

Research Progress of TCM External Treatment on Opioid-related Constipation in Cancer Pain

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Abstract: Pain is one of the most common symptoms of malignant tumors. Opioids are the first-line drugs for the treatment of moderate to severe cancer pain. At present, there is no clear, effective and safe method for the prevention and treatment of its adverse reactions. Opioid-induced constipation (OIC) is a very common symptom of cancer patients who use opioids. An opioid induced Constipation (OIC) has a great impact on patients' quality of life, tumor treatment and many other aspects. Therefore, an effective prevention and treatment of cancer pain OIC is of great clinical significance. The traditional Chinese medicine external treatment method is simple, convenient, testing and cheap, and has unique advantages in the treatment of OIC. In this paper, we summarized and analyzed the research on the treatment of opioid-related constipation by external treatment of traditional Chinese medicine in recent years, in order to provide reference value for clinical treatment.

Keywords: Opioid-related Constipation; Cancer Pain; External Treatment of Chinese Medicine.

1. Introduction

In the current situation of the continuous improvement of the average life expectancy of human beings, the increase in the incidence of cancer has become an unavoidable problem. According to statistics, there will be 4.56 million new cancer patients in China in 2020, accounting for 23.7% of the global cancer incidence [1]. Cancer pain is one of the most common concomitant symptoms of cancer patients, and opioids have an unshakable status as the most commonly used means to suppress cancer pain in clinical practice. However, an adverse reaction of opioid-induced constipation (OIC) can occur anytime after the use of opioid analgesics. An increase in the drug dose does not make patients tolerate it. Studies have shown that more than 90% of patients with cancer pain have OIC after using opioid analgesics [2]. Opioids can inhibit gastrointestinal peristalsis and digestive fluid secretion to a certain extent, inducing constipation [3]. In addition, OIC is often present throughout the course of treatment. OIC not only reduces the quality of life of patients, but also easily induces cardiovascular and cerebrovascular diseases. For patients with cancer pain, OIC can also lead to reduced compliance with opioids and reduce the effectiveness of drugs. Therefore, the effective intervention of OIC for cancer pain has important clinical significance. Some scholars believe that the emergence of OIC is not only a problem of the gastrointestinal tract, but is related to various organs, especially for cancer patients, long-term disease will make the lungs, spleen, kidney and other organs occur different degrees of deficiency damage. Therefore, in the treatment of OIC patients with cancer pain, the comprehensive treatment led by Chinese medicine has its unique advantages [4]. The external treatment of TCM is based on the theory of zang fu meridians, including acupuncture, applying, massage, fumigation, ear points, foot therapy, poultices, acupoint injection and many other methods. It has the advantages of simple, convenient, testing and incorruptible. For cancer pain OIC, especially for patients who resist taking drugs internally, the external treatment of traditional Chinese medicine is particularly important.

2. Acupoint Application Therapy

Acupoint application therapy is a commonly used clinical external treatment of traditional Chinese medicine, which is ground into fine powder with water and ginger juice as a blending agent, then mixed into paste, then made into pills or paste, etc., and applied locally on the human acupoint [5]. The treatment method is to select a specific point, apply the appropriate Chinese medicine or prescription to the point, so that the drug force can penetrate into the body through the meridian points, direct to the disease, to achieve the purpose of treatment. Traditional Chinese medicine believes that the impact of OIC on gastrointestinal function is mainly manifested in "gastrointestinal heat, qi, blood and body fluid deficiency" caused by intestinal moistening, fluid deficiency, abnormal rise and fall, conduction disturbance. Therefore, the treatment should be based on supplementing the middle and supplementing the qi, eliminating the accumulation and moistening the bowel, and relaxing the bowels.

Wu Liqin et al. [7] divided 80 patients into control group and treatment group by random number table method for cancer pain OIC with Qi deficiency and fluid deficiency. The control group was given oral Maren pill, 6g once, twice a day. The treatment group was treated with autonomous traditional Chinese medicine pill applied at Shenque point (Astragalus, Baizhu, Radix adenoginseng, scrophulariae, sesame seed), 1 pill, 2 hours each time, 3 times/day. Both groups were treated for 21 days. The total effective rate was 87.77% based on the constipation symptoms, constipation score and TCM clinical symptoms before and after treatment. It demonstrates that Xu Zhuanxi mentioned in "Medical source Theory · Thin paste theory": "Stick with paste, block its gas, make the drug from the pores into its rationale, through the meridian, or out, or attack and disperse, compared with medicine especially powerful, this is the most wonderful method", acupoint paste is better than the effect of internal medicine. At the same time, it also shows the remarkable effect of the treatment of both attack and tonic in the constipation of Qi deficiency and fluid deficiency. Lu Lingling et al. [8] applied paste rhubarb

powder prepared with ginger juice to Shenque Point once a day. The course of treatment was 10 days. The total effective rate of OIC for cancer pain was 93.33%. It embodies the exact curative effect of the method of attack and drainage. Ouyang Yilan et al. [9] applied defecation ointment (raw rhubarb, angelica sinensis, Xuanming powder, Magnolia officinalis, areca nut, fructus aurantii, orange peel, and male clove) to Shenque point, 2d/ stick, combined with lfructosum oral solution once/twice /d, for 14 days as a course of treatment, and the total effective rate was 98.53%. Clinical symptoms, quality of life have been significantly improved, acupoint application and internal medicine complement each other, and promote the absorption of internal medicine while playing a role. Yao Lili et al. [10] applied pasted fine powder of Cornus officinus at Shenque point, once /d, combined with warm and electric moxibustion (bilateral Tianshu, branch gou, Zusanli and Shangjuxu), 30min each time, once /d, and took 10d as a course of treatment. The total effective rate was 78.00%.

For patients with chronic and serious cancer pain, the efficacy of a single treatment is ultimately insufficient, and the high degree of adaptation of acupoint application makes it ensure its own efficacy at the same time, not only will not affect the development of other therapeutic measures, but also improve its efficacy. Therefore, the application of Shenque acupoint as the main position reflects its important clinical value in the treatment of cancer pain OIC with its characteristics of simple operation, high patient compliance, wide adaptation group, few adverse reactions, and remarkable efficacy.

3. Acupuncture Therapy

Acupuncture therapy is based on the theory of meridians and acupoints, and adopts metal needles to stimulate the acupoints of the human body to achieve the purpose of treatment. There are many common methods in clinical practice, such as millimeter needle acupuncture, electric acupuncture, warm acupuncture, small needle knife and so on. It has the clinical characteristics of minimally invasive, safe, simple and effective. Li Sheng et al. [11] selected Oics (Tianshu, Jigou, Daheng, Fenglong, Hegu, Qihai, and Zusanli) for the treatment of cancer pain by acupuncture and retained the needle for 30min. The needle was injected once every 15min, once a day, and the treatment lasted for 30 days. The total effective rate was 90.00%. "Plain Question · Six Micro purposes" said: "On the heaven pivot, the weather is the Lord; Under the heaven pivot, the earth Qi is the ruler of... That's what that means. " This method takes Tianshu point as the main point and uses all the points together to play the role of promoting qi and guiding stagnation, moistening intestine and clearing heat, invigorating qi and nourishing Yin. It shows the remarkable effect of acupuncture on OIC of cancer pain. Li Tianmiao et al. [12] adopted the tiaoshitong Fu-fu acupuncture method (main points: Neiguan, Sanyin Jiao, Zhong Shui, Zuo Hui Hui, Zuo Wai Hui and Zuo Wai Shui, auxiliary points: Weizhong, Chizze and Ji Quan) to assist warm acupuncture and moxibustion (main points: Xiawan, Zhongwan, Qi Hai and Guanyuan, auxiliary points: Daheng, Tianshu, Jigou and Shangjuxu), and the total effective rate was 95.65%. "On the source of diseases" records: "Stool patients, by the five viscera is not adjusted, Yin and Yang partial deficiency and reality, that the three jiao discord is cold and hot and knot. " With the method of regulating Shentong Fu-organs combined with warm acupuncture and moxibustion to regulate Sanjiao, the use of benefiting air

temperature Yang, grasp the theory of local and whole Chinese medicine, and get together the effect of guiding fu-qi and relieving constipation. Li Jingang et al. [13] applied acupuncture (Zhongwan, Tianshu, Qihai, Shangjuxu, Zusanli, Zhaohai) combined with auricular points to the king without leaving seeds. The total effective rate was 85.00%. It is far more effective than oral drug treatment, simple acupuncture or auricular points. It shows the remarkable curative effect of acupuncture and auricular point. Guo Yingying [14] used acupuncture (Tianshu, Shangjuxu, Dan-Dan-Yu, jigou, Waiqi, Erbai and Zusanli). Apply in Zhongwan and Shenque with Liqitongfu external prescription (Rhubarb, Fructus aurantii, Magnolia officinalis, licorice, stir-fried white peony, ginger pinellia, poria cocos, wood fragrance, sand kernel). The total effective rate was 91.30%.

Acupuncture treatment of cancer pain OIC has a significant effect, although many doctors use different acupuncture methods, acupuncture point selection and combined with different other treatments, but are to regulate the fu-qi, tonifying qi and blood, promoting gastrointestinal peristalsis as the center to expand. Moreover, the diversity of acupuncture points provides doctors with more choices when facing the complicated syndromes of cancer patients.

4. Moxibustion Therapy

Moxibustion therapy uses different techniques to stimulate the skin and acupoints by burning moxa heat generated by moxa wool. It has the characteristics of simple, safe, low cost and good curative effect. Studies have shown that OIC moxibustion for cancer pain has a good effect on thermal and medicinal effects [15]. Yan Yan et al. [16] used moxibustion (Tianshu, Shenque, Guanyuan) in the form of circular moxibustion combined with routine nursing. The total effective rate was 94.4%. Ge Yingzi et al. [17] conducted a randomized controlled experiment on the effects of electronic moxibustion at different temperatures on OIC of cancer pain. The study showed that the total effective rate of electronic moxibustion at 50°C was 86.21%. In the case that the human body can tolerate, the higher the temperature of moxibustion, the better the effect. Studies have shown that moxibustion in the treatment of constipation, the main effect is to improve the fasting and post-meal gastrin levels of patients [18]. Moxibustion in the treatment of cancer pain OIC, for deficiency syndrome, can play a role in supplementing the positive qi, regulating the spleen and stomach, warming the lower jiao; According to the empirical evidence, it can play a two-way regulation of heat inducing heat to go out or dispelling cold.

5. Massage Therapy

Massage therapy is a kind of physical therapy which is based on the theory of meridians of traditional Chinese medicine and acts on specific parts of the human body by means of pushing, holding, pinching and lifting. It can play the effect of dredging meridians, harmonizing qi and blood, and assisting healthy qi. Tian Xiaojing [19] et al. adopted the method of Jiugong abdominal massage to carry out targeted massage by means of pushing, holding, dotting and kneading in accordance with the order of Jiugong bagu. It can effectively relieve the symptoms and intestinal function of OIC patients with cancer pain. Yan Qingyan et al. [20] used the method of affixing Wang Kuixing to acupoints (Zusanli, Hegu, Tianshu, Jigou, Guanyuan) for acupressure. The total

effective rate was 94.4%. It can not only treat cancer pain OIC, but also regulate the function of viscera, so as to treat both symptoms and root causes. Han Lijun et al. [21] adopted the method of TCM ointment rubbing. They applied the refined herbs to the diseased parts of patients, and made the drugs penetrate better through acupoints and massage, so as to achieve the effect of treating diseases. Whether it is simple massage treatment, or with other therapies have a significant effect.

6. Other Therapies

Other therapies include needle therapy, enema therapy, TCM umbilical therapy and so on.

For the treatment of OIC for cancer pain, some researchers [22] have adopted the method of embedding the press needle into Tianshu, Venjie, Zhongwan, Dantan Shu, and Dantan Shu together with other related treatments [23], which have good efficacy.

Some researchers have used traditional Chinese medicine retention enema to add flavor to Tiaoweichengqi Tang [24] (30g sesame seed, 0g Xianhecao, 15 g hyalagon, sligelaria, Zhonglou, 15 g achyranthes, 10 g rhubarb, Yanhu, 5g mirabilis and Xianchorice) TCM enema prescription [25] (30g Rhubarb, 30g North Astragalus, 30g Magnolia officinalis, 30g hyalagon officinalis) Good results were obtained.

In TCM umbilical therapy, studies have shown [26] that TCM umbilical therapy bag (rhubarb, mirabarite, cinnamon, cloves, wood balm, Astragalus, angelica, Poncirus aurantii) is a good choice for patients who cannot eat or have poor gastrointestinal tumor.

7. Peroration

TCM classifies OIC as "constipation" based on its symptoms. "Su Wen" said that "the large intestine, the conduction of the official, change out", that the large intestine conduction function should be used as the basis for diagnosis and treatment of diseases. "Shengji General Record · Volume ninety-seventh constipation" mentioned that "Big constipation, cover is not a syndrome, all Rongwei is not consistent, Yin and Yang Qi is also... There is also a shelter." The etiology and pathogenesis of constipation are complex and varied. For the complex and diverse etiology and pathogenesis of cancer pain OIC, it may be difficult to achieve the expected efficacy of a single internal or external treatment, so it may be better to cooperate with a variety of treatment methods according to the individual situation of the patient.

Shenque acupoint in the umbilicus, belongs to any pulse, the blood line, also known as "umbilicus", "life", "health door", for the essence, Qi, God, blood exchanges. "Lizheng Massage to the technique" records: "umbilical through the five viscera, the door of true qi exchange also", umbilical contains a wealth of blood vessels, lymphatic vessels and various nerve tissues, its strong permeability to ensure the efficacy of drugs. Therefore, many scholars chose Shenque point as the main position of syndrome differentiation when treating OIC by acupoint application. Cancer pain OIC patients due to the lack of positive qi, in the acupuncture treatment, select points, points with the spleen and stomach, qi tonifying blood, promote intestinal function, more use of Zusanli, Sanyin Jiao, Tianshu and other points. In the treatment of constipation can also play a role in the

intervention of pain. The warming effect of moxibustion often plays a bidirectional regulating role in the face of the pathogenesis of deficiency and accumulation in cancer patients. Acupoint application, acupuncture, moxibustion, massage, enema, acupuncture and other external treatment methods in the treatment of diseases have their own unique features. Therefore, one or more treatments should be applied dialectically in clinical practice. To relieve the patient's pain and promote the improvement of the condition for the purpose. At the same time of treatment, the patient's mental counseling is also of great help to the improvement of the disease. In the face of the complex disease changes of cancer pain OIC, external treatment is only one of the means to treat the disease, should take the improvement of the patient's condition as the goal, both internal and external consideration, all methods and application, comprehensive treatment. Individualized and integrated treatment should be more conducive to the diagnosis and treatment of diseases.

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