FEATURE ARTICLE

Effect of Traditional Chinese Medicine for Treating Human Immunodeficiency Virus Infections and Acquired Immune Deficiency Syndrome: Boosting Immune and Alleviating Symptoms*

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ABSTRACT To respond to the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) epidemic in China, the integration of antiretroviral therapy (ART) and traditional Chinese medicine (TCM) has important implications in health outcomes, especially in China where the use of TCM is widespread. The National Free TCM Pilot Program for HIV Infected People began in 5 provinces (Henan, Hebei, Anhui, Hubei, and Guangdong) in 2004, and quickly scaled up to 19 provinces, autonomous regions, and municipalities in China including some places with high prevalence, 26,276 adults have been treated thus far. Usually, people with HIV infection seek TCM for four main reasons: to enhance immune function, to treat symptoms, to improve quality of life, and to reduce side effects related to medications. Evidences from randomized controlled clinical trials suggested some beneficial effects of use of traditional Chinese herbal medicine for HIV infections and AIDS. More proofs from large, well-designed, rigorous trials is needed to give firm support. Challenges include interaction between herbs and antiretroviral drugs, stigma and discrimination. The Free TCM Program has made considerable progress in providing the necessary alternative care and treatment for HIV-infected people in China, and has strong government support for continued improvement and expansion, establishing and improving a work mechanism integrating Chinese and Western medicines.

KEYWORDS human immunodeficiency virus, traditional Chinese medicine, immune, symptoms

Human immunodeficiency virus (HIV) has become a significant public health issue in China, and an increasing number of HIV-infected individuals are in need of care. Current reports confirm about 497,000 cases of HIV infection and estimate that approximately 810,000 people are now infected with HIV at the end of October, 2014. Most of these cases have occurred in young, poor adults living in rural areas.[1]

Although HIV infection was first reported in China in 1985, the magnitude of its spread was not evident until the epidemic among former plasma donors across central China was realized. Poor, rural farmers sold plasma to unscrupulous collectors under unsanitary conditions during the early to mid-1990s, resulting in untold numbers of infections.[2] China's National Free Antiretroviral Therapy (ART) Program was piloted in 2002 and was scaled up in 2003, initially to former plasma donors and then to the rest of the country, leading to a significant reduction of mortality among its participants. Prior to this time, few people in China had access to ART, and clinical expertise in HIV/acquired immune deficiency syndrome (AIDS) medicine was limited to major centers in a few eastern cities.[3] The availability of ART has markedly improved the survival rate and quality of life (QOL) in patients infected with HIV, data from the China ART program shows virological suppression, increased $CD4^+$ cell counts, and a pronounced decrease in mortality in patients who have received treatment.[4] However, there is still no cure for HIV. ART is still by no means

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perfect and is not the ultimate answer to controlling and ending the HIV epidemic. Adverse events, emergence of drug-resistant viral strains, maintenance of adherence, sustainability, and cost are just some of the concerns. The persistence of prolonged HIV reservoirs in patients on effective antiretroviral therapy is the main hurdle to HIV eradication.[5]

Three types of treatment systems are practiced in Chinese society: (a) ART offered by health care professionals in clinics and hospitals; (b) tonic, which is over-the-counter popular medicine and includes teas, soups, tablets, herbal preparations, and tonics, which are similar to herb supplements used in some Western countries; and (c) traditional Chinese medicine (TCM), provided by trained Chinese practitioners, which incorporates a wide range of theories, therapies, and practices. Many Chinese people use all three types of treatment simultaneously. Generally, people with HIV infection use TCM for four main reasons: to enhance immune function, to treat symptoms, to improve QOL, and to reduce side effects related to medications.[6] TCM has been used in Chinese society for more than 5,000 years. In ancient times, Chinese medical practitioners tasted medicinal herbs to test the efficacy in treating diseases, and from the practical experience of the pioneers to improve their medical skills. TCM has been widely and successfully used to treat diseases from inflammation to cancer and retains an important role in the healthcare system of China today. In the TCM approach, the body is recognized and treated as a whole entity, and diseases are identified as conditions caused by internal imbalances. The role of doctors is to identify imbalances and then correct them; the body is then expected to be able to heal itself.[7] Because of the chronic disease course, poor QOL and high possible occurrences of severe complications and death, HIV infected people are likely to seek TCM therapy, particularly in some rural areas with limited medical resources. Different from conventional Western medicine system, TCM treating patients individually, when HIV infection occurs in someone, who has enough vital force and strong self-adjustment ability; he might be living concurrently with infection and becomes a long-time HIV carrier, with a retarded entering from asymptomatic stage to AIDS stage.

To respond to the HIV/AIDS epidemic in China, the integration of ART and TCM has important implications in health outcomes, especially in China where the use of TCM is widespread.

The National Free TCM Pilot Program for HIV Infected People

Governments may have contradictory attitudes towards the use of alternative medicines for AIDS, fearing the toxicity of drugs, or that these medicines will interact with anti-retroviral medication and lead to discontinuation of ART therapy. An exception is the Chinese government, which officially supports a complementary medicine program for AIDS care and research. WANG Guo-qiang, vice-minister of the National Health and Family Planning Commission and vice-commissioner of the State Administration of Traditional Chinese Medicine (SATCM), delivered a speech on The National Work Conference on HIV/AIDS Prevention and Treatment in Beijing on December 8, 2014, he mentioned that government should make full use of TCM, establish and improve a work mechanism integrating Chinese and Western medicines.

National Free TCM Pilot Program (NFTPP) had been launched by SATCM and the Chinese Ministry of Health by 2004, and quickly scaled up from 2,582 cases in 5 provinces (Henan, Hebei, Anhui, Hubei, and Guangdong) to 19 provinces, autonomous regions, and municipalities in China including some places with high prevalence, treating 26,276 cases accumulatively by September 2014 (Figure 1).

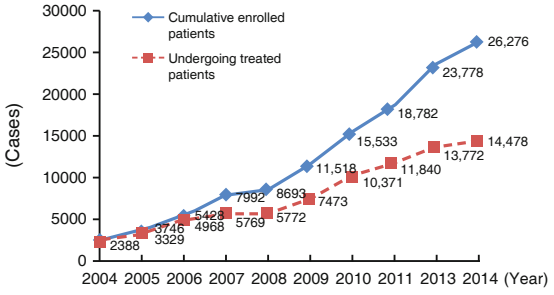

Figure 1. Cumulative and Undergoing Cases of Patients Receiving Free TCM by Year

Enrolled Patients

HIV infected people who meet any one of the following items were enrolled in the program. (1) HIV infected people who were treatment naive, (2) patients who suffered side effects from ART therapy, (3) patients who had opportunistic infections, (4) patients who had failure immune reconstitution, (5)

patients who had poor QOL, and (6) patients who were volunteered to take TCM. Pregnant women and children were excluded.

Treatment and Care Model

NFTPP began in 2004, Center of AIDS Treatment with Traditional Chinese Medicine (CATTCM), China Academy of Chinese Medical Sciences was established in 2004, and provides guidance and technical assistance for this program. The care model in this program was designated hospitals and village healthcare service centers based and involves the provision of decoction at the county level with routine follow-up, consulting, and care at the village or township level. Experts at provincial and national level provide consultative referral and guidance to the county and prefecture level clinicians as required. Provincial Bureaus of Traditional Chinese Medicine manage treatment within the province, including the appointment of experts to treat patients every three month. The SATCM and Chinese Ministry of Health oversee the management and supervision of treatment and care, including the development of clinical technical guidelines and manual (Figure 2), training, and technical guidance. Clinical Practice Guideline of Traditional Medicine for People Living with HIV infections and AIDS sponsored by China Academy of Chinese Medical Sciences and WHO Western Pacific Region has been published by 2011. Until September, 2014, there were 163 designated hospitals and village healthcare service centers for the program.

Figure 2. Clinical Technical Guidelines and Manuals for the Program

Funding

The central government's NFTPP-related budget increased from 9 million (RMB) in 2004 to 82.26 million in 2014, the funding primarily goes to NFTPP and reagents for CD4 cell counts and viralload testing, training, and program management.

Training

The CATTCM oversees and conducts training for infectious disease specialists; county, village and township practitioners; nurses; and public health workers. Training consists of two-day didactic courses, which have educated nearly 900 TCM practitioners. Additional training takes place at the local level.

Free Database

Since late 2004, CATTCM has been developing a free TCM database to monitor patients in the free program. Information is collected at treatment initiation and each follow-up visit. CATTCM is in charge of collecting and analyzing data. Collected data reflect care in all provinces and regions providing free TCM and includes demographic information, laboratory test results, clinical signs and symptoms, mortality, QOL questionnaire and patient-reported outcome questionnaire.

Some Data Analysis Outcome from the Database

According to some report, the therapeutic effects on 8,946 cases from pilot program are as follows: most of the cases maintained stable immune function, main symptoms and signs like fever, cough, fatigue, poor appetite, diarrhea had significantly been improved, no adverse reaction was found in TCM treatment.[8] A total of 1,666 people living with HIV who enrolled in NFTPP in October 2004 and ended by October 2010 were analyzed to provide survival estimates in rural area of Henan province, China. The retrospective study showed that the total mortality rate over the study period was 3.6 per 100 person-years, which was lower than the rate of world. The cumulative survival rate was 95.9% at 1 year [95% confidence interval (CI): 94.8, 96.8] and 80.4% at 6 years (95% CI: 78.4–82.3).[9] An observation based on syndrome differentiation involving 1,200 people living with HIV at asymptomatic stage claimed that TCM significantly improved the patient's QOL, in which World Health Organization (WHO) QOL-HIV scale (Chinese version) was used.[10]

Challenges and Responses

Clinical Observation

Evidences from randomized controlled clinical trials have demonstrated a positive association between use of TCM and immune promotion, symptoms relief of people living with HIV/AIDS, which

compared Chinese herbal medicines with placebo or antiretroviral drugs in patients with HIV infection, HIV-related disease or AIDS.[11-13] These studies exhibit a wide variety of TCM treatment principles like supplementing qi and nourishing yin, promoting qi and activating blood circulation, clearing heat and dispelling dampness, removing toxic substance.[11-13] Some studies support the Chinese herb and antiretroviral drug combination therapy. Wang, et al[14] provide evidence in improving symptoms and a lower risk for the decrease of $CD4^+$ cell counts for patients with combined therapy using TCM herb Aining Granule (艾宁颗粒). Studies of diarrhea and oral candidiasis, which are challenging symptoms of AIDS, were demonstrated to have positive effects.[15] Study of peripheral leukocytes, which are a side effect of antiretroviral drugs, suggested that an integrated treatment approach may be of benefit.[16]

A report of 3-year outcome on $CD4^+$ lymphocyte count of 807 cases of HIV/AIDS enrolled in the program, results showed that the overall $CD4^+$ lymphocyte count maintained stable at the 6th and 12th month, declined significantly at the 18th, 24th and 30th month, then elevated to the pre-treatment level at the 36th month. Patients with pre-treatment $CD4^+$ lymphocyte count level<200/mm^3, who possibly combined highly active ART, had $CD4^+$ lymphocyte count elevated significantly after all visits. Patients with pre-treatment $CD4^+$ lymphocyte count level between 200 and 350/mm^3 maintained stable before the 36th month, and then rose significantly, which implicated the long-term effect of TCM. Patients with pre-treatment $CD4^+$ lymphocyte count level>350/mm^3, had $CD4^+$ lymphocyte count declined significantly after all visits.[17] A randomized double blind placebo-controlled clinical trial using Aifukang Capsule (艾复康胶囊) involving 198 patients showed significant effect in improving immune function and clinical symptoms such as fatigue, anorexia, headache, skin rash and insomnia.[18]

Evidences from some of those trials suggested some beneficial effects of use of TCM herb for HIV infections and AIDS. However, considering the small sample and limitations of the trials (most of trials had participants less than 30, duration arranging from 3 months to 1 year).

In response to the challenges, future trials should be rigorous in methodology and address clinical outcomes such as patients reported outcome, QOL, or symptom relief. Participants should be stratified according to their stages, such as asymptomatic HIV-infection, HIV-related diseases or AIDS. The quality of herbal medicine to be tested should be warranted through *in vitro* or *in vivo* experimental studies, and the adherence should be evaluated in the trials. More evidence from large, well-designed, rigorous trials is needed to give firm support.

Interaction between Herbs and Antiretroviral Drugs

TCM use is common in Chinese society and it is generally perceived as "safe," despite evidence of either harmful or harmless interactions between some herbal medicines and medical treatments and the evidence of associated risks. Specifically, recent studies have shown that herbal medicines can interact with ART in such a way as to contribute to treatment failure or success.[19-22] A randomized double blind placebo-controlled clinical trial using Immune No.2 Granule involving 264 patients that failure to immune reconstitution showed significant increase in CD4, CD45RA, CD45RO compared with the control group.[23]

In response to the challenges, physicians and health care providers should be aware of potential toxicities and drug interactions related to the use of TCM and ART in China, they should routinely discuss TCM therapies with patients. Beginning a conversation with patients about the casual use of complementary alternative medicine might enhance the provider-patient relationship. Patients also should be informed that TCM use at a time interval from ART in order not to affect the latter's effectiveness. An important focus for these discussions should be on the risks and benefits of taking TCM and ART simultaneously, with explicit information on how to effectively integrate TCM practices into ART regimens to maximize the patient's health and safety.[24]

Furthermore, providers should explore the pros and cons of each type of treatment with patients, given the individual clinical and social situation of the patient as well as his or her values regarding these different therapies with the goal of supporting a good balance between ART and TCM in Chinese patients.

Stigma and Discrimination

When consulting TCM practitioners at an

ordinary clinic or hospital (not from the pilot program), patients usually do not inform doctors about their HIV status. The key factor lies in stigma about HIV. Remarkable progress have been made by Chinese government to eliminate HIV stigma, but it is still exists, sometimes stigma comes from even medical workers. Efforts to combat the stigma have been insufficient. In 2006, the Chinese government came up with recommendations to eliminate legal and public prejudices against infected individuals, but these have yet to be turned into clear legal guidelines. Policy-makers must make discrimination against HIV-positive individuals punishable by law, and include sufficient incentives or penalties to ensure that the policies are enforced. We also believe that legislation should include punishment for knowingly exposing another person to HIV, and requirements for HIV-infected patients to notify their physician and partners when they are diagnosed with HIV.

Summary

In the past 10 years, China has made significant strides in the fight against HIV/AIDS. The program has evolved from a pilot response to a standardized treatment and care system. Given the size and complexity of the country, however, many challenges remain and well-coordinated efforts will be needed for continued progress. Increased funding, development of the health care system, and greater attention to the interaction between TCM and ART will help the program achieve its goal of nationwide access to TCM.

China is not the only nation treating HIV infections and AIDS with alternative medicines; the market of alternative medicines for HIV/AIDS is dynamic. More interdisciplinary research is needed on the experience of people living with HIV/AIDS with these alternative medicines, and on the ways in which these products interact or not with ART at pharmacological as well as psychosocial levels. More research is also needed to assess the economic impact of these therapies, since people seem to be spending much on these 'other' medicines while ART is provided for free. To be able to inform patients better, more clinical research is needed on the benefits and risks of those alternative medicines that are perceived to be beneficial by people living with HIV and AIDS.

There is no strong evidence-based proof to suggest that these alternative treatment are particularly effective for HIV, while in the real world, you may practice evidence-based medicine, but your patients living with HIV don't.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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