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Clinical Study of Huaier Granule Combined with Auricular Point Seed Pressing in Postoperative Treatment of Primary Liver Cancer Patients Undergoing Transcatheter Arterial Chemoembolization

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Abstract

Background: This study aims to explore the curative effect of Huaier granule combined with auricular point seed pressing on primary liver cancer after transcatheter arterial chemoembolization. **Methods:** Clinical data of 80 patients with primary liver cancer treated in our hospital from March 2022 to March 2023 were retrospectively analyzed. 40 patients receiving Huaier granule combined with auricular point seed pressing therapy after transcatheter arterial chemoembolization were assigned into the observation group, and 40 patients receiving auricular point seed pressing therapy after transcatheter arterial chemoembolization were allocated into the control group. The clinical efficacy in the two groups was compared, and the effect of different treatment methods on traditional Chinese medicine (TCM) symptom score, liver function indicators measured using an automatic biochemical analyzer, including serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL) and albumin (ALB), and quality of life of patients was observed, and the safety was analyzed. **Results:** The total remission rate in observation group was significantly higher than that in control group ($p < 0.05$). After treatment, the TCM symptom score and the levels of ALT, AST, serum TBIL and ALB in the two groups were significantly decreased ($p < 0.05$). The levels of abovementioned indexes in observation group were obviously lower than those in control group ($p < 0.05$). Quality of life scores in both groups were apparently elevated ($p < 0.05$), and the scores in observation group were distinctly higher than those in control group ($p < 0.05$). There was no statistical significance in the incidence of adverse reactions between the two groups ($p > 0.05$). **Conclusion:** Huaier granule combined with auricular point seed pressing in the treatment of primary liver cancer after transcatheter arterial chemoembolization may have a good curative effect, which can improve the symptoms of TCM and help to recover patients' liver function and quality of life, with a high safety.

1 Introduction

Primary liver cancer is a common malignant disease with insidious onset; there are no specific symptoms in the early stage, and more obvious symptoms appear in the middle and late stages, including jaundice, ascites, and pain in the liver area, so most of the patients with this disease are diagnosed in the middle and late stages, which are difficult to be treated, with the average survival period of 4-6 months [1-4]. Transcatheter arterial chemoembolization is the preferred modality for the clinical treatment of primary liver cancer, which has the characteristics of low trauma and high safety [5]. However, patients are prone to abdominal pain and liver function damage, which are not conducive to recovery [5]. Therefore, it is important to develop effective ways for improving the postoperative condition of primary liver cancer patients undergoing transcatheter arterial chemoembolization.

In recent years, traditional Chinese medicine (TCM) has shown unique advantages in the treatment of cancer-related adverse events, and according to TCM, the pathogenesis of cancer-related pain is the stagnation of stasis and toxins as well as the obstruction of qi and blood [6-9]. The common auricular point seed pressing therapy can stimulate the auricular acupuncture points and regulate the balance of the organism according to the characteristics of the meridians, so as to promote the circulation of qi, relieve pain and prevent diseases; however, its efficiency is low and the treatment cycle is longer when used alone [6-9]. In addition, Huaier granule, made from Huaier aqueous extract, is a kind of anticancer Chinese patent medicine containing a variety of organic ingredients, with the effects of activating the blood and enhancing the body resistance, which is widely used in postoperative adjuvant treatment of tumors [10]. A recent study reported that Huaier granule in the postoperative treatment of patients with viral hepatitis B-related liver cancer can enhance immunity and improve liver function of patients [11]. In addition, the combination of transcatheter arterial chemoembolization and Huaier granule has a significant effect on the treatment of primary liver cancer, which can prolong the patient's survival time, ameliorate their negative emotions, and improve their quality of life [12].

In this study, by observing and comparing the therapeutic efficacy of auricular point seed pressing alone or in combination with Huaier granule on patients with primary liver cancer after transcatheter arterial chemoembolization, we explored the application value of Huaier granule combined with auricular point seed pressing on primary liver cancer after transcatheter arterial chemoembolization, which can provide reference and guidance for the treatment of clinical primary liver cancer after transcatheter arterial chemoembolization.

2 Data and methods

2.1 Sample data collection

Clinical data of 80 patients with primary liver cancer treated in our hospital from March 2022 to March 2023 were retrospectively analyzed. 40 patients receiving Huaier granule combined with auricular point seed pressing therapy after transcatheter arterial chemoembolization were first allocated into the observation group, and 40 patients receiving auricular point seed pressing therapy after transcatheter arterial chemoembolization were assigned into the control group. There was no statistically significant difference in the comparison of gender, age, disease duration, tumor diameter and tumor staging in the two groups ($\rho > 0.05$), but these data were comparable, as shown in Table 1.

Table 1 Comparison of the sample data in two groups.

Groups	Cases	Gender (cases)		Age (years old)	Disease duration (years)	Tumor diameter (cm)	Tumor staging (cases)		
		Male	Female				Massive type	Nodular type	Diffuse type
Observation group	40	19	21	48.48 ± 9.33	2.50 ± 1.37	7.18 ± 1.25	21	8	11
Control group	40	20	20	49.40 ± 10.19	2.62 ± 1.65	7.22 ± 1.31	22	10	8
X^2/t		0.050		0.421	0.354	0.140		0.719	
p		0.823		0.675	0.724	0.889		0.698	

2.2 Inclusion and exclusion criteria

2.2.1 Inclusion criteria

(1) Patients who met the diagnostic criteria for primary liver cancer according to the Guidelines for the Diagnosis and Treatment of Primary Liver Cancer (2019 Edition) [13]. (2) Patients aged 14 to 70 years.

2.2.2 Exclusion criteria

(1) Patients whose expected survival no more than 3 months. (2) Patients with secondary liver cancer. (3) Patients who were allergic to the drugs used in this study. (4) Patients with other malignant tumors. (5) Patients with cardiac, hepatic, and renal organ insufficiency. (6) Those with coagulation disorders. (7) Patients with psychiatric disorders, and poor adherence to the treatment. (8) Patients with incomplete clinical data. (9) Pregnant and lactating women.

2.3 Treatment method

All patients underwent transcatheter arterial chemoembolization and were given routine postoperative symptomatic treatment including liver protection, hemostasis, and anti-infection. The patients in control group were given auricular point seed pressing therapy on the basis of abovementioned treatment. One day before surgery, acupoint selection was performed on one side of the auricular acupuncture points, with Shenmen, Gan, Zhen, Jiaogan, and Pizhixia as the main acupoints, taking E (frontal acupoint), Fu (abdomen acupoint), Dan (Biliary acupoint) as the matching acupoints according to the related symptoms. One day after surgery, acupoint selection was performed on contralateral auricle. The auricle was disinfected and tender points were sought and marked. During the intervention, the seed of cowherb was adhered in the center of a 0.6 cm × 0.6 cm adhesive tape, and was applied to the tender points, being alternated between the two ears and replaced once every 2-3 days. The ear acupoints were pressed until feeling bloating, numb, and painful, with flushing auricle, which was continuously performed 4-5 times a day for one month, with 1-2 minutes per time. On the basis of treatment in the control group, patients in observation group were continuously given Huaier granule (Qidong Gaitianli Pharmaceutical Co., Ltd, National Medical Products Administration (NMPA) Approval No.: Z20000109, Specification: 10 g) for 1 month (3 times/day, 20 g/time).

2.4 Observational indexes

2.4.1 Clinical efficacy

Clinical efficacy in the two groups was recorded and compared. The efficacy was assessed after 1 month of treatment, with reference to the assessment criteria for new response in solid tumors below. Complete remission: complete disappearance of lesions for more than 1 month; partial remission: shrinkage of original lesions ⩾ 50%, without new lesions for at least 1 month; stable: no new lesion, with original lesions enlarged < 25% or shrunk < 50% for more than 1 month; disease progression: the increase of lesions ⩾

25% or the appearance of new lesions [14]. Overall remission rate = (number of cases in complete remission + number of cases in partial remission)/total number of cases × 100%.

2.4.2 TCM symptom scores

TCM symptom scores in the two groups were collected and compared before treatment and after 1 month of treatment. According to the relevant standards in Guiding Principles for Clinical Research of New Chinese Medicines, the main symptomatic changes of the patients, such as discomfort in the liver area, lack of appetite and fatigue, abdominal distension and physical emaciation, were scored from 0, 1, 2, and 3 points according to the severity of the symptoms, and the higher scores indicated the more severe symptoms [15].

2.4.3 Liver function

Liver functions of patients in both groups were determined and compared before treatment and after 1 month of treatment. Before and after 1 month of treatment, 5 mL of fasting peripheral venous blood was drawn from patients in both groups in the early morning, stood at room temperature for 30-60 min and centrifuged at 3000 r/min for 10 min. Then, the serum was separated and stored at -20 ℃. The serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL) and albumin (ALB) were measured using an automatic biochemical analyzer from Shanghai Kehua Experimental Systems Co., Ltd.

2.4.4 Quality of life

The quality of life in the two groups before treatment and after 1 month of treatment was assessed using the Quality of Life Scale (SF-36) and compared. The scale was divided into eight aspects such as physical function, emotional function, and role physical, with a total of 36 entries and a total score of 100 points. The higher scores indicated the better quality of life [16].

2.4.5 Safety analysis

The incidence of adverse reactions in the two groups during the treatment period was collected and compared.

2.5 Statistical methods

Statistical analysis was performed using SPSS 20.0 and count data were expressed as cases (%). Intergroup comparisons were made using the X^2 test, and one-way ordered type count data were compared between groups using Wilcoxon rank sum test. Measurement data are expressed as mean ± standard deviation. Independent samples t-test was applied for the comparisons between two groups and paired samples t-test was adopted for the comparison of the same group before and after treatment. $p < 0.05$ was regarded as a statistically significant difference.

3 Results

3.1 The observation group was more clinically effective than the control group

The total remission rate in observation group was significantly higher than that in control group ($p < 0.05$), as displayed in Table 2.

3.2 The observation group showed lower TCM symptom scores compared with the control group

Before treatment, there was no statistically significant difference in TCM symptom scores of discomfort in liver region, lack of appetite and fatigue, abdominal distension and physical emaciation between the two groups ($p > 0.05$). After treatment, these TCM symptom scores in the two groups were obviously reduced ($p < 0.05$), and those in observation group were apparently lower than those in control group ($p < 0.05$). The results were listed in Table 3.

Table 2 Comparison of clinical efficacy between the two groups [cases (%)].

Groups	Cases	Complete remission	Partial remission	Stable	Disease progression	Total remission rate
Observation group	40	6 (15.00)	25 (62.50)	6 (15.00)	3 (7.50)	31 (77.50)
Control group	40	3 (7.50)	18 (45.00)	16 (40.00)	3 (7.50)	21 (52.50)
X^2						15.332
p						<0.001

Table 3 Comparison of TCM symptom scores between the two groups (mean ± standard deviation, point).

Groups	Cases	Discomfort in liver region		Lack of appetite and fatigue	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	2.55 ± 1.11	1.25 ± 0.59 *	2.80 ± 0.85	1.43 ± 0.50 *
Control group	40	2.45 ± 1.04	1.88 ± 0.79 *	2.85 ± 0.83	1.78 ± 0.73 *
t		0.416	4.041	0.266	2.502
p		0.679	<0.001	0.791	0.015
Groups	**Cases**	**Abdominal distension**		**Physical emaciation**	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	2.55 ± 0.50	1.38 ± 0.54 *	2.35 ± 0.48	1.33 ± 0.47 *
Control group	40	2.48 ± 0.51	1.75 ± 0.93 *	2.43 ± 0.50	1.73 ± 0.68 *
t		0.620	2.176	0.730	3.060
p		0.537	0.033	0.468	0.003

Note: vs. before treatment, * $p < 0.05$.

3.3 The observation group showed a better improvement of liver function compared with the control group

Before treatment, there was no statistically significant difference in the levels of ALT, AST, TBIL, and ALB between the two groups ($p > 0.05$). After treatment, the levels of ALT, AST, TBIL, and ALB in both groups were dramatically reduced ($p < 0.05$), and the levels in observation group were significantly lower than those in control group ($p < 0.05$). The results were displayed in Table 4.

3.4 The observation group showed a better improvement of life quality compared with the control group

There was no statistically significant difference in life quality scores of physical function, emotional function, role physical, mental health, social function, body pain, dynamism and overall health between the two groups before treatment ($p > 0.05$). After treatment, these quality of life scores in both groups were obviously increased ($p < 0.05$), and those in observation group were significantly higher than those in control group ($p < 0.05$). The results were shown in Table 5.

3.5 The two groups had no significant difference in adverse reactions

There was no statistically significant difference in the incidence of adverse reactions including gastrointestinal reactions, cutaneous hand-foot syndrome, lacking in strength, myelosuppression and hair loss between the two groups ($p > 0.05$). The results were exhibited in Table 6.

Table 4 Comparison of liver function between the two groups (mean ± standard deviation).

Groups	Cases	ALT (U/L)		AST (U/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	244.36 ± 55.28	82.22 ± 26.58 *	227.04 ± 45.11	88.46 ± 29.93 *
Control group	40	245.17 ± 54.08	161.47 ± 69.28 *	228.09 ± 48.67	144.28 ± 45.18 *
t		0.066	6.755	0.100	6.514
p		0.947	<0.001	0.921	<0.001
Groups	Cases	TBIL (μmol/L)		ALB (g/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	29.58 ± 6.24	23.11 ± 3.87 *	44.09 ± 4.71	33.13 ± 4.27 *
Control group	40	29.47 ± 6.59	26.16 ± 3.46 *	45.46 ± 4.74	37.84 ± 5.07 *
t		0.077	3.838	1.297	4.494
p		0.939	<0.001	0.199	<0.001

Note: vs. before treatment, * $p < 0.05$.

Table 5 Comparison of quality of life scores between the two groups (mean ± standard deviation, point).

Groups	Cases	Physical function		Emotional function	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	55.20 ± 3.43	61.03 ± 4.36 *	59.90 ± 3.76	64.38 ± 4.57 *
Control group	40	55.40 ± 2.91	58.15 ± 3.13 *	59.68 ± 3.63	61.73 ± 3.69 *
t		0.281	3.417	0.266	2.853
p		0.779	0.001	0.791	0.006
Groups	Cases	Role physical		Mental health	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	51.75 ± 5.50	57.98 ± 76.86 *	61.88 ± 3.87	69.33 ± 5.20 *
Control group	40	52.48 ± 4.99	54.95 ± 5.40 *	60.38 ± 3.94	64.20 ± 4.44 *
t		0.622	2.195	1.718	4.745
p		0.536	0.031	0.090	<0.001
Groups	Cases	Social function		Body pain	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	54.60 ± 2.93	65.38 ± 2.96 *	60.43 ± 4.72	68.90 ± 4.53 *
Control group	40	53.98 ± 3.31	61.60 ± 4.09 *	61.18 ± 4.70	65.65 ± 5.19 *
t		0.887	4.735	0.712	2.984
p		0.378	<0.001	0.479	0.004
Groups	Cases	Dynamism		Overall health	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	40	57.88 ± 4.25	64.95 ± 4.56 *	55.73 ± 2.91	62.10 ± 3.39 *
Control group	40	58.40 ± 3.96	62.65 ± 5.05 *	55.38 ± 2.96	58.45 ± 3.39 *
t		0.566	2.138	0.533	4.815
p		0.573	0.036	0.595	<0.001

Note: vs. before treatment, * $p < 0.05$.

Table 6 Comparison of adverse reactions between the two groups [cases (%)].

Groups	Gastrointestinal reactions	Cutaneous hand -foot syndrome	Lacking in strength	Myelosuppression	Hair loss	Total adverse reactions
Observation group	3 (7.50)	4 (10.00)	2 (5.00)	1 (2.50)	1 (2.50)	11 (27.50)
Control group	3 (7.50)	3 (7.50)	2 (5.00)	2 (5.00)	2 (5.00)	12 (30.00)
X^2						0.061
p						0.805

4 Discussion

In order to improve the clinical efficacy of primary liver cancer, this study discussed the curative effect of Huaier granule combined with auricular point seed pressing on primary liver cancer after transcatheter arterial chemoembolization. The results showed that Huaier granule combined with auricular point seed pressing in the treatment of primary liver cancer may have a good curative effect.

Primary liver cancer belongs to the categories of “mass in the abdomen” and ”mass in the liver” in TCM, and TCM symptoms include disturbance of the liver-qi, stagnation of qi and blood, and gathering dampness to form phlegm [17]. A decrease in TCM symptom scores indicates an improvement in the condition of the patients with primary liver cancer [17]. Our study suggested that the treatment of Huaier granule combined with auricular point seed pressing on primary liver cancer after transcatheter arterial chemoembolization can reduce the tumor lesions in patients and relieve abdominal distension and physical emaciation. The recovery of patients’ conditions was more obvious. Based on the performance of the human meridian acupoints and the relationship between the ear and internal organs and meridians, auricular point seed pressing is a therapy that the seed of cowherb was applied to adhere to the patient’s auricular acupuncture points, and the corresponding acupuncture points were stimulated through the maximum degree of pressure, thus promoting the movement of qi and blood in the body’s meridians to achieve the effects of dredging the channels and collaterals and regulating the yin and yang of the organs [18]. Huaier granule can inhibit the proliferation of tumor cells and induce the cell apoptosis [19]. This drug can also reverse the drug resistance of liver cancer cells, playing a role in killing these cells [20,21]. Likewise, Huaier granule can inhibit the invasion and metastasis of liver cancer cells by blocking the signaling pathway, reduce the regeneration of tumor blood vessels, and enhance the immune function of the body, and its therapeutic effect will be enhanced when combined with auricular point seed pressing [20,21]. Therefore, Huaier granule combined with auricular point seed pressing in the postoperative treatment of primary liver cancer patients undergoing transcatheter arterial chemoembolization may have a good curative effect, which can improve the symptoms of TCM.

ALT, AST, TBIL and ALB are commonly used in clinical assessment of liver function, and a decrease in their levels indicates an improvement in liver function [22]. This study confirmed that improvement of liver function in patients treated with Huaier granule combined with auricular point seed pressing was more obvious. Through auricular point seed pressing, Shenmen, Gan, Zhen, Jiaogan, and Pizhixia points are continuously stimulated to activate the twelve meridians, which exerts the efficacy of quenching evil heat in the liver, tonifying spleen, and normalizing gallbladder to cure jaundice, thus effectively relieving patients’ symptoms of liver depression, qi stagnation, and weakness of the spleen and the stomach, and improving the liver function [23]. Huaier granule can

enhance the activity of healthy cells and antioxidant capacity, induce the apoptosis of liver cancer cells, inhibit the body's oxidative stress response, promote the regeneration of liver cells, and accelerate the recovery of liver function [24,25]. Huaier granule contain the components of polyglycoprotein, which can promote the production of specific antibodies, enhance the activity of immune cells, effectively regulate liver function microcirculation, and improve the function of the liver [24,25]. Hence, Huaier granule combined with auricular point seed pressing in the treatment of primary liver cancer after transcatheter arterial chemoembolization may be conducive to recovering patients' liver function.

According to the results in our study, Huaier granule combined with auricular point seed pressing in the treatment of primary liver cancer after transcatheter arterial chemoembolization can significantly improve patients' quality of life. The reason may be that the complications and pain brought by the surgical treatment have reduced the patients' quality of life to a certain extent, and auricular point seed pressing therapy has the effects of calming the mind and relieving the pain at the acupuncture points [26]. Huaier granule can effectively inhibit the activity of the cancer cells, enhance the immune function of the body, and reduce the damage of the disease to the liver [27,28]. Our findings showed that their combined treatment can enhance the therapeutic effect. Thus, Huaier granule combined with auricular point seed pressing in the treatment of primary liver cancer after transcatheter arterial chemoembolization may be beneficial to improving the patients' quality of life.

During transcatheter arterial chemoembolization, due to the use of a large number of chemotherapy drugs and contrast agents, psychological factors such as fear and tension, direct stimulation of blood vessels, and decreased blood sugar regulation ability, patients may experience some adverse reactions, such as gastrointestinal reactions and lacking in strength [29]. In addition, our results presented that during the treatment period, Huaier granule combined with auricular point seed pressing in the treatment of primary liver cancer after transcatheter arterial chemoembolization did not increase the occurrence of adverse reactions, including gastrointestinal reactions and cutaneous hand-foot syndrome, with a high safety.

Due to the limited review time and number of sample cases in this study, our results were contingent and insufficient to represent the situation of all patients, and the long-term therapeutic effects of Huaier granule combined with auricular point seed pressing need to be further experimented and explored.

In conclusion, Huaier granule combined with auricular point seed pressing in the treatment of primary liver cancer after transcatheter arterial chemoembolization may have a good curative effect, which can improve the symptoms of TCM and contribute to recovering patients' liver function and improving their quality of life, with a high safety.

Acknowledgements

Not applicable.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization, G.L.; Data curation, X.S.; Formal analysis, G.L.; Methodology, X.S.; Writing-Original draft, G.L.; Writing-review and editing, X.S.; All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee, and the patients were informed and

consented.

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Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Material

Not applicable.

References

[1] Ma L, Wang B, Long Y, et al. Effect of traditional Chinese medicine combined with Western therapy on primary hepatic carcinoma: a systematic review with meta-analysis. *Frontiers in Medicine* 2017; 11(2): 191-202.

[2] Pu Q, Yu L, Wang X, et al. Immunomodulatory Effect of Traditional Chinese Medicine Combined with Systemic Therapy on Patients with Liver Cancer: A Systemic Review and Network Meta-analysis. *Journal of Cancer* 2022; 13(11): 3280-3296.

[3] Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians* 2021; 71(3): 209-249.

[4] Liu K, Liu Y, Song H, et al. Application of traditional Chinese medicine and hyperbaric oxygen after TACE for treatment of patients with primary liver cancer. *Journal of Practical Liver Disease* 2020; 23(5): 755-756.

[5] Wang H, Pan Y, Xia J, et al. Clinical effect of transcatheter arterial chemoembolization in treatment of primary liver cancer: application and research advances. *Journal of Clinical Hepatology* 2018; 34(2): 414-418.

[6] Ni M, Wang H, Wang M, et al. Investigation on the Efficiency of Chinese Herbal Injections for Treating Non-small Cell Lung Cancer with Vinorelbine and Cisplatin Based on Multidimensional Bayesian Network Meta-Analysis. *Frontiers in Pharmacology* 2021; 11: 631170.

[7] Wang D, Wu C, Liu D, et al. Ginsenoside Rg3 Inhibits Migration and Invasion of Nasopharyngeal Carcinoma Cells and Suppresses Epithelial Mesenchymal Transition. *BioMed Research International* 2019; 2019: 8407683.

[8] Sun C, Dong F, Xiao T, et al. Efficacy and safety of Chinese patent medicine (Kang-ai injection) as an adjuvant in the treatment of patients with hepatocellular carcinoma: a meta-analysis. *Pharmaceutical Biology* 2021; 59(1): 472-483.

[9] Li L, Tan W, Qin J, et al. The Intervention Study of Auricular Point Press on Malignant Tumor Patients in Middle and Advanced Stage. *Journal of Hunan University of Chinese Medicine* 2016; 36(7): 68-70.

[10] Chen Q, Shu C, Laurence AD, et al. Effect of Huaier granule on recurrence after curative resection of HCC: a multicentre, randomised clinical trial. *Gut* 2018; 67(11): 2006-2016.

[11] Zhang L, Lu H. Clinical Observation on Huaier Granule in Postoperative Treatment of Patients with Viral Hepatitis B-Related Liver Cancer. *Modern Medicine and Health Research* 2023; 7(8): 25-28.

[12] Wang R. Observation on Therapeutic Effect of Transcatheter Arterial Chemoembolization Combined with Huaier Granule on Primary Liver Cancer. *Contemporary Medicine Forum* 2022; 20(10): 60-62.

[13] Guidelines for the Diagnosis and Treatment of Primary Liver Cancer (2019 Edition). *Infectious Disease Information* 2020; 33(6): 481-500.

[14] Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *European Journal of Cancer* 2009; 45(2): 228-247.

[15] National Administration of Traditional Chinese Medicine. *Guiding Principles for Clinical Research of New Chinese Medicines*; China Medical Science and Technology Press: Beijing, China, 2002; pp. 208-216.

[16] Lins L, Carvalho FM. SF-36 total score as a single measure of health-related quality of life: Scoping review. *SAGE Open Medicine* 2016; 4: 2050312116671725.

[17] Zhong H, Liu X, Fei X, et al. Clinical observation of Huaier Granule combined with microwave ablation assisted endoscopic Hepatectomy in the treatment of primary liver cancer. *Chinese Science and Technology of Traditional Chinese Medicine* 2022; 29(6): 1046-1047.

[18] He K, Xiong Y, Zhang W. Effects of Zhenqi Fuzheng Capsules combined with auricular point seed pressing in patients with advanced primary liver cancer. *Northwest Pharmaceutical Journal* 2023; 38(3): 189-195.

[19] Liu Y, Zhang YJ, Li BY, et al. Effects of Huaier Particles on the proliferation and apoptosis of human ovarian cancer

SKOV3 cells in vitro. *Tumor* 2016; 36(6): 644-649.

[20] Dong D, Liu Z. Research advances in Huai'er granules combined with transarterial chemoembolization in treatment of hepatocellular carcinoma. *Journal of Clinical Hepatobiliary Disease* 2017; 33(10): 2021-2024.

[21] Zhao GS, Liu Y, Zhang Q, et al. Transarterial chemoembolization combined with Huaier granule for the treatment of primary hepatic carcinoma: Safety and efficacy. *Medicine* 2017; 96(29): e7589.

[22] Liu CG, Wang XL, Jiang DY, et al. Effects of Gandakang (GDK) on ALT, AST, TP, ALB and TBIL in Serum of Hepatic Injury Rats Induced by DMN. *Information on Traditional Chinese Medicine* 2012; 29(4): 74-76.

[23] Ji J, Wei G, Yin G, et al. Clinical observation on auricular points plaster therapy in treating adverse reactions of primary liver cancer after TACE. *Western Traditional Chinese Medicine* 2020; 33(10): 124-126.

[24] Wang C, Li L, Sun C. Effect of Huaier Granules on liver function, T lymphocytes and quality of life in patients with liver cancer after operation. *Journal of Integrated Traditional Chinese and Western Medicine in Hepatology* 2022; 32(7): 610-613.

[25] Yang Z, Liao X, Lu Y, et al. Add-On Therapy with Traditional Chinese Medicine Improves Outcomes and Reduces Adverse Events in Hepatocellular Carcinoma: A Meta-Analysis of Randomized Controlled Trials. *Evidence-Based Complementary and Alternative Medicine* 2017; 2017: 3428253.

[26] Chi CY, Fu YH, Zhi M. Treatment of 60 Cases of Neurogenic Headache with Simple Auricular Point Sticking. *Journal of Changchun University of Chinese Medicine* 2013; 29(6): 1066-1067.

[27] Zhou XC, Zhu AL. Research Progress in Mechanism of Huaier Granule against Colorectal Cancer. *Medical Recapitulate* 2021; 27(20): 4041-4045.

[28] Wang CJ, Li L, Sun C. Effect of Huaier Granules on liver function, T lymphocytes and quality of life in patients with liver cancer after operation. *Chinese Journal of Integrated Traditional and Western Medicine on Liver Diseases* 2022; 32(7): 610-613.

[29] Shao SD, Li HS, Zhang XJ. Observation and nursing of adverse reactions during TACE in patients with primary liver cancer. *China Foreign Medical Treatment* 2009; 28(33): 150.