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Original Article

A Meta-Analysis of the Efficacy and Safety of Huai'er Granules as an Adjuvant Therapy for Breast Cancer in Combination with Western Medicine

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Abstract:
Objective: To systematically evaluate the efficacy and safety of Huairu Granules combined with Western medicine in the treatment of breast cancer. Methods: Randomized controlled trials (RCTs) comparing Huairu Granules combined with Western medicine and Western medicine alone in the treatment of breast cancer were retrieved from Pubmed, Web of Science, CNKI, VIP, Wanfang, and Chinese Biomedical Database (CBM) from the establishment of the databases to September 2025. The quality of the included studies was evaluated using the AMSTAR quality assessment form. Relevant data were extracted, and Review 5.4 was used to conduct a meta-analysis of the relative risk (*RR*) and odds ratio (*OR*) of the reference indicators, and the 95% confidence interval (*CI*) was listed. Results: A total of 17 RCTs were included, involving 1655 patients, with 833 in the experimental group and 822 in the control group. The meta-analysis results showed that the Karnofsky Performance Status (KPS) score of the experimental group treated with Huairu Granules (*MD* = 9.66, 95% [7.05, 12.28], $P < 0.00001$), clinical efficacy including objective response rate (*OR* = 1.35, 95% *CI*[1.03, 1.76], $P = 0.03$), disease control rate (*RR* = 1.16, 95% [1.01, 1.33], $P = 0.03$), 2-year survival rate (*RR* = 1.18, 95% [1.02, 1.37], $P = 0.03$), reduction in 2-year recurrence and metastasis rate (*RR* = 0.27, 95%*CI* [0.13, 0.56] , $P = 0.0005$), reduction in adverse reactions (gastrointestinal reactions, bone marrow suppression, liver function damage), peripheral blood CD3+ T cells, CD4+ T cells, CD8+ T cells, NK cells, and CD4+/CD8+ levels were all superior to those of the control group, with statistically significant differences ($P < 0.05$). Conclusion: Based on the results of the meta-analysis, it can be preliminarily inferred that Huairu Granules combined with Western medicine can improve the efficacy and safety of breast cancer patients, but more strictly designed large-sample, prospective clinical studies are still needed for confirmation.

Key words: Huaier Granules; Breast Cancer; Meta-analysis

Introduction

Breast cancer is the most common malignant tumor among women worldwide [2], and a significant cause of cancer-related deaths among women, with a standardized mortality rate of 4.96 per 100,000. Its global incidence is increasing at a rate of 3.1% annually and shows a trend of affecting younger women. Different regions also exhibit distinct characteristics, with studies reporting that the incidence rate in low-income areas is approximately four times that in high-income areas[1]. For different molecular subtypes of breast cancer, various treatment regimens are commonly adopted in clinical practice [3]. Chemotherapy has always played a crucial role in the comprehensive treatment of breast cancer. Appropriate adjuvant chemotherapy regimens

during diagnosis and treatment can achieve the maximum therapeutic effect, minimize adverse reactions, reduce the risk of tumor recurrence, and thereby improve patient survival rates[4]. However, while chemotherapy brings survival benefits, its side effects cannot be ignored, including gastrointestinal reactions[5], liver function damage, bone marrow suppression, and neurotoxicity. Some patients discontinue treatment due to their inability to tolerate the side effects of chemotherapy. Huairu Granules, a type of fungus growing on the trunks of old "Chinese locust" trees, mainly contain proteoglycans[6], and have the functions of tonifying the body, promoting blood circulation, and eliminating tumors. They can improve blood stasis and weakness of the body. Currently, in clinical practice, they are used for the adjuvant treatment of various malignant tumors such as gastric cancer, liver cancer, and breast cancer through their pharmacological effects of inhibiting angiogenesis, reversing drug resistance in chemotherapy-resistant tumor cell lines, and promoting tumor cell apoptosis[7]. A large number of literature studies have reported that the combination of Huairu Granules and Western medicine in the treatment of breast cancer can enhance the patient's immune function, reduce the incidence of adverse reactions, and improve survival rates and recurrence and metastasis rates. However, there is a lack of systematic evaluation reports, which to some extent limits the application of Huairu Granules in the treatment of breast cancer. Therefore, this study aims to collect relevant literature and conduct a Meta-analysis on the efficacy and safety of Huairu Granules combined with Western medicine in the treatment of breast cancer, in order to provide more drug options for the adjuvant treatment of breast cancer.

1. Materials and Methods

1.1 Literature Search and Screening

The computer was used to search for relevant literature on the combination of Huai'er Granule and Western medicine in the databases of CNKI, VIP, Wanfang, CBM, PubMed, and Web of Science. In addition, manual searches were conducted for other literature. The search period was from the establishment of the databases to September 2025. The median search terms were freely combined with "Breast Neoplasms", "Breast Tumors", "Breast Cancer", "Huaier Granule", and "Breast Carcinoma" as the main words or keywords. Two researchers screened the literature according to the inclusion and exclusion criteria. In case of disagreement, the third researcher would assist in making the judgment.

Inclusion Criteria

1.2.1 Research Type: All were RCT studies comparing the efficacy of Huai'er Granules combined with Western medicine in treating breast cancer, regardless of whether blinding was used or not.

1.2.2 Research Subjects: All patients diagnosed with breast cancer through imaging tests, biopsy or surgical pathology, regardless of their age, race or gender.

1.2.3 Intervention Measures: The control group received conventional Western medical treatments, including surgery, chemotherapy, radiotherapy, targeted therapy, and endocrine therapy. The experimental group added Huai'er Granules to the treatment regimen of the control group.

1.2.4 Outcome Indicators : ① 2-year survival rate, 2-year recurrence and metastasis rate; ② Quality of life. Measured according to the KPS scoring standard[8]; ③ Clinical efficacy. Evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST)[9]. The therapeutic effect is classified as complete response (CR), partial response (PR), disease stability (SD), disease progression (PD), objective remission rate (Objective Remission Rate, *ORR*) = (number of CR cases + number of PR cases) / total number of cases × 100%, disease control rate (Disease

Control Rate, DCR) = (number of CR cases + number of PR cases + number of SD cases) / total number of cases × 100%; ④ Immune indicators. Changes in the contents of peripheral blood CD3+, CD4+, CD8+, NK cells and the ratio of CD4+/CD8+ cells; ⑤ Adverse reactions to anti-cancer treatment. Gastrointestinal reactions, liver function impairment, bone marrow suppression[10].

1.3 Exclusion Criteria : ① Non-RCT studies or non-high-quality RCT studies; ② Reviews, case reports, animal experiments, systematic reviews; ③ Incorrect statistical methods; ④ The reported outcomes in the literature do not match the expected outcomes.

1.4 Quality Evaluation Carefully read the literature and conduct quality evaluation of the included studies using the AMSTAR quality evaluation form[11]. The evaluation results will be classified into three levels: high risk, unclear risk, and low risk. Cross-evaluate the results. If there are conflicts, read the literature again and negotiate to resolve them.

1.5 Statistical Methods: A Meta-analysis was conducted using Cochrane Collaboration's RevMan 5.3. For binary variables, relative risk (*RR*) was used; for continuous variables, mean difference (*MD*) was employed. Both indicators were expressed with 95% confidence intervals (*CI*). Chi-square test was used to examine heterogeneity among the included studies. If there was no heterogeneity or the heterogeneity was small (I2 < 50%), a fixed-effect model (FE) was adopted; if the heterogeneity was large (I2 > 50%), a random-effect model was used and the reasons were analyzed. The significance level was set at $P < 0.05$, and the statistical results were analyzed using forest plots.

2. Result

2.1 Search Results of Literature

This study retrieved a total of 266 relevant articles through computer and manual searches, among which 256 were in Chinese, including 71 from CNKI, 50 from VIP, 76 from Wanfang, and 59 from CBM; 10 were in English, including 3 from PubMed and 7 from Web of Science. A total of 176 duplicate publications were initially excluded through computer and manual screening; after carefully reading the titles and abstracts, 68 were eliminated; and after carefully reading the full texts and strictly following the inclusion and exclusion criteria, 17 articles were finally included in the study. The flowchart of literature screening is shown in Figure 1.

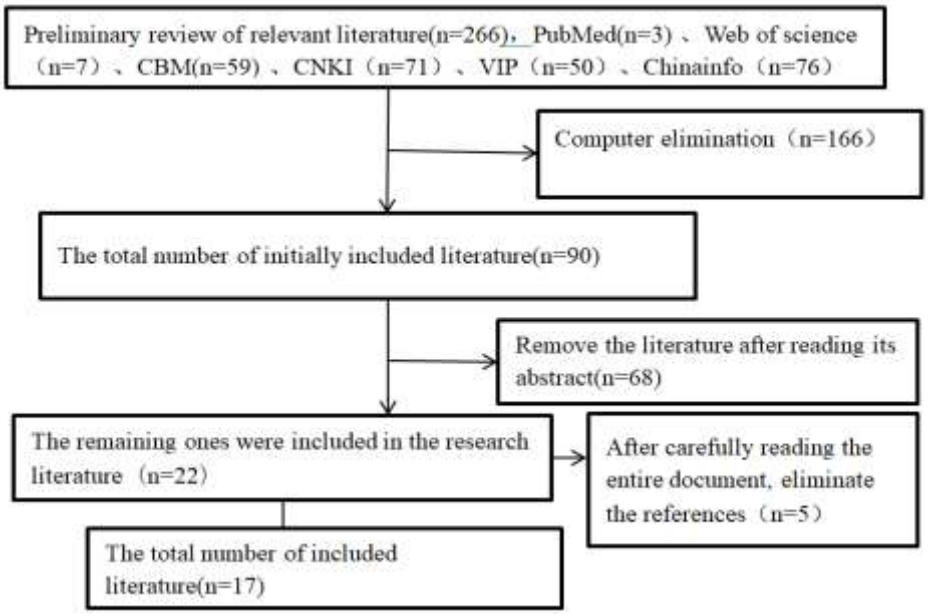

Figure 1 Flowchart of Literature Inclusion and Screening Process

2.2 Basic Characteristics of Included Literature

A total of 17 studies were included in this research, involving 1,655 patients. Among them, 833 were in the experimental group and 822 were in the control group. All were female patients, with the youngest being 18 years old and the oldest 85 years old. Except for 3 studies[12,13,14] which did not mention the consistency of baseline data, the remaining studies compared the general information of the experimental group and the control group, and the differences were not statistically significant ($P > 0.05$). The experimental group all received Huai'er Granules combined with Western medicine therapy. The course of Huai'er Granules ranged from 3 weeks to 2 years, and the usage was according to the drug instructions "20g per time, 3 times per day"; the control group all received conventional Western medical therapy, which included surgical treatment, radiotherapy, chemotherapy, targeted therapy, and endocrine therapy. Both the experimental group and the control group were regularly re-examined and followed up after treatment. Regarding the observation indicators, 8 studies reported adverse reactions (gastrointestinal reactions, liver function damage, bone marrow suppression), 7 studies reported changes in immune indicators (CD3+, CD4+, CD8+, NK, CD4+/CD8+), 4 studies reported KPS scores, 3 studies reported short-term clinical efficacy (objective response rate, disease control rate), 4 studies reported the 2-year recurrence and metastasis rate, and 3 studies reported the 2-year survival rate. The basic characteristics of the included studies are shown in Table 1.

Table 1 Basic Characteristics of Included Studies

	Time	Samples		Age(year)	Intervening methods		Dosage time of Hyaier granule	Evaluation index
		Experiental	Control		Experiental	Control		
Chen Y	2020	50	50	42-75 (range)	Chemotherapy+ AP Huaier granule		6 weeks	①②③④⑤
Dai YG	2007	34	34	29-55 (range)	Chemotherapy+ VE Huaier granule		8-12weeks	⑦⑧⑨
Shan CY	2018	46	46	34-73 (range)	Chemotherapy+ PT Huaier granule		18 wssks	③④⑤
Guan RD	2011	77	88	26-85 (range)	Operation+Chemotherapy+Huaier granule	Operation+ Chemotherapy (Not provided)	12-18 weeks	⑪
Guo FD	2014	25	25	55-76 (range)	Chemotherapy+ Huaier granule	Chemotherapy (Not provided)	≥12 weeks	⑪
Han SJ	2017	33	33	20-70 (range)	Chemotherapy+ AC*4-T*4 Huaier granule		Not provided	⑦⑩③⑤
Li SM	2021	40	40	18-65 (range)	Chemotherapy+ AT Huaier granule		24 weeks	

Mu NR	2005	43	46	Not provided	Radiotherapy+ Huaier granule	Radiotherapy	5-6 weeks	③④
Qu SX	2020	35	30	60-79 (range)	Chemotherapy+ Huaier granule	TC	2 years	⑥⑦⑧⑨
Tang Y	2006	25	25	Not provided	Chemotherapy+ Huaier granule	Chemotherapy (Not provided)	30 days	⑤⑦
Wang W	2019	48	48	29-65 (range)	Chemotherapy+ Huaier granule	FEC	24 weeks	③④⑤
Xu F	2009	32	28	18-65 (range)	Chemotherapy+ Huaier granule	TAC	5-6 weeks	⑦⑧⑨
Xiong F	2015	52	40	19-67 (range)	Chemotherapy+ Huaier granule	TAC	18 weeks	⑦⑧
Yang Z	2017	30	30	30-67 (range)	Chemotherapy+ Huaier granule	TP	6 weeks	③⑥
Ying X	2013	20	20	60-75 (range)	Operation+Radiotherapy++Huaier granule	Operation +Radiotherapy	6 weeks	⑪
Zhang M	2020	30	30	34-74 (range)	Chemotherapy+ Huaier granule	FEC	6-7 weeks	①②
Zhao ZW	2020	31	31	29-70 (range)	Chemotherapy+ Huaier granule+Targered therapy	Chemotherapy+Targeted therapy (Not provided)	3 weeks	⑥⑦

Notes：① Objective remission rate；② Disease control rate；③ Myelosuppression；④ liver function lesion；⑤ gastrointestinal reaction；⑥ KPS score；⑦ $CD4^+$, $CD8^+$, $CD4^+/CD8^+$；⑧ NK；⑨ $CD3^+$；⑩ Two-year survival rate；⑪ Two-year recurrence and metastasis rate

AP：Pemetrexed Disodium + Cis-platinum；VE：Gemcitabine + Cyclophosphamide；PT：Pirarubicin + Paclitaxel；AC-T：Cyclophosphamide + Pirarubicin - Paclitaxel；AT：Pharmorubicin + Pirarubicin；TC：Cyclophosphamide + Docetaxel；FEC：Fluorouracil + Pharmorubicin + Cyclophosphamide；TAC：Docetaxel + Pirarubicin + Cyclophosphamide；TP：Paclitaxel + Paraplatin

2.3 Inclusion of Literature Quality Evaluation

The included literature, except for 2 articles [12,15], all mentioned random grouping. Among them, 8 article[16,17,18,19,20,14,21] described the grouping methods (random number table method, balanced randomization method)s; 4 articles did not clearly explain the statistical conclusions[7,21,12,23]; 3 articles mentioned allocation concealment and the use of blinding[20,19,24]; 5 articles[7.12.23.21.16] may have selective bias; the results of the bias risk assessment of the included literature are shown in Figures 2 and 3.

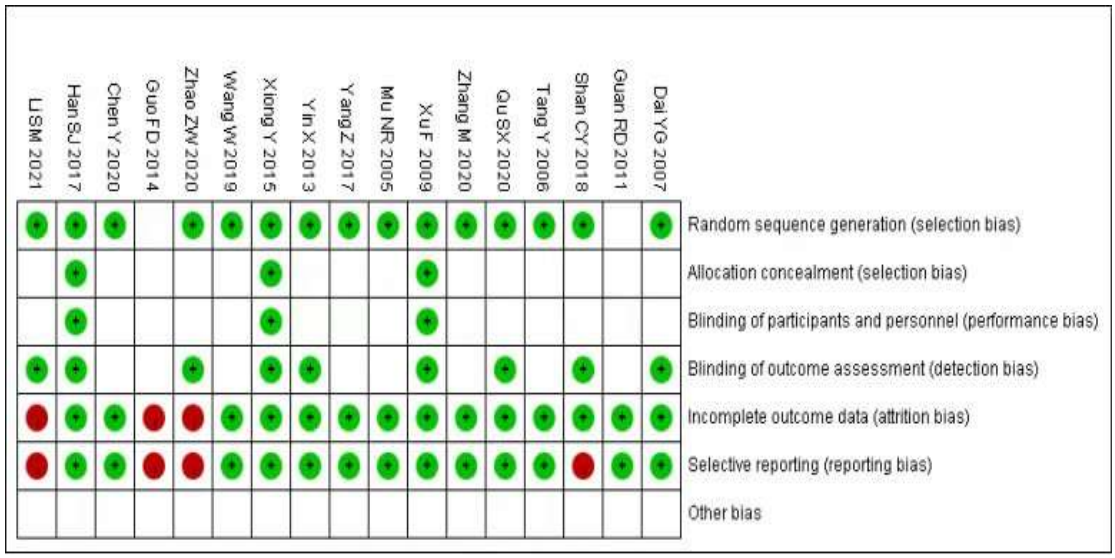

Figure 2 Risk Diagrams of Bias in Each Study

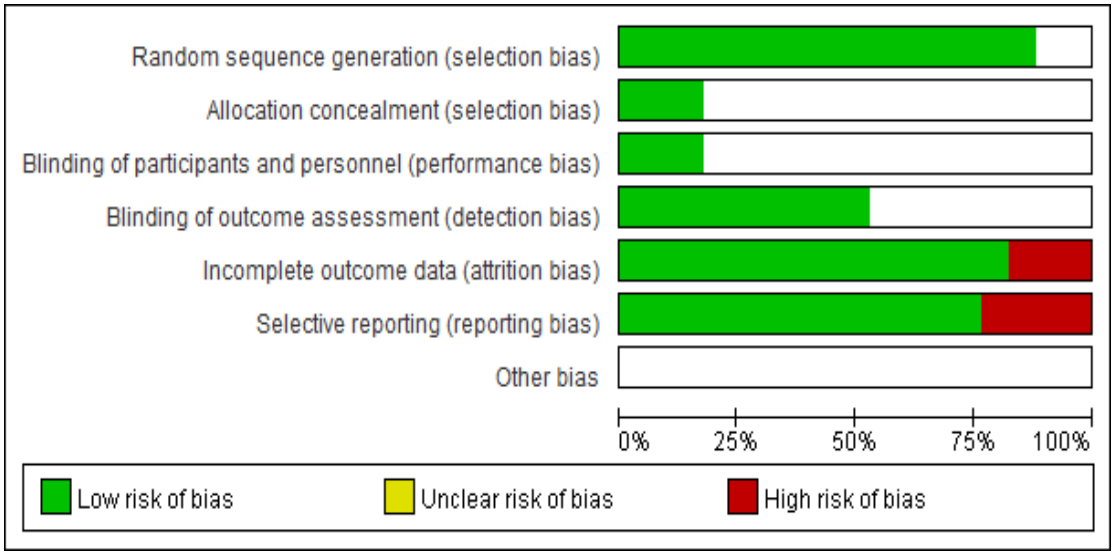

Figure 3 Percentage of each bias risk

2.4 Evaluation of the Therapeutic Effect of Huai'er Granules in the Treatment of Breast Cancer

2.4.1 Immune Function A total of 7 studies [25.18.26.13.19.20.21] analyzed the changes in immune indicators of breast cancer patients. Among them, 4 studies[13,19,25,26] analyzed the changes in the total value of T lymphocytes (CD3+), 7 studies[25,18,26,13,19,20,21] analyzed the changes in helper T cells (CD4+), 7 studies[25,18,26,13,19,20,21] analyzed the changes in cytotoxic T cells (CD8+), 7 studies2[5,18,26,13,19,20,21] analyzed the changes in the CD4+/CD8+ ratio, and 4 studies [25,26,19,20] analyzed the changes in natural killer cells (NK). The heterogeneity result test showed that there was no significant heterogeneity in the CD4+/CD8+ ratio among the studies (P = 0.20, I^2 = 30%), and a fixed-effect model was adopted; the other indicators all showed heterogeneity: CD3+ (P = 0.0001, I^2 = 86%), CD4+ (P < 0.00001, I^2 = 88%), CD8+ (P < 0.00001, I^2= 90%), NK (P = 0.0004,I^2= 83%), which might be related to the baseline differences of patients, drug formulation, dose, treatment course, etc. Therefore, a random-effect model was adopted. The differences in immune indicators among the studies were statistically significant (P < 0.05).

See Table 2. Therefore, it can be inferred that Huai'er Granules can improve the immune function of patients.

Table2 Meta-analysis of immunization indicators

Immune indice	literature quantity	Sample		MD	I^2 (%)	95%*CI*	*P*值
		Experiment	Control				
CD3+	4	126	117	4.53	86	0.43，8.62	0.03
CD4+	7	230	223	5.35	88	2.62，8.07	0.0001
CD8+	7	230	223	-1.99	96	-6.40，2.32	0.38
CD4+/CD8+	7	230	223	-2.96	30	-5.70，-0.21	<0.00001
NK	4	126	117	3.68	83	1.08，6.28	0.006

2.4.2 Quality of Life A total of 4 studies analyzed the quality of life of patients after comprehensive treatment through KPS scores. The heterogeneity test showed that there was significant heterogeneity among the studies (P < 0.00001, I^2 = 90%), so the random effects model was selected for the Meta-analysis. The results showed that all 4 studies fell on the right side of the null line (see Figure 4). There was a statistically significant difference in the quality of life between the experimental group and the control group [*MD* = 10.07, 95% *CI* (7.00, 13.14), P < 0.00001], proving that Huai'er Granules can improve the quality of life of breast cancer patients.

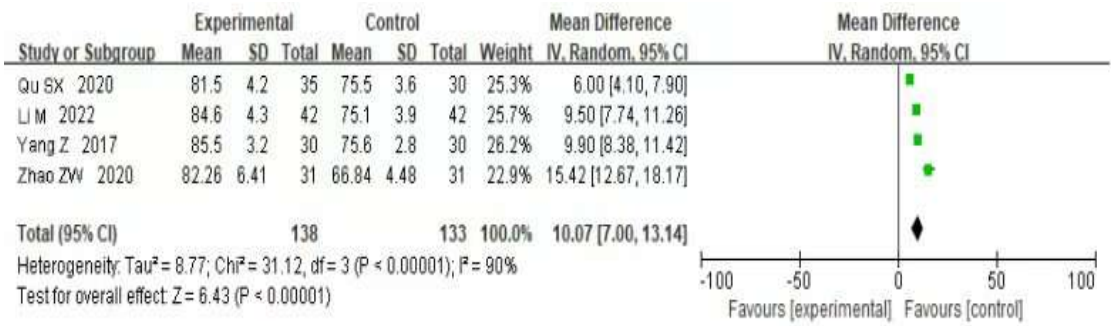

Figure 4 Forest plot comparing the quality of life between the experimental group and the control group

2.4.3 2-year survival rate and recurrence/metastasis rate A total of 5 studies[12, 24,27,15,17] analyzed the 2-year recurrence/metastasis rate, among which 4studies [12, 24, 27, 15] analyzed the 2-year recurrence/metastasis rate, and 3 studies[24, 17, 12] analyzed the 2-year survival rate. The heterogeneity test results showed that there was no heterogeneity in the 2-year survival rate (I^2 = 0%, P =0.57) and the 2-year recurrence/metastasis rate (I^2 = 0%, P = 0.86). The fixed-effect model was adopted. The 2-year survival rate results were [*RR* = 1.18, 95% *CI* (1.02, 1.37), P = 0.03], and the 2-year recurrence/metastasis rate results were [*RR* = 0.27, 95% *CI* (0.13, 0.56), P = 0.0005]. See Figure 5.6. The differences between the experimental group and the control group were statistically significant (P < 0.05), proving that Huai'er Granules can improve the 2-year survival rate and recurrence/metastasis rate of patients.

2.4.4 Clinical Efficacy A total of 3 studies[14, 17, 22] reflected the clinical efficacy through objective response rate and disease control rate. The

heterogeneity results showed that there was no heterogeneity in the objective response rate among the studies (I^2 = 0%, P = 0.39) and the disease control rate (I^2= 11%, P = 0.33) (see Figure 6.7). All used the fixed-effect model. The objective response rate results were [*RR* = 1.35, 95% *CI* (1.03, 1.76), P = 0.03], and the disease control rate results were [*RR* = 1.16, 95% *CI* (1.01, 1.33), P = 0.03]. See Figure 7.8. The differences in clinical efficacy values among the groups were statistically significant (P < 0.05), indicating that Huai'er Granules can improve the clinical efficacy of patients.

2.5 Evaluation of the Safety of Huai'er Granules in the Adjuvant Treatment of Breast Cancer

A total of 8 studies[22,16,24,17,18,28,29,30] analyzed adverse reactions. Among them, 7 studies[16,24,17,18,29,22,28] analyzed gastrointestinal reactions, 8 studies[22,16,24,17,18,28,29,30] analyzed bone marrow suppression, and 5 studies[16,18,28,29,22] analyzed liver function damage. The heterogeneity results showed that there was no heterogeneity in adverse reactions among the studies: gastrointestinal reactions (P = 0.92, I^2 = 0%), bone marrow suppression (P = 0.36, I^2 = 9%), liver function damage (P = 0.76, I^2 = 0%). Therefore, the fixed-effect model was selected. The differences in adverse reactions among the groups were statistically significant (P < 0.05). See Table 3. Therefore, it can be inferred that Huai'er Granules as an adjuvant treatment can reduce the occurrence of adverse reactions in patients.

3. Discussion

Although significant progress has been made in the diagnosis and treatment of cancer, the incidence and mortality rates of breast cancer remain high due to its high heterogeneity, potential invasiveness, and complex biological characteristics. Although a variety of treatment methods for breast cancer have emerged, surgery remains the main treatment approach. Chemotherapy is used to inhibit the distant metastasis and spread of the tumor, and radiotherapy is used to improve the therapeutic effect. A comprehensive assessment of factors such as the patient's age, tumor stage, and patient's wishes is also conducted, and neoadjuvant chemotherapy (Neoadjuvant Chemotherapy, NACT) can be administered first. NACT can reduce the tumor diameter and even achieve pathological complete remission (Pathological Complete Remission, PCR), providing patients with the opportunity for surgery. The adjuvant treatment of breast cancer has an undeniable effect on improving efficacy, but it also damages normal cells and brings significant toxic side effects, such as gastrointestinal reactions, bone marrow suppression, and liver function impairment. These side effects not only reduce the quality of life of patients but may also affect the progress of tumor treatment. Appropriate intervention measures can minimize or eliminate tumor recurrence and reduce drug resistance and toxicity. One of the main challenges currently faced by the scientific community is how to reverse drug resistance and develop an ideal drug combination for patients to improve survival rates[37]. In recent years, traditional Chinese medicine has received increasing attention worldwide due to its potential anti-tumor effects. Huai'er Granules is an important traditional Chinese medicine preparation in China. The glycoproteins extracted by high-temperature-ultrahigh-pressure gradient ethanol precipitation method are its main active components[32]. It focuses on tonifying deficiency, promoting blood circulation, and has the effects of strengthening the body's defenses, consolidating the foundation, and promoting blood circulation and eliminating symptoms[31].It is currently widely used in the adjuvant treatment of malignant tumors such as liver cancer, breast cancer, and gastric cancer.

Huaier Granules are a traditional Chinese

medicine with proven efficacy. They can exert anti-tumor effects through various pathways. Caspase-3 is a key participant in the apoptotic signaling pathway. Studies have shown that Huaier Granules can promote the expression of cleaved Caspase-3, increase the activity of Caspase-3 enzymes in tumor cells, and induce cell apoptosis. In addition, Huaier Granules can also increase the Bax/Bcl-2 ratio, damage the integrity of the tumor cell membrane, and indirectly lead to cell apoptosis[34]. Estrogen receptor (ER) is currently an important target for the treatment of ER-positive breast cancer. Xiaolong Wang et al. [35] reported that Huaier Granules are also a promising drug for the treatment of ER-positive breast cancer. It reverses the activation of the estrogen-inducing factor κB (NFκB) pathway and thereby inhibits the proliferation of cells stimulated by estrogen. In terms of inhibiting tumor cell migration, Huaier Granules affect the proliferation, migration, and adhesion ability of tumor vascular endothelial cells, and weaken the function of breast stem cells, thereby reducing the systemic metastasis of tumor cells[38]. As a drug for reversing drug resistance, Huaier Granules exert its resistance-reversing effect by down-regulating the expression of multidrug resistance gene MDR1 and its encoded cell membrane P-glycoprotein (P-gp)[36].

A total of 17 RCT studies were included in this research, involving 1,655 patients. The meta-analysis results showed that the combined use of Huai'er Granules as an adjunct to Western medical therapy was statistically significantly different from the control group in improving the patient's quality of life, 2-year survival rate, objective response rate, disease control rate, and reducing the 2-year recurrence and metastasis rate ($P < 0.05$). At the same time, Huai'er Granules could significantly reduce the drug toxic side effects brought by the sole Western medical therapy, mainly including digestive tract reactions, such as nausea, vomiting, abdominal pain, diarrhea, constipation, etc.; bone marrow suppression, including a decrease in white blood cells and platelets; and liver function damage, including jaundice, dull pain in the liver area, and elevated transaminases and bilirubin levels. In addition, there were also skin and neurological damage, due to the lack of relevant literature, this was not included in this study.

This research strictly followed the inclusion and exclusion criteria to search for relevant literature. The basic information, treatment plans, treatment courses, and screening indicators of the patients were carefully recorded after detailed reading of the literature. However, there were certain limitations: ① During the literature search, the number of English literature included was insufficient, and all were excluded during the literature screening, which may lead to possible literature search omissions. Therefore, in the future, it is necessary to expand the English database to reduce bias and increase the reliability of the meta-analysis. ② The age and tumor stage of the breast cancer patients in the included studies were uneven, and the Huai'er Granules and Western medical therapy plans, courses were different, which may lead to clinical heterogeneity. ③ When evaluating the quality of the included studies, most did not mention whether blind methods were used, and some did not mention the randomization grouping method, suggesting that some of the included literature were not high-quality RCT studies. ④ This study did not discuss long-term survival rate and recurrence and death rate, so more prospective trials need to be included in the future.

In conclusion, through a systematic review of clinical research reports on the treatment of breast cancer using Huai'er Granules in combination with Western medicine, it is suggested that the efficacy and safety of Huai'er Granules as an adjunct to Western medicine are superior to that of Western medicine alone. It not only improves the clinical efficacy of patients, enhances their

immune function and quality of life, but also reduces the incidence of adverse reactions. This provides a basis for the adjunctive treatment of breast cancer with Huai'er Granules.

Reference

1. Winters S,Martin C,Murphy D, et al.Breast Cancer Epidemiology, Prevention, and Screening. Prog Mol Biol Transl Sci. 2017;151:1-32.
2. Trayes KP, Cokenakes SEH. Breast Cancer Treatment. Am Fam Physician. 2021;104(2):171-178.
3. Barrios CH, Reinert T. Open questions and controversies in the systemic treatment of breast cancer. Curr Opin Oncol. 2021;33(6):591-596.
4. Chidley P,Foroudi F,Tacey M, et al. Neoadjuvant radiotherapy for locally advanced and high-risk breast cancer. J Med Imaging Radiat Oncol. 2021;65(3):345-353.
5. Naito Y, Kai Y, Ishikawa T, et al. Chemotherapy-induced nausea and vomiting in patients with breast cancer: a prospective cohort study. Breast Cancer. 2020;27(1):122-128.
6. Hao S, Sun H, Li HF, et al. Observation on the Therapeutic Effect of Huairu Combined with Chemotherapy on Nude Mice with Breast Cancer [J]. Chinese Journal of Chronic Disease Prevention and Control, 2021, 29(12): 946-949 + 967.
7. Li SM, Hao JW, Hong Y, et al. The effect of Huairu Granules on endocrine hormones and survival period during the postoperative adjuvant chemotherapy period of breast cancer [J]. Guangzhou Medical Journal, 2021, 52(05): 109-112.
8. An E, Lo C, Hales S, et al. Demoralization and death anxiety in advanced cancer. Psychooncology. 2018;27(11):2566-2572.
9. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009 Jan;45(2):228-47.
10. Brown T, Sykes D, Allen AR. Implications of Breast Cancer Chemotherapy-Induced Inflam mation on the Gut, Liver, and Central Nervou s System. Biomedicines. 2021;9(2):189. Publi shed 2021 Feb 13.
11. 11.Xiong J, Chen R. AMSTAR: A Tool for Evaluating the Methodological Quality of Systematic Reviews/Meta-Analyses [J]. Chinese Journal of Evidence-Based Medicine, 2011, 11(09): 1084-1089.
12. Guo FD. Clinical Efficacy Analysis of Huai'er Granules in Treating Elderly Breast Cancer [J]. Chinese and Foreign Medical Journal, 2014, 33(13): 26-27.
13. Tang Y, Li R, Wu X. Observation on the Immune Function Regulatory Effect of Huai'er Granules on Breast Cancer Patients after Surgery [J]. Journal of Military Medical College, 2006(03): 170-171.
14. Zhang M, Zhang CY, Chen SY. The inhibitory effect of Huai'er Granules combined with chemotherapy on advanced triple-negative breast cancer and its influence on tumor angiogenesis [J]. Inner Mongolia Medical Journal, 2020, 52(10): 1169-1171.
15. Guan RD, Zheng Y, Chen QJ. A Retrospective Cohort Study on the Effect of Huai'er Granules in Preventing Short-Term Recurrence and Metastasis of Operable Breast Cancer [J]. Guangdong Medical Journal, 2011, 32(11): 1490-1492.
16. Shan CY, Di Y, Huang S, et al. The efficacy of Huai'er Granules combined with neoadjuvant chemotherapy in breast cancer and its influence on the levels of P53, Ki-67, MMP-2 and MMP-9 [J]. Hebei Medical Journal, 2018, 24(04): 579-583.
17. Li M, Wang T. Analysis of the therapeutic effect of Huai'er Granules combined with pemetrexed disodium and cisplatin in the treatment of breast cancer [J]. Clinical Medicine Practice, 2022, 31(08): 586-588 +

598.
18. Liang YQ, Yin WJ, Qian W, et al. The influence of Huai'er Granules combined with systemic chemotherapy on the immune function and prognosis of patients with advanced breast cancer [J]. Chinese Journal of General Surgery and Clinical Medicine, 2015, 22(12): 1482-1486.
19. Xu F, Tang ZG. The Effect of Jin Kechao's Ears on the Cellular Immune Function of Breast Cancer Patients Undergoing Neoadjuvant Chemotherapy [J]. Chinese Journal of General Surgery, 2009, 18(05): 524 -526.
20. Xiong Y, Zhu YL, Xu XD. The influence of Huier Granules combined with TAC chemotherapy regimen on the postoperative immune function and prognosis of patients with triple-negative breast cancer [J]. International Journal of Surgery, 2015, 42(9): 608-611.
21. Zhao ZW, Yao YQ. Observation on the Anti-Drug Resistance Effect of Pyrrolidinib Combined with Huai'er Granules in Patients with Advanced Breast Cancer Positive for Human Epidermal Growth Factor Receptor 2 [J]. Journal of Clinical Military Medicine, 20 20, 48(3): 284-286.
22. Chen Y, Liu JZ. Clinical Study on the Treatment of Breast Cancer with Huai'er Granules Combined with AP Regimen [J]. Modern Drugs and Clinical Practice, 2020, 35 (01): 52-55.
23. Li Y. Clinical Study on the Effect of Huier Granules on Recurrence and Metastasis after Breast Cancer Surgery [J]. China Health Care and Nutrition, 2017, 27(13): 42-24.
24. Han SJ, Jin XM, Qiu F, et al. Clinical Application of Huier Granules in Postoperative Adjuvant Treatment of Triple-Negative Breast Cancer [J]. China Emergency Medicine, 2017, 37(z1): 4-6.
25. Dai YG, Cun YL. The Effect of Huai'er Granules Combined with Chemotherapy on the Cellular Immune Function of Breast Cancer Patients [J]. Modern Oncology Medicine, 2007(10): 1438-1439.
26. Qu SX, Han T, Liu YG, et al. The influence of Huai'er Granules on the safety and immune function of elderly breast cancer patients during TC chemotherapy as an adjuvant treatment [J]. China Modern TCM & Distance Education, 2020, 18(03): 73-76.
27. Yin X, Hou YC, Wang MY, et al. Observation on the clinical efficacy of Huai'er Granules in the treatment of elderly breast cancer [J]. China Medical Guide, 2013, 11(20): 280-281.
28. Mu NR, Chen H.et al.Application of Huier Gr anules in Breast Cancer Radiotherapy [J]. Jour nal of Oncology, 2005, 11(6): 461-462.
29. Wang W, Shi Lb, Zhang ML, et al. The efficacy of postoperative chemotherapy for breast cancer combined with Huai'er Granules and its influence on some marker factors [J]. Western Medicine, 2019, 31(1): 113-117.
30. Yang Z. Clinical Efficacy Observation of Huai'er Granules Combined with Chemotherapy in Postoperative Patients with Breast Cancer [J]. China Modern Drug Application, 2017, 11(5): 93-95.
31. Shi J, Zhou YQ, Yuan F, et al. "Comparison of the Effects of Qinggan Huodong Zhuyu Decoction and Huailie Granules on Immune Function and Survival Time of Patients with Liver Cancer after TACE" [J]. Jiangsu Traditional Chinese Medicine, 2021, 53(04): 41-44.
32. Wang YX, Yuan HS. Research Progress on Chemical Components and Antitumor Activity of Huaili Baiye Kongmycelium (Huailie) [J]. Journal of Mycology, 2021, 40 (03): 411-422.
33. Wang YY, Wu ZG. Study on the In Vitro Effects of Huai'er Qing Ointment on K562 Cells [J]. Chinese Journal of Pediatric Hematology and Oncology, 2008(03): 104-10 7 + 145.
34. Chen Y, Wu H, Wang X, et al. Huaier

Granule extract inhibit the proliferation and metastasis of lung cancer cells through down-regulation of MTDH, JAK2/STAT3 and MAPK signaling pathways. Biomed Pharma - cother. 2018;101:311-321.

35. Wang X, Zhang N, Huo Q,et al . Huaier aqueous extract suppresses human breast cancer cell proliferation through inhibition of estrogen receptor α signaling. Int J Oncol. 2013;43(1):321-328.
36. Li R, Xie S, Zhang L, et al. The preliminary mechanism of Huai'er Granule in reversing the drug resistance of human breast cancer cell MCF-7 [J]. China Practical Medicine, 20 09, 4(17): 1-3.
37. Anastasiadi Z, Lianos GD, Ignatiadou E,et al. Breast cancer in young women: an overview. Updates Surg. 2017;69(3):313-317.
38. Zhang Y, Wang X, Chen T. Efficacy of Huaier granule in patients with breast cancer. Clin Transl Oncol. 2019;21(5):588-595.