, *et al.* Treatment of tumor patients with deep venous thrombosis by removing blood stasis and dredging collaterals. *Study Journal of Traditional Chinese Medicine* 2004, 22: 160.
14. Tang ZY. *Modern oncology*. Shanghai, Shanghai Medical University Press 1993: 129-429.
15. Ma ZL, Fan SH, Ge LZ, *et al.* Clinical study on the relationship between cancer pain and immune level. *Chinese Journal of Pain Medicine* 1999, 5: 133-135.
16. Sunagawa M, Okada M, Guo SY, *et al* . Splenic natural killer cell activity is suppressed by ligation of unilateral mental nerve in rats. *Masui* 2000, 49: 250-254.
17. C XL. Discussion on the mechanism of Chinese medicine in relieving cancer pain. *Chin J Mod Drug Appl* 2008, 2:113-115.
18. Li Z. Eight ways of treating cancer pain by TCM. *Chinese Journal for Clinicians* 2000, 28: 40.
19. Zhou J, Li ZT. Eight ways of treating cancer pain by TCM. *J Luzhou Med Coll* 2005, 28: 326-327.
20. Zhao CN, Shui YP. Chinese medicine and tumor immunity. *Tianjin J Tradit Chin Med* 2004, 21: 227-228.