

Postprint of Research on Traditional Chinese Medicine External Therapies for Opioid-Related Constipation

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Abstract

Opioid analgesics are common clinical agents for the treatment of cancer pain. Opioid-induced constipation (OIC) is highly prevalent among cancer pain patients, severely compromising their quality of life and carrying the risk of precipitating cardiovascular and cerebrovascular events. The prevention and management of OIC thus hold significant clinical importance. This article reviews and summarizes recent advances in the understanding of OIC pathogenesis in traditional Chinese medicine (TCM) and related external therapeutic modalities, including acupuncture, auricular point pressing, moxibustion, and acupoint application, aiming to provide references for optimized TCM interventions and scientific research in cancer pain-related OIC.

Full Text

Study on External Treatment of Traditional Chinese Medicine for Opioid-Induced Constipation

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Abstract

Opioid analgesics are commonly used in clinical practice for cancer pain management. Opioid-induced constipation (OIC) is highly prevalent among cancer pain patients, severely impacting their quality of life and posing risks for cardiovascular and cerebrovascular events. The prevention and treatment of OIC hold significant clinical importance. This article summarizes recent advances in understanding the Traditional Chinese Medicine (TCM) pathogenesis of cancer pain-related OIC and reviews developments in external TCM therapies including acupuncture, auricular point pressing, moxibustion, and acupoint application, aiming to provide references for optimizing TCM interventions and scientific research on cancer pain OIC.

Keywords: external treatment of Traditional Chinese Medicine; opioid drugs; constipation; pain; integrated traditional Chinese and western medicine; moxibustion

Cancer is the second leading cause of death globally, with data from the International Agency for Research on Cancer of the World Health Organization showing that opioid analgesics (such as controlled-release oxycodone, codeine, and tramadol hydrochloride tablets) are the first-line drugs for treating and improving cancer pain symptoms in middle and advanced-stage cancer patients. However, long-term opioid use commonly causes adverse reactions including nausea, vomiting, and urinary retention, with studies indicating that a significant percentage of cancer pain patients develop OIC. The interdisciplinary consensus on OIC diagnosis considers any of the following that occurs after initiating opioid use as OIC: reduced bowel frequency, progressively worsening difficulty in defecation, or hardened stool.

Traditional Chinese Medicine is a medical science with a long historical and cultural tradition, unique diagnostic theories, and therapeutic techniques that have been continuously summarized, enriched, and improved over thousands of years. External TCM therapies such as acupuncture, massage, herbal application, auricular point pressing, and moxibustion have demonstrated preventive and therapeutic effects on constipation, offering simplicity, convenience, and minimal side effects while showing unique advantages in clinical studies for OIC prevention and treatment. This review examines the current application status of external TCM therapies in OIC.

1. TCM Understanding of the Etiology and Pathogenesis of Constipation

The mechanism of OIC is more complex than that of ordinary constipation. Ancient literature contains no specific records of OIC, and clinical diagnoses still show variations today, with individual differences among patients. The *Huangdi Neijing* states that “the large intestine is the official of transmission, through

which transformation is discharged,” highlighting the importance of the large intestine as an excretory organ. Dysfunction of large intestine transmission is closely related to organ dysfunction, deficiency of qi, blood, and body fluids, and imbalance of yin and yang. Normal large intestine transmission depends on the nourishment of blood, the moistening of body fluids, and the propulsion of qi. Most cancer patients receiving opioid analgesics are in middle and advanced stages, often presenting with deficiency of vital qi, imbalance of yin and yang, and depletion of qi and blood. Opium is a poppy extract, with aliases in historical materia medica including afurong, yapian, and yingzisu. The *Bencao Gangmu* records it as “sour, astringent, warm, and slightly toxic,” primarily treating chronic dysentery. Qing dynasty warm disease scholar Wang Shixiong considered it warm and astringent, intensely hot and toxic, easily damaging true yang.

Modern elucidation of OIC mechanisms also provides references for effective TCM interventions. For instance, opioids share similar structures and functions with endogenous opioid peptides and represent dose- and concentration-dependent replacement therapy, while acupuncture can promote endogenous opioid peptide secretion. Therefore, employing acupuncture for analgesia or organ function regulation during opioid use can achieve good pain relief while preventing or improving OIC. Additionally, opioids inhibit nerve impulses and neurotransmitter synthesis, reducing gastrointestinal motility—a mechanism by which they affect gastrointestinal function. TCM can directly or indirectly stimulate specific acupoints, the auricle, and the gastrointestinal tract through syndrome differentiation to systematically coordinate organs and improve intestinal function. Research also indicates that gut microbiota and the brain-gut-microbiota axis have extensive connections with constipation and significantly influence intestinal epithelial metabolism, with TCM having unique theoretical foundations and clinical experience in regulating gut microbiota. These perspectives provide scientific explanations and references for syndrome-differentiation-based optimized interventions for cancer pain OIC.

2. External TCM Therapies

2.1 Acupuncture Therapy

Acupuncture, guided by basic TCM theory and based on meridian and acupoint theory, uses filiform needles to stimulate specific body parts for disease prevention and treatment. Cancer patients with OIC present with deficiency of vital qi, further compromised by surgery, radiotherapy, and chemotherapy, leading to spleen-stomach damage, impaired transportation, and aggravated constipation. Acupuncture supports vital qi, dispels pathogenic factors, unblocks meridians, and regulates yin-yang. Acupoints such as Tianshu (ST25, the front-mu point of the Large Intestine Meridian), Dachangshu (BL25, the back-shu point), and Shangjuxu (ST37, the lower he-sea point) effectively treat constipation. Yang et al. followed the principle of “treating yin disease with yang and yang disease with yin,” needling the spleen front-mu point Qimen (LR14), stomach front-mu

point Zhongwan (CV12), and large intestine front-mu point Tianshu to draw yang from yin and supplement original qi deficiency, combined with back-shu points of the spleen, stomach, and large intestine to treat yin from yang, significantly improving constipation symptoms and reducing adverse events in cancer pain patients. Li et al. selected Tianshu and Zhigou (TE6) to unblock sanjiao qi, supplemented with Fenglong (ST40) and Daheng (SP15) to unblock the fu organs and regulate the spleen-stomach, using Hegu (LI4) for heat-pattern constipation. After treatment, patients showed significantly reduced CSS scores and TCM syndrome scores, with elevated KPS scores. Zhao et al. selected acupoints including Tianshu, Zhongwan, Qihai (CV6), Xiajuxu, Zusanli (ST36), Yinlingquan (SP9), Taixi (KI3), Taichong (LR3), and Zhigou, where Tianshu and Zhongwan eliminate turbidity and regulate fu qi, Qihai supports vital qi and consolidates deficiency, Taichong guides qi downward and clears liver fire, and Zusanli promotes digestion and supplements middle qi. After treatment, patients showed significant improvements in single defecation time, stool characteristics, defecation intervals, straining, as well as symptoms such as anal discomfort, heaviness, and abdominal distension. Zou et al. noted that acupuncture for OIC is simple, cost-effective, and effective, embodying the TCM principle that the rationale of external treatment corresponds to internal treatment, with good therapeutic effects and high patient acceptance.

2.2 Auricular Point Pressing Therapy

The ear is closely connected to meridians. The *Lingshu* records that “the ear is where the zang-fu organs and meridians converge,” and the *Weisheng Baojian* states that “the five zang-organs, six fu-organs, and twelve meridians all connect to the ear,” establishing the ear as a local representation of the whole body. When internal organs or 躯体 lesions occur, corresponding auricular areas exhibit changes such as discoloration, deformation, desquamation, papules, tenderness, and altered skin resistance—collectively termed positive reactions. Auricular point pressing is a TCM therapy that uses alcohol to clean the auricle, then applies vaccaria seeds on adhesive tape precisely to auricular points, with appropriate kneading, pressing, and pinching to generate heat, numbness, distention, and pain stimuli for disease prevention and treatment. Zhang et al. noted that OIC mostly results from qi stagnation, qi deficiency, or blood deficiency causing intestinal dryness and heat accumulation, suggesting that auricular therapy should address both root and branch, combining local and whole-body approaches by selecting points based on both location and syndrome differentiation. A systematic review showed that auricular plaster therapy effectively prevents and treats constipation in cancer patients using opioids, offering safety advantages by avoiding gastrointestinal stimulation from oral medications. Primary point selection includes Large Intestine, Spleen, Lower Rectum, Constipation Point, and Sanjiao to regulate intestinal function and stimulate peristalsis. Zhu et al. selected Rectum, Large Intestine, Abdomen, Sanjiao, and Constipation Point, using tender points as sensitive points with pressure tolerable to patients, achieving notable efficacy. Zhang et al. intervened with

Constipation Point, Sanjiao, Abdomen, Spleen, Stomach, Liver, Lung, Large Intestine, and Subcortex, with results showing the average time to first constipation occurrence was longer than in control groups taking lactulose alone.

2.3 Moxibustion Therapy

Moxibustion is a traditional TCM treatment. Mugwort is acrid, warm, and bitter; burning it achieves qi-moving, blood-activating, meridian-warming, cold-dispersing, and pain-relieving effects. The warming stimulation on meridian points warms meridians, disperses cold, unblocks collaterals, regulates qi-blood circulation, and warms yang to supplement qi, allowing stomach qi to flourish and yang qi, essence, and blood to become abundant. Cancer patients often present with vital qi deficiency. Yan et al. selected Tianshu, Shenque (CV8), and Guanyuan (CV4), applying mild moxibustion until local warmth without burning pain was achieved, observing reduced constipation scores and higher total effective rates in the treatment group. Zhou studied the clinical effects of heat-sensitive moxibustion on OIC and its improvement of patients' quality of life, applying alternating heat-sensitive moxibustion on two groups of points every other day with significant results. Moxibustion may offer ideal long-term efficacy, is simple to operate, non-invasive, and provides good patient comfort, warranting broader promotion.

2.4 Acupoint Application Therapy

Acupoint application works through two mechanisms: indirect action, where drug stimulation of specific locations enhances immunity to reduce disease incidence and improve symptoms; and direct action, where applied drugs penetrate the skin at corresponding points, reach the disease site via blood circulation to exert therapeutic effects. Acupoint application offers numerous advantages, avoiding gastrointestinal interference and inactivation, reducing inter- and intra-individual variability, decreasing dosing frequency and total dosage, minimizing adverse reactions, and providing simple operation. For malignant tumor patients with OIC, the Shenque (CV8) point is commonly selected. As the origin of congenital essence located at the umbilicus center on the Ren Meridian, Shenque is also where the Chong and Du Meridians circulate, making it a convergence point of three meridians that connects with all vessels, thus possessing effects of cultivating original qi, consolidating yang, rescuing collapse, and harmonizing the stomach and intestines. Various medicinals through Shenque can unblock sanjiao qi, allowing drugs to directly enter the yangming meridian of the large intestine, harmonize yin-yang and qi-blood, and promote gastrointestinal peristalsis to achieve bowel movement. Jin dynasty Ge Hong's *Zhouhou Beiji Fang* recorded treating malaria by applying a mixture of vinegar and aconite powder on the back. Qing dynasty external treatment master Wu Shiji systematically elaborated various umbilical therapies in his monograph *Li Yue Pian Wen*. Multiple studies have applied herbal formulas to Shenque to regulate gastrointestinal function and cultivate original qi, showing higher effective rates

than control groups. Zhao et al. used rhubarb powder on Shenque to prevent constipation in tumor patients taking oral oxycodone, reducing constipation incidence. Feng et al. used astragalus and mirabilite application on Shenque with good results. A meta-analysis by Zhao et al. showed that acupoint application effectively improves constipation caused by opioid use in cancer patients.

2.5 Abdominal Massage

TCM holism holds that normal function of all zang-fu organs depends on the connection and communication of the meridian system, with acupoints bridging the relationship between body surface and internal organs. Abdominal massage provides certain stimulation to intestinal qi-blood circulation, benefiting improvement of intestinal mucosal neurotrophs. Kneading corresponding abdominal acupoints can regulate zang-fu functions, with kneading Zhongwan, Tianshu, Guanyuan, and other points regulating the spleen-stomach, modulating large intestine activity, stimulating intestinal peristalsis, and thus promoting defecation. Chen et al. applied abdominal massage daily during the Mao hour (5-7 am) according to the midnight-noon circulation theory, showing that abdominal massage effectively improves OIC treatment efficacy, reduces BFI fatigue scores, and increases patient satisfaction. Tian used clockwise abdominal massage combined with kneading Zhongwan, Tianshu, Hegu (LI4), and Guanyuan to treat advanced lung cancer OIC, demonstrating good prognosis and high clinical satisfaction. Rao et al. compared three different abdominal massage techniques for OIC, using manual external force to mobilize intestinal tubes and contents, accelerating food residue movement.

2.6 Rectal Administration and Integrated Chinese-Western Approaches

Rectal administration is one of the oldest drug therapies. Eastern Han dynasty Zhang Zhongjing pioneered rectal suppositories and enema techniques, Eastern Jin dynasty Ge Hong invented enema equipment, and Tang dynasty Sun Simiao developed the earliest retention enema technology. With modern pharmaceutical development, many new rectal dosage forms have emerged, such as thermosensitive liquid suppositories, micro-enemas, thermosensitive rectal gels, and nanoparticle rectal formulations. Rectal administration avoids direct gastric stimulation, reduces patient suffering from oral Chinese medicine, and allows approximately % of drugs to be absorbed through intestinal mucosa directly into blood circulation without passing through the liver, thereby reducing hepatotoxicity and side effects. Combined therapies using multiple external TCM methods, rectal administration, and integrated Chinese-western approaches for OIC have synergistic effects of supporting vital qi, dispelling pathogenic factors, enhancing efficacy, and reducing toxicity, with their application value gradually becoming a research hotspot. Studies have shown that oral probiotic yogurt combined with acupuncture effectively improves constipation and functional status in OIC patients. Yao et al. applied Shenque acupoint application com-

bined with electronic moxibustion for OIC with definitive efficacy. Mai used ointment-rubbing therapy combined with heat-sensitive moxibustion, preparing herbal ointments combined with massage techniques to warm and unblock meridians, regulate qi-blood, and improve organ function, significantly relieving constipation symptoms.

3. Conclusion

Cancer-associated pain is an important factor affecting patient quality of life, and controlling cancer pain is a key component of malignant tumor treatment. Opioid analgesics are the main drugs for moderate to severe cancer pain, with OIC being a common adverse reaction that worsens with increasing dosage and treatment duration, affecting subsequent therapy. As society pays greater attention to traditional medicine and the continuous development of TCM, more experts and scholars have recognized the unique value of Chinese medicine in treating OIC, with proven effectiveness. Future research on the modern medical significance and mechanisms of numerous TCM therapies—including acupuncture, auricular point pressing, acupoint application, abdominal massage, and herbal enemas—still requires support from larger sample sizes and multicenter laboratory and clinical data. The development and advancement of TCM still face challenges.

Conflict of Interest Statement: The authors declare no conflicts of interest.

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