Future Integrative Medicine **2025** vol. 4(4) | 233–239
DOI: 10.14218/FIM.2025.00035

Review Article

Traditional Chinese Medicine in Febrile Neutropenia Treatment: Advances and Prospects

Kangdi Cao[1,2#], Jinkun Wang[2#], Jiawei Wang[1], Shuo Wang[1], Dandan Wang[1], Shuaihang Hu[1], Bingjie Fan[1], Lanxin Zhang[1], Wei Hou[1*] and Xueqian Wang[1*]

[1]*Department of Oncology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China;* [2]*Department of Graduate School, Beijing University of Chinese Medicine, Beijing, China*

Received: June 10, 2025 | **Revised:** October 21, 2025 | **Accepted:** December 02, 2025 | **Published online:** December 30, 2025

Abstract

Febrile neutropenia (FN) is one of the acute and serious complications of chemotherapy-induced myelosuppression in tumor patients. Antibiotics and granulocyte colony-stimulating factor are the mainstays of its treatment. However, this therapy still faces many challenges and may trigger drug resistance, as well as adverse effects such as bone pain and vasculitis. How to minimize treatment-related toxicity while ensuring therapeutic efficacy has become a key issue to be addressed in current clinical practice. In recent years, traditional Chinese medicine (TCM) has demonstrated unique advantages in the prevention and treatment of FN. We conducted a comprehensive search of the PubMed, Web of Science, and CNKI databases using keywords such as TCM and FN, covering the period from their establishment to May 2025. Clinical studies have shown that the combination of TCM and modern medicine can significantly reduce the incidence of FN, while also enhancing the number of granulocytes, shortening the duration of fever, improving the quality of life of patients, and reducing other toxic effects of chemotherapy. These results suggest that TCM is a promising and safe complementary therapy. However, more high-quality trials are needed to verify its benefits. This review summarizes the latest progress in the treatment of FN with TCM and discusses future development directions.

Introduction

Febrile neutropenia (FN) is a common acute condition during tumor treatment. There is a clear international consensus on its diagnostic criteria: a single oral temperature ≥38.3°C or a sustained temperature ≥38.0°C for more than 1 h (defined by the European Society for Medical Oncology as 2 h), and an absolute neutrophil count of $<0.5 \times 10^9$/L or expected to fall to $<0.5 \times 10^9$/L within 48 h.[1–3] Despite advances in prevention and treatment, FN remains one of the most serious complications of oncologic chemotherapy. Epidemiologic data show that FN occurs in seven to eight cases per 1,000 cancer patients receiving chemotherapy.[4] A U.S. study that included 41,779 hospitalized FN patients showed an in-hospital mortality rate of 9.5%.[5] The multiple burdens of FN on tumor patients cannot be ignored. Firstly, as the primary line of defense against infection, the absence of neutrophils significantly increases the risk of serious infections, endangering patients' lives. Secondly, it affects the process of anti-tumor therapy, which may lead to a reduction or delay in the chemotherapy dose, thus affecting therapeutic efficacy and survival prognosis.[6,7] Furthermore, FN seriously affects the quality of life of patients. From a health economics perspective, FN significantly increases the medical burden, with studies indicating an average length of stay of six days and an average hospitalization cost of up to 40,000 dollars, and has become a significant public health problem.[8,9]

Considering the hazardous nature of FN, it is important to find effective management options. Presently, the Multinational Association for Supportive Care in Cancer scoring system is the main clinical tool for FN risk assessment, which is effective in identifying low-risk patients.[10] Recent guidelines indicate that risk factors for FN include advanced age, advanced disease, poor physical status, a history of neutropenia/FN, infections, recent surgery or open wounds, prior chemotherapy, myelosuppression, and the presence of pulmonary, renal, hepatic, or cardiovascular comorbidities. The incidence of FN can be effectively reduced by identifying these risk factors and implementing preventive measures.[1,11,12]

Keywords: Traditional Chinese medicine; Febrile neutropenia; Efficacy; Safety; Advance; Prospect.

***Correspondence to:** Xueqian Wang and Wei Hou, Department of Oncology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China. ORCID: https://orcid.org/0000-0002-5694-222X (XW); https://orcid.org/0000-0002-6166-6039 (WH). Tel: +86-010-88001192 (XW); +86-010-88001500 (WH), E-mail: wxq791875354@126.com (XW); houwei1964@163.com (WH)

[#]These authors contributed equally to this work.

How to cite this article: Cao K, Wang J, Wang J, Wang S, Wang D, Hu S, *et al*. Traditional Chinese Medicine in Febrile Neutropenia Treatment: Advances and Prospects. *Future Integr Med* 2025;4(4):233–239. doi: 10.14218/FIM.2025.00035.

The current prevention and treatment of FN rely mainly on antibiotics and granulocyte colony-stimulating factor (G-CSF).[9,13] Although studies have confirmed that antibiotics and G-CSF show good efficacy and can reduce the incidence of FN and mortality,[14–17] there are still obvious limitations: antibiotic use can trigger drug resistance,[18] while G-CSF can cause adverse effects such as skeletal muscle pain, vasculitis, and an increased risk of secondary tumors.[19–21] Therefore, there is an urgent need to explore new adjuvant therapeutic strategies to optimize existing regimens.

Traditional Chinese medicine (TCM), as a complementary treatment for FN, demonstrates unique advantages. In contrast to the direct intervention mode of modern medical therapies, TCM emphasizes integrated regulation and dialectical treatment to improve symptoms and quality of life by restoring the balance of yin and yang (yin and yang are regulatory systems that describe the mutual antagonism and dynamic balance within the human body) in the body.[22] A plethora of extant studies have demonstrated that TCM, whether employed as a standalone modality or in conjunction with modern medicine, has yielded favorable outcomes in enhancing the number of granulocytes and regulating fever.[23–25] These findings provide a novel framework for the combined treatment of FN with TCM and modern medicine. However, further research is required to fully explore this potential. There is a lack of systematic reviews on the treatment of FN with TCM. This review aims to summarize the etiology, pathogenesis, and treatment principles of FN in TCM, to sort out clinical practice experience, and to explore its prospects, in order to provide a new theoretical basis and practical guidance for optimizing the treatment protocols of FN.

Theoretical basis for the treatment of FN in TCM

TCM is a systemized medical practice that has been developed and refined over millennia. It draws upon a rich tapestry of traditional Chinese cultural and medical knowledge, resulting in a unique theoretical framework, diagnostic methodologies, and therapeutic approaches.[26] As one of the complementary and alternative medicine systems recognized by the World Health Organization, TCM has demonstrated unique advantages in the treatment of complex diseases.[27] Records of FN can be traced back to the Chinese medical text Huang Di Nei Jing, which was written more than 2,000 years ago. FN can be categorized as "fatigue" and "fever". Ancient physicians, through long-term clinical observation, categorized the causes of FN as external evils, improper diet, and internal injuries to emotions. These pathogenic factors work together to disrupt the balance of yin and yang in the human body, impairing the function of the internal organs and leading to weakness of qi and blood (qi and blood refer to the energy substances that maintain life activities), which in turn triggers a series of clinical manifestations of FN. It is worth noting that this pathological process often forms a vicious circle: weakness of qi and blood leads to a decline in the body's ability to resist disease and evil, while the invasion of external evil further depletes qi and blood, and so on, aggravating the condition. Despite the absence of a contemporary notion of micro-medicine within the framework of TCM, this medical system accurately identified the fundamental pathological characteristics of FN through the diagnostic and therapeutic method of "external and internal". The "fever from internal injuries" mentioned in the Shanghan Zabing Lun provided an important idea for the treatment of FN. The theories of "fever due to qi deficiency" and "fever due to blood deficiency," put forward by Zhang Jingyue, a physician of the Ming Dynasty, are highly consistent with the pathogenesis of modern FN.[28,29] These ancient wisdoms have laid a solid theoretical foundation for modern Chinese medicine in the diagnosis and treatment of FN.

With the development of modern medicine, the name, diagnostic criteria, and pathogenesis of FN have been clarified. On this basis, modern TCM, combined with Western medical theories, elaborates the etiology and pathogenesis of FN more systematically. The first factor is drug toxicity (mainly referring to the toxicity of chemotherapy drugs), the second is the invasion of external evil (i.e., pathogen infection), and the remaining factors include internal injury of emotion and spirit (including psychological factors such as emotional disorders) and improper diet.[28,30] Within this theoretical framework, contemporary renowned Chinese medicine practitioners have proposed distinctive treatment principles. Prof. Bingkui Piao pointed out through in-depth research that most toxic effects after chemotherapy are caused by loss of qi and blood, disorders of the spleen and stomach, and deficiencies of the liver and kidneys, and advocated tonifying qi and blood.[31] Prof. Daihan Zhou, based on the theory of "Wei qi and Ying blood", believes that the essence of granulocyte decline is that "Wei qi is not solid and Yang qi is deficient", and advocates the therapeutic principle of warming Yang and benefiting Qi.[32] Prof. Rencun Yu paid special attention to the key role of the spleen and kidney in the prevention and treatment of FN and proposed the treatment method of strengthening the spleen and kidney.[33]

In clinical treatment, TCM is characterized by its adherence to the holistic concept and dialectical treatment (Fig. 1). The holistic concept views the human body as an organically connected system, and treatment focuses on regulating the entire system. When prescribing a prescription, doctors not only need to consider the symptoms of FN itself, but also many other factors, such as the patient's primary tumor condition, the functional status of the relevant organs, and the Western treatment protocols that the patient is undergoing. This holistic treatment concept aims to restore the dynamic balance between the body's various organ systems and provide each patient with a comprehensive treatment strategy. At the same time, dialectical treatment, as another major feature of TCM, emphasizes precise interventions targeting the patient's core disease mechanism. It is a clinical decision-making model that involves a comprehensive analysis of an individual's overall functional status, personalized diagnosis, and dynamic treatment adjustment. For example, qi deficiency is treated by qi tonification, blood deficiency is treated by blood tonification, and blood stasis is treated by blood activation. This individualized approach ensures that the treatment plan is precisely tailored to the patient's condition. Studies have shown that this TCM mode, which combines holistic regulation and dialectical treatment, demonstrates unique advantages in the prevention and treatment of FN.[34] As modern medicine has deepened its understanding of FN, theories developed in TCM have evolved and advanced, thus offering increased potential for addressing this clinical challenge.

Clinical evidence of TCM in FN treatment

In recent years, with increasing research on the modernization of TCM, the clinical efficacy of TCM in FN treatment has been increasingly reported in international medical journals. However, in most cases, TCM is still mainly used as part of an integrated treatment approach to enhance overall FN management. Clinical data have shown that the combination of TCM and modern medicine can significantly reduce the incidence of FN, as well as enhance the number of granulocytes, shorten the duration of fever, improve the quality of life of patients, and reduce other toxic effects of chemotherapy (Fig. 2).[34] More importantly, TCM intervention can

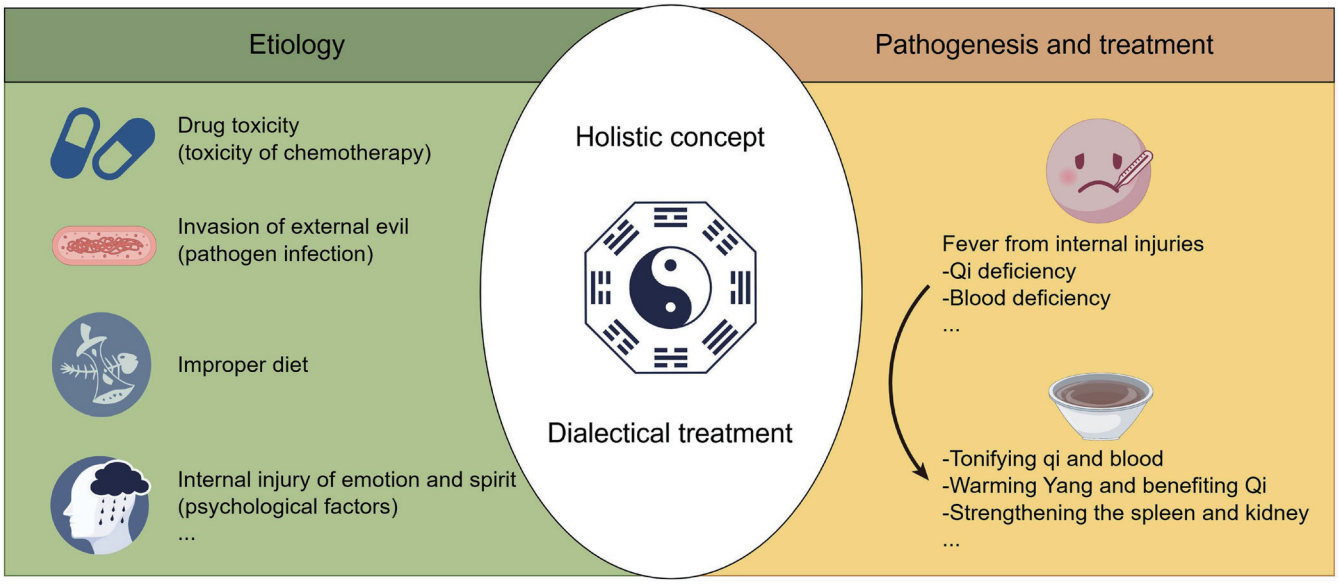

Fig. 1. Theoretical basis for the treatment of FN in TCM. The holistic concept and dialectical treatment guide TCM treatment of FN. From the perspective of TCM, the etiology of FN includes drug toxicity (toxicity of chemotherapy), invasion of external evil (pathogen infection), improper diet, and internal injury of emotion and spirit (psychological factors). The pathogenesis of FN involves internal injury fever (such as fever due to qi deficiency and fever due to blood deficiency). Treatment of FN includes tonifying qi and blood, warming yang and benefiting qi, strengthening the spleen and kidney, and other related approaches. FN, febrile neutropenia; TCM, traditional Chinese medicine.

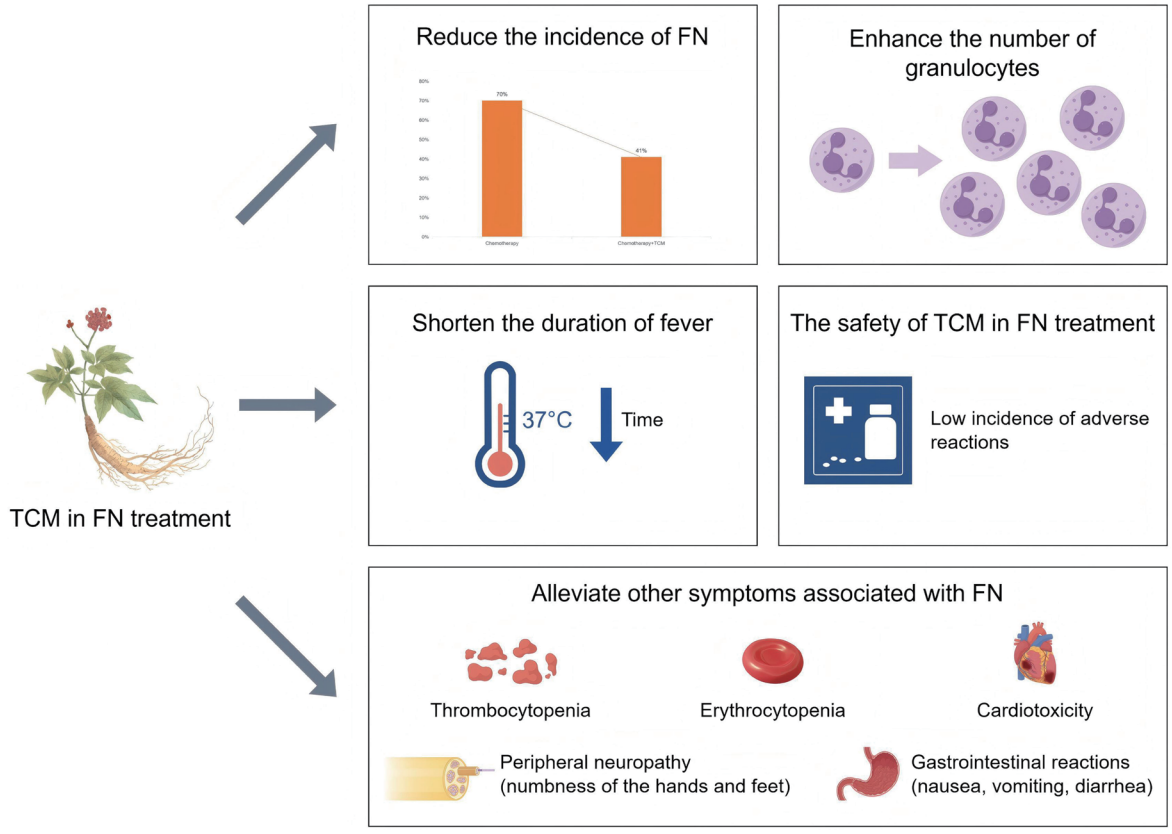

Fig. 2. Efficacy and safety of TCM in FN treatment. TCM treatment can reduce the incidence of FN, enhance the number of granulocytes, shorten the duration of fever, and alleviate other symptoms associated with FN. TCM interventions for FN have a good safety and tolerability profile. FN, febrile neutropenia; TCM, traditional Chinese medicine.

Table 1. Clinical study on the treatment of FN with TCM

Author, year	TCM Type	Clinical Application	Methods	sample sizes	Major findings
Wang, 2023[34]	The formula of benefiting qi and nourishing yin (the main ingredients of which are huangqi, codonopsis pilosula, radix pseudostellariae, etc.)	Combined with biapenem and rhG-CSF	RCT	64	The average time for the body temperature to return to normal was shortened by 52 hours, the recovery time of neutrophils was advanced by 4 days, the total effective rate of clinical symptom improvement was increased by 26.67% (96.67% vs. 70.00%), and the improvement of the quality of life scores was significantly greater.
Tian *et al.*, 2015[35]	TCM intervention (with spleen strengthening, qi nourishing and blood regeneration for marrow production as the basic treatment)	Combined with chemotherapy	retrospective study	792	The incidence of FN has significantly decreased.
Chen *et al.*, 2024[36]	TCM intervention (tonify the spleen and stomach, clear Yin Fire, and support Yang)	Combined with antibiotics and G-CSF	case report	1	After 10 days of intervention, her absolute neutrophil count had gradually increased. Additionally, after two weeks of treatment, her fever subsided.

FN, febrile neutropenia; RCT, randomized controlled trial; rhG-CSF, recombinant human granulocyte stimulating factor; TCM, traditional Chinese medicine.

often regulate the overall functional status of the body rather than just targeting a single symptom, which reflects the TCM treatment concept of "treating the disease at its root". To accurately evaluate the effectiveness of TCM in treating FN, we conducted a comprehensive search of the PubMed, Web of Science, and CNKI databases, covering the period from their establishment to May 2025, and summarized clinical studies on FN treated with TCM. The search terms included TS1 = "Medicine, Chinese Traditional" OR "Traditional Chinese Medicine", and TS2 = "Febrile Neutropenia". We screened the titles and full texts and ultimately obtained three studies. Table 1 summarizes the existing clinical studies.[34–36]

TCM treatment reduces the incidence of FN, enhances the number of granulocytes, and shortens the duration of fever

The standard modern medical treatment regimen for FN relies on the combination of antibiotics and G-CSF.[37] Antibiotics are used to control infection, while G-CSF promotes neutrophil production. However, as clinical practice evolves, mounting evidence suggests that integrating TCM with this established treatment protocol may yield substantial synergistic effects and offer more comprehensive therapeutic benefits for patients with FN.[38] Several clinical studies have provided strong evidence for this combined TCM and modern medicine treatment model. A rigorously designed randomized controlled trial (RCT) included 64 patients with FN. The control group was treated with standard antibacterial therapy using biapenem combined with recombinant human G-CSF, while the observation group was treated with a formula for benefiting qi and nourishing yin (the main ingredients of which are huangqi, Codonopsis pilosula, Radix Pseudostellariae, etc.) based on the standard therapy. The results of the study showed that the combined TCM and modern medicine group was significantly better than the control group in several efficacy indices: the average time for body temperature to return to normal was shortened by 52 h, the recovery time of neutrophils was advanced by four days, the total effective rate of clinical symptom improvement was increased by 26.67% (96.67% vs. 70.00%), and improvement in quality-of-life scores was significantly greater.[34] These data fully demonstrate the added value of TCM in accelerating FN recovery and improving patient symptoms. More noteworthy is the unique advantage of TCM in FN prevention. A large-scale retrospective study that included 792 patients undergoing chemotherapy for tumors showed that the incidence of FN was significantly lower in the group of patients who started TCM intervention (with spleen strengthening, qi nourishing, and blood regeneration for marrow production as the basic treatment) immediately before the chemotherapy cycle than in the control group (43% vs. 71%). An in-depth subgroup analysis further confirmed that this protective effect was observed in different chemotherapy regimens (such as those containing anthracyclines, paclitaxel, and docetaxel).[35] This finding provides an important basis for the wide application of TCM in tumor supportive therapy. TCM also shows unique therapeutic potential for G-CSF–insensitive cases, which are more difficult to treat in clinical practice. A case report provided evidence for this potential. An 18-year-old woman with cancer developed FN after chemotherapy. Despite the use of antibiotics and G-CSF, FN persisted for two months. After approximately 10 days of treatment with TCM decoctions (tonifying the spleen and stomach, clearing yin fire, and invigorating yang), the absolute neutrophil count gradually increased. Two weeks later, the patient's fever also subsided.[36] Although limited by sample size, these clinical observations provide new ideas and options for the treatment of refractory FN. Synthesizing the available clinical evidence shows that the combined application of TCM and standard modern medical treatments can improve FN outcomes in multiple dimensions. Effective formulas include the Benefiting Qi and Nourishing Yin Decoction and the Shengyang Sanhuo Decoction. These formulas contain commonly used herbs such as huangqi, Codonopsis pilosula, Radix Pseudostellariae, Cimicifugae Rhizoma, and Bupleuri Radix. These findings provide a reference for the clinical treatment of FN using TCM. However, methodological limitations must also be acknowledged, including modest sample sizes and inadequate implementation of randomization methods and blinding. These factors affect the reliability and extrapolation of the study findings to a certain extent. Consequently, the need for high-quality clinical studies in this domain remains paramount.

TCM treatment to alleviate other symptoms associated with FN

In addition to FN, tumor patients experience a range of other toxic effects during chemotherapy, such as thrombocytopenia, erythrocytopenia, gastrointestinal reactions (nausea, vomiting, diarrhea),

peripheral neuropathy (numbness of the hands and feet), and cardiotoxicity (cardiac arrhythmias, myocardial damage).[39] Notably, TCM has demonstrated unique advantages in comprehensive conditioning for these concomitant symptoms while combating FN. Several systematic reviews and meta-analyses (including only RCTs) have confirmed that the combined application of TCM and chemotherapy can significantly reduce the incidence of leukopenia, erythrocytopenia, and thrombocytopenia compared with chemotherapy alone.[40,41] The sample sizes covered by these meta-analyses all exceeded 1,500, further supporting the reliability of this conclusion. This result reflects the comprehensive protective effect of TCM on the hematopoietic system. In terms of gastrointestinal adverse reactions, multiple reviews have shown that Chinese herbs such as Pinellia ternata and ginger can effectively alleviate digestive symptoms, including nausea, vomiting, bloating, and loss of appetite. Multiple clinical trials have validated this conclusion, and the mechanisms have been preliminarily revealed in animal experiments.[39,42,43] For chemotherapy-induced peripheral neuropathy and cardiotoxicity, TCM has also shown good results in prevention and treatment. A meta-analysis involving 2,356 patients found that external TCM treatment reduced the incidence of peripheral neuropathy by 20%, increased the overall recovery rate by 30%, and increased the effective rate of symptom severity scores by 35%.[44] A review showed that qi- and heart-nourishing prescriptions can significantly reduce abnormal elevations of cardiotoxicity indicators (such as troponin and BNP) and protect cardiac function.[45] These clinical benefits are achieved because of the guiding advantage of the holistic concept of TCM. Rather than targeting the isolated symptom of FN, TCM treatment improves the overall functional status of the body by regulating internal balance, thereby achieving multi-system and multi-target comprehensive regulation and a beneficial transformation of the treatment model. This therapeutic feature of holistic regulation aligns with the needs of modern tumor supportive therapy.[46] With continued research, the comprehensive value of TCM in tumor supportive therapy is expected to be more fully demonstrated.

The safety of TCM in FN treatment

Existing studies have shown that, with regulated medication use, TCM interventions for FN have a good safety and tolerability profile.[35] Clinical data show that adverse reactions to TCM compound preparations are generally low. They are dominated by mild gastrointestinal discomfort (such as nausea and abdominal distension), which can be relieved on its own within a short period without special treatment.[47] From the perspective of long-term drug safety, the incidence of liver and kidney function abnormalities was not statistically different from that of the control group in patients who continued to use TCM for three to six months.[48] In the treatment of FN with TCM, clinical data show that, compared with drugs such as G-CSF, TCM does not cause significant adverse reactions such as bone pain and vasculitis, nor does it increase the risk of secondary tumors.[35] The good safety characteristics of TCM are mainly due to the treatment concept of "dialectical treatment". This approach allows adjustment of the medication plan according to the patient's constitution and condition characteristics, thus avoiding adverse drug reactions to the greatest extent possible. However, to ensure medication safety, drug interactions need to be guarded against in elderly patients receiving multiple medications. Special herbs, such as insects and minerals, should also be strictly controlled with regard to indications.[49,50] In short, TCM is a low-risk therapy that can be applied to FN.

Strengths, challenges, and prospects

TCM for FN has unique clinical value and development potential. Its core advantages are mainly reflected in the overall regulatory effect of multiple targets, the individualized advantage of dialectical treatment, and the preventive health care value associated with high safety. Nevertheless, the efficacy of TCM is often questioned. Therefore, this review aims to evaluate the effectiveness of TCM within an evidence-based medicine framework by synthesizing existing clinical evidence, including systematic reviews and meta-analyses, RCTs, retrospective studies, case-control studies, and safety data. The results suggest that an integrated approach combining TCM and modern medicine is more effective than modern medicine alone. However, the treatment of FN with TCM still faces many challenges. Firstly, the criteria for dialectical treatment have not been fully unified, which affects the reproducibility of treatment protocols. Secondly, the quality of existing clinical studies varies, and large-sample, multicenter, high-quality studies are still insufficient. Thirdly, current research suggests that TCM may play a role through multiple pathways and targets, including immune regulation, improvement of the hematopoietic microenvironment, and anti-inflammatory and antiviral.[51,52] However, there is still a relative lack of basic experimental research on the treatment of FN with TCM. These mechanisms are mostly based on preliminary speculation and have not yet been fully validated by solid experimental data. In addition, the components of TCM compound formulas are complex, and their effective ingredients and mechanisms of action remain unclear. Systematic research on the material basis and pharmacological mechanisms still needs to be further explored. Finally, in the treatment of acute and severe FN, the positioning, timing, and mode of TCM intervention still need to be further clarified, and the synergistic approach with Western medicine treatment requires optimization. Future development of TCM for FN should focus on the following directions. First, diagnostic and therapeutic norms should be established based on evidence-based medicine, with unified dialectical criteria formulated. Second, multicenter clinical trials conducted in accordance with international norms should be carried out to provide higher-level evidence. Third, the optimal mode of combining TCM and modern medicine should be explored to form therapeutic plans with complementary advantages. Fourth, modern scientific and technological methods, such as network pharmacology,[53,54] should be used to further elucidate the mechanisms of TCM compounding. At the same time, research on drug interactions between TCM and modern drugs should be strengthened to promote the modernization and internationalization of TCM.

Conclusions

This review systematically analyzes the application value of TCM in the treatment of FN. The results show that TCM, as a promising and safe complementary therapy, exhibits unique clinical advantages in the comprehensive treatment of FN. Existing clinical evidence demonstrates that the combination of TCM and modern medicine significantly reduces the incidence of FN, effectively increases granulocyte counts, shortens the duration of fever, improves patients' quality-of-life scores, and attenuates other toxicities associated with chemotherapy compared with modern medicine alone. However, it should be emphasized that some current clinical studies have limitations, such as small sample sizes, irregular randomization methods, and non-strict implementation of blinding. These methodological shortcomings may affect the reliability of the study results. Therefore, there is an urgent need for

large-sample, multicenter, randomized, double-blind, high-quality clinical trials to further validate the clinical efficacy of TCM for FN. With continuous improvement in study design and deeper exploration of underlying mechanisms, TCM is expected to play a more important role in the prevention and treatment of FN, ultimately benefiting patients worldwide.

Acknowledgments

Thanks to Figdraw.

Funding

This work was supported by the Fundamental Research Funds for the Central Public Welfare Research Institutes (No. ZZ14-YQ-013); the National Key Research and Development Program of China (No. 2023YFC3503300 and No. 2023YFC3503301); and the High-Level Chinese Medical Hospital Promotion Project (No. HLCMHPP2023034 and No. HLCMHPP2023085).

Conflict of interest

The authors have no conflicts of interest related to this publication.

Author contributions

Conceptualization (KDC, WH, XQW), data curation (KDC), formal analysis (KDC), investigation (KDC, JKW), project administration (KDC, WH, XQW), visualization (KDC, JKW), resources (WH, XQW), supervision (WH, XQW), writing – original draft (KDC, JKW, JWW, SWA, DWA, SHH, BJF, LXZ, XQW), writing – review and editing (KDC, JKW, JWW, SWA, DWA, SHH, BJF, LXZ, WH, XQW). All authors made significant contributions to this work and approved the final manuscript.

References

[1] Klastersky J, de Naurois J, Rolston K, Rapoport B, Maschmeyer G, Aapro M, *et al*. Management of febrile neutropaenia: ESMO Clinical Practice Guidelines. Ann Oncol 2016;27(suppl 5):v111–v118. doi:10.1093/annonc/mdw325, PMID:27664247.

[2] Flowers CR, Seidenfeld J, Bow EJ, Karten C, Gleason C, Hawley DK, *et al*. Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol 2013;31(6):794–810. doi:10.1200/JCO.2012.45.8661, PMID:23319691.

[3] Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, *et al*. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. Clin Infect Dis 2011;52(4):e56–e93. doi:10.1093/cid/cir073, PMID:21258094.

[4] Rasmy A, Al Mashiakhi M, Ameen A. Chemotherapy-Induced Febrile Neutropenia in Solid Tumours. Gulf J Oncolog 2017;1(25):77–84. PMID:29019336.

[5] Kuderer NM, Dale DC, Crawford J, Cosler LE, Lyman GH. Mortality, morbidity, and cost associated with febrile neutropenia in adult cancer patients. Cancer 2006;106(10):2258–2266. doi:10.1002/cncr.21847, PMID:16575919.

[6] Lyman GH, Abella E, Pettengell R. Risk factors for febrile neutropenia among patients with cancer receiving chemotherapy: A systematic review. Crit Rev Oncol Hematol 2014;90(3):190–199. doi:10.1016/j.critrevonc.2013.12.006, PMID:24434034.

[7] Logan C, Koura D, Taplitz R. Updates in infection risk and management in acute leukemia. Hematology Am Soc Hematol Educ Program 2020;2020(1):135–139. doi:10.1182/hematology.2020000098, PMID:33275701.

[8] Pathak R, Giri S, Aryal MR, Karmacharya P, Bhatt VR, Martin MG. Mortality, length of stay, and health care costs of febrile neutropenia-related hospitalizations among patients with breast cancer in the United States. Support Care Cancer 2015;23(3):615–617. doi:10.1007/s00520-014-2553-0, PMID:25556610.

[9] Boccia R, Glaspy J, Crawford J, Aapro M. Chemotherapy-Induced Neutropenia and Febrile Neutropenia in the US: A Beast of Burden That Needs to Be Tamed? Oncologist 2022;27(8):625–636. doi:10.1093/oncolo/oyac074, PMID:35552754.

[10] Klastersky J, Paesmans M, Rubenstein EB, Boyer M, Elting L, Feld R, *et al*. The Multinational Association for Supportive Care in Cancer risk index: A multinational scoring system for identifying low-risk febrile neutropenic cancer patients. J Clin Oncol 2000;18(16):3038–3051. doi:10.1200/JCO.2000.18.16.3038, PMID:10944139.

[11] Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, *et al*. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2015;33(28):3199–3212. doi:10.1200/JCO.2015.62.3488, PMID:26169616.

[12] Becker PS, Griffiths EA, Alwan LM, Bachiashvili K, Brown A, Cool R, *et al*. NCCN Guidelines Insights: Hematopoietic Growth Factors, Version 1.2020. J Natl Compr Canc Netw 2020;18(1):12–22. doi:10.6004/jnccn.2020.0002, PMID:31910384.

[13] Stohs EJ, Abbas A, Freifeld A. Approach to febrile neutropenia in patients undergoing treatments for hematologic malignancies. Transpl Infect Dis 2024;26(2):e14236. doi:10.1111/tid.14236, PMID:38349035.

[14] Forcano-Queralt E, Lemes-Quintana C, Orozco-Beltrán D. Ambulatory management of low-risk febrile neutropenia in adult oncological patients. Systematic review. Support Care Cancer 2023;31(12):665. doi:10.1007/s00520-023-08065-y, PMID:37921996.

[15] Wang L, Baser O, Kutikova L, Page JH, Barron R. The impact of primary prophylaxis with granulocyte colony-stimulating factors on febrile neutropenia during chemotherapy: a systematic review and meta-analysis of randomized controlled trials. Support Care Cancer 2015;23(11):3131–3140. doi:10.1007/s00520-015-2686-9, PMID:25821144.

[16] Aras E, Bayraktar-Ekincioglu A, Kilickap S. Risk assessment of febrile neutropenia and evaluation of G-CSF use in patients with cancer: a real-life study. Support Care Cancer 2020;28(2):691–699. doi:10.1007/s00520-019-04879-x, PMID:31127438.

[17] Tsuchihashi K, Ito M, Okumura Y, Nio K, Ozaki Y, Nishio H, *et al*. Therapeutic use of granulocyte colony-stimulating factor (G-CSF) in patients with febrile neutropenia: a comprehensive systematic review for clinical practice guidelines for the use of G-CSF 2022 from the Japan Society of Clinical Oncology. Int J Clin Oncol 2024;29(6):700–705. doi:10.1007/s10147-024-02541-z, PMID:38696053.

[18] Schmidt-Hieber M, Teschner D, Maschmeyer G, Schalk E. Management of febrile neutropenia in the perspective of antimicrobial de-escalation and discontinuation. Expert Rev Anti Infect Ther 2019;17(12):983–995. doi:10.1080/14787210.2019.1573670, PMID:30686067.

[19] Lyman GH, Yau L, Nakov R, Krendyukov A. Overall survival and risk of second malignancies with cancer chemotherapy and G-CSF support. Ann Oncol 2018;29(9):1903–1910. doi:10.1093/annonc/mdy311, PMID:30099478.

[20] Muzzana M, Pedrazzoli P, Lasagna A. G-CSF and G-CSF-related vasculitis: a systematic review of the literature and intriguing future research perspectives. Future Oncol 2021;17(33):4619–4634. doi:10.2217/fon-2021-0701, PMID:34431371.

[21] Li X, Zheng H, Yu MC, Wang W, Wu XH, Yang DM, *et al*. Is PEGylated G-CSF superior to G-CSF in patients with breast cancer receiving chemotherapy? A systematic review and meta-analysis. Support Care Cancer 2020;28(11):5085–5097. doi:10.1007/s00520-020-05603-w, PMID:32621264.

[22] Su XL, Wang JW, Che H, Wang CF, Jiang H, Lei X, *et al*. Clinical application and mechanism of traditional Chinese medicine in treatment of lung cancer. Chin Med J (Engl) 2020;133(24):2987–2997. doi:10.1097/CM9.0000000000001141, PMID:33065603.

[23] Jiang HZ, Jiang YL, Yang B, Long FX, Yang Z, Tang DX. Traditional Chinese medicines and capecitabine-based chemotherapy for colorectal cancer treatment: A meta-analysis. Cancer Med 2023;12(1):236–255. doi:10.1002/cam4.4896, PMID:35650714.
[24] Lv LY, Lv P, Duan Y, Yang GW, Li Q, Wu WY, *et al*. Multicenters,Randomized Controlled Clinical Study on Qijiaoshengbai Capsules in Prevention and Treatment of Leukopenia (Qi and Blood Deficiency Syndrome) Caused by Chemotherapy of Lung Cancer. World Chinese Medicine 2021;16(19):2915–2921.
[25] Bu Z, Xu Y, Zhou X, Wang X, Liu S, Wang L, *et al*. Exploring the therapeutic potential of "Xiaochaihu Decoction": a systematic review and meta-analysis on the clinical effectiveness and safety in managing cancer-related fever. Front Pharmacol 2024;15:1359866. doi:10.3389/fphar.2024.1359866, PMID:38803432.
[26] Li S, Xutian S. New Development in Traditional Chinese Medicine: Symbolism-Digit Therapy as a Special Naturopathic Treatment. Am J Chin Med 2016;44(7):1311–1323. doi:10.1142/S0192415X16500737, PMID:27785941.
[27] Yu Z, Li T, Zheng Z, Yang X, Guo X, Zhang X, *et al*. Tailoring a traditional Chinese medicine prescription for complex diseases: A novel multi-targets-directed gradient weighting strategy. J Pharm Anal 2025;15(4):101199. doi:10.1016/j.jpha.2025.101199, PMID:40297631.
[28] Yin L, Xin R, Qi Y, Miao X, Li M. Discussion on the Mechanism of Danggui Buxue Decoction in the Treatment of Granulocyte Deficiency with Fever Caused by Myelosuppression after Chemotherapy (in Chinese). Guangming Journal of Chinese Medicine 2023;38(11):2217–2220. doi:10.3969/j.issn.1003-8914.2023.11.055.
[29] Zhao ZK, Yuan XT, Chen SL, Du GL. Pathogenesis and treatment of fever in Traditional Chinese Medicine (in Chinese). Journal of Guangxi University of Chinese Medicine 2025;28(2):1–4.
[30] Su K, Si WT, Hou AH. Advances in the Treatment of Chemotherapy-induced Bone Marrow Suppression by Chinese Medicine (in Chinese). Journal of Oncology in Chinese Medicine 2020;2(5):87–91. doi:10.19811/j.cnki.ISSN2096-6628.2020.05.018.
[31] Zheng HG, Piao BK. A Brief Discussion on the Traditional Chinese Medicine Causes of Toxic and Side Effects of Radiotherapy and Chemotherapy (in Chinese). Chinese Journal of Basic Medicine in Traditional Chinese Medicine 2007;13(10):751–752.
[32] Li Z, Li JY, Huang L, Huang F, Jiang JW, Zhou DH. Exploration of Traditional Chinese Medicine Based on Blood Cell Analysis for the Diagnosis and Treatment of Bone Marrow Inhibition with "Heavy Formula Therapy" and "Reverse Stress Treatment" (in Chinese). Hubei Journal of Traditional Chinese Medicine 2024;46(5):51–55.
[33] Rong ZH, Hua BJ, Yu RC. Professor Yu Rencun's experience in preventing and treating bone marrow suppression (in Chinese). Jilin Journal of Chinese Medicine 2013;33(7):658–661. doi:10.3969/j.issn.1003-5699.2013.07.005.
[34] Wang XF. Clinical Observation on the Treatment of Neutropenia with Fever after Chemotherapy in Acute Leukemia with Yiqi Yangyin Formula (in Chinese) [Dissertation]. Zhengzhou: Henan University of Chinese Medicine; 2023.
[35] Tian H, Qin W, Wu W, Guo P, Lu Y, Liu P, *et al*. Effects of Traditional Chinese Medicine on Chemotherapy-Induced Myelosuppression and Febrile Neutropenia in Breast Cancer Patients. Evid Based Complement Alternat Med 2015;2015:736197. doi:10.1155/2015/736197, PMID:26347793.
[36] Chen CH, Ou SC, Wang SH, Chang TT. Alternative therapy for lymphoma with febrile neutropenia using traditional Chinese medicine: A case report. Explore (NY) 2024;20(6):103057. doi:10.1016/j.explore.2024.103057, PMID:39244905.
[37] Georgala A, Klastersky J. Can febrile neutropenia re-invent its self? Curr Opin Oncol 2025;37(2):163–167. doi:10.1097/CCO.0000000000001116, PMID:39869037.
[38] Pan L, Zhang T, Cao H, Sun H, Liu G. Ginsenoside Rg3 for Chemotherapy-Induced Myelosuppression: A Meta-Analysis and Systematic Review. Front Pharmacol 2020;11:649. doi:10.3389/fphar.2020.00649, PMID:32477128.
[39] Zhang X, Qiu H, Li C, Cai P, Qi F. The positive role of traditional Chinese medicine as an adjunctive therapy for cancer. Biosci Trends 2021;15(5):283–298. doi:10.5582/bst.2021.01318, PMID:34421064.
[40] Yang J, Zhu X, Yuan P, Liu J, Wang B, Wang G. Efficacy of traditional Chinese Medicine combined with chemotherapy in patients with non-small cell lung cancer (NSCLC): a meta-analysis of randomized clinical trials. Support Care Cancer 2020;28(8):3571–3579. doi:10.1007/s00520-020-05433-w, PMID:32266566.
[41] Li R, Zhang T, Yan SH, Yan YZ, Ding YC, Wang YS, *et al*. Chinese Medicine Combined with Adjuvant Chemotherapy for Improving Myelosuppression in Colorectal Cancer Patients: A Systematic Review and Network Meta-Analysis. Chin J Integr Med 2024;30(7):643–652. doi:10.1007/s11655-023-3558-7, PMID:38212495.
[42] Zhao YZ, Dai YZ, Nie K. Research Progress on the Antiemetic Effect of Traditional Chinese Medicine Against Chemotherapy-Induced Nausea and Vomiting: A Review. Front Pharmacol 2021;12:790784. doi:10.3389/fphar.2021.790784, PMID:35222008.
[43] Lv C, Shi C, Li L, Wen X, Xian CJ. Chinese herbal medicines in the prevention and treatment of chemotherapy-induced nausea and vomiting. Curr Opin Support Palliat Care 2018;12(2):174–180. doi:10.1097/SPC.0000000000000348, PMID:29697417.
[44] Li QY, Cai FH, Lu Y, Liu H, Wang X, Li FL, *et al*. External Treatment With Chinese Herbal Medicine for Chemotherapy-Induced Peripheral Neuropathy: A Systematic Review and Meta-Analysis. Front Pharmacol 2022;13:764473. doi:10.3389/fphar.2022.764473, PMID:35250555.
[45] Wang JW, Shao H, Zhang YN, Ge T, Chen XY, Mou XZ. Traditional Chinese medicine as a protective strategy against chemotherapy-induced cardiotoxicity: An overview of the literature. J Tradit Complement Med 2025;15(2):107–118. doi:10.1016/j.jtcme.2024.06.010, PMID:40060147.
[46] Theunissen I, Bagot JL. Supportive cancer care: is integrative oncology the future? Curr Opin Oncol 2024;36(4):248–252. doi:10.1097/CCO.0000000000001027, PMID:38842016.
[47] Xu MF, Xu ML. Analysis of the use and adverse reactions of traditional Chinese medicine decoction pieces in the oncology department of a tertiary hospital from 2022 to 2023 (in Chinese). Journal of Traditional Chinese Medicine Management 2025;33(5):86–88. doi:10.16690/j.cnki.1007-9203.2025.05.065.
[48] Wang XQ, Zhang Y, Hou W, Wang YT, Zheng JB, Li J, *et al*. Association between Chinese Medicine Therapy and Survival Outcomes in Postoperative Patients with NSCLC: A Multicenter, Prospective, Cohort Study. Chin J Integr Med 2019;25(11):812–819. doi:10.1007/s11655-019-3168-6, PMID:31471834.
[49] Liu SH, Chuang WC, Lam W, Jiang Z, Cheng YC. Safety surveillance of traditional Chinese medicine: current and future. Drug Saf 2015;38(2):117–128. doi:10.1007/s40264-014-0250-z, PMID:25647717.
[50] Cai P, Qiu H, Qi F, Zhang X. The toxicity and safety of traditional Chinese medicines: Please treat with rationality. Biosci Trends 2019;13(5):367–373. doi:10.5582/bst.2019.01244, PMID:31564696.
[51] Gu S, Zheng Y, Chen C, Liu J, Wang Y, Wang J, *et al*. Research progress on the molecular mechanisms of Saikosaponin D in various diseases (Review). Int J Mol Med 2025;55(3):37. doi:10.3892/ijmm.2024.5478, PMID:39717942.
[52] He D, Dan W, Du Q, Shen BB, Chen L, Fang LZ, *et al*. Integrated Network Pharmacology and Metabolomics Analysis to Reveal the Potential Mechanism of Siwu Paste on Aplastic Anemia Induced by Chemotherapy Drugs. Drug Des Devel Ther 2022;16:1231–1254. doi:10.2147/DDDT.S327433, PMID:35517983.
[53] Li X, Liu Z, Liao J, Chen Q, Lu X, Fan X. Network pharmacology approaches for research of Traditional Chinese Medicines. Chin J Nat Med 2023;21(5):323–332. doi:10.1016/S1875-5364(23)60429-7, PMID:37245871.
[54] Zhang P, Zhang D, Zhou W, Wang L, Wang B, Zhang T, *et al*. Network pharmacology: towards the artificial intelligence-based precision traditional Chinese medicine. Brief Bioinform 2023;25(1):bbad518. doi:10.1093/bib/bbad518, PMID:38197310.