

## Asymptomatic stage of human immunodeficiency virus infection is the optimal timing for its management with Traditional Chinese Medicine

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**Supported by** the National Special Science and Technology Program on Major Infectious Diseases (No. 2012ZX10005010-001, 2012ZX1005001-005, 2013ZX100500Z-001); Henan Province Colleges and Universities Key Youth Teachers Scheme (No. 2013GGJS-095); Research Project for Practice Development of National TCM Clinical Research Bases (No. JDZX2012023) and Henan Province Basic and Advanced Technology Research Project (No. 132300413215)

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**Accepted:** June 13, 2014

worldwide public health problem and an incurable disease. The roles of Traditional Chinese Medicine (TCM) on AIDS had been recognized and accepted by more and more people. Being a relatively long period, to initiate combination antiretroviral therapy (cART) for the asymptomatic human immunodeficiency virus (HIV) infection patient is not consensus. According to TCM theory, not only the imbalance of *Yin* and *Yang* but also the disharmony of internal body function and external natural environment had occurred in the body of the patient, the imbalance and the disharmony should be adjusted by the means of the treatment based on the patterns identified among the symptoms in terms of TCM. We aimed to analyze the feature of patients with asymptomatic infection, and compare the advantages and disadvantages of the usage of cART for asymptomatic infection, explored the possible mechanism underlying TCM treatment of the asymptomatic infection, by reviewing the TCM treatment progress on asymptomatic HIV infection.

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**Key words:** Acquired immunodeficiency syndrome; Medicine, Chinese traditional; Antiretroviral therapy, highly active; Asymptomatic infections

### INTRODUCTION

Acquired immune deficiency syndrome (AIDS) is a quite complex disease caused by the human immunodeficiency virus (HIV) infection.<sup>1</sup> The immune system

### Abstract

Acquired immune deficiency syndrome (AIDS) is a

would be destroyed gradually once HIV invades human body and leaves the body vulnerable to opportunistic infections and life-threatening cancers. Being an emerging infectious disease, the prospect of an effective HIV vaccine to contain the pandemic remains uncertain,<sup>2</sup> and there was no recognized cure for the conditions except for a few cured cases reported.<sup>3,4</sup>

Since 1996, the combination antiretroviral therapy (cART) was introduced for the to treat the patients with advanced AIDS, it has reduced HIV-related the morbidity and mortality drastically.<sup>5</sup> But the effect of cART on patients with asymptomatic infection is still uncertain.

In this article, we will analysis the feature of patients with asymptomatic infection, compare the advantages and defects of the usage of cART for asymptomatic infection, explore the possible mechanism behind the treatment of asymptomatic infection with Traditional Chinese Medicine (TCM) by reviewing the TCM treatment progress on asymptomatic HIV infection.

## FEATURE OF ASYMPTOMATIC HIV INFECTION

The progresses of AIDS can be divided into such three stages: acute HIV infection stage, asymptomatic HIV infection stage, and AIDS stage.<sup>6</sup>

Generally, following the stage of acute infection, regardless of detectable or undetectable symptoms, patients enter a stage of asymptomatic infection which always is regarded as a relatively longest period, people who are infected with HIV may have no symptoms (i.e. AIDS defined symptoms or diseases) for almost 6-8 years or longer, but only for a week or month in acute HIV infection stage, and less than 2-3 years in early symptomatic HIV infection and advanced AIDS stage. So the asymptomatic HIV infection stage is regarded as the longest period among those three stages.

In asymptomatic stage, the progress of the disease is still going on, some dangers and risks are existing (the immune system would be weakened gradually, HIV can be transmitted from HIV+ patient to the others, some HIV-related or no-HIV-related symptoms and signs are still common). Those symptoms or signs might negatively affect quality of life, adherence, virological response and survival,<sup>7</sup> and should be treated immediately. Furthermore, the patient often suffers the stigma and discrimination from social and family, and the the quality of life is much lower than the normal one.

Therefore, it is necessity to offer treatments or interventions for those patients with asymptomatic HIV infection, and to prolong the asymptomatic HIV infection stage through various methods is also important.

## ADVANTAGES AND DISADVANTAGES OF cART FOR THE TREATMENT OF THE ASYMPTOMATIC INFECTION

The cART is a effective therapy in the advanced AIDS stage, but the HIV cannot be eliminated from patient's body, so they must take lifelong medication.

However, there is still no consensus on the right timing for administering cART in individuals infected with HIV,<sup>8</sup> especially no consensus on that any HIV+ persons in asymptomatic HIV-infection with CD4+T cell counts above 350 cells/ $\mu$ L should initiate cART (i.e. early therapy);<sup>9</sup> e.g. the 2013 World Health Organization (WHO) treatment guidelines strongly recommend cART should be initiated for all patients with CD4+Tcell counts 500 cells/ $\mu$ L or less;<sup>10</sup> cART always is recommend in any HIV-positive person with a current CD4+T cell counts below 350 cells/ml and considered below 500 CD4+Tcells/ $\mu$ L in the guidelines of European AIDS Clinical Society (EACS)<sup>11</sup> and UK;<sup>12</sup> and the United states recommended that cART be administered for any HIV-positive persons no matter what their CD4 T cell counts were.<sup>13</sup>

It is noteworthy that the benefits and risks of the early therapy are still under discussion. Some researches demonstrated the benefits from early treatment recently,<sup>14</sup> for example, the early therapy can reduce rates of sexual transmission of HIV-1 and clinical events,<sup>15</sup> improve the survival rate of patients living with HIV,<sup>16</sup> delay the progression of asymptomatic HIV infection to AIDS,<sup>17</sup> decrease the risk of opportunity infections and non-AIDS defined incidents<sup>18</sup> (prominently included hepatic, cardiovascular, and pulmonary diseases, as well as non-AIDS malignancies), and enhance the reconstruction of impaired immune function.<sup>19</sup> As some researchers have worried, there may be some risks and dangers for early therapy, such as increasing the adverse effects of cART, reducing the patient treatment compliance, enhancing the drug resistance, and reducing the opportunity of using cART.<sup>20</sup>

Briefly, the timing of initiating cART is not absolutely consensus, the benefits and shortcomings from early therapy should be confirmed through more researches, for we have to find a best joint-point between individual benefits (reduced risk of mortality, progression to AIDS or death, and diagnosis of an AIDS defining illness) and population benefits (prevention of HIV-1 infection) for earlier initiation of cART.

## POSSIBLE MECHANISM UNDERPINNED THE TREATMENT OF ASYMPTOMATIC INFECTION WITH TCM

TCM has a long history of thousands years. Its thera-

peutic philosophy and treatment methods are different from the convenient medicine.<sup>21</sup>

TCM has a theory system rooting in clinical application. Its practitioners do believe that the diseases are understandable, preventable and curable. The thought of "preventive treatment theory" has existed for thousands years, which emphasizes the importance of disease prevention and early-stage treatment and stands for the characteristic and essence of the TCM. In order to hold back or delay the progression after HIV infection, they often suggest their patients pay more attentions to recuperating, and regulating emotion, diet section, moderate exercise and initiate the early therapy, when they treat their patients.

TCM plays an important role in primary care in China. It often is used for infection disease treating, and some infection diseases had been successfully cured and controlled such as severe acute respiratory syndromes,<sup>22</sup> influenza A virus subtype H1N1,<sup>23</sup> epidemic encephalitis B,<sup>24</sup> and hepatitis,<sup>25</sup> etc.

According to TCM theory, AIDS is an infectious disease because of the invasion of the pathogen. Although the asymptomatic HIV infection stage is quite long, and the progress of the disease is still going on rather than no progress. In asymptomatic HIV infection stage, not only the imbalance of *Yin* and *Yang* but also the disharmony of internal body function and external natural environment had occurred in the body of the patient for TCM believes that the human body is an organic whole which is made of "*Yin* and *Yang*" or "*Qi* and *Xue*", and the imbalance and/or disharmony should be adjusted to avoid further damages. In other words, if we give positive intervention to eliminate the discomfort of patient with asymptomatic stage, the disease progression would be prolonged and other dangers would be decreased, especially when the effect of early therapy is not confirmed. So the asymptomatic HIV infection stage is a prime time to manage for TCM.

## PROGRESSE ON THE TREATMENT OF ASYMPTOMATIC INFECTION WITH TCM

In the last 30 years, the progress on TCM treatment of AIDS has been made promoted by the State Administration of Traditional Chinese Medicine of China. A pilot program was conducted to treat AIDS by combining TCM with anti-retroviral therapy funded by National Science Foundation, National 973 Program, and National 863 Project etc.

As we had known, TCM practitioners had demonstrated the clinical effects of TCM on AIDS stage, such as reducing plasma HIV viral loads,<sup>27</sup> increasing CD4+T cell counts,<sup>28</sup> promoting immunity reconstitution,<sup>29</sup> ameliorating symptoms and signs,<sup>30</sup> improving the health related quality of life,<sup>31</sup> and counteracting against the effects of anti-retroviral drugs,<sup>32</sup> etc.

By contrast, the far fewer studies or observations of TCM had been carried out for patient with asymptomatic HIV infection than to AIDS patient. But researcher had initiated to believe that TCM can be used to treat patient with asymptomatic HIV infection,<sup>33</sup> some studies had demonstrated that TCM can be used to treat patients with asymptomatic HIV infection,<sup>34,35</sup> and the progression of asymptomatic HIV infection can be delayed significantly by TCM intervention.<sup>36,37</sup>

Briefly, the importance of the treatment effects of patients with asymptomatic HIV infection with TCM has been recognized and accepted by some of patients and TCM practitioners in China, and the further research had been carried out to confirm those effects of the treatment of asymptomatic HIV infection with TCM founded by the national major projects since 11th 5-year period.

## EVALUATION OF TCM EFFECT ON THE ASYMPTOMATIC CONDITION INFECTED WITH HIV

AIDS caused by HIV infection. If the infection is not detected and treated, the immune system gradually weakens and AIDS develops. As a matter of course, CD4+T cell counts and HIV loads had been recommended as evaluation and monitoring approach for cART,<sup>38</sup> and has been used globally.

By contrast, efficacy assessment of TCM may be quite different to that of WM. For TCM rely on a holistic approach, conventional efficacy assessment measures may not be adequate. Thus, it is difficult to evaluate the treatment of TCM on AIDS simply through CD4+T cell counts and plasma HIV viral loads.

In general, TCM practitioners mainly focus on the clinical complaints of the patient and all those abnormal symptoms and signs according to the theory of treatment based on pattern and disease identification. Thus they evaluate the treatment effects through the improvements of troublesome symptoms and signs, health related quality of life, mental and spiritual, the side-effects of cART, CD4+T cell counts and/or levels of HIV loads; when they treat or change their strategy for patients for the various objectives. Furthermore, some researchers had adopted delayed time of asymptomatic HIV infection to AIDS stage as evaluation endpoints in their studies.<sup>39</sup>

## CONCLUSION

The roles of TCM on AIDS had been recognized and accepted by more and more people. The asymptomatic HIV infection stage is a relatively long period. From the viewpoints of TCM, not only the imbalance of *Yin* and *Yang* but also the disharmony of internal body function and external natural environment had occurred during the asymptomatic HIV infection stage.

The imbalance and the disharmony can be restored by TCM methods based on the patterns identified from the symptoms for treatment. We do believe that asymptomatic HIV infection stage is a good timing of using TCM to manage the condition.

## ACKNOWLEDGMENT

The authors are grateful for the people who contributed to the foundation of our work.

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