

# *To Explore the Application Rule of Pinellia in Chemotherapy-Related Vomiting of Cancer Patients Based on Classical Prescription*

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**Abstract:** We consider Cancer is the most deadly disease in the world. Chemotherapy is an effective treatment for tumors, but the side effects, mainly nausea and vomiting, also seriously affect is the survival quality and prognosis of tumor patients. In this paper, we analyze the application rules of Pinellia ternata in the Jing formula based on the Jing formula, clarify the details and explore the true meaning of its application, to provide a reference for the use of Ban Xia in clinical treatment. I discuss it as follows.

We consider cancer is the deadliest disease in the world and one of the highest human mortality rates. Chemotherapy is an effective and widely used treatment for cancer [1], and platinum-based antineoplastic drugs are among the important chemotherapeutic agents. However, chemotherapy-induced nausea and vomiting (CINV) is not only a serious side effect of cancer treatment, but also one of the most feared side effects of patients in oncology treatment, and according to statistics, the percentage of patients with varying degrees of nausea and vomiting symptoms during chemotherapy reaches According to statistics, the proportion of patients with varying degrees of nausea and vomiting during chemotherapy is 70%-80%. Severe gastrointestinal reactions cause fear of chemotherapy and anxiety and depression in patients, which reduces their compliance with treatment.

## 1. Pathogenesis of CINV

The medulla oblongata vomiting center controls the pharynx, gastrointestinal tract, and several chemoreceptor trigger areas involved in vomiting occurrence. When visceral nerves, cerebral nerves or vestibular organs, and so forth are stimulated, signals will be transmitted via afferent nerves to the brainstem, which processes them for the vomiting reflex and then transmits efferent signals to the relevant tissues and organs, thus triggering vomiting. 5-HT<sub>3</sub> receptors, substance P and NK-1 receptors, and dopamine are the main neurotransmitters and receptors involved in vomiting. [2]

## 2. CINV Clinical Classification

Chemotherapeutic agents are classified into four classes according to their risk of causing nausea and vomiting: highly emetogenic (HEC) in  $\geq 90\%$ , moderately emetogenic (MEC) in 30-90%, and low and minimal emetogenic chemotherapy in 10-30% and  $\leq 10\%$ , respectively. The HEC drugs include high-dose cisplatin, carmustine, cyclophosphamide, dacarbazine, trimethoprim, streptomycin, and anthracycline, MEC chemotherapeutic agents include but are not limited to carboplatin, doxorubicin, irinotecan, oxaliplatin, etc. It belongs to the low-emetogenic drugs such as paclitaxel, gemcitabine, docetaxel, pemetrexed, etc. Finally, bevacizumab, trastuzumab, vinorelbine, nivolumab, and pembrolizumab are the drugs with minimal risk of emesis. In addition, according to the latest guidelines for the prevention and treatment of CINV [3], tCINV according to the treatment time of occurrence and treatment effect, CINV is usually classified as acute, retarding, expect nature, explosive and difficult to treat. And late-onset CINV is generally more prevalent than acute CINV, which may be due to more aggressive prevention strategies in chemotherapy.

## 3. Progress in CINV Treatment in Western Medicine

Many antiemetic agents with different mechanisms of action have been developed and used to treat CINV, most of which are used as prophylactic agents. Currently, the most commonly used drugs with antiemetic and anti-nausea functions are 5-HT<sub>3</sub> antagonists, corticosteroids, and NK1 receptor antagonists.

### 3.1 5-HT<sub>3</sub> Antagonist

Chemotherapeutic drugs stimulate the mucosa of the gastrointestinal tract and cause damage to the intestinal epithelial chromophores to release neurotransmitters such as 5-HT [4], which are transmitted to the vagal 5-HT<sub>3</sub> receptors and cause a series of responses such as excitation of the vomiting center [5]. In contrast, 5-HT<sub>3</sub> receptor antagonists are highly selective in blocking 5-HT<sub>3</sub> receptors in peripheral vagal nerve terminals and central chemoreceptors, so they have a dual antiemetic effect. Commonly used 5-HT<sub>3</sub> receptor antagonists to treat CINV include Ondansetron, Granisetron, Dolasetron, and palonosetron.

### 3.2 Corticosteroid

Corticosteroids [6] are the primary treatment of acute and tardive CINV. Although the exact mechanism of the antiemetic action of corticosteroids is unknown, many studies have shown that corticosteroids mainly provide "potentiation" to other antiemetic drugs, therefore, corticosteroids are often used in combination with other antiemetic drugs to enhance the antiemetic effect, with dexamethasone being one of the most commonly used corticosteroids.

### 3.3 NK1 Receptor Antagonists

The mechanism of antiemesis by NK1 receptor antagonists [7] is primarily acting both peripherally and centrally by blocking the binding of substance P to NK1 receptors. The most common drugs, such as aprepitant, fosapitant, and lolapitant, are mostly NK1 receptor antagonists in combination with 5-HT<sub>3</sub> antagonists, corticosteroids, in clinical use.

### 3.4 Other Antiemetic Drugs

Other medications used to treat CINV include olanzapine and dopamine receptor antagonists, benzodiazepines, and cannabis. Olanzapine [8], an atypical antipsychotic that blocks dopaminergic and 5-hydroxytryptaminergic neurotransmission, has been used to treat acute, delayed, and breakthrough CINV, and some studies have shown [9] that olanzapine is effective in treating acute and delayed CINV when combined with a 5-HT<sub>3</sub> antagonist, dexamethasone. The most recent guidelines recommend the use of olanzapine in combination with a 5-HT<sub>3</sub> receptor antagonist and dexamethasone, with or without an NK receptor antagonist.

The antiemetic effect of dopamine receptor antagonists [10] is through inhibition of the central emesis pathway and a prokinetic effect on esophageal and small bowel motor function (through choline action and the 5-HT<sub>4</sub> receptor). Benzodiazepines [11] are anxiolytics that have been used for predictive nausea and vomiting, but may also be included in regimens to treat breakthrough or refractory CINV. Several studies have suggested [12] that the mechanism of delayed nausea and vomiting may involve cannabinoid-1 receptors, and thus cannabinoids may also be used as an adjunctive treatment for breakthrough CINV.

## 4. TCM for the Treatment of CINV

TCM(Traditional Chinese medicine ) is the most distinctive treatment method, especially in the treatment of cancer patients. Based on the analysis of the frequency of Chinese herbal medicines to treat CINV by L.Y. Fang et al. [13] based on network pharmacology, it was concluded that Licorice, *Pinellia ternata*, *Poria*, bighead *atractylodes* rhizome, and dried tangerine or orange peel had the highest frequency, and it was concluded that the Chinese herbal medicines to treat CINV were mostly deficiency tonifying, phlegm-relieving, and qi-relieving medicines. “Treatise on Febrile Diseases”, “*Jingui Yaolüe*” have many theories can be used to treat vomiting, such as *Pinelliae* Decoction for Purging Stomach-Fire , *Xiao Chai Hu* Tang, and Big *pinellia* soup, among which, *Pinellia ternata*, is one of the most commonly used herbs, is the sacred medicine for vomiting, and its efficacy in the treatment of nausea and vomiting has been evaluated in some clinical trials.

### 4.1 Pharmacological Effects of *Pinellia Ternata*

*Pinellia pinum* *Pinellia pinis* the dry tuber of the family *Ceraceae*. In May, *Pinellia ternata* is born. We also know it as the half of the summer, so it's called *pinellia pinellia* [14]. It is pungent in taste, warm, poisonous, and belongs to the lung, spleen, and stomach meridians. The efficacy of *Pinellia ternata* was first described in “*Shennong Ben Cao Jing*”, “treating typhoid fever and cold, sub cardiac firmness, hypochondrium, swelling and pain in the throat and throat, head dizziness, chest distension, coughing, intestinal tinnitus, and stopping sweating”. Most of the modern day is the same as it.

Pharmacological experiments have shown that hesperidin alkaloids are the main active components of hesperidin antiemetic, which are useful in preventing chemotherapeutic nausea and vomiting. Zhang Qilong et al. [15] found that the antagonistic effects of Semi-summer alkaloids on four receptor agonists, namely 5-HT, SP, selective 5-HT<sub>3</sub> receptor agonist, and 2-methyl-5-hydroxytryptamine, showed a certain dose dependence. This paper shows that *pinellia* alkaloids block both 5-HT<sub>3</sub> receptor and NK1 receptor on the ileum. Inference may be one of the important mechanisms for preventing chemotherapeutic nausea and vomiting. Zhang Xiangnong et al. [16] and Zhang Tian et al. [17] showed that the decoction-immersed extract in *pinellia terellia* had a certain control effect on CINV. Chen Yalin et al. showed that besides the antiemetic effect, the total alkaloids of *Semen sylvestris* could also cause DNA damage situation in human gastric

cancer cell line SGC-7901 cells, thus keeping tumor cell growth and thus achieving anti-tumor effects.

## 4.2 Exploring the Clinical Application of Pinellia Based on the Prescription

In the "Shanghan Zabing Lun", the pinellia is raw, and raw pinellia is poisonous and needs to be used after prepare, "Jin Kui Yu Huan Jing", the seventh volume of the "The prescription processing" cloud: "where the pinellia is not hey chewed, to soup wash ten times, so that the water is clear and slippery exhausted, wash unripe poisonous". The "Shuowen Jiezi" cloud: "soup, hot water, too", the raw pinellia half of the herb with hot water scalding dozens of times, until the water is clear and the half of the surface secretion of sticky saliva slippery material washed clean, Until the water is clear and the surface of the half-summer secreted sticky saliva slippery substance is washed away, the sticky slippery substance on the surface is one of the sources of toxicity. Modern research has shown that the mucus on the surface of pinellia contains calcium oxalate crystals, which are decocted in hot water for toxicity reduction. Modern experimental studies have found that the toxic components of raw pinellia are resistant to high temperature and insoluble in water and are present only in the herb itself, while the decoction is safe and non-toxic. Chen Baoping treated over 500 patients with raw pinellia, and no uncomfortable reaction was seen and came to the same conclusion: raw pinellia still has a strong stimulating effect after long decoction, but its decoction is safe, so raw pinellia can be used clinical. Most Chinese doctors consider vomiting because of the loss of stomach harmony and lowering and upward rebellion of stomach qi. Zhang Zhongjing emphasizes "Know what to do, along with the evidence of governance," and clinical treatment requires evidence-based treatment. As far as pinellia is concerned, according to vomiting, the dosage varies, Wu-Tang discussed that "one or two to lower the rebellion, two or two to sleep" is the same.

## 5. The Dosage Pattern of Pinellia in the Treatment of Vomiting in the "Shanghan Zabing Lun"

The Qing Dynasty physician Wang Qingren said, "The taste of the medicine is important, but the quantity is even more important". According to the "Shanghan Zabing Lun", which was written in the Eastern Han Dynasty, the conventional dosage of half a liter of Radix Rehmanniae is recorded in the book. According to the tutor, Director Wang Keqiong, who has spent over ten years exploring the original dosage of prescriptions and striving to state the unspoken words of the ancients, "the secret of Chinese medicine is that the dosage is not transmitted", therefore, concerning Associate Professor Chen Renxu of the Chengdu University of Traditional Chinese Medicine, the dosage of half a liter of Radix Rehmanniae = 200ml. Weighing, one liter of pinellia is about 130g, and more raw pinellia is used, and the decoction method, according to the sutra formula, has achieved miraculous results. And the sutra prescription of pinellia dosage law is summarized: 1. Pinellia dosage of two liters: "'Jin Kui Yu Huan Jing- abdominal fullness of cold hernia and persistent food disease'" say "stomach regurgitation and vomiting, Big pinellia soup is the main", where the most amount of pinellia, up to two liters of 260g, where the stomach regurgitation refers to the morning and evening vomiting, vomiting at night, enough to see the severity of vomiting, which is with the pinellia dosage of a liter: Pinellia summer soup, Pinellia soup plus tuckahoe soup ; 3. Pinellia dosage of half a liter: Xiao Chai Hu Tang, small doses, such as "micro vomiting" as the main symptom of Chai Hu Gui Zhi Tang, only used two and a half, 32g.

## 6. Conclusion

This paper outlines the progress of chemotherapy-associated vomiting treatment in Chinese and Western medicine, summarizes the use of pinellia ternata in chemotherapy-associated vomiting in

tumor patients based on the classical prescription combined with Wang keqiong's experience in the clinical application of pinellia ternata, and explores the original dose and traces the origin. We also hoped that we can integrate "theory, method, prescription, medicine and dosage" in the diagnosis and treatment, to maximize the development of Chinese medicine inheritance and innovation.

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