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Research Progress on the Integrated Traditional Chinese and Western Medicine Therapy for Cancer-Related Anemia

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Abstract: ***Cancer-related anemia (CRA) is a common complication in patients with malignant tumors, which not only affects their quality of life but may also reduce the efficacy and tolerance of radiotherapy and chemotherapy. In recent years, integrated Traditional Chinese and Western medicine (TCM-WM) has demonstrated unique advantages in treating CRA. Modern medicine primarily employs therapies such as erythropoietin, iron supplementation, and blood transfusion, which have limitations and potential risks. Traditional Chinese Medicine (TCM), through treatment approaches like fortifying the spleen and nourishing the kidney, replenishing qi and blood, and activating blood circulation to remove stasis, improves the hematopoietic microenvironment and regulates the body's immune function, showing increasing promise in recent years. By combining the strengths of both systems, integrated TCM-WM exhibits synergistic effects in elevating hemoglobin levels, improving clinical symptoms, reducing side effects of Western medical treatments, and enhancing the quality of life. Current research confirms its safety and efficacy; however, more high-quality, large-sample clinical studies are needed in the future to further explore its mechanisms of action and optimize diagnosis and treatment protocols.***

Keywords: Cancer-related anemia, Integrated Traditional Chinese and Western medicine, Research progress, Clinical studies**.**

1. Introduction

Malignant tumors rank as the second leading cause of death globally [1]. It is predicted that by 2050, the number of new cancer cases worldwide will increase by 77% [2]. Cancer-related anemia (CRA) is one of the common complications of malignant tumors, referring to anemia that occurs during the development of the disease or its treatment [3]. Biochemically, it is primarily characterized by a decrease in red blood cell count or hemoglobin (Hb) concentration per unit volume of peripheral blood [4]. Clinically, it often manifests as fatigue, pale skin and mucous membranes, dizziness, palpitations, shortness of breath, and similar symptoms. CRA not only reduces patients' quality of life but also affects treatment progress and efficacy, thereby shortening overall survival. Therefore, exploring treatment methods with fewer side effects and stable, long-lasting efficacy is crucial. Western medical treatments primarily include the use of ESAs, supplementation of hematopoietic raw materials, and blood transfusion, while Traditional Chinese Medicine (TCM) approaches involve oral administration of classical formulas, acupuncture, and others. Given the current diversity of treatment methods, integrated Traditional Chinese and Western medicine therapy can achieve synergistic effects. This article will review the latest research and literature on the integrated treatment of CRA.

2. Incidence of CRA

2.1 Types of CRA

CRA can primarily be classified into two types: treatment-unrelated CRA and treatment-related CRA. Treatment-unrelated CRA is mainly caused by tumor-related factors, such as bone marrow infiltration by the tumor, malnutrition, iron metabolism disorders, cancer-related bleeding, impaired renal function, or the impact of tumor-associated cytokines on bone marrow hematopoiesis. Treatment-related CRA is primarily induced by cancer treatments, including the myelosuppressive effects of surgical interventions, chemotherapy, targeted therapy, immunotherapy, and radiotherapy.

2.2 Incidence of CRA in Different Types of Tumors

The incidence of CRA is associated with factors such as tumor type, clinical stage, and interventional therapy [5]. Anemia is quite common in hematologic malignancies. For solid tumors, foreign statistics [6] indicate that the incidence rates, in descending order, are: digestive system tumors (62.0%), female reproductive system tumors (52.1%), urinary system tumors (45.0%), soft tissue sarcomas (33.3%), lung cancer (32.8%), head and neck tumors (30.8%), and breast cancer (26.3%). Similar statistics exist in China. Pei Wangwei et al. [7] analyzed 20,500 CRA cases from Zhejiang Cancer Hospital in 2018, reporting incidence rates in descending order as: female gynecological tumors (28.9%), digestive system tumors (28.8%), urinary system tumors (24.9%), lung cancer (23.3%), breast cancer (16.5%), head and neck tumors (13.5%), and other tumors (18.9%). Differences in CRA incidence between countries may relate to national conditions, geographical variations, and patient characteristics, but it is undeniable that incidence is associated with tumor type. Furthermore, the incidence is related to whether the cancer patient has received interventional therapy. Before cancer intervention, 20%-30% of solid tumor patients have CRA. During treatment, the proportion of patients developing CRA increases significantly to 60%-70%. In the early stages of cancer, the incidence of CRA is relatively low, whereas when the tumor progresses to middle and advanced stages, 60%-80% of patients develop CRA [5].

3. Pathogenesis of CRA

3.1 Western Medical Etiology

3.1.1 Hemorrhage

Studies have shown that cancer patients with a history of hemorrhage are four times more likely to develop anemia than those without such a history [8]. Cancers with a higher incidence of anemia associated with hemorrhage primarily include gastric cancer, colorectal cancer, and gynecological cancers. Occult bleeding is a characteristic feature of colorectal cancer, which explains the high proportion of anemic patients among those with colorectal cancer. Most patients with gynecological tumors have a history of bleeding [8]. For cervical cancer patients, genital bleeding is the most common complication, and the degree of anemia during radiotherapy can also be influenced by the disease stage and tumor size. Additionally, bleeding alone can lead to anemia in cervical cancer patients [9].

3.1.2 Reduced Raw Materials for Hb Synthesis

Deficiencies in iron, folic acid, and vitamin B12 can all impair hemoglobin synthesis, leading to anemia. Iron deficiency is closely associated with anemia; when the body's iron levels decrease severely enough to compromise erythropoiesis, iron deficiency anemia occurs, with chronic anemia being the most common type [10]. In gastric cancer patients, iron deficiency results from reduced iron absorption. A study by Tang et al. [11] indicated that a significant proportion of gastric cancer patients have iron deficiency anemia, with 80% of patients suffering from anemia. Research by Ludwig et al. [12] showed that iron deficiency anemia is present in most patients across different tumor types and stages, and is more severe in patients with advanced pancreatic cancer, colorectal cancer, and lung cancer. However, no significant correlation with iron deficiency was found in patients with hematologic malignancies. Additionally, cancer patients often experience malnutrition, leading to insufficient raw materials such as iron, folic acid, and vitamins for hemoglobin synthesis, which can also contribute to anemia.

3.1.3 Inflammatory Factors

According to 2012 epidemiological statistics, over one-quarter of cancers worldwide can be attributed to chronic inflammatory responses [13]. Inflammation can affect hematopoiesis in multiple ways, leading to anemia. Studies have shown that a complex network involving immune system activation, iron metabolism dysregulation, and impaired erythropoiesis collaboratively drives the key pathological processes of cancer-related anemia [14]. Elevated levels of inflammatory factors are present in cancer patients. Certain inhibitory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interferon-gamma (IFN-γ), stimulate the production of hepatic hepcidin. This limits the iron supply to erythroid cells, subsequently causing anemia due to insufficient iron for their survival needs. Furthermore, these inflammatory factors can directly inhibit the proliferation and differentiation of erythroid precursor cells and suppress the production of endogenous erythropoietin (EPO), thereby contributing to anemia [15]. Among these, interleukin-6 (IL-6), a pro-inflammatory cytokine released by tumor cells and immune cells, plays a pivotal role in the pathogenesis of CRA.

3.1.4 Bone Marrow Infiltration, Metastasis, and Necrosis

Hematologic malignancies such as leukemia, lymphoma, and multiple myeloma can almost all progress to bone marrow infiltration in advanced stages [16-17]. Additionally, cancer cells from solid tumors like advanced lung cancer, breast cancer, prostate cancer, colorectal cancer, thyroid cancer, and melanoma can also develop bone marrow metastases [18]. The bone marrow is the body's primary hematopoietic tissue. When cancer cells spread into the bloodstream during advanced clinical stages, they can readily invade the bone marrow. Due to cancer metastasis or the infiltration of bone marrow by hematologic malignant cells, along with fibrotic bone marrow replacing normal hematopoietic stem cells as the dominant proliferating cells, normal hematopoiesis in the bone marrow is directly suppressed, ultimately leading to anemia [19]. Cancer-related bone marrow necrosis is an extremely rare but serious complication. It refers to a tumor-associated condition characterized by extensive necrosis of hematopoietic tissue and stromal cells in the bone marrow, resulting in the destruction of normal bone marrow architecture. Studies have shown that hematolymphoid malignancies (such as acute leukemia) and metastatic solid tumors are the most common underlying causes of bone marrow necrosis [20]. The mechanism by which it leads to CRA also involves the invasion of this primary hematopoietic organ and the release of inflammatory factors, which further suppress erythropoiesis and cause anemia.

3.1.5 Treatment-Induced Myelosuppression

The myelosuppressive effects of chemotherapy are a significant factor contributing to anemia in patients undergoing cytotoxic treatment. An analysis of red blood cell transfusion data in cancer patients receiving chemotherapy indicates that the probability of anemia developing in lymphoma, lung cancer, gynecological (ovarian) cancer, and genitourinary cancer ranges from 50% to 60% [21]. Cytotoxic drugs such as platinum-based agents and anthracyclines not only target and kill tumor cells but also affect the bone marrow, thereby impairing hematopoiesis and leading to anemia. Cisplatin, whose primary side effect is nephrotoxicity, can also interfere with the secretion of erythropoietin, resulting in reduced red blood cell production.

3.1.6 Increased Red Blood Cell Destruction

The primary causes of increased red blood cell destruction include cancer-related microangiopathic hemolytic anemia and autoimmune hemolytic anemia. Cancer-related microangiopathic hemolytic anemia (CR-MAHA) is a type of paraneoplastic syndrome (PNS). It occurs when tumor-related factors cause microvascular endothelial injury, leading to the mechanical destruction of red blood cells. Its clinical manifestations include hemolytic anemia, jaundice, thrombocytopenia, the presence of schistocytes on peripheral blood smear, elevated plasma hemoglobin, elevated lactate dehydrogenase, and frequent renal failure [22]. CR-MAHA is relatively uncommon compared to other cancer complications.

In 2012, Lechner et al. [22] analyzed 168 patients with CR-MAHA. The results indicated that CR-MAHA often occurs in patients with gastric cancer, breast cancer, prostate cancer, lung cancer, lymphoma, cancer of unknown primary, abdominal cancer, genitourinary cancer, and endocrine cancer. Autoimmune hemolytic anemia (AIHA) is another common paraneoplastic syndrome in oncology. It arises from immune system dysregulation, leading to the production of autoantibodies that accelerate red blood cell destruction (hemolysis). Anemia occurs when this destruction surpasses the bone marrow's compensatory capacity. In the context of cancer, AIHA is frequently observed in lymphoproliferative malignancies such as chronic lymphocytic leukemia and non-Hodgkin lymphoma, but is relatively rare in solid tumors like renal cell carcinoma, ovarian cancer, and thymic carcinoma [23].

3.2 Etiology and Pathogenesis in Traditional Chinese Medicine

CRA is a complex pathological process arising from the influence of "cancer" and/or "toxin," with "deficiency," "toxin," and "stasis" as its core elements. This leads to a reduction or depletion of blood, involving disorders of multiple organs such as the heart, liver, spleen, stomach, and kidney, as well as an imbalance of qi, blood, yin, and yang. Based on the TCM Classification and Nomenclature of Common Blood Diseases [24] and the national "13th Five-Year Plan" innovative higher education TCM textbook Hematology in Traditional Chinese Medicine [25], experts have collectively recommended using the TCM disease name "Cancer Toxin Blood Depletion Disease" for CRA.

Etiology and Pathogenesis in Traditional Chinese Medicine (Continued)

The development of CRA stems from two fundamental aspects: "decline of healthy qi" and "exuberance of pathogenic factors". Major or chronic illness, prolonged treatment without cure, disease progression, or inadequate recuperation can lead to depletion of healthy qi and deficiency of blood, making recovery difficult. On the other hand, tumors form under the combined action of pathological factors such as "toxin" and "stasis". Furthermore, treatments aimed at eliminating pathogens—such as surgery, radiotherapy, chemotherapy, and immunotherapy/targeted therapy—further consume the body's healthy qi, exacerbating imbalances in the zang-fu organs, qi, blood, yin, and yang.

This not only damages the spleen and stomach, leading to impaired transportation and transformation, but can also directly injure the liver, kidney, and bone marrow, cutting off the source of essence and blood generation. Impairment of the spleen and stomach disrupts reception, digestion, and transformation of food and water, leading to inadequate production of qi and blood. Damage to the kidney, directly reaching the bone marrow, results in kidney essence deficiency and emptiness of the marrow sea, undermining the foundation for generating essence and blood. Injury to the liver compromises its free-flowing function, causing qi stagnation and blood stasis; if static blood is not resolved, new blood cannot be produced.

Qi deficiency leads to weak movement and inability to propel blood circulation, giving rise to phlegm-turbidity, fluid retention, and blood stasis. Coupled with exuberant cancer toxin, over time, deficiency and stasis become interwoven. The vicious cycle of "deficiency generating toxin, and toxin further aggravating deficiency" constitutes the basic pathological evolution, ultimately resulting in the outcome of "failure to generate new blood."

Clinically, it often manifests as a lusterless complexion, brittle nails, dizziness, palpitations, chest tightness, poor appetite, and insomnia. The disease nature is generally deficiency-based, characterized by root deficiency and superficial excess, often complicated by toxin accumulation, blood stasis, and qi stagnation. The disease location is in the bone marrow and is closely related to the spleen, stomach, kidney, liver, and heart.

4. Treatment

CRA is characterized by high incidence, low early diagnosis rates, and low treatment rates. The primary Western medical treatments include the use of Erythropoiesis-Stimulating Agents (ESA), iron supplementation, and blood transfusion. Traditional Chinese Medicine primarily employs methods such as oral decoctions, proprietary Chinese patent medicines, and acupuncture. Integrated Traditional Chinese and Western Medicine therapy offers unique advantages and distinctive features. It can not only increase hemoglobin levels, correct anemia, and improve the overall treatment response rate, but also alleviate patient symptoms, enhance functional status, and improve quality of life [26].

4.1 Western Medical Treatment

4.1.1 Erythropoiesis-Stimulating Agents (ESA)

(1) EPO

The primary approach in Western medicine for treating CRA is the use of Erythropoiesis-Stimulating Agents. EPO is the most commonly used and extensively studied ESA in clinical practice. It is an active glycoprotein secreted by the kidneys that acts on erythroid progenitor cells in the bone marrow, promoting red blood cell production, steadily increasing hemoglobin levels, effectively improving anemia, and reducing the need for blood transfusions.

The use of EPO has specific indications, namely for anemia in cancer patients with moderate to severe renal impairment, and for anemia caused by or occurring during cancer treatment [27]. EPO therapy is initiated when Hb levels are ≤100 g/L. The target is to achieve an Hb level of 110–120 g/L; if the Hb reaches or exceeds 120 g/L, it is recommended to discontinue EPO or reduce the dosage based on an individual patient assessment. Iron status should be evaluated before and during EPO treatment, as iron deficiency can impair its efficacy. Since EPO increases the risk of thromboembolism, thrombotic risk assessment is crucial before initiating therapy.

(2) Roxadustat

Roxadustat is a novel Hypoxia-Inducible Factor (HIF) Prolyl Hydroxylase Inhibitor (PHI) that has achieved certain results in treating CRA. A US Phase II clinical study demonstrated its efficacy and acceptable safety profile in treating chemotherapy-associated anemia in patients with myeloid malignancies [28]. A Chinese Phase III clinical study showed that, compared to EPO, Roxadustat exhibited non-inferiority and a favorable safety profile in treating chemotherapy-induced anemia in patients with non-myeloid malignancies [29].

The initiation timing and Hb target value for Roxadustat can both reference the standards for EPO. The starting dose should be selected based on body weight:40 to <50 kg: 100 mg orally per dose 50 to 60 kg: 120 mg orally per dose 60 kg: 150 mg orally per dose Administered three times per week.

4.1.2 Supplementation of Hematopoietic Raw Materials

Most cancer patients experience iron deficiency, which can sometimes appear even earlier than anemia. The indications for iron supplementation are as follows: it is only applicable to four types: absolute iron deficiency, potential iron deficiency, functional iron deficiency, and potential functional iron deficiency. Iron preparations are divided into oral and intravenous forms, and the appropriate type can be selected based on the specific iron deficiency: Oral Iron Preparations are suitable for absolute iron deficiency. However, only about 10% of oral iron is absorbed, and it may cause gastrointestinal side effects such as abdominal pain [30]. Intravenous Iron Preparations are suitable for functional iron deficiency. This is because functional iron deficiency leads to hepcidin-mediated inhibition of intestinal iron absorption and reduced iron transport within the body, making intravenous iron more effective [30]. Common oral iron preparations include ferrous sulfate, iron dextran, ferrous succinate, iron proteinsuccinylate, and polysaccharide-iron complex. Commonly used Chinese patent medicines include Yizhongshengxue Capsules (Tablets), Yiqiweixue Granules (Capsules, Tablets), Zaizaoshengxue Tablets (Capsules), Compound Ejiao Jiang, Shengxuening Tablets, and Jianpishengxue Granules (Tablets). Intravenous iron preparations include iron dextran, iron sucrose, and ferric derisomaltose. The efficacy of these intravenous iron formulations is comparable. After intravenous infusion, patients should be observed in the hospital to promptly identify and manage any potential adverse reactions [31-32]. In addition to iron, for patients deficient in folic acid or vitamin B12, combining iron supplementation with folic acid yields better efficacy in correcting anemia [33]. When taking oral iron, attention should also be paid to supplementing with Vitamin C.

4.1.3 Blood Transfusion

For patients with CRA, blood transfusion is not the primary treatment of choice. While red blood cell transfusion can rapidly increase hemoglobin concentration and quickly improve anemia, it is generally reserved for cancer patients with severe anemia, those with severe anemia due to acute bleeding, asymptomatic anemic patients with comorbid conditions such as heart disease, chronic lung disease, or cerebrovascular disease, and patients unresponsive to EPO therapy.

However, due to the specific etiology of CRA, the increase in Hb levels achieved through transfusion is often short-lived. Furthermore, transfusion carries risks such as allergic reactions, hemolytic reactions, alloimmunization, and viral infections. Some studies also suggest that blood transfusion may increase the risk of thrombosis in cancer patients and potentially promote tumor growth and recurrence. Therefore, transfusion therapy should be chosen cautiously [34].

4.1.4 Other Novel Therapeutic Strategies

Several innovative strategies for treating CRA are emerging, notably those that combine potential therapeutic targets for CRA into single agents. The goal of these combination drugs is to achieve dual effects: anti-tumor and anti-anemia. Currently, preliminary evidence confirms that certain drug combinations possess these dual properties. For CRA treatment, these novel therapeutic strategies hold significant promise.

4.2 Traditional Chinese Medicine Treatment

Expert consensus opinions indicate that combining TCM with EPO therapy can enhance clinical efficacy without increasing clinical risks, while also improving patients' quality of life [35]. Furthermore, when used alongside oral or intravenous iron supplementation, TCM can effectively promote iron absorption and utilization, improve clinical outcomes, alleviate patient discomfort, and enhance tolerance to iron preparations. Some Chinese patent medicines with clear indications for iron deficiency anemia even demonstrate clinical efficacy comparable to that of iron preparations when used alone [36-37]. Collectively, this evidence underscores the unique advantages of TCM in treating CRA.

4.2.1 Classical TCM Formulations

Different medical practitioners hold varying opinions on the syndrome differentiation of Cancer Toxin Blood Depletion Disease. To establish a unified classification, Li Xiao [38] and colleagues from the Oncology Committee of the Beijing Association of Integrated Traditional Chinese and Western Medicine organized a panel of experts. By referencing relevant domestic and international consensus documents, guidelines, clinical research findings, and integrating clinical reality and practical experience, they engaged in repeated discussions and revisions. This process led to the established consensus, building upon the Expert Consensus on TCM Prevention and Treatment of Cancer-Related Anemia published in 2021.

(1) Syndrome of Deficiency of Both Qi and Blood

Main symptoms: shortness of breath with reluctance to speak, spontaneous sweating.

Secondary symptoms: pale nails, dizziness and blurred vision, palpitations and insomnia, numbness in hands and feet. Common tongue and pulse presentation: pale tongue with thin white coating, thready and weak pulse. Diagnosis: This pattern is diagnosed if two main symptoms, or one main

symptom plus two secondary symptoms, are present. (Other syndrome types are diagnosed using the same principle.) Treatment principle: For this pattern identified as Deficiency of Both Qi and Blood, the treatment principle is to tonify Qi and nourish Blood. Representative formulas: Danggui Buxue Decoction (Nei Wai Shang Bian Huo Lun), Bazhen Decoction (Rui Zhu Tang Jing Yan Fang), and Shiquan Dabu Pill (Tai Ping Hui Min He Ji Ju Fang).Huang Zhihui et al. conducted a study involving 60 CRA patients, which showed that Modified Danggui Buxue Decoction could improve the treatment efficacy for CRA compared to conventional Western medicine [39].Huang Ju, through a randomized controlled clinical observation, found that combined treatment with Modified Danggui Buxue Decoction and EPO was more effective in treating CRA than EPO alone [40].Clinical research has found that Bazhen Decoction, used as an adjunct to Pemetrexed Disodium + Cisplatin chemotherapy in lung cancer patients, can reduce the degree of myelosuppression and inhibit tumor progression [41].Zhang Xu [42] randomly divided 94 post-operative gastric cancer patients into groups. The control group received chemotherapy and conventional care, while the experimental group received Bazhen Decoction combined with Thunder-fire Moxibustion. The results indicated that Bazhen Decoction with Thunder-fire Moxibustion effectively alleviated chemotherapy-induced myelosuppression, thereby reducing CRA.

(2) Spleen-Stomach Weakness Syndrome

Main symptoms: poor appetite, abdominal distension and fullness. Secondary symptoms: nausea, epigastric discomfort, irregular bowel movements. Common tongue and pulse presentation: pale tongue, or tongue with teeth marks; thin white or white greasy coating; thready and weak pulse. Treatment principle: For this pattern identified as Spleen-Stomach Weakness, the treatment principle is to fortify the spleen and harmonize the stomach. Representative formulas: Buzhong Yiqi Decoction (Pi Wei Lun), Xiangsha Liujunzi Decoction (Gu Jin Ming Yi Fang Lun), Huangqi Jianzhong Decoction (Jin Gui Yao Lue), and Yigong Powder (Xiao Er Yao Zheng Zhi Jue).Su Ke, through clinical research, found that compared to Western medicine treatment alone, combining Western medicine with Buzhong Yiqi Decoction and electronic moxibustion demonstrated a significantly better effect in preventing and treating chemotherapy-induced myelosuppression and could promote the recovery of hemoglobin levels [44].

(3) Deficiency of Both Heart and Spleen Syndrome

Main symptoms: palpitations, shortness of breath, abdominal distension after eating. Secondary symptoms: dizziness, blurred vision, poor appetite, insomnia, dream-disturbed sleep, irregular bowel movements. Common tongue and pulse presentation: pale tongue with thin white coating, thready and weak pulse. Treatment principle: For this pattern identified as Deficiency of Both Heart and Spleen, the treatment principle is to tonify the Heart and Spleen. Representative formulas: Guipi Decoction (Jisheng Fang) and Renshen Guipi Pill (Jisheng Fang). Clinical studies have shown that compared to EPO therapy alone, combining Guipi Decoction with EPO for CRA can alleviate anemia symptoms and increase levels of red blood cells, hemoglobin, and hematocrit [45]. Chen Shuang, through clinical observation, concluded that Guipi Decoction combined with recombinant human erythropoietin can effectively improve anemia symptoms in breast cancer patients after chemotherapy [46].

(4) Yin Deficiency of the Liver and Kidney Syndrome

Main symptoms: dizziness, tinnitus, soreness and weakness in the lower back and knees.

Secondary symptoms: dry eyes, dry throat, tidal fever, night sweats, insomnia, dream-disturbed sleep. Common tongue and pulse presentation: red tongue with scant coating, thready and rapid pulse. Treatment principle: For this pattern identified as Yin Deficiency of the Liver and Kidney, the treatment principle is to nourish and tonify the Liver and Kidney. Representative formulas: Zhibai Dihuang Decoction (Yi Zong Jin Jian) combined with Danggui Buxue Decoction (Nei Wai Shang Bian Huo Lun), Zuogui Pill (Jing Yue Quan Shu), and Liuwei Dihuang Pill (Xiao Er Yao Zheng Zhi Jue). Li Qinghua et al. [47], through clinical research, also found that Liuwei Dihuang Pill combined with the FOLFOX6 regimen in treating advanced gastric cancer could reduce chemotherapy-induced myelosuppression and inhibit tumor growth.

(5) Yang Deficiency of the Spleen and Kidney Syndrome

Main symptoms: coldness and soreness in the lower back and knees, frequent and clear urine. Secondary symptoms: listlessness, aversion to cold, cold limbs, loose stools. Common tongue and pulse presentation: pale tongue with a thin white or white and greasy coating, thready and weak pulse. Treatment principle: For this pattern identified as Yang Deficiency of the Spleen and Kidney, the treatment principle is to warm and tonify the Spleen and Kidney. Representative formulas: Yougui Pill (Jing Yue Quan Shu) combined with Danggui Jianzhong Decoction (Qian Jin Yi Fang), and Jinkui Shenqi Pill (Jin Gui Yao Lue).

(6) Syndrome of Internal Binding of Toxin and Static Blood

Main symptoms: dull or sallow complexion, pain (stabbing or dull, fixed in location, worse at night), dark or purplish lips. Secondary symptoms: masses in the hypochondrium, scaly dry skin, petechiae or ecchymoses on the skin, fullness and discomfort in the chest and hypochondrium, afternoon tidal fever or low-grade fever at night, dry and hard stools. Common tongue and pulse presentation: dark purplish tongue, or tongue with petechiae/ecchymoses; thready and choppy pulse. Treatment principle: For this pattern identified as Internal Binding of Toxin and Static Blood, the treatment principle is to dispel stasis and resolve toxin. Representative formulas: Xuefu Zhuyu Decoction or Gexia Zhuyu Decoction (Yi Lin Gai Cuo) combined with Xijiao Dihuang Decoction (Wai Tai Mi Yao) or Jiedu Pill (San Yin Ji Yi Bing Zheng Fang Lun).

(7) Syndrome of Internal Phlegm-Dampness Accumulation

Main symptoms: stuffiness and fullness in the epigastrium and abdomen, chest tightness with wheezing and

breathlessness, nausea and poor appetite, vomiting or coughing with expectation of phlegm and thin mucus, subcutaneous nodules or scrofula. Secondary symptoms: heaviness in the head and body, dizziness and blurred vision, sticky sensation in the mouth or bland taste in the mouth, absence of thirst or thirst without desire to drink, puffy face and swollen limbs, loose stools. Common tongue and pulse presentation: pale tongue, or a swollen and tender tongue body; white, greasy, watery-slippery, or pus-fur-like coating; soggy or wiry pulse. Treatment principle: For this pattern identified as Internal Phlegm-Dampness Accumulation, the treatment principle is to dispel phlegm and resolve dampness. Representative formulas: Erchen Decoction (Tai Ping Hui Min He Ji Ju Fang), Banxia Houpu Decoction (Jin Gui Yao Lue), Linggui Zhugan Decoction (Jin Gui Yao Lue), and Shenling Baizhu Powder (Tai Ping Hui Min He Ji Ju Fang).

4.2.2 Chinese Patent Medicines

[Consensus Opinion] The clinical application of Chinese patent medicines to treat or assist Erythropoiesis-Stimulating Agents (ESAs) in managing CRA has demonstrated clear efficacy. They can not only increase patients' hemoglobin concentration and red blood cell levels, improving the overall treatment response rate, but also enhance patients' quality of life [35]. (Category 2A evidence, Grade II recommendation) Chinese patent medicines should be used according to their primary functions and based on the principle of treatment determined by syndrome differentiation. To facilitate application by physicians, they are primarily categorized into those leaning towards fortifying the spleen and those leaning towards tonifying the kidney. Medicines leaning towards fortifying the spleen include: Compound Ejiao Jiang (supplements Qi and nourishes Blood), Yizhong Shengxue Capsules (Tablets) (fortifies the spleen and harmonizes the stomach, supplements Qi and generates blood), Qijiao Shengbai Capsules (nourishes blood and supplements Qi), Yiqi Weixue Granules (Capsules, Tablets) (nourishes blood and supplements Qi), Shengxuening Tablets (supplements Qi and nourishes blood), Jianpi Shengxue Granules (Tablets) (fortifies the spleen and harmonizes the stomach, nourishes blood and calms the spirit), The above medicines are suitable for: Syndrome of Deficiency of Both Qi and Blood, Spleen-Stomach Weakness Syndrome, and Deficiency of Both Heart and Spleen Syndrome (Category 2A evidence, Grade II recommendation). Medicines leaning towards tonifying the kidney include: Shengxuebao Mixture (nourishes and tonifies the liver and kidney, supplements Qi and generates blood), Zaizao Shengxue Capsules (Tablets) (tonifies and benefits the liver and kidney, supplements Qi and nourishes blood), Compound Zaofan Pills (warms the kidney and strengthens the marrow, supplements Qi and nourishes Yin, generates blood and stops bleeding), Yixuesheng Capsules (fortifies the spleen and tonifies the kidney, generates blood and replenishes essence), Xueshusheng Granules (supplements Qi and warms Yang, nourishes blood and activates blood), Zhenqi Fuzheng Granules (Capsules, Tablets) (supplements Qi and nourishes Yin. The above medicines are suitable for: Syndrome of Deficiency of Both Qi and Blood, Yin Deficiency of the Liver and Kidney Syndrome, and Yang Deficiency of the Spleen and Kidney Syndrome (Category 2A evidence, Grade II recommendation).

4.2.3 Other Therapies

The most commonly used methods are acupuncture and moxibustion. Moxibustion: Common acupoints selected include Zusanli (ST36), Geshu (BL17), Shenshu (BL23), Pishu (BL20), Dazhui (GV14), Guanyuan (CV4), Qihai (CV6), and Shenque (CV8). The primary method is moxa stick moxibustion, although ginger-interposed moxibustion, grain-sized moxibustion, moxa cone moxibustion, herb-partitioned moxibustion, heat-sensitive moxibustion, and thunder-fire moxibustion may also be selected as appropriate. Acupuncture: Common acupoints selected include Sanyinjiao (SP6), Zusanli (ST36), Xuehai (SP10), Geshu (BL17), Shenshu (BL23), Ganshu (BL18), Pishu (BL20), Neiguan (PC6), Hegu (LI4), Dazhui (GV14), Guanyuan (CV4), Qihai (CV6), and Shenque (CV8). Routine needle acupuncture is the primary technique, with other options such as intradermal needles (press needles), electroacupuncture, or warm needle moxibustion used as appropriate. Explanation of Acupoint Selection: Zusanli (ST36) is the most frequently used point. As the He-Sea point of the Stomach Meridian and a key point for treating deficiency, its function of fortifying the spleen and harmonizing the stomach aims to promote the transformation of Qi and Blood by the spleen and stomach. Dazhui (GV14), the meeting point of the six Yang meridians and the Governor Vessel, is selected to stimulate and strengthen Yang Qi. The three back-shu points, Geshu (BL17), Shenshu (BL23), and Pishu (BL20), are points where the essence of the Zang-fu organs infuses on the back. Specifically, Geshu is the influential point for Blood. Combined with Pishu (Spleen) and Shenshu (Kidney), they regulate both the congenital and acquired constitutions, thereby regulating and nourishing blood. Guanyuan (CV4), Qihai (CV6), and Shenque (CV8) are used to cultivate and supplement original Qi, boost Qi, and consolidate the root. Qigong, which regulates the mind, breath, and body, can also be employed. Under the guidance of qualified instructors, practices such as Wuqinxi (Five-Animal Frolics), Baduanjin (Eight-Section Brocade), Taijiquan (Tai Chi), or Yijinjing (Muscle-Tendon Change Classic) may be chosen [48].

5. Conclusion

Cancer-related anemia (CRA) is a common complication that affects the quality of life and treatment outcomes of patients with malignant tumors. While Western medicine alone can effectively increase hemoglobin levels, it has limitations such as poor response, iron metabolism disorders, thrombotic risks, and transfusion-related side effects. In recent years, the integrated approach of Traditional Chinese and Western medicine has demonstrated unique advantages and broad prospects in treating CRA. This synergistic model not only mitigates the side effects of Western treatments and enhances their efficiency in correcting anemia but also, through holistic regulation, improves patients' overall symptoms, physical strength, and quality of life, thereby supporting anti-cancer therapy and embodying the wisdom of "addressing both the root cause and symptoms."

However, current research in this field still faces several challenges, including the need for standardization of TCM syndrome differentiation and efficacy evaluation, a lack of

high-quality, large-sample randomized controlled trials, and the requirement for further elucidation of its mechanisms of action at the molecular and cellular levels. In the future, efforts should focus on establishing standardized diagnosis and treatment protocols for the integrated prevention and management of CRA, utilizing modern scientific technologies to deeply explore its scientific basis, and conducting more rigorously designed clinical studies to provide high-level evidence-based medical support.

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