ORIGINAL RESEARCH

Clinical effects of adjunctive spleen- and kidney-invigorating Chinese herbal therapy combined with highly active antiretroviral treatment on immune recovery and nutritional status in people living with HIV

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Abstract

Objective

To evaluate whether adding a spleen- and kidney-invigorating Chinese herbal decoction to highly active antiretroviral therapy (HAART) improves immune recovery and nutritional status in people living with HIV.

Methods

Forty adults living with HIV were randomly allocated to receive either standard HAART alone or HAART plus a Chinese herbal decoction composed of astragalus, Chinese yam, dangshen, poria cocos, white atractylodes rhizome, radix pseudostellariae, and rehmannia glutinosa. Immune indices (CD4□, CD8□ T cells, Th17 cells), inflammatory cytokines (interferon-γ [IFN-γ], tumor necrosis factor-α [TNF-α]), hematological and nutritional parameters (hemoglobin, serum albumin), adverse drug reactions, and Medical Outcomes Study HIV Health Survey (MOS-HIV) scores were compared between groups.

Results:

Compared with HAART alone, HAART plus Chinese herbal decoction produced more marked immune reconstitution. At 6-12 months, the combination group had higher CD4□ counts (37.58 ± 3.76 vs 30.25 ± 3.02 cells/μL, $P < 0.0001$), lower CD8□ counts (22.41 ± 2.25 vs 28.62 ± 2.65 cells/μL, $P < 0.0001$), and higher Th17 levels (2.26 ± 0.23 vs 1.89 ± 0.19 cells/μL, $P < 0.0001$). IFN-γ and TNF-α concentrations were significantly reduced, while hemoglobin (126.87 ± 12.68 vs 116.32 ± 11.65 g/L, $P = 0.009$), serum albumin (38.82 ± 3.84 vs 32.45 ± 3.26 g/L, $P < 0.0001$), and MOS-HIV scores (80.36 ± 8.07 vs 72.58 ± 7.25, $P = 0.0026$) were higher in the combination group. The incidence of adverse reactions was similar between the two groups.

Conclusion

Adjunctive use of a spleen- and kidney-invigorating Chinese herbal decoction with HAART may help restore the balance of T-lymphocyte subsets, attenuate systemic inflammation, enhance immune function, and improve nutritional status in patients with acquired immune deficiency syndrome.

Keywords: Acquired Immune Deficiency Syndrome, Highly Active Antiretroviral Therapy, Chinese Traditional Medicine, T Lymphocyte Subsets, Nutritional Status

Introduction

Acquired immune deficiency syndrome (AIDS) develops after infection with human immunodeficiency virus (HIV)[1]. As the disease progresses, HIV invades and destroys helper T lymphocytes, impairing immune cells and increasing susceptibility to malignancies, pneumonia, and other serious diseases[2]. With the continuous exploration of modern clinical researchers, highly active antiretroviral therapy (HAART) was gradually applied to the clinical treatment of AIDS in the late 1990s, which can effectively reduce the viral load of patients, increase the number of CD4+ T lymphocytes, rebuild immune function, and with superior efficacy[3]. However, long-term HAART may induce adverse effects, drug resistance, and treatment failure[4].

According to traditional Chinese medicine, AIDS is often caused by kidney and essence damage due to exposure to epidemic viruses or excessive sexual activity, classified under "warm disease" and "overuse injury," and can be treated by invigorating the spleen and kidney[5]. The decoction of astragalus, Chinese yam, dangshen, poria cocos, white atractylodes rhizome, radix pseudostellariae, and rehmannia glutinosa is believed to strengthen the spleen and kidney. Previous studies reported its efficacy in combination with calcium dobesilate for diabetic nephropathy[6], but its role in people living with HIV remains unclear.

This study aimed to evaluate the clinical efficacy of the decoction combined with HAART on T lymphocyte regeneration and nutritional status in people living with HIV.

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Methods

General data

Forty people living with HIV who received therapy at our hospital between April 2022 and December 2023 were included. Sample size was estimated using G*Power 3.1 software, assuming a medium effect size (Cohen's d = 0.7), a two-tailed $\alpha = 0.05$, and a power $(1–\beta) = 0.80$. The calculation indicated that at least 18 participants per group were required; therefore, a total of 40 patients (20 per group) were included to ensure adequate statistical power. Through the random number table method, an electronically generated random sequence created using SPSS 21.0 software was used to divide the patients into the HAART group and the combination group, with 20 cases in each group. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes prepared by an independent researcher not involved in recruitment or assessment. Laboratory technicians and statisticians conducting the analyses were blinded to group allocation to minimize potential bias.

The HAART group included 10 males and 10 females (mean age 41.52 ± 3.69 years, body mass index (BMI) 23.14 ± 1.22 kg/m^2). The combination group included 12 males and 8 females (mean age 41.55 ± 3.72 years, BMI 23.18 ± 1.23 kg/m^2). No significant differences in demographics or baseline plasma HIV viral loads were observed ($P > 0.05$).

Baseline plasma HIV viral loads were assessed before randomization, and no significant difference was found between the HAART group and the combination group ($P > 0.05$). All patients received standardized HAART regimens administered under direct supervision by clinical pharmacists to ensure medication adherence throughout the study. Participants with severe comorbid conditions such as liver cirrhosis, renal failure, or malignancy were excluded, ensuring comparability of baseline health status across groups.

Inclusion criteria: (1) Patients diagnosed with AIDS; (2) Patients signed informed consent; (3) Age ≥18 years. Exclusion criteria: (1) Drug, alcohol, or psychiatric disorders; (2) Communication barriers; (3) Pregnancy or lactation period; (4) Severe infection, fatal complications and multiple organ failure. This study has been approved by the Medical Ethics Committee of the Affiliated Hospital of Shaoxing University (Approval No. 2023(reserach)-006-01).

Treatments

The HAART group received HAART treatment: The patient was treated with oral zidovudine tablets (Shanghai Desano Pharmaceutical Group Co., LTD.), 300 mg/time; oral lamivudine tablets (Shaanxi Xingbang Pharmacevtical Co., Ltd.) treatment, 150 mg/time; oral nevirapine (Shanghai Shyndec Pharmaceutical Co., Ltd.) treatment, 200 mg/time.

The combination group received decoction of invigorating spleen and kidney on the basis of HAART. The prescription of decoction of invigorating spleen and kidney was as follows: astragalus 30 g, Chinese yam 30 g, dangshen 30 g, poria cocos 15 g, white atractylodes rhizome 15 g, radix pseudostellariae 15 g, and rehmannia glutinosa 15 g. The prescription was mixed and boiled with 800 mL water, concentrated to about 250 mL, 1 dose a day.

Both groups were treated for 12 months.

Observation indicators

(1) 3 mL fasting venous blood was gathered from patients, centrifuged, and the CD3+, CD4+, and CD8+ T lymphocyte subsets were measured using flow cytometry.

(2) 3 mL fasting venous blood was gathered from patients, centrifuged, and the Th17 cells were detected by flow cytometry.

(3) 3 mL fasting venous blood was gathered from patients, centrifuged, and the levels of interferon-γ (IFN-γ) as well as tumor necrosis factor-α (TNF-α) were detected by enzyme-linked immunosorbent assay (ELISA).

(4) 3 mL fasting venous blood was collected from patients, centrifuged, and the plasma was stored at -20^{0}C. The hemoglobin and serum albumin levels of the two groups were compared.

(5) The adverse drug reactions, such as diarrhea, gastrointestinal reactions, blood system abnormalities, nausea and vomiting, were compared between 2 groups.

(6) Medical Outcomes Study HIV Health Survey (MOS-HIV) was used to evaluate the quality of life of 2 groups 7, including 11 areas such as physical function, social function, mental health, pain, and cognitive function, with a total of 35 items. The original score was obtained by accumulating first and then converted into a 100-point scale. The higher the score, the better the quality of life was.

Statistical analysis

SPSS 21.0 was used for analysis. Continuous and categorical data are presented as mean ± SD and n (%), respectively. Comparisons were performed using t-tests or χ^2 tests, with $P < 0.05$ considered statistically significant.

Results

Number of T lymphocyte subsets in 2 groups

Before therapy, no difference was seen in the number of CD3$^+$, CD4$^+$, along with CD8+ T lymphocyte subsets between 2 groups ($P>0.05$, Figure 1). After 3 months of treatment, CD3$^+$ counts in the combination group (49.68 ± 5.02 cells/μL) were significantly higher than in the HAART group (45.23 ± 4.52 cells/μL, $P = 0.006$). At 6 months, the combination group also showed higher CD3$^+$ counts (54.72 ± 5.48 cells/μL) compared with the HAART group (50.06 ± 5.07 cells/μL, $P = 0.008$). After 3 months, CD4$^+$ counts in the combination group (30.65 ± 3.06 cells/μL) were significantly higher than in the HAART group (25.64 ± 2.56 cells/μL, $P < 0.0001$). At 6 months, the combination group also showed higher CD4$^+$ counts (37.58 ± 3.76 cells/μL) compared with the HAART group (30.25 ± 3.02 cells/μL, $P < 0.0001$). After 3 months, CD8$^+$ counts in the combination group (28.65 ± 2.87 cells/μL) were significantly lower than in the HAART group (32.41 ± 3.25 cells/μL, $P = 0.0005$). At 6 months, the combination group showed further reduction in CD8$^+$ counts (22.41 ± 2.25 cells/μL) compared with the HAART group (28.62 ± 2.65 cells/μL, $P < 0.0001$).

Number of Th17 cells in 2 groups

Th17 cell counts increased over time in both groups. At baseline, there was no significant difference between the HAART group (1.39 ± 0.14 cells/μL) and the combination group (1.40 ± 0.14 cells/μL, $P = 0.82$, Figure 2). After 6 months, Th17 counts in the combination group (1.86 ± 0.18 cells/μL) were significantly higher than in the HAART group (1.62 ± 0.16 cells/μL, $P < 0.0001$).

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Table 1 Incidence of adverse drug reactions in 2 groups

Groups	n	Diarrhea	Gastrointestinal reactions	Blood system abnormalities	Nausea and vomiting	Total incidence rate
HAART group	20	0	1	0	1	2 (10.00%)
Combination group	20	1	1	1	1	4 (20.00%)
χ^2						0.784
P						0.375

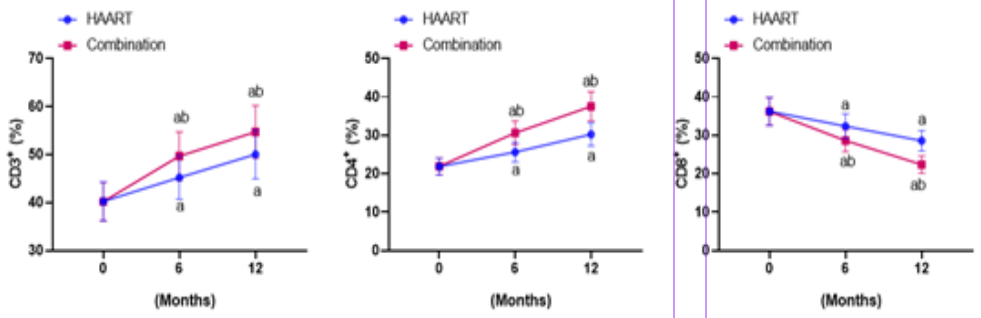

Figure 1 Number of T lymphocyte subsets in 2 groups. aP<0.05, in contrast to before therapy. bP<0.05, in contrast to HAART group

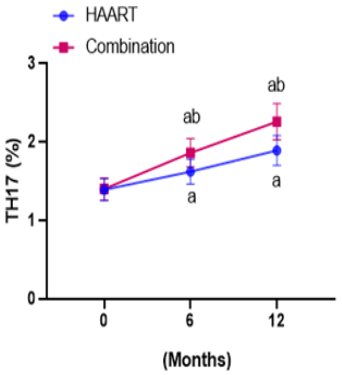

Figure 2 Number of Th17 cells in 2 groups. [a]P<0.05, in contrast to before therapy. [b]P<0.05, in contrast to HAART group

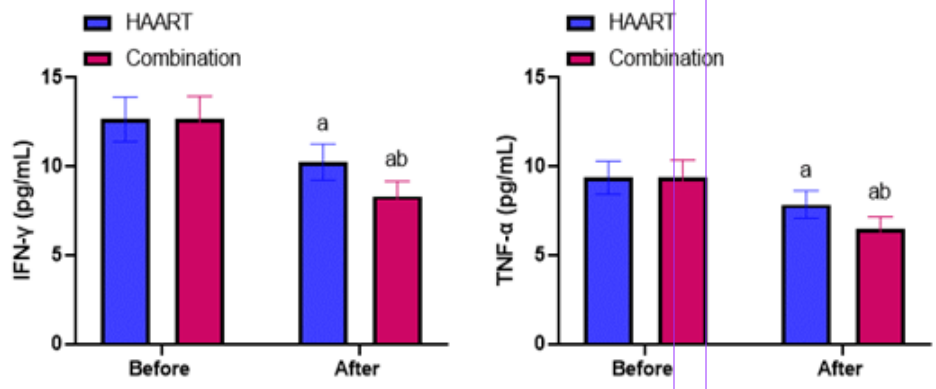

Figure 3 Inflammation in 2 groups. aP<0.05, in contrast to before therapy. bP<0.05, in contrast to HAART group

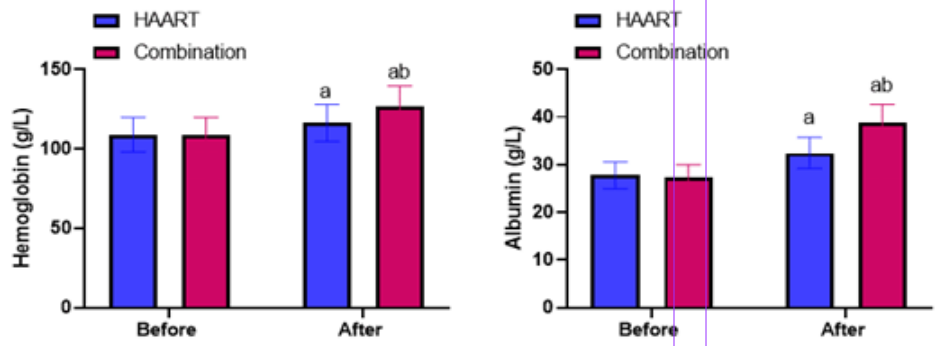

Figure 4 Nutritional status in 2 groups. [a]P<0.05, in contrast to before therapy. [b]P<0.05, in contrast to HAART group

At 12 months, the combination group also showed higher Th17 counts (2.26 ± 0.23 cells/μL) compared with the HAART group (1.89 ± 0.19 cells/μL, P < 0.000, Figure 2).

Inflammation in 2 groups

Before therapy, no difference was seen in IFN-γ and TNF-α levels between 2 groups (P>0.05, Figure 3). After treatment, IFN-γ levels in the combination group (8.32 ± 0.83 pg/mL) were significantly lower than in the HAART group (10.23 ± 1.03 pg/mL, P < 0.0001). After treatment, TNF-α levels in the combination group (6.51 ± 0.65 pg/mL) were

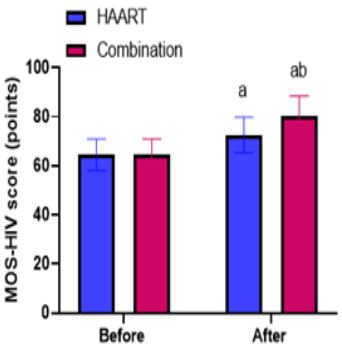

Figure 5 Quality of life in 2 groups. aP<0.05, compared with before therapy. bP<0.05, compared with HAART group

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significantly lower than in the HAART group (7.85 ± 0.78 pg/mL, P < 0.0001).

Nutritional status in 2 groups

Before therapy, no difference was seen in hemoglobin and serum albumin levels between 2 groups (P>0.05, Figure 4). After treatment, hemoglobin levels in the combination group (126.87 ± 12.68 g/L) were significantly higher than in the HAART group (116.32 ± 11.65 g/L, P = 0.009), and serum albumin levels in the combination group (38.82 ± 3.84 g/L) were significantly higher than in the HAART group (32.45 ± 3.26 g/L, P < 0.0001).

Incidence of adverse drug reactions in 2 groups

There was no significant difference in the incidence of adverse reactions between the HAART group and the combination group (P>0.05, Table 1).

Quality of life in 2 groups

Before therapy, no difference was seen in MOS-HIV score between 2 groups (P>0.05, Figure 5). After treatment, the combination group showed significantly higher MOS-HIV scores (80.36 ± 8.07) than the HAART group (72.58 ± 7.25, P = 0.0026).

Discussion

When the human body is infected with HIV, the immune system will be seriously damaged, humoral immunity, cellular immunity is destroyed, resulting in the collapse of the human immune system, and with the progress of the disease, immune function can gradually decline, the ability to clear the virus is also reduced, and eventually induce immune function deficiency, progress to AIDS[8]. The process of HIV infection to AIDS is long, usually about 8 to 10 years, most of the time are in the asymptomatic period, if the intensive antiviral treatment at this stage, it can delay the transition time from the asymptomatic period to the AIDS period, and promote patients to be in the asymptomatic period for a long time to improve the quality of life[9].

HAART is the mainstream treatment for HIV infection[10]. Zidovudine, lamivudine, and Nevira are commonly used broad-spectrum antiviral drugs on average. The combined use of the three drugs can not only maximize the inhibition effect of HIV virus, reduce the damage of immune system, but also reduce the drug resistance caused by single drug, thus delaying the progression of the disease and ensuring that the patient remains asymptomatic for a long time[11]. Because HAART therapy is to give patients a variety of drugs at the same time, and requires to be used for a long period, the toxic and side effects brought by this therapy has become a prominent problem in clinical AIDS treatment at present, and the prognosis of patients is not good[12].

The treatment of AIDS by traditional Chinese medicine has a history of over 30 years[13]. From the current clinical research, traditional Chinese medicine has the advantages of higher safety and less adverse reactions[14]. When the human body is infected with HIV, the virus continues to replicate in the body and damage the human body's positive qi, the pathogenesis of the disease is characterized by the combination of qi deficiency, poison, and dampness[15]. If given a simple antiviral treatment, it is difficult to support the positive qi; if given a simple supporting treatment, the poison is difficult to remove; if only use of resolving dampness treatment, the poison damage is difficult to treat. Therefore, in the treatment of AIDS, it is necessary to strengthen body resistance and eliminate evil, supplement qi and tonify deficiency as the treatment principle, which can help to adjust the immune function of the body, promote the improvement of clinical symptoms[16].

In the prescription of decoction of invigorating spleen and kidney, astragalus, dangshen and radix pseudostellariae can tonifying primordial qi and invigorate spleen and kidney[17-19]; Chinese yam, poria cocos and white atractylodes rhizome can strengthen the spleen and nourish the stomach and supplement qi[20-22]; rehmannia glutinosa can nourish kidney and replenish vital essence[23]. The combination of all kinds of drugs can play the function of invigorating spleen and kidney. As reported previously, decoction of invigorating spleen and kidney has been reported to have effective clinical efficacy in treating many diseases, such as asthma[24], chronic hepatitis B virus[25], and myasthenia gravis[26].

In our study, the results suggested that compared to before therapy, and the improvements of CD3+, CD4+, along with CD8+ T lymphocyte subsets in the combination group were more significant as comparing with HAART group, the number of Th17 cells in the combination group presented higher as comparing with HAART group, IFN-γ along with TNF-α levels in the combination group were lower as comparing with HAART group, hemoglobin and serum albumin levels in the combination group were higher as comparing with HAART group, and MOS-HIV score in the combination group was higher as comparing with HAART group. All these results suggested that decoction of invigorating spleen and kidney combined with HAART could promote the balance of T lymphocyte subsets, reduce the inflammatory response, improve the immune function, and promote the nutritional status of people living with HIV. Consistently, Zhang et al. have indicated that Chinese medicine of invigorating spleen and kidney detoxification has immune regulation effect in simian immunodeficiency virus-infected rhesus macaque[27]. Wei et al. have indicated that the therapeutic principles of invigorating the liver and kidney can strengthen the viability and improve the nutrition state of patients with peritoneal dialysis for chronic renal failure[28].

Several bioactive components in the herbal prescription may contribute to the observed immunological improvements. Astragalus membranaceus contains polysaccharides and saponins that can enhance T-cell proliferation and promote $CD4^+$ T-cell differentiation by activating the PI3K/Akt and MAPK signaling pathways, thereby improving the Th1/Th2 balance and reducing pro-inflammatory cytokines such as TNF-α and IFN-γ[29,30]. Rehmannia glutinosa has been shown to regulate the hypothalamic-pituitary-adrenal axis and inhibit NF-κB activation, which may suppress excessive inflammatory responses while supporting immune restoration[31]. Poria cocos polysaccharides exert immunomodulatory effects by activating dendritic cells and macrophages, promoting cytokine secretion (IL-2, IL-10), and indirectly enhancing T-cell subset recovery[32]. Together, these mechanisms may underlie the improved T-cell subset balance and reduced inflammatory cytokine levels observed in the combination group.

These herb-driven effects align with several key immunological processes known to govern HIV pathogenesis and immune recovery. Early and sustained loss of mucosal $CD4^+$ subsets-particularly Th17 cells—compromises gastrointestinal barrier integrity and promotes microbial translocation, a major driver

of chronic systemic immune activation in HIV infection; restoring Th17 function therefore can reduce translocation and downstream immune activation[33]. Reducing systemic immune activation is crucial because persistent activation both drives bystander CD4+ T-cell loss and impairs effective immune reconstitution despite viral suppression with ART[34]. By inhibiting NF-κB/MAPK-mediated pro-inflammatory cytokine production (for example lowering TNF-α and IFN-γ) and by promoting antigen-presenting cell maturation and T-cell proliferative responses, the herbal components could therefore (a) decrease pathogenic immune activation and (b) enhance the capacity for CD4+ T-cell recovery and functional restoration under HAART[35]. Finally, because chronic HIV infection is associated with T-cell exhaustion and dysfunctional antiviral responses, interventions that reduce antigenic/inflammatory burden and improve APC–T cell interactions may indirectly limit exhaustion and permit better qualitative recovery of T-cell function, complementing quantitative CD4+ gains observed clinically[36].

Our findings also have practical relevance in the context of current HIV/AIDS management. Globally, the Joint United Nations Programme on HIV/AIDS (UNAIDS) emphasizes achieving sustained viral suppression and functional immune recovery through antiretroviral therapy optimization and patient-centered care[37].

In China and other Asian regions, integrative treatment combining HAART with traditional Chinese medicine has been incorporated into national HIV management guidelines as a complementary approach to enhance immune recovery and mitigate HAART-related toxicity[38,39]. Previous studies have shown that traditional Chinese medicine interventions improve the immune reconstruction and improve CD4+ T-cell recovery and alleviate fatigue, gastrointestinal intolerance, and hepatic dysfunction associated with HAART[40-42]. Our results are consistent with these findings and suggest that integrating herbal immunomodulation with standardized HAART may provide a translational pathway to enhance long-term immune restoration and quality of life in people living with HIV, especially in regions where traditional Chinese medicine resources and clinical expertise are readily available.

This study has several limitations that should be acknowledged. First, the sample size was relatively small and recruited from a single center, which may limit the generalizability of the findings. Second, although baseline viral loads were assessed, longitudinal viral load monitoring during treatment was not performed, preventing a direct evaluation of viral suppression as a contributing factor to immune recovery. Third, the lack of long-term follow-up data restricts the assessment of sustained immune function and nutritional improvements. Future multicenter studies with larger sample sizes and comprehensive viral load monitoring are warranted to validate and extend these findings.

Conclusion

Our study demonstrates that decoction of invigorating spleen and kidney combined with HAART can promote the balance of T lymphocyte subsets, reduce the inflammatory response, improve the immune function and promote the nutritional status of people living with HIV.

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