Analysis of the Clinical Efficacy of Tenofovir Tablets Combined with Liqi Fuzheng Decoction in the Treatment of Acquired Immune Deficiency Syndrome

XINLI RU, HAIYAN XU, YANPING XU AND HAIYAN SONG*

Department of Infectious Diseases, Zhuji people's Hospital, Zhuji, Zhejiang Province 311800, P. R. China

This study attempts to discuss the clinical efficacy of tenofovir tablets combined with Liqi Fuzheng decoction (consist of *Radix pseudostellariae* 30 g, fruit of citron or trifoliate orange 9 g, inula 12 g, *Pinellia ternata* 9 g, pericarpium citri reticulatae viride 9 g, dried tangerine peel 9 g, costus root 9 g, corydalis 15 g, rice sprout 30 g, malt 30 g, dandelion 30 g, its indications for gastrointestinal disorders) in the treatment of acquired immune deficiency syndrome patients with immune reconstitution and liver and kidney damage. We selected 70 acquired immune deficiency syndrome patients treated in our dermatology department from January 2019 to June 2020. Then randomly divided them into observation group (35 patients treated with tenofovir tablets and Liqi Fuzheng decoction) and control group (35 patients treated with tenofovir tablets), compare the serum cytokine concentration levels and immune function index levels of both groups of patients before and after treatment, and compare the changes in liver and kidney function and clinical efficacy after treatment. After 6 mo treatment, interleukin-2, interleukin-5, interleukin-4, interleukin-10, interferon gamma and interferon alpha levels in the serum of observation group decreased more remarkably than control group, it possessed statistical significance ($p<0.05$); observation group had greater decrease trend of cluster of differentiation 8^+ T lymphocytes and regulatory T cells than control group, which was statistically significant ($p<0.05$); observation group had greater uptrend of cluster of differentiation 4^+ T lymphocytes and T helper 17 cells than control group, which was statistically significant ($p<0.05$). Both groups had no remarkable divergence in liver and kidney function (alanine transaminase, creatinine) before and after treatment, and it possessed no statistical significance ($p>0.05$). The total clinical effective rate of observation group (94.29 %) was remarkably higher than control group (82.86 %), it possessed statistical significance ($p<0.05$). The combination of tenofovir tablets and Liqi Fuzheng decoction for long term treatment of acquired immune deficiency syndrome patients' increases cluster of differentiation 4^+ T lymphocytes and T helper 17 cells levels, improves the clinical efficiency and has no liver and kidney damage. It is a safe and effective treatment plan and is worth popularizing in clinic.

Key words: Tenofovir, Liqi Fuzheng decoction, acquired immune deficiency syndrome, clinical efficacy

In 2016, the World Health Organization (WHO) showed that 1 60 453 people were new infection of Human Immunodeficiency Virus (HIV) in 51 European countries every year, it is equivalent to 18.2 new infection of HIV infections per 1 00 000 people. According to statistics, about 15 % of HIV infected people do not know that they have been infected with HIV[1]. Although the clinical, immunological and virological course of untreated HIV infection varies, there is evidence of HIV progression during follow-up for 8-10 y [2]. Most patients who have not received Antiretroviral Therapy (ART) will die within 2 y after the onset of Acquired Immune Deficiency Syndrome (AIDS). At the same time, ART treatment can transform AIDS patients from an advanced disease state to a chronic disease[3]. After 1 y of ART treatment, Cluster of Differentiation 4 ($CD4^+$) T cell of patients reaches at least 350 cells/µl and their life expectancy is close to normal people[4]. The current ART treatment has evolved from monotherapy to triple therapy, tenofovir disoproxil fumarate is currently the main treatment drug, but it is also exploring combination drugs, such as

***Address for correspondence**
E-mail: shy751120wom@163.com

a combination of two drugs[5]. AIDS is caused by the body's pathogenesis such as the conflict between the right and the evil, the imbalance of yin and yang, and the disorder of qi and blood after the human body is infected with the virus. It can be known from symptomatology that a variety of Chinese medicine combinations regulate the body's immune function and inhibit the activity of HIV. Liqi Fuzheng decoction can improve human immunity[6,7]. Under these conditions, we attempt to discuss the clinical efficiency of tenofovir tablets combined with Liqi Fuzheng decoction in treating AIDS and influence of patients' serum cytokines and immune indexes and we seek to provide a reference for finding safe and effective methods to improve the clinical efficacy and prognosis of AIDS patients, let us check the following reports. We selected 70 AIDS patients who received treatment in our dermatology department from January 2019 to June 2020. Inclusion criteria includes patients met the standard of "Chinese guidelines for diagnosis and treatment of HIV/AIDS (2018)"[8] and are diagnosed with AIDS after clinical examination; patients without communication or mental disorders; patients without immune system diseases; patients and their families signed an informed consent form. Exclusion criteria includes pregnant women and patients with liver and kidney diseases; patients with cardiovascular diseases; patients with unstable vital signs; patients with known malignancy; minor patients, patients allergic to the study drug. We divided patients into control group and observation group (n=35). 21 males and 14 females included in control group, ages were from 41 to 71 y old, average were about (52.8±8.27) y old, including 12 cases sexual contact, 21 cases drug taking and 3 cases blood contact. 19 males and 16 females included in experimental group, ages were from 39 to 72 y old, average were about (53.22±9.64) y old, including 14 cases sexual contact, 19 cases drug taking and 2 cases blood contact. All patients included in the study received informed consent, general information such as gender and age of both groups possessed no significant difference and can be compared. Control group adopted tenofovir tablets (Anhui Biochemmedical sales Co., Ltd. NMPN: H20193014, size: 300 mg), 300 mg/time, once a day. After receiving the same therapy as control group, combined with Liqi Fuzheng decoction, its main prescription: Dangshen 15 g, *Atractylodes macrocephala* 15 g, Aucklandia 10 g, Fructus aurantii 10 g, Jineijin 10 g, peach kernel 15 g, *Radix pseudostellariae* 30 g, *Astragalus* 30 g. Decoct 300 ml in water, take it warm twice in the morning and evening, 1 dose/d. Both groups received 6 mo treatment then evaluated the clinical efficacy. Collect 5 ml of fasting elbow vein of patients in control group and observation group in the morning of the 2nd d of admission and put it into two centrifuge tubes, 3 ml for each. Left standing one tube at room temperature for 30 min, centrifuged in a 3500 r/min centrifuge (4°) for 10 min, extracted the supernatant, adopted enzyme linked immune sorbent assay to exam cell factor (Interleukin (IL)-2, IL-5, IL-4, IL-10, Interferon gamma (IFN-γ) and Interferon alpha (IFN-a)) and immune function index ($CD4^+$ T, T helper 17 (Th17), $CD8^+$ T, regulatory T cells (Treg)) levels in peripheral blood serum. After 6 mo treatment, detected concentration of cell factors and immune function index in the serum. We set "Chinese guidelines for diagnosis and treatment of HIV/AIDS (2018)" as efficacy criteria, evaluated the clinical efficacy according to three indexes: Symptoms, signs and laboratory examination; the patient's condition improved significantly and the three indexes recovered completely or one of them did not recover completely; the condition improved effectively after treatment and 2~3 of the three indexes still did not fully recover; the condition has not improved significantly, even aggravated (Significantly effective+Effective)/Total cases=Total clinical effective rate. Use Statistical Package for the Social Sciences (SPSS) 22.0 software to analyze all data. Express the count data as n %, comparison of both groups tested by χ^2. Measurement data conforms to normal distribution and homogeneity of variance as ($\bar{x}\pm s$). Use t test for comparison between groups. $p<0.05$ was considered to possess statistical significance. Compare cell factors (IL-2, IL-5, IL-4 and IL-10) concentration of both groups before treatment, they had no remarkable difference, so it possessed statistical significance ($p>0.05$); after treatment, cell factors (IL-2, IL-5, IL-4 and IL-10) concentration of both groups decreased remarkably, but observation group decreased more, so it had statistical significance ($p<0.05$), as shown in Table 1. $CD4^+$ T lymphocyte, Th17 cells, $CD8^+$T lymphocyte and Treg cells levels of both groups had no difference, so it had no statistical significance ($p>0.05$); after 6 mo treatment, $CD8^+$ T lymphocyte and Treg cells levels of observation group decreased more than control group, it possessed statistical significance ($p<0.05$); $CD4^+$ T lymphocyte and Th17 cells of observation group increased more than control group, it possessed statistical significance ($p<0.05$), as shown in Table 2. Liver function index Alanine Transaminase (ALT) and kidney function index Creatinine (Cr) of both groups before and after treatment

were all in the normal scopes, increasing Liqi Fuzheng decoction had no influence on liver and kidney function, so it possessed no statistical significance ($p<0.05$), as shown in Table 3. After 6 mo treatment, the total clinical effective rate of observation group (94.29 %) was remarkably higher compared with control group (82.86 %). They were obviously different and it possessed statistical significance ($p<0.05$). As shown in Table 4. HIV is a retrovirus leading to AIDS, which affects tens of millions of people worldwide, despite recent progress in the treatment and prevention of HIV, millions of new HIV infections and AIDS related deaths are still dying each year[9]. Decades of investigation have made significant progress in HIV treatment and prevention. However, 2.1 million new HIV infections occurred worldwide in 2015, constant HIV infection in developing countries may indicate new prevention and treatment methods to curb the severe epidemic, then reducing the above incidence rate and China's AIDS mortality[10]. Moreover, nearly 37 million people are HIV infectors and it causes 1 million deaths in the same year[11]. Despite we have developed and optimized many Antiretroviral (ARV) therapies, microbicides and protective barriers, but HIV epidemic in African countries is still at an alarming high level. At present, we need an effective HIV-1 vaccine to curb the epidemic of AIDS[12]. Tenofovir dipivoxil fumarate (oral preparation of tenofovir) has got approval for HIV and Hepatitis B Virus (HBV) treatment. A new alternative to tenofovir alleviates toxic adverse reactions such as kidney and bone, while maintaining a high drug resistance barrier[13]. Neither tenofovir dipivoxil fumarate nor its active metabolite is the substrate of CYP3A4. At the same time, tenofovir dipivoxil fumarate is eliminated through glomerular filtration and renal tubular secretion[14], If there are no severe nephrotoxicity patients, almost all HIV patients receive tenofovir (dipivoxil fumarate) and kanamycin[15]. Several studies have shown that the daily oral regimen of ntriptabine combined with tenofovir fumarate has got approval for pre exposure prevention of HIV infection[16]. Specific $CD8^+$ T cells have key effect on immune control of HIV[17], $CD4^+$ T cells are the main targets of HIV-1 infection, the gradual loss of $CD4^+$ T cells in chronic HIV infectors is the key mechanism of AIDS development[18], $CD4^+$ T cell death is the result of multiple cytopathic effects, such as viral DNA integration triggering apoptosis and the presentation of viral peptides on the cell surface[19], this leads to cytotoxic T lymphocyte mediated killing and cytokines are released after cell death, thus it shows that HIV infection is the main mechanism leading to chronic inflammation, $CD4^+$ T cell exhaustion, T cell steady-state misadjustment and finally AIDS[20]. This study indicates that after effective treatment IL-2, IL-5, IL-4, IL-10 concentration in the serum of groups decreased remarkably, $CD8^+$ lymphocyte and Treg cells levels of AIDS patients had a greater downtrend while $CD4^+$ T lymphocyte and Th17 cells levels had a greater uptrend. It indicates that the combination of tenofovir and Liqi Fuzheng decoction has obvious curative effect on immune system reconstruction of AIDS patients, which is consistent with previous studies. This study also has some short comings. At present, the combined use of Chinese and Western medicines is still in preliminary trials in the treatment of AIDS patients, the combination of traditional Chinese medicine and antiviral drugs is to enhance its antiviral effect, how to play the role of antiviral, which traditional Chinese medicine component has the greatest curative effect has not been verified by experiment, these problems need to be further studied in the future. At the same time, we study the situation that small sample size will also cause result bias. This study proves that tenofovir tablets combined with Liqi Fuzheng decoction in the treatment of AIDS liver and kidney function (ALT, Cr) had no remarkable difference before and after treatment, and it possessed no statistical significance ($p>0.05$), the total clinical effective rate of observation group (94.29 %) was remarkably higher compared with control group (82.86 %), it possessed statistical significance ($p<0.05$). Tenofovir tablets combined with Liqi Fuzheng decoction for long-term treatment of AIDS patients' increases $CD4^+$ T lymphocytes and Th17 cells levels, improve the clinical efficiency and has no liver and kidney damage. It is a safe and effective treatment plan and is worth popularizing in clinic.

TABLE 1: COMPARISON OF SERUM CELL FACTORS LEVELS OF BOTH GROUPS BEFORE AND AFTER TREATMENT (pg/ml) (x̄±s)

Item	Before and after treatment	Observation group (n=35)	Control group (n=35)	t	p
IL-2	Before treatment	14.18±9.04	13.54±9.23	0.23	0.84
	After treatment	6.54±3.23	9.69±5.21	3.57	0.008
IL-4	Before treatment	16.15±11.09	15.59±9.96	0.35	0.71
	After treatment	7.06±3.31	10.78±5.94	6.35	0.001
IL-5	Before treatment	6.18±9.04	6.54±2.53	0.46	0.53
	After treatment	3.25±1.56	4.69±2.05	11.13	0.000
IL-10	Before treatment	10.02±5.35	11.03±5.67	0.35	0.49
	After treatment	5.24±2.46	8.06±3.26	5.03	0.001
IFN-γ	Before treatment	29.18±19.35	28.59±19.01	0.36	0.69
	After treatment	13.47±9.29	19.06±11.21	4.34	0.002
IFN-α	Before treatment	8.68±4.74	8.59±4.27	0.66	0.47
	After treatment	4.03±1.53	6.07±2.45	7.57	0.001

TABLE 2: COMPARISON OF IMMUNE FUNCTION INDEX LEVELS BEFORE AND AFTER TREATMENT (x̄±s)

Item	Before and after treatment	Observation group (n=35)	Control group (n=35)	t	p
$CD4^+$ T lymphocyte (pc/μl)	Before treatment	185±47	186±45	0.27	0.76
	After treatment	441±61	211±49	9.25	0.001
$CD8^+$ T lymphocyte (pc/μl)	Before treatment	165±37	162±36	0.19	0.72
	After treatment	111±22	142±23	6.02	0.001
Th17 cells (%)	Before treatment	1.62±0.46	1.56±0.41	0.46	0.52
	After treatment	2.46±0.39	1.79±0.31	7.17	0.001
Treg cells (%)	Before treatment	9.1±1.4	8.9±1.3	0.35	0.61
	After treatment	4.9±0.9	6.5±1.1	4.26	0.003

TABLE 3: COMPARISON OF ALT AND CR LEVELS IN THE SERUM OF BOTH GROUPS BEFORE AND AFTER TREATMENT

Item	Before and after treatment	Observation group (n=35)	Control group (n=35)	t	p
ALT (U/l)	Before treatment	35.93±8.64	34.22±8.12	0.27	0.76
	After treatment	37.54±9.03	39.62±9.21	0.25	0.66
Cr (μmol/l)	Before treatment	56.72±12.67	54.79±11.52	0.19	0.72
	After treatment	58.35±13.07	57.39±11.87	0.46	0.75

TABLE 4: COMPARISON OF CLINICAL EFFICACY AFTER TREATMENT

	Significantly effective	Effective	Invalid	Total clinical effective rate
Observation group	19 (54.28 %)	14 (40 %)	2 (5.7 %)	33 (94.29 %)
Control group	16 (45.71 %)	13 (37.14 %)	6 (17.14 %)	29 (82.86 %)
χ^2				5.68
p				0.006

Conflict of interests:

The authors declared no conflicts of interest.

REFERENCES

1. Parikh UM, McCormick K, van Zyl G, Mellors JW. Future technologies for monitoring HIV drug resistance and cure. Curr Opin HIV AIDS 2017;12(2):182-9.
2. Bandera A, Gori A, Clerici M, Sironi M. Phylogenies in ART: HIV reservoirs, HIV latency and drug resistance. Curr Opin Pharmacol 2019;48:24-32.
3. Smith MK, Jewell BL, Hallett TB, Cohen MS. Treatment of HIV for the prevention of transmission in discordant couples and at the population level. Adv Exp Med Biol 2018;1075:125-62.
4. Noy A. Optimizing treatment of HIV-associated lymphoma. Blood 2019;134(17):1385-94.
5. Bale MJ, Kearney MF. HIV-1 phylogeny during suppressive antiretroviral therapy. Curr Opin HIV AIDS 2019;14(3):188-93.
6. Oti VB. Nanoparticles and its implications in HIV/AIDS therapy. Curr Drug Discov Technol 2020;17(4):448-56.
7. Flexner C, Owen A, Siccardi M, Swindells S. Long-acting drugs and formulations for the treatment and prevention of HIV infection. Int J Antimicrob Agents 2021;57(1):106220.
8. AIDS and hepatitis C professional group, Society of infectious diseases, Chinese Medical Association; Chinese Center for Disease Control and Prevention. Chinese guidelines for diagnosis and treatment of HIV/AIDS (2018). Zhonghua Nei Ke Za Zhi 2018;57(12):867-84.
9. Cadiñanos J, Montejano R, de Miguel Buckley R, Marcelo C, Arribas JR. Risks and benefits of reducing the number of drugs to treat HIV-1 infection. Expert Opin Drug Saf 2021;20(4):397-409.
10. Glass TR, Günthard HF, Calmy A, Bernasconi E, Scherrer AU, Battegay M, *et al.* The role of Human Immunodeficiency Virus (HIV) asymptomatic status when starting antiretroviral therapy on adherence and treatment outcomes and implications for test and treat: The Swiss HIV cohort study. Clin Infect Dis 2021;72(8):1413-21.
11. Wong LM, Jiang G. NF-κB sub-pathways and HIV cure: A revisit. EBioMedicine 2021;63:103159.
12. Waymack JR, Sundareshan V. Acquired immune deficiency syndrome. StatPearls; 2021.
13. Thornhill J, Orkin C. Long-acting injectable HIV therapies: The next frontier. Curr Opin Infect Dis 2021;34(1):8-15.
14. Chen BC. A new drug for the treatment of human immunodeficiency virus type I multidrug resistance-Fortesavir sustained release tablets. Herald Med 2021;40(3):425-34.
15. Skelton WM, Cardaciotto L, O'Hayer CV, Goldbacher E. The role of self-compassion and shame in persons living with HIV/AIDS. AIDS Care 2021;33(6):818-26.
16. Schank M, Zhao J, Moorman JP, Yao ZQ. The impact of HIV- and ART-induced mitochondrial dysfunction in cellular senescence and aging. Cells 2021;10(1):174.
17. Huang S, Lv SQ, Duan HF. Cohort Study on the influence of opportunistic infections pathogens on the distribution of peripheral blood T lymphocyte subsets in newly acquired AIDS patients during antiretroviral therapy. J Kunming Med Univ 2021;42(11):159-65.
18. Brown I, Finnigan NA. Fever of Unknown Origin (FUO). StatPearls; 2018.
19. da Silva Prates G, Malta FM, de Toledo Goncalves F, Monteiro MA, Fonseca LA, R Veiga AP, *et al.* AIDS incidence and survival in a hospital-based cohort of HIV-positive patients from São Paulo, Brazil: The role of IFN-λ4 polymorphisms. J Med Virol 2021;93(6):3601-6.
20. Lieber M, Chin-Hong P, Whittle HJ, Hogg R, Weiser SD. The synergistic relationship between climate change and the HIV/AIDS epidemic: A conceptual framework. AIDS Behav 2021;25(7):2266-77.]

This article was originally published in a special issue, "New Advancements in Biomedical and Pharmaceutical Sciences" Indian J Pharm Sci 2022:84(2) Spl Issue "98-102"