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## Reviews

### Thoughts on Intervention in HIV/AIDS with Traditional Chinese Medicine

WU Xin-fang 吴欣芳, WANG Jie 王阶, LI Yong 李勇, Tang Yan-li 汤艳莉, and Zhao Dan-dan 赵丹丹

**Abstracts:** HIV/AIDS has become a worldwide pandemic and highly active antiretroviral therapy (HAART) is the only generally recognized effective therapy at present. However, various unresolvable problems appear with the widespread use of HAART. Traditional Chinese Medicine shows good efficacy for intervention in HIV/AIDS and could become an effective treatment option.

**Keywords:** HIV/AIDS; Traditional Chinese Medicine; immunological nonresponders; asymptomatic HIV infection; adverse effects; highly active antiretroviral therapy

Since the first AIDS case was reported in the early 1980s, it has become a worldwide pandemic and has the fourth highest mortality in humans. It is crucial to find appropriate clinical management for HIV/AIDS patients. Highly active antiretroviral therapy (HAART) is currently the only generally recognized therapy for HIV/AIDS. It can maximally suppress viral replication in the plasma, delay progress of AIDS, and reduce morbidity and mortality. However, some unresolvable problems such as intolerable adverse effects, cross-resistance among antiretroviral drugs, and high costs occur with extensive use of HAART. Thus, other therapeutic methods are urgently needed.

#### POSSIBILITY OF INTERVENTION WITH TRADITIONAL CHINESE MEDICINE

Traditional Chinese Medicine (TCM) and Western medicine have different viewpoints about pathology and therapeutic principles. In Western medicine, it is considered that a disease is caused by one or more specific pathogenic factors, whereas, in TCM, a disease is thought to develop from an imbalance between *yin* and *yang* in the body. Therefore, in treatment, Western medicine focuses on elimination of the specific pathological factors, but TCM tends to concentrate on restoring human functional balance.

TCM has been reported as effective in preventing and treating infectious diseases such as severe acute respiratory syndrome (SARS), influenza and infectious hepatitis. In *Su Wen* (素问 *Plain Questions*), a famous ancient Chinese medical text, infectious diseases are described. After thousands years of clinical practice and theory, many methods and prescriptions have been developed to treat infectious diseases. The first AIDS case in China was reported in 1985, and many TCM workers began to consider how to treat HIV/AIDS with TCM. Since September 1988, TCM experts have been sent by the China State Administration of Tradition Chinese Medicine to Tanzania to treat AIDS patients, and have observed the therapeutic effect of TCM and

considered which Traditional Chinese Medicines might be effective. Meanwhile, basic experimental studies have also been conducted to elucidate the therapeutic mechanism of these TCM agents. Currently, the cooperation is continuing and a lot of practical experience is being accumulated. In the past 30 years, the pathogenic factors and pathogenesis of AIDS have been proposed based on TCM theory, and the syndrome pattern and a number of formulae have been developed in clinical practice. Furthermore, more clinical trials and basic experiments have been carried out and have proven the efficacy of TCM intervention in AIDS.

Early experimental studies showed that many Chinese herbs had HIV inhibition activity. For example, Luo, et al.<sup>1</sup> have reported that among 1000 herbs screened, >140 different have been found to possess HIV inhibitory activity, and >20 herbs cause significant inhibition. However, these experiments were all conducted *in vitro*, and the *in vivo* effects are unknown.

#### POSSIBLE AREAS IN WHICH TCM WILL WORK WELL

Currently, TCM therapy is not as potent as HAART in inhibiting HIV replication. Thus, some researchers consider that, in AIDS treatment with TCM, the emphasis should not be on HIV inhibition and propose several areas in which TCM will work well.

#### Promoting Immune Restoration of Immunological Nonresponders

Most patients who achieve successful inhibition of HIV replication after HAART exhibit increases in their peripheral CD4<sup>+</sup> T-cell count.<sup>2</sup> However, many early studies have revealed that 17%–40% of AIDS patients do not exhibit any increase in CD4<sup>+</sup> T cells despite complete virus suppression.<sup>3-6</sup> These patients are called

Guang'an men Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China

Correspondence to: Prof. WU Xin-fang, Tel.: 86-1351102629.

immunological nonresponders (INRs).<sup>7</sup> The US Department of Health and Human Services prefers to define INRs as patients with no more than 350–500 cells/mL after 4–7 years of effective HAART.<sup>8</sup> Yeni, et al.<sup>9</sup> hold that the criteria for INRs should be an increase by <30% in CD4<sup>+</sup> T-cell count and an absolute CD4<sup>+</sup> T-cell count  $\leq$ 200 cells/mL during the first 6–12 months of effective HAART. INRs are at increased risk of HIV/AIDS progress and death.<sup>10</sup> Interleukin (IL)-2, IL-7 and regulatory T cells have been used for intervention in INRs, but have not been widely adopted clinically as yet, because of unproven safety and efficacy.<sup>11–13</sup>

Two thousand years ago, TCM physicians realized the importance of immune function. *Huang Di Nei Jing* (黄帝内经 *The Yellow Emperor's Internal Medicine*) recorded that “sufficient vital *qi* in the body can prevent invasion by pathogens, intrusion of pathogens certainly results from insufficiency of vital *qi*”. This is in accordance with the defense, homeostasis and surveillance of the immune system in Western medicine. Here, the vital *qi* refers to the normal immune function of the human body. Many therapeutic methods of TCM have been developed to treat immune deficiency diseases,<sup>14</sup> such as supplementing and invigorating vital *qi*, reinforcing and strengthening the kidneys, promoting blood circulation and removing blood stasis, and clearing away heat and toxic materials. In HIV/AIDS, HIV as evil *qi* during the entire disease course gradually weakens the vital *qi*. However, the vital *qi* can be regulated or strengthened to normal levels with appropriate TCM therapy based on the patients' different signs and symptoms. The vital *qi* dispels HIV and promotes restoration of immune function. Therefore, in INRs, TCM can be used together with HAART to improve the immunological response and induce reconstitution of the CD4<sup>+</sup> T-cell compartment.

### Early Intervention in Asymptomatic HIV-infected Patients

In Western medicine, it is not suggested to initiate antiretroviral therapy in HIV-infected patients with CD4 counts >350 cells/ $\mu$ L,<sup>15</sup> due to side effects of HAART and drug resistance, and no effective intervention method is used for these patients at present. The vast majority of untreated patients with HIV infection will develop AIDS within an average of 7–10 years.<sup>16</sup> If some intervention measures are taken in the early stage of AIDS, the disease progress will be delayed and life will be prolonged.

Prevention is considered to be an important component in TCM. Disease prevention was first proposed in the early medical classic *Huang Di Nei Jing* (黄帝内经 *The Yellow Emperor's Internal Medicine*) and has been adopted as one of the therapeutic principles in clinical practice for many centuries. A number of clinical studies have been carried out to observe the effect of TCM on

asymptomatic HIV-infected patients. Guo, et al.<sup>17</sup> have demonstrated that Fuzheng Paidu Granules (扶正排毒颗粒), composed of Xi Yang Shen (*Radix Panacis Quinquefolii*), Yin Yang Huo (*Herba Epimedii*), Shan Yao (*Rhizoma Dioscoreae*), Bai Zhu (*Rhizoma Atractylodis Macrocephalae*), and other components, have a good clinical effect on asymptomatic HIV-infected patients with CD4 counts of 200–350/ $\mu$ L, and improves the CD4 cell counts. Another study<sup>18</sup> has shown that Yi Ai Kang Capsules (益艾康胶囊), consisting of Ren Shen (*Radix Ginseng*), Huang Qi (*Radix Astragali*), Chao Bai Zhu (*Fried Rhizoma Atractylodis Macrocephalae*), Fu Ling (*Poria*), and other components, are effective in preventing further decline in CD4 cells and delaying disease progression. Almost all studies have shown that TCM can delay disease progression by preserving immune function. Therefore, TCM can be considered as a therapy for patients with asymptomatic HIV infection.

### Alleviating Adverse Effects of HAART

HAART has a wide range of adverse effects in humans,<sup>19</sup> such as gastrointestinal reactions, bone marrow suppression, fatigue, headache, skin rash, peripheral neuropathy, and hepatotoxicity. These adverse effects are the most common reason for poor compliance and discontinuation of HAART, and they have a detrimental effect on quality of life. Combined use of HAART and TCM could lower the adverse effects of HAART and improve quality of life.

Huang, et al.<sup>20</sup> have demonstrated that Dang Gui Shao Yao San (当归芍药散) can alleviate HAART-induced liver dysfunction, by reducing elevated liver enzyme levels, and improving symptoms such as abdominal distension, diarrhea, poor appetite and hypochondriac pain. Liu, et al.<sup>21</sup> have found that Tang Yuan Kang Capsules (糖元康胶囊) are effective in alleviating bone marrow suppression and improving syndrome scores and increasing Karnofsky Performance Status. The effect of Tang Yuan Kang Capsules (糖元康胶囊) in alleviating bone marrow suppression has been confirmed in mice with zidovudine-associated bone marrow suppression.<sup>22</sup>

### Relieving HIV/AIDS-associated Symptoms

Common symptoms in HIV/AIDS include fever, diarrhea, coughing, fatigue, and poor appetite. Many studies have demonstrated that TCM has some effect in controlling HIV/AIDS-associated symptoms. Fever is one of the most common symptoms. Yu, et al.<sup>23</sup> have demonstrated that for African patients with late-stage AIDS, *Yin* deficiency is the main cause of fever, and nourishing *Yin* and clearing away heat is used, with the TCM formulae Qinghao Biejia Jian (青蒿鳖甲煎) and Xiao Chaihu Decoction (小柴胡汤) showing a good therapeutic effect. Diarrhea is commonly seen in late-stage HIV/AIDS patients and the effect of antibiotics is not obvious. In TCM theory, diarrhea is related to dysfunction of the spleen, kidney and the dampness evil. Li, et al.<sup>24</sup> have

reported that Xiang Sha Liu Jun Zi (香沙六君子) combined with Si Shen Wan (四神丸) control diarrhea and reduce mortality in AIDS patients better than Western medicine does. Besides the Chinese drugs, acupuncture and moxibustion, and Tuina also show good effects in treating AIDS-related diarrhea.<sup>25,26</sup> In addition, TCM is also effective in treating other HIV/AIDS-related symptoms including cough, headache, lymphangiectasia, kidney calculi, and herpes zoster.

### CHALLENGES AND PROSPECTS

At present, HIV/AIDS patients are increasingly seeking help from TCM. In 2002, it was reported that 18.6% of HIV/AIDS adults in the United States were treated with herbal medicines.<sup>27</sup> A study conducted in Hong Kong revealed that 59.2% of HIV/AIDS patients had used TCM, with 20% infrequently and 60% frequently.<sup>28</sup> The popularity of TCM has led many people to wonder whether it is beneficial to human health. Although many studies have shown the efficacy of TCM for preventing and treating AIDS, few of these studies were strictly designed and their evidence is not sufficiently strong. Furthermore, Ma, et al.<sup>28</sup> have demonstrated that the main indications of TCM are for general health maintenance and/or treatment of minor illness, rather than specifically for HIV/AIDS. Also, some people have questioned whether there is any antagonism between Chinese herbs and antiretroviral drugs. To resolve these problems, first, future studies should be more strictly designed and randomized clinical trials with specific assessment criteria of therapeutic effects for TCM should be used to provide conclusive evidence of the efficacy of TCM intervention in AIDS. Second, studies should focus on the areas in which TCM could work well in HIV/AIDS treatment. Last, further rigorous basic studies should be designed to demonstrate the pharmacokinetic and pharmacodynamic interactions between medicinal herbs and antiretroviral drugs. We conclude that TCM is an effective HIV/AIDS treatment option and will play an important role in future treatment.

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