Chinese Medicine for Treatment of Chronic Hepatitis B

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ABSTRACT Contemporary Western medicines approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic hepatitis B (CHB), although available in China, have high costs, or major side effects and limited effectiveness. Research efforts have focused on looking for natural products as alternative medicines with low cost and good safety for CHB treatment. Chinese medicine (CM) has ancient, time-honored theories about methods of diagnosis and treatment for liver diseases. In recent decades, a large number of clinical trials and preclinical studies, which were performed in China and other countries, indicated that CM has potential benefits in several aspects of the treatment of CHB, e.g., anti-inflammatory, anticancer, antioxidant, immunomodulating, antifibrosis, and antiviral. However, there are many concerns regarding the study design and the quality of clinical trials. Further, larger, stringently designed, double-blind, placebo control, randomized clinical trials and long-term follow-up are needed to provide conclusive evidence of their efficacy and safety. Components of CM deserve further study in preclinical models of HBV infection and in clinical trials worldwide.

KEYWORDS chronic hepatitis B, natural products, Chinese medicine, Western medicine, clinical trial

China has a long history of using Chinese medicine (CM) to treat chronic liver diseases. Today, CM is still one of the major medicines in China, and is also being used more commonly in Western countries. Chronic viral hepatitis B (CHB) is a global health problem. China has the largest population affected by this viral hepatitis. CHB is caused by infection with the hepatitis B virus (HBV). Chronic infection with HBV can significantly impair the quality of life and life expectancy of patients because of the potential for disease progression, which can lead to fibrosis, cirrhosis, liver failure and hepatocellular carcinoma. CM is used widely in CHB treatment in China as well as other countries. Clinical surveys revealed that over 90% of patients with CHB in China received CM therapy. More than 80% of natural products thought useful for management of liver diseases are Chinese herbs and/or their extracts, and over 80% of the Chinese publications regarding hepatitis and hepatic fibrosis are CM-related. These are far higher proportions than those for Western medicines used in China. In Western medicine, interferon (IFN) and lamivudine (LAM) or other nucleoside analogues (e.g. adefovir dipivoxil, tenofovir, entecavir) are the currently approved remedies for hepatitis B.

Regarding the treatment CHB with CM, major questions are "Are CMs effective therapeutic agents for CHB? If yes, how to explain the large population infected by HBV in China?" and "If they are, why are so many millions of Chinese chronically infected with the HBV?" There are both medical and cultural dimensions to these questions. In recent decades, a number of clinical trials have been performed in China to assess the efficacy and safety of CMs for CHB infection. Studies have looked at the effects of CMs on CHB, both alone, and in combination with Western medicines. Results have been compared with those from studies employing only conventional Western therapies.

To understand better the current patterns of use of CMs in management of CHB in China, in 2010, we searched the database of the China National Knowledge Infrastructure (CNKI, from January 1998 to June 2008) and PubMed (January 1966 to June 2008) using the key words CM, herb, plant, herbal extract and hepatitis B. The reports of CM clinical trials that included prospective randomized clinical trials (RCTs), non-randomized clinical trials (non-RCTs), and summaries of clinical experience were selected for analysis. The clinical trials included single blind, double blind or not blinded studies

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Our study also revealed that the CMs used for HBV treatment in different formulations are very similar. The most commonly used herbs include *Radix Astragali* (Huangqi), *Radix Salviae Miltiorrhizae* (Danshen), *Rhizoma Polygoni Cuspidati* (Huzhang), and *Herba Hedyotis Diffusa* (Bai Hua She She Cao). Interestingly, milk thistle (Shui Fei Je), which is widely used for viral hepatitis and other liver diseases in Europe and North America, was not ranked in the top 20 most commonly used clinical herbs, suggesting that CM practitioners choose herbs for HBV mainly based on CM theory. Like CMs, milk thistle and its extracts (e.g., silymarin) have been used for medicinal purposes since the time of ancient Greece, and continue to attract attention for their touted liver-health properties. Although some studies reported successful treatment of patients infected with HBV with milk thistle, these findings were not replicated in higher quality clinical trials. The U.S. Agency for Healthcare Research and Quality reported in a systematic review of clinical trials of milk thistle that milk thistle improved liver function in people with mild liver disease but did not work as well for those with severe liver disease such as cirrhosis. According to the National Center for Complementary and Alternative Medicine of the U.S. National Institutes of Health, milk thistle may benefit the liver by protecting and promoting the growth of liver cells, fighting oxidation (a chemical process that can damage cells), and inhibiting inflammation in laboratory animal studies.

The art of Chinese medicine emphasizes the whole human body as a unit, and then uses a formula with several herbs, which are selected based upon the individual properties of the herbs and their purported ability to work in a complementary fashion to treat a disease in numerous domains. Hundreds of herbs have...