

Management of Primary Hepatic Carcinoma by Traditional Chinese Medicine

Cheng Jinlai^{1*}, Leng Jing¹ and Xia Meng²

¹Guangxi University of traditional Chinese Medicine, China

²Basic Medical School of Guangxi University of Traditional Chinese Medicine, China

*Corresponding author: Cheng Jinlai, PhD Student, Guangxi University of Traditional Chinese Medicine, China, Tel: 15677163660; E-mail: 479484528@qq.com

Rec date: August 30, 2018; Acc date: September 08, 2018; Pub date: September 17, 2018

Copyright: © 2018 Jinlai C, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Citation: Jinlai C, Jing L, Meng X (2018) Management of Primary Hepatic Carcinoma by Traditional Chinese Medicine. Herb Med. Vol.4 No.2:04.

Abstract

Primary hepatic carcinoma is one of the types with high incidence of cancer. It has the characteristics of hidden disease, long incubation period, rapid development and easy metastasis, and the prognosis is poor, which seriously affects the quality of life of patients. Although much progress has been made in its research, the complex mechanisms of its onset and deterioration are not fully understood. This article summarizes the diagnosis and treatment of primary liver cancer in modern medicine and traditional Chinese medicine and provides the future prospects for the treatment of primary liver cancer from the perspective of overall and personalized Chinese medicine.

Keywords: Primary hepatic carcinoma; Traditional chinese medicine treatment; Western medicine treatment.

- Non-viral factors: excessive drinking causes cirrhosis and is easily degraded to liver cancer [7]; lower doses of aflatoxin (AFT) in moldy food can cause DNA genetic information to be wrong, leading to genetic mutations that induce liver cancer; Contamination of blue-green algae toxins in unclean drinking water can also induce liver lesions to liver cancer.

Due to the special physiological characteristics of the liver, the molecular mechanism of liver cancer is complex, including:

- Activation of proto-oncogenes and inactivation of tumor suppressor genes [8]. Common proto-oncogenes mainly include N-ras and HBVx [9], the tumor suppressor genes mainly include p53, Rb, p21 and PTEN [10], and the proto-oncogene and tumor suppressor gene maintain a dynamic balance in normal physiological conditions.
- Abnormal activation of multiple molecular signaling pathways: Abnormal activation of Wnt/ β -catenin signaling pathway may promote liver cancer [7]; Hedgehog signaling pathway is not expressed in mature normal liver tissue, but in liver cancer cells Abnormally active expression [11]; Other signaling pathways, such as Notch signaling pathway, mitogen-activated protein kinase (MAPK) pathway, AKT signaling pathway and extraregulatory protein kinase (ERK) signaling pathway, are important in the process of liver cancer Regulatory pathway.
- Related protein expression: such as proliferating cell antigen and stathmin 1, 14-3-3 γ are highly expressed in liver cancer cells, and liver cancer may be related to abnormal expression of certain growth factors in the body.

Traditional Chinese Medicine (TCM) usually includes a personalized diagnosis and an herbal formula using 10-20 separate herbal ingredients selected from thousands of herbal material medicines that can be used as boiled water decoctions, dried herbs extract or as a pill [12]. The principles of diagnosis and treatment are based on the understanding of the pathology of Chinese medicine. A good TCM practice is generally considered to require a TCM syndrome model based on clinical performance, and then an individualized Chinese herbal decoction suitable for addressing each patient-specific TCM model [13]. As treatment will change with changes in TCM patterns and clinical performance. TCM is a dynamic,

Introduction

Primary hepatic carcinoma (PHC) is characterized by high morbidity and mortality. It is the fifth most common malignant tumor in the world, ranking third in the cause of cancer death. More than 500,000 people worldwide suffer from liver cancer every year. More than half of them are in China and have shown a clear upward trend [1].

The occurrence of PHC is a multi-factor cumulative result, the cause of which is not fully understood, mainly related to the following factors:

- Hepatitis virus: mainly Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV), especially in vivo the role of viral infection and the external environment [2]. HBV DNA and HCV RNA are the main causes of liver cancer [3,4], and HBV surface antibody (HBsAg) and surface e-antibody (HBeAg) in patients' serum are closely related to the occurrence of liver cancer [5,6]. Further deterioration of the hepatitis virus will lead to liver fibrosis and eventually to liver cancer.

highly responsive medical system that is increasingly emphasized in systems biology strategies with the use of multiple methods for optimal diagnosis and individualized treatment to account for variable responses to modern drugs.

In the TCM theory, the incidence of PHC is mostly caused by emotions, diet or toxins, resulting in visceral qi deficiency, qi ji dysfunction, and wet phlegm, and phlegm. According to the TCM treatment of PHC, the doctors of previous generations classified the liver cancer into Chinese medicine models (phenotypes) with different characteristics according to their clinical manifestations. Some scholars [14] compiled the Chinese medicine research articles on PHC from CNKI from 1979 to 2010, showing that there are 33 types of PHC, including stagnation of liver-QI with deficiency of the spleen, qi-stagnancy and blood stasis, hepatocholic hydropyrexia, deficiency of liver-yin and kidney-yin. Types are more common, which requires different treatments for Chinese medicine. This article summarizes the theory and treatment of PHC in modern medicine and traditional Chinese medicine and provides the future prospects for PHC treatment from the perspective of system biology.

Diagnosis of PHC

The incidence of PHC is high, which seriously threatens the life and health of patients. Therefore, early screening and improving the accuracy of diagnosis are of great significance to improve the survival rate of patients. Alpha fetoprotein (AFP) is a single chain serum glycoprotein. It is secreted by the yolk sac and liver in the early development of the fetus, and the blood content is very low in healthy adults. AFP has been an important clinical tool for detecting hepatocellular carcinoma since 1970's when researchers found that AFP was elevated in the serum of patients with hepatocellular carcinoma. However, in recent years, more and more PHC patients with negative AFP have been found, and a large number of missed diagnoses have been found in clinical work. People are increasingly suspicious of its sensitivity and specificity in screening and diagnosis of liver cancer. Therefore, it is of great significance for early diagnosis of PHC and guiding clinical diagnosis and treatment to put forward more meaningful serum tumor markers and adopt a variety of indicators for joint detection.

Alpha fetoprotein Variant 3 (AFP-L3) is unique to HCC cells. In recent years, AFP-L3 has been increasingly recognized as the diagnostic marker of sensitivity over AFP [15]. Abnormal prothrombin (DCP) is carboxylated in liver microsomes catalyzed by Vit K-dependent glutamyl and γ -carboxylase. In recent years, it has been found that the expression of DCP is closely related to the size and number of hepatocellular carcinoma lesions and whether there is intrahepatic or extrahepatic metastasis.

Golgi transmembrane glycoprotein 73 (GP73) levels are significantly elevated in the serum of patients with liver cancer, which is of great significance for the diagnosis of liver cancer [16]. DKK1 is a secreted inhibitory factor, which is closely related to Wnt signaling pathway. Wnt signaling plays an important role in the occurrence and development of

hepatocellular carcinoma. α -L-fucosidase (AFU) is a lysosomal acid hydrolase that is mainly involved in the catabolism of fucose-containing carbohydrate complexes, which are widely present in mammals, in liver and kidney. The highest activity in tissues. When hepatocytes become cancerous, serum AFU levels rise, making it an important marker of liver cancer. Alkaline phosphatase (ALP) is an enzyme that is excreted through the liver to the outside of the gallbladder. It is widely distributed in tissues such as the liver, bones, intestines, kidneys, and placenta, and is distributed more in the liver and bones. Under normal conditions, ALP binds tightly to the liver cell membrane and levels in serum are low. When hepatocytes become cancerous, hepatocytes overproduce ALP. Due to poor excretion in the intrahepatic biliary tract, ALP reversely flows into the blood and causes the expression of serum ALP to increase significantly, which makes it have a certain diagnostic value for PHC.

Glypican 3 (GPC3) is a heparan sulfate glycan protein that plays an important role in the proliferation and metastasis of liver cancer cells [17]. Transforming growth factor β 1 (TGF- β 1) is an important regulator that strongly inhibits the proliferation of hepatocytes. Studies have shown that TGF- β 1 can promote the growth of tumor cells by inhibiting the growth of paraneoplastic cells, and its serum level is negatively correlated with the occurrence of hepatocellular carcinoma. Carcinoembryonic antigen (CEA) is an acid glycoprotein study [18], CEA is an independent predictor of hepatocellular carcinoma through epithelial-mesenchymal transition and tumor angiogenesis recurrence. Cancer antigen 125 (CA125) is derived from glycoproteins in the body cavity of embryonic development. When the body becomes cancerous, the level of CA125 is increased, which plays a crucial role in the early detection of tumors. CA199 is a non-specific tumor-associated oligosaccharide antigen, which is extremely low in healthy people. In many epithelial malignancies differentiated from endoderm cells, serum CA199 levels can be significantly increased.

CA153 is a very specific and important specific marker for the diagnosis of breast cancer, which is closely related to human breast cancer. Serum ferritin (Fer) is a complex formed by deferoxin and iron core Fe^{3+} . It is synthesized in the liver and has the function of storing iron and regulating iron metabolism. When the liver is damaged or cancerous, it is released into the blood in large quantities, resulting in an increase in the level of Fer in the blood. Fer is increasingly being used to diagnose liver cancer. Tumor-specific growth factor (TSGF) is a polypeptide substance produced by tumor cells and closely related to the growth, invasion and metastasis of tumor cells. Therefore, the early metastasis and recurrence of tumors can be judged by measuring the level of TSGF in serum.

At present, the main joint detection methods include: joint detection of AFP, AFP-L3, DCP [19]; joint detection of AFP, DCP, GP73 [20]; joint detection of AFP, DCP, DKK1 [21]; AFP, AFU, Combined detection of ALP [22]; AFP, GPC3, TGF- β 1 combined detection [23]; AFP, CEA, CA125, CA199 combined detection [24]; AFP, CEA, Fer, CA153, CA125, CA199, TSGF combination

Detection [25]. These combined tests have greatly improved the diagnostic rate of primary liver cancer.

Treatment of PHC in Modern Medicine

Modern treatment of PHC usually includes: (1) surgery, minimally invasive interventional therapy and liver transplantation; (2) radiotherapy and chemotherapy; (3) biopharmaceutical treatment; (4) cardiac adjuvant therapy.

Surgery and minimally invasive interventional techniques for the treatment of PHC

Surgical resection of PHC is currently the most widely used radical treatment. Early PHC surgery has a good prognosis and high survival rate after surgery. In the middle and late stage PHC, especially large liver cancer or multiple cancer, the rate of radical resection is low, and the prognosis is poor [26]. According to the statistical analysis [27], the survival rate within 5 years after PHC resection is less than 40%, and the recurrence and metastasis rate is as high as 70%.

Interventional therapy is another important method after surgical treatment, mainly for transcatheter arterial chemoembolization (TACE), which has less effect on postoperative depression than surgery. Shi YZ [28] compared the anxiety and depression of patients with PHC after surgical resection and TACE combined with microwave ablation (PMCT). The incidence of anxiety and depressive symptoms in the PMCT group was significantly lower than that in the surgical resection group. However, TACE is a topical treatment, making it less desirable for long-term clinical efficacy of PHC, and the tumor recurrence rate is still high. Liver transplantation is currently considered to be an effective method for the treatment of end-stage liver disease with PHC, but the survival rate of liver transplant patients after liver transplantation is still not very high [29].

Radiofrequency ablation (RFA), as an interventional therapy, can well control local tumors and is more effective in combination with partial hepatectomy. With the continuous development of science and technology, RFA has significantly expanded the surgical indications of patients with primary liver cancer and improved the survival rate of patients [30]; the study found that [31] focused on the HCC perioperative patients, can significantly reduce Patients with anxiety and depression improve the patient's sleep quality and improve patient compliance, but the size of the tumor is a major limitation for the implementation of RFA.

Radiotherapy and chemotherapy for the treatment of PHC

Current methods of radiotherapy include: three-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), and image-guided radiotherapy (IGRT), such as TOMO and cyberknife. These new methods can make the energy radiation area consistent with the tumor, irradiate

the tumor, and have little damage to the surrounding normal tissue. The treatment research of IMRT and IGRT has become a hot issue [32].

For patients with PHC who are both inoperable and unable to intervene in the advanced stage, it is currently considered that systemic chemotherapy is superior to general supportive therapy without obvious contraindications. Currently commonly used chemotherapy drugs are: fluorouracil and its derivatives, platinum drugs, anthracyclines, mitomycin, hydroxycamptothecin, gemcitabine and so on. However, patients with advanced HCC have a very poor prognosis, with a natural course of only 4-8 months. Systemic chemotherapy is ineffective and does not significantly prolong the survival time of patients [33].

Biopharmaceutical treatment of PHC

Biopharmaceutical treatment PHC has also been widely carried out, including: molecular targeted therapy, gene therapy, immunotherapy and many other aspects. Biotherapy is to enhance the body's immunity by regulating the physiological functions of the body, inhibiting the growth of tumor cells, improving the survival rate of patients and reducing the recurrence rate of tumors. However, most biotherapeutic techniques are still immature and still need to be developed [34]. Most studies [35,36] found that postoperative drug intervention has a good effect on PHC.

Postoperative neuropsychiatric treatment

As a kind of adjuvant therapy, psychotherapeutic therapy has been widely used in clinical nursing. Postoperative psychological rehabilitation of patients can significantly improve the mood and life treatment of patients and improve the prognosis of patients. Studies have shown that, mental intervention can improve the patient's postoperative anxiety, depression and other emotions, and help patients recover [37].

Chinese Medicine Treatment PHC

The causes of PHC in traditional Chinese medicine are mostly caused by emotions, diet or toxins, resulting in viscera deficiency of vital energy, the movement imbalance of gas and wet, blood stasis, and sputum. Liver Qi stagnation is the root cause, leading to the occurrence and development of liver cancer. From the current research literature, the main pathogenesis of PHC concurrency depression can be summarized as stagnation of liver-Qi with deficiency of the spleen, Qi-stagnancy and blood stasis, dampness and heat accumulation, deficiency of liver-yin and kidney-yin, and when the body's positive Qi is weak, Qi, blood, phlegm, stasis, poison and dampness are linked to the viscera. Therefore, the treatment strategies of Chinese medicine include invigorating the spleen and invigorating Qi and relieving the stagnation of the liver; Qi activating blood circulation, removing stasis and eliminating accumulation; antipyretic, diarrhea and detoxification; nourishing water and culvert and relieving stagnation of liver.

Treatment of primary liver cancer according to Chinese medicine mode

TCM syndrome differentiation is a method to analyze and characterize the clinical manifestations of diseases. It is a process that takes into account the geographical location,

nature, occurrence and development of pathological and pathogenic factors. Once the specific syndrome of the PHC patient is determined, specific treatments will be used to correct or alleviate the patient's disease symptoms. **Table 1** provides a summary of the typical TCM classification of PHC and its subsequent treatment.

Table 1 The typing, prescription, and treatments for different syndromes of PHC.

Prescription	Medicinal herb ingredients
Stagnation of liver-QI with deficiency of the spleen	
Xiaoyao San	Bupleuri Radix, Angelicae Sinensis Radix, Paeoniae Radix Alba, Menthae Haplocalycis Herba, Poria, Atractylodis Macrocephalae Rhizoma, Glycyrrhizae Radix Et Rhizoma.
Shugan Jieyu Capsule	Hyperici Perforati Herba, Acanthopanax Senticosi Radix Et Rhizoma Seucaulis.
Jianpi Fuzheng Soup	Astragali Radix, Codonopsis Radix, Atractylodis Macrocephalae Rhizoma, Poria, Glycyrrhizae Radix Et Rhizoma, Citri Reticulatae Pericarpium, Aurantii Fructus, Pinelliae Rhizoma, Bambusae Caulis in Taenias, Coicis Semen, Ligustri Lucidi Fructus, Dendrobii Caulis.
Chaihu Shugan Powder	Citri Reticulatae Pericarpium, Bupleuri Radix, Chuanxiong Rhizoma, Cyperi Rhizoma, Aurantii Fructus, Paeoniae Radix Alba, Glycyrrhizae Radix Et Rhizoma.
Invigorating Spleen and Removing Stasis Prescription	Astragali Radix, Pseudostellariae Radix, Atractylodis Macrocephalae Rhizoma, Poria, Spraganii Rhizoma, Polygoni Cuspidati Rhizoma Et Radix, Curcumae Rhizoma Citri Reticulatae Pericarpium Viride, Citri Reticulatae Pericarpium, Citri Sarcodactylis Fructus, Akebiae Caulis, Tetrastigma hemsleyanum Diels et Gilg, Hedyotis diffusa, Toad skin, Scutellariae Barbatae Herba, Pinelliae Rhizoma, Hordei Fructus Germinatus, Coicis Semen, Setariae Fructus Germinatus, Galli Gigerll Endothelium Comeum.
Bupleurum and Peony Six Gentlemen Decoction	Bupleuri Radix, Paeoniaeradix Rubra, Codonopsis Radix, Atractylodis Macrocephalae Rhizoma, Poria, Pinelliae Rhizoma, Citri Reticulatae Pericarpium, Cuspidati Rhizoma Et Radix, Curcumae Radix, Germinatus, Trionycis Carapax, Scorpio, Glycyrrhizae Radix Et Rhizoma.
Capsule of the Heart	Curcumae Rhizoma, Edible tulip, Bruceae Fructus Strychni Semen, Vespaenidus
Soft Liver and Lidan Decoction	Bupleuri Radix, Scutellariae Radix, Pinelliae Rhizoma, Ginseng Radix Et Rhizoma Rubra, hypericum japonicum Thunb, Sedum sarmentosum Bunge. The root of red-rooted salvia, Carapax, Concha ostreae, Selfneal, Edible tulip, the bulb of fritillary Corydalis tuber, Curcumae Longa Rhizoma, Glycyrrhizae Radix Et Rhizoma.
Powder for Regulating Liver and Spleen	Persicae Semen, Carthami Flos, Angelicae Sinensis Radix, Rehmanniae Radix, Achyranthis Bidentatae Radix, Chuanxiong Rhizoma, Platycodonis Radix, Paeoniaeradix Rubra, Aurantii Fructus, Glycyrrhizae Radix Et Rhizoma, Bupleuri Radix.
Qi-Stagnancy and Blood Stasis	
Infra-diaphragmatic Expelling Decoction	Stasis- Chuanxiong Rhizoma, Angelicae Sinensis Radix, Tree Peony Bark, Paeoniaeradix Rubra, Persicae Semen, Carthami Flos, Curcumae Radix, Cyperi Rhizoma, Bupleuri Radix, Glycyrrhizae Radix Et Rhizoma.
Bai Dan Shugan Recipe	Lilii Bulbus, The root of red-rooted salvia, Trichosanthis Fructus, Bupleuri Radix, Cyperi Rhizoma, Atractylodis Macrocephalae Rhizoma, Astragali Radix, Crataegi Fructus, Magnoliae Officinalis Cortex Paeoniae Radix Alba, Galli Gigerll Endothelium Comeum Angelicae Sinensis Radix, Curcumae Radix, Artemisiae Scopariae Herba, Rhei Radix Et Rhizoma.
Clearing Liver and Removing Stasis	Scutellariae Barbatae Herba, Hedyotis diffusa, Spraganii Rhizoma, Curcumae Rhizoma Astragali Radix.
Xuefu Zhuyu Decoction	Persicae Semen, Carthami Flos, Angelicae Sinensis Radix, Rehmanniae Radix, Achyranthis Bidentatae Radix, Chuanxiong Rhizoma, Platycodonis Radix, Paeoniaeradix Rubra, Aurantii Fructus, Glycyrrhizae Radix Et Rhizoma Bupleuri Radix.
AiTongXiao Granule	Angelicae Sinensis Radix, Chuanxiong Rhizoma, Paeoniaeradix Rubra, Hedyotis diffusa, Scutellariae Barbatae Herba, Astragali Radix.
Bupleurum Soothing Liver and Peach Red Siwu Soup	Bupleuri Radix Citri Reticulatae Pericarpium, Chuanxiong Rhizoma, Aurantii Fructus, Cyperi Rhizoma, Paeoniae Radix Alba, Persicae Semen, Carthami Flos, Angelicae Sinensis Radix, Tree Peony Bark, Rehmanniae Radix, Astragali Radix, Pseudostellariae Radix, Atractylodis Macrocephalae Rhizoma, Poria, Glycyrrhizae Radix Et Rhizoma.
Ruangan Compound	Artemisiae Scopariae Herba, Polygoni Cuspidati Rhizoma Et Radix, Curcumae Radix, Citri Sarcodactylis Fructus. The root of red-rooted salvia, Paeoniaeradix Rubra, Scutellariae Barbatae Herba, Hedyotis diffusa, Phyllanthus urinaria L, Ganoderma atrum, Sophorae Ronkinensis Radix Et Rhizoma, Atractylodis Macrocephalae Rhizoma, Poria, Trionycis Carapax, Manis Squama.
Xiao Ji Huayu pill	Panacis Quinquifolii Radix, Scutellariae Barbatae Herba, Cervi Cornus Colla, Aquilariae Lignum Resinatum, Bombyx batryticatus, Curcumae Rhizoma, pseudo-ginseng, Scorpio, Scolopendra, Dendrobii Caulis Vespaenidus.
Dampness and Heat Accumulation	
Pill of Eight Treasures	Bovisc Alculus, Snake gall Saigae Tataricae Cornu, pearl pseudo-ginseng, musk.

Artemisia Gardenia Qinggan Pill	Artemisiae Annuae Herba, Gardenia jasminoides EllisMagnoliae Officinalis Cortex, Coicis SemenBupleuri RadixCorydalis Rhizoma, Scutellariae Barbatae Herba, Glycyrrhizae Radix Et Rhizoma, Codonopsis Radix.
Capsule of the Heart	Curcuma Rhizoma, Edible tulip, Bruceae Fructus, Strychni Semen, Vespaenidus.
Deficiency of Liver-yin and Kidney-yin	
Bushen Jianpi Recipe	Rehmanniae Radix Praeparata, Corni Fructus, Dioscoreae Rhizoma, Codonopsis Radix, Poria, Alismatis Rhizoma, Tree Peony Bark, Glycyrrhizae Radix Et Rhizoma.
Huazheng Sanji Prescription	Scolopendra, Wall lizard, Scutellariae Barbatae Herba, Cuspidati Rhizoma Et Radix, Rehmanniae Radix, Rhei Radix Et Rhizoma, Arecae Pericarpium, Paeoniae Radix Alba, Glycyrrhizae Radix Et Rhizoma.
Yiguan Jian	Rehmanniae Radix, Ltoll Fructus. The root of straight ladybell, Ophiopogonis Radix, Angelicae Sinensis Radix, Toosendan Fructus, Anemarrhenae Rhizoma, Trionycis Carapax, Poria, Glycyrrhizae Radix Et Rhizoma.

Invigorating the spleen and invigorating qi and relieving the stagnation of the liver: This type is the main type of liver cancer, the clinical manifestations of two rib pain, bloating pain, general weakness, low spirit pessimism, insomnia and more dreams. The main pathogenesis is due to obstruction of liver Qi, resulting in dysfunction of the spleen and stomach, leading to liver depression and spleen deficiency. Treatment method is invigorating the spleen and invigorating Qi and relieving the stagnation of the liver. Chinese medicine prescriptions commonly used in clinic include: Xiaoyao San [38], Shugan Jieyu capsule [39], Jianpi Fuzheng soup [40], Chaihu shugan powder [41], Invigorating spleen and removing stasis prescription [42], Bupleurum and Peony Six Gentlemen Decoction [43], Capsule of the heart [44], Soft liver and Lidan Decoction [45], Powder for Regulating Liver and Spleen [46]. However, the clinical use of traditional Chinese medicine combined with minimally invasive surgery is now more effective than traditional Chinese medicine or surgery.

Qi activating blood circulation, removing stasis and eliminating accumulation: The main clinical manifestations of this type of patients are hypochondriac rib pain, dark complexion, restlessness, emotional depression, thinking and movement retardation, purple tongue, etc. The main pathogenesis is stagnation of liver Qi and Qi stagnation, and the gas machine is not smooth. The result was blood stasis. Treatment method is qi activating blood circulation, removing stasis and eliminating accumulation. Treatment method is invigorating the spleen and invigorating Qi and relieving the stagnation of the liver. Chinese medicine prescriptions commonly used in clinic include: Infra-diaphragmatic stasis-expelling decoction [47], Bai Dan Shugan recipe [48], clearing liver and removing stasis [49], Xuefu zhuyu decoction [50], Ai Tong Xiao Granule [51], Bupleurum soothing liver and peach red Siwu soup [52], Ruangan compound [53], Xiao Ji Huayu pill [54].

Antipyretic, diarrhea and detoxification: The main clinical manifestations of this type of patients are: heavy body weight, irritability, depression, fever, thirst, insomnia, dizziness and nausea, unclean defecation, less urine and yellow and yellowish tongue. The main pathogenesis is stagnation of liver Qi and Qi stagnation, the internal heat of the body, internal heat injury, resulting in poor movement of body fluid, stopping in the viscera, turning to damp heat, and disturbing the disease of the viscera. Treatment method is antipyretic,

diarrhea and detoxification. Chinese medicine prescriptions commonly used in clinic include: Pill of Eight Treasures [55], Artemisia Gardenia Qinggan pill [56], Capsule of the heart [57].

Nourishing water and culvert and relieving stagnation of liver: The clinical manifestations of this type of patients are mainly emaciation, asthma, anorexia, thirst, oliguria, upset, insomnia, tongue red, and no moss. Its pathogenesis is liver dysfunction, stagnation of Qi and stagnation of liver Qi, leading to internal heat, and then internal heat damages body fluid, resulting in Yin deficiency of liver and kidney. Treatment method is nourishing water and culvert and relieving stagnation of liver. Chinese medicine prescriptions commonly used in clinic include: Bushen Jianpi recipe [58], Huazheng Sanji prescription [59], Yiguan Jian [60].

Experimental study on the treatment of primary liver cancer with Chinese medicine monomer

Inhibit the proliferation of liver cancer cells: Normal cell proliferation is regulated by the body, and the formation of tumors is an infinitely proliferating process in which cells are not controlled. Inhibition of hepatocarcinoma cell proliferation assay is a basic study of the mechanism of action of anti-hepatocarcinoma drugs. Traditional Chinese medicine can inhibit the growth and proliferation of abnormal hepatocytes by regulating the expression of abnormal genes and the level of cytokines. Studies have found that Chinese medicine monomers that can inhibit the proliferation of liver cancer cells include: Curcumin [61], Dihydroartemisinin [62], and Diterpenoids in JD [63].

Inducing apoptosis of liver cancer cells: Apoptosis is an intrinsic programmed suicide mechanism in which cells are controlled to disintegrate into apoptotic bodies, which are then recognized and phagocytosed by phagocytic cells, which is an important mechanism for maintaining a constant number of organs and a stable inner loop. It plays an important role in the process of tumor development and elimination. Studies have found that Chinese herbal medicines that can induce apoptosis of liver cancer cells include: Scutellaria extract β -elemene [64], Tanshinone IIA [65], Piperine [66], and Icariin [67].

Anti-hepatocarcinoma invasion and metastasis: Primary tumor invasion and metastasis are the basic biological

characteristics of malignant tumors and are the lethal factors of most tumor patients in clinical practice. Liver cancer is easy to metastasize and easy to relapse, and the therapeutic effect is difficult to fundamentally improve. In recent years, Chinese medicine has made great progress in this research. Studies have found that Chinese herbal medicines with anti-hepatocarcinoma invasion and metastasis include: Total saponins of paeonia [68] and Ginsenoside Rg3 [69].

Affecting telomerase activity: Telomerase is a ribonucleoprotein composed of RNA and protein belongs to a reverse transcriptase. Normal somatic cells hardly express telomerase activity, while malignant tumor cells have telomerase activity as high as 80-90%. Telomerase has now become a specific marker for tumors, and telomerase as a "target" is a new strategy for the treatment of tumors. Studies have found that the water flavonoid DMC [70] can affect the activity of telomerase.

Regulating cell signal transduction: Obstacles or abnormalities in the signal transduction process lead to a series of biological behavior abnormalities such as cell growth, proliferation, differentiation, metabolism, and apoptosis, causing various diseases and even tumors. Studying tumor cell signal transduction, you can understand the mechanism of tumor formation and development, using bioengineering techniques and means to target a specific molecular target or signal transduction pathway, block the signal transduction pathway of tumor growth, so inhibit tumor the occurrence and development. It was found that vitexin VB-1 [71] down-regulates the phosphorylation levels of ERK and FoxO3a, thus inhibiting the proliferation of liver cancer cells. The traditional Chinese medicine monomer berberine [72] may inhibit tumor cell proliferation by inhibiting the activity of tumor invasion-associated signal VEGF/PLCr1.

Conclusion

Early screening of PHC and improved diagnostic accuracy are important for improving patient survival. At present, the main diagnostic and diagnostic index for liver cancer is alpha-fetoprotein, but the accuracy of single diagnosis is not high. It is considered that more meaningful serum tumor markers are proposed, and combined detection of multiple indicators is used for early diagnosis of primary liver cancer. Diagnosis and treatment are of great significance. At present, there are various treatments for primary liver cancer. Due to the complex symptoms and symptom characteristics of such patients, such as the use of a single treatment, it is difficult to achieve the desired effect, combined therapy is currently a more common method. At present, traditional Chinese medicine combined with modern medical means is ideal for the treatment of primary liver cancer, and can alleviate the suffering of patients, relieve their anxiety and improve the quality of life. The research on the therapeutic effect of traditional Chinese medicine on liver cancer also provides a new research direction for the pathogenesis and treatment of liver cancer.

The high incidence of PHC is difficult to treat. In addition to further research on its pathogenesis, it is more important to continuously study the most effective methods for treating PHC, to bring patients treatment hope and to reduce the economic burden of treatment as much as possible. It is necessary to conduct in-depth research on the basis of giving full play to the advantages of traditional Chinese medicine and rationally combining other treatment methods. In addition to the symptomatic treatment of Western medicine, improving the quality of life is regarded as the primary task in the treatment of advanced liver cancer. The combination of traditional Chinese and Western medicine shows us the main direction and provides a useful reference for further progress.

References

- White DL, Kanwal F, El-Serag HB (2012) Association between nonalcoholic fatty liver disease and risk for hepatocellular cancer, based on systematic review. *Clinical Gastroenterology and Hepatology* 10: 1342-1359.
- Fattovich G, Stroffolini T, Zagni I, Donato F (2004) Hepatocellular carcinoma in cirrhosis: incidence and risk factors. *Gastroenterology* 127: S35-S50.
- Chen G, Lin W, Shen F, Illoeje UH, London WT, et al. (2006) Past HBV viral load as predictor of mortality and morbidity from HCC and chronic liver disease in a prospective study. *The American Journal of Gastroenterology* 101: 1797.
- Lee MH, Yang HI, Lu SN, Jen CL, Yeh SH, et al. (2010) Hepatitis C virus seromarkers and subsequent risk of hepatocellular carcinoma: long-term predictors from a community-based cohort study. *J Clin Oncol* 28: 4587-4593.
- Tian S, Hui X, Fan Z, Li Q, Zhang J, et al. (2014) Suppression of hepatocellular carcinoma proliferation and hepatitis B surface antigen secretion with interferon- λ 1 or PEG-interferon- λ 1. *The FASEB Journal* 28: 3528-3539.
- Boyd A, Gozlan J, Maylin S, Delaugerre C, Peytavin G (2014) Persistent viremia in HIV-hepatitis B co-infected patients undergoing long-term tenofovir: virologic and clinical implications. *Hepatology* 60: 497-507.
- Bruix J, Sherman M (2011) Management of hepatocellular carcinoma: an update. *Hepatology* 53: 1020-1022.
- Wang G, Zhang ZM (2013) Molecular mechanisms underlying the development of hepatocellular carcinoma and molecular targeted therapy. *World Chinese Journal of Digestology* 21: 1791.
- Zhao M, He HW, Sun HX, Ren KH, Shao RG (2009) Dual knockdown of N-ras and epiregulin synergistically suppressed the growth of human hepatoma cells. *Biochemical and Biophysical Research Communications* 387: 239-244.
- Jeon YE, Lee SC, Paik SS, Lee KG, Jin SY, et al. (2011) Histology-directed matrix-assisted laser desorption/ionization analysis reveals tissue origin and p53 status of primary liver cancers. *Pathology International* 61: 449-455.
- Berman DM, Karhadkar SS, Maitra A, De Oca RM, Gerstenblith MR, et al. (2003) Widespread requirement for Hedgehog ligand stimulation in growth of digestive tract tumours. *Nature* 425: 846.

12. Jia W, Gao W, Tang L (2003) Antidiabetic herbal drugs officially approved in China. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives* 17: 1127-1134.
13. Jia W, Gao WY, Yan YQ, Wang J, Xu ZH, et al. (2004) The rediscovery of ancient Chinese herbal formulas. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives* 18: 681-686.
14. Si FC, Yue JY, Liu ZY (2011) Analysis of TCM syndromes and medication rules of clinical primary liver cancer in recent 30 years. *World Journal of Integrated Traditional and Western Medicine* 6: 8-10.
15. Cheng J, Wang W, Zhang Y, Liu X, Li M, et al. (2014) Prognostic role of pre-treatment serum AFP-L3% in hepatocellular carcinoma: systematic review and meta-analysis. *PLoS one* 9: e87011.
16. Zhang Q, He DF, Li HV (2015) Significance of Golgi protein73(GP73) for diagnosis and treatment of the hepatocellular carcinomas. *Mod Oncol*.
17. Wang L, Yao M, Pan LH, Qian Q, Yao DF (2015) Glypican-3 is a biomarker and a therapeutic target of hepatocellular carcinoma. *Hepatobiliary & Pancreatic Diseases International* 14: 361-366.
18. Yoshikawa M, Morine Y, Ikemoto T, Imura S, Higashijima J, et al. (2017) Elevated Preoperative Serum CEA Level Is Associated with Poor Prognosis in Patients with Hepatocellular Carcinoma Through the Epithelial-Mesenchymal Transition. *Anticancer Research* 37: 1169-1175.
19. Lim TS, Kim DY, Han KH, Kim HS, Shin SH, et al. (2016) Combined use of AFP, PIVKA-II, and AFP-L3 as tumor markers enhances diagnostic accuracy for hepatocellular carcinoma in cirrhotic patients. *Scandinavian Journal of Gastroenterology* 51: 344-353.
20. Huo Q, Zheng Z, Liu J, Li C, Hu C (2015) Diagnosis value of combined detection of serum golgi protein 73, desgamma carboxy prothrombin and α -fetoprotein in primary hepatic carcinoma. *Zhonghua yi xue za zhi* 95: 757-760.
21. Qin QF, Weng J, Xu GX, Chen CM, Jia CK (2017) Combination of serum tumor markers dickkopf-1, DCP and AFP for the diagnosis of primary hepatocellular carcinoma. *Asian Pacific Journal of Tropical Medicine* 10: 409-413.
22. Song ST, Zhu F, Sun Y (2017) Diagnostic value of combined detection of serum AFP, AFU and ALP levels in patients with primary liver cancer. *International Journal of Digestive Diseases* 37: 177-179.
23. Zhang CC, Chu RH, Han P (2012) Diagnosis value analysis of serum AFP, GPC3, TGF- β 1 single and combined testing on primary liver cancer. *Qingdao Medical Journal* 44: 108-110.
24. Wu LL, Shao XX, Zhang M (2015) Clinical value of combined detection of serum tumor markers in diagnosis of primary hepatocellular carcinoma. *Laboratory Medicine and Clinic*, pp: 754-755.
25. He WJ (2013) Diagnostic value of combined detection of 7 tumor markers for primary liver cancer. *International Journal of Laboratory Medicine* 34: 734-736.
26. Zhu PL, Yin C, Feng JL (2015) Progress in comprehensive treatment of primary liver cancer. *J Clin Hepatol* 31: 965-968.
27. Huang X, Zhang S (2015) The research progress of primary liver cancer treated by integrative Chinese and western medicine. *International Journal of Traditional Chinese Medicine* 3: 278-282.
28. Shi YZ, Lian B, Wu H (2016) The Contrast Analysis on Anxiety and Depression Condition of Small Primary Liver Cancer Patients under Surgical Resection/PMCT Treatment. *Journal of Chengdu Medical College* 11: 35-39.
29. Yang WW, Hou EC (2016) The research progress of primary hepatic carcinoma treatment. *Journal of Modern Oncology* 24: 3495-3499.
30. Ma KS (2015) Current status of radiofrequency therapy for liver cancer. *Chinese Journal of Bases and Clinics in General Surgery*, pp: 1161-1163.
31. Tan N (2016) Effects of solution-focused approach on anxiety-depression and sleep quality in perioperative patients with liver cancer. *China Modern Medicine* 23: 166-168.
32. Xue H, Zhong Q, Liu H (2015) Efficacy and prognostic factors of cyberknife treatment combined with transcatheter arterial chemoembolization therapy for primary liver cancer. *Infectious Disease Information* 28: 301-305.
33. Zaanen A, Williet N, Hebban M, Dabakuyo TS, Fartoux L, et al. (2013) Gemcitabine plus oxaliplatin in advanced hepatocellular carcinoma: a large multicenter AGEO study. *Journal of Hepatology* 58: 81-88.
34. Yao DX, Qin CY (2013) Progress in non-surgical treatment of primary hepatic carcinoma. *Medical Recapitulate* 58: 81.
35. Wu YD (2012) Efficacy of domestic adenosylmethionine in the treatment of hepatocellular carcinoma with depression. *Chinese Medicine Modern Distance Education of China* 10: 39.
36. Zhang YW, Tan C, Pang WD (2016) Effect of drug intervention on anxiety, depression and prognosis of patients with simple liver cancer during perioperative period. *World Latest Medicine Information* 16: 107-108.
37. Greer JA, Traeger L, Bemis H, Solis J, Hendriksen ES, et al. (2012) A pilot randomized controlled trial of brief cognitive-behavioral therapy for anxiety in patients with terminal cancer. *The Oncologist*.
38. Zhu Z, Yang CW, Chen YQ (2017) Observation on treating liver tumor with Danzhi Xiaoyao San plus ablation. *Clinical Journal of Chinese Medicine* 9: 54-55.
39. Qing XY (2015) Clinical observation of Shu Gan Jie Yu capsule assisted sertraline tablets in the treatment of depression in patients with liver cancer. *Chinese Community Doctors* 31: 97-98.
40. Yang JB, Zhang J, Ma CZ (2017) The clinical efficacy of Jianpifuzheng decoction and effect on Immune function and quality of life in patients with terminal primary hepatoma. *Pharmacology and Clinics of Chinese Materia Medica*.
41. Cheng RW, Li P, Deng LP (2016) Effect of TACE Combined with Chaihu Shugan Powder on Hepatocellular Carcinoma of Liver Depression and Spleen Deficiency. *Guiding Journal of Traditional Chinese Medicine and Pharmacology*, pp: 20-23.
42. Chen K, Zhang YF (2017) Clinical Curative Observation of Using Jianpi Huayu Decoction Combined with Chemotherapy in the Treatment of 78 Cases of Primary Hepatocellular Carcinoma (Liver-depression and Spleen-deficiency Syndrome). *Journal of Sichuan of Traditional Chinese Medicine*, pp: 108-110.
43. Zhang H, Wang YY, Zhang ZF (2007) Clinical observation of Chai Shao and Six Gentlemen Decoction in prevention and treatment

- of syndrome of liver depression and spleen deficiency after interventional chemoembolization. *Journal of Traditional Chinese Medicine University of Hunan* 27: 55-57.
44. Zheng DH, Zheng DJ, Zheng WH (2015) An old Chinese medicine doctor Zheng Weida used Cidan Capsule to treat 4 cases of liver stagnation and spleen deficiency type liver cancer. *World Chinese Medicine*, pp: 1739-1740.
 45. Zeng LH (2017) Research on clinical application of Ruangan Lidan Decoction mitigate TACE adverse reactions in the treatment of primary hepatocellular carcinoma. *Guangxi University of Chinese Medicine*.
 46. Huang DS, Guan J (2018) The improvement of TCM syndrome and prognosis of primary liver cancer treated with jiawei sinisan. *Nei Mongol Journal of Traditional Chinese Medicine* 37: 1-2.
 47. Rao K, Zhang TC, Yang Q (2017) Evaluation of the effect of modified Ge Xia Zhuyu Decoction in treating liver cancer with qi stagnation and blood stasis. *Contemporary Medicine Forum* 15: 33-35.
 48. Lu ZY, Dang DJ, Wang JY (2017) Effect observation of treating liver cancer patients with qi stagnation and blood stasis by using Bai Dan Shu Gan Fang. *World Latest Medicine Information*.
 49. Zhang ZY, Dong BZ, Li FL (2017) Clinical study of Qinggan Huayu Decoction Combined with TACE in the treatment of primary liver cancer. *Journal of Sichuan of Traditional Chinese Medicine* 35: 111-113.
 50. Lu DY, Ye XW (2016) Clinical Efficacy of Xuefu Zhuyu Decoction in Treatment of Pain with Qi Stagnation and Blood Stasis after Transcatheter Arterial Chemoembolization for Primary Liver Cancer: An Analysis of 30 Cases. *Journal of Anhui Traditional Chinese Medical College* 35: 45-47.
 51. Qiao LJ (2010) The Syndrome and Clinical Research of Aitongxiao Decoction with TACE on Primary Hepatic Carcinoma. *China Journal of Chinese Medicine* 25: 393-395.
 52. Wu HN (2017) Clinical observation on the effect of chaihu shugan powder combined with pink siwu decoction on qi stagnation and blood stasis after liver cancer tace operation. *Heilongjiang University of Chinese Medicine*.
 53. Wu ZP, Cheng JJ, Zhu XP (2017) Clinical Observation on Ruangan Decoction in Treatment of Advanced Primary Liver Cancer. *Journal of Hubei College of Traditional Chinese Medicine* 19: 64-66.
 54. Liang YY (2017) Clinical study of Xiao Ji Huayu pill combined with TACE in the treatment of primary liver cancer. *Guangxi University of Chinese Medicine*.
 55. Ye SL, Zeng PH, Gao WH (2016) Clinical efficacy of Babaodan capsules combined with interventional therapy with Brucea javanica oil emulsion in treatment of damp-heat accumulation type primary liver cancer. *Hunan Journal of Traditional Chinese Medicine* 32: 1-4.
 56. Sheng QS, Guo HW, Wang M (2016) Clinical observation on 60 cases of advanced primary liver cancer (damp heat syndrome) treated by Hao Zhi Qing Gan pill combined with radio knife *World Latest Medicine Information*, pp: 77-78.
 57. Zheng WH, Zheng DJ, Zheng DH (2015) An old Chinese medicine doctor Zheng Weida uses Cidan Capsule to treat liver and gallbladder damp-heat type liver cancer. *World Chinese Medicine* 10: 1904-1905.
 58. Zhong MH (2018) Regulating effect of Bushen Jianpi Recipe on TCM Syndromes of patients with primary liver cancer after percutaneous coronary intervention. *Chinese Journal of Cancer Prevention and Treatment* 25: 1.
 59. Jin DS (2014) The disease spread product flavored Clinical research for the treatment of primary liver cancer (syndrome of yin deficiency of liver and kidney). *Changchun University of Chinese Medicine*.
 60. Huang WX (1995) Therapeutic effect of consistent decoction plus reduction on liver and kidney yin deficiency in primary liver cancer. *Fujian Journal of Traditional Chinese Medicine*, p: 33.
 61. Tian J, Li HP, Ren PY (2014) Curcumin inhibits proliferation of human hepatoma cell line HL-7702 by activating AMPK. *Chinese Journal of Gerontology* 34: 1897-1898.
 62. Sheng QS, Wang W, Guo HW (2015) Research on dihydroarteannuin contained serum inhibit the activity of cancer cells SMMC-7721. *Pharmacology and Clinics of Chinese Materia Medica*, pp: 40-43.
 63. Chen FY, Tao WW, Chen KY (2016) Effects of diterpenoid peginenal of *Euphorbia pekinensis* Rupr. On proliferation, cell cycle and apoptosis of hepatoma cells. *Chinese Pharmacological Bulletin* 32: 519-524.
 64. Ou YJ, Shen H, Liu JL (2014) Study on the mechanism of apoptosis induced by β -Elemene in anti-hepatoma. *Modernization of Traditional Chinese Medicine and Materia Medica-World Science and Technology*, pp: 738-742.
 65. Xia XH, Liu M (2014) Effect of tanshinone II A and salvianolic acid B on HepG2 cell line and its mechanism. *Journal of Chinese Medicinal Materials* 37: 652-655.
 66. Qiao YJ, Bo GRLT (2015) Study of Liver Cancer Cell Apoptosis Induced by Piperine in Vitro. *The Practical Journal of Cancer*, pp: 803-805.
 67. Sun L, Peng Q, Qu L (2015) Anticancer agent icaritin induces apoptosis through caspase-dependent pathways in human hepatocellular carcinoma cells. *Molecular Medicine Reports* 11: 3094-3100.
 68. Yang Y, Wang S, Meng XS (2015) Study on Migration of SMMC-7721 Hepatocarcinoma Cells Included by Total Paeony Glucosides and Its Preliminary Mechanism. *Chinese Journal of Experimental Traditional Medical Formulae* 21: 108-112.
 69. Yin TX, Wang YY (2015) Effect of ginsenoside Rg3 on the proliferation, adhesion, migration and apoptosis of human hepatoma cell lines and the mechanism. *Basic & Clinical Medicine* 35: 303-307.
 70. Ye CL, Lai YF, Liu XJ (2014) Study on mechanism of inducing apoptosis in human hepatoma SMMC-7721 cells by DMC, a chalcone from buds of *Cleistocalyx operculatus*. *China Journal of Chinese Materia Medica* 39: 2942-2946.
 71. Zheng XX, Zhang RS, Zhou YJ (2014) Role of ERK/FoxO3a signal axis in inhibitory effect of vitexin 1(VB-1) in HepG2 cell proliferation. *China Journal of Chinese Materia Medica* 39: 1276-1279.
 72. Wang J, Xie B, Liu Y (2015) Inhibitory Effects of Berberine on Invasion in Hepatocellular Carcinoma Cells by Down-regulating PLC γ 1. *Journal of Hubei Medical University* 34: 23-25.