

Original Article

Impact of programmatic intervention on the treatment compliance of patients with HIV/TB dual infection

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Abstract: To study the treatment compliance impact of Programmatic intervention to acquired immune deficiency syndrome (AIDS) patients with Mycobacterium tuberculosis (TB) dual infection. 90 cases HIV/TB dual infection patients were selected and randomly divided into the observation group (n=45) and the control group (n=45). The observation group was treated after the programmatic interventions, whereas the control group followed the conventional treatment. CD₄⁺ T lymphocyte level, treatment compliance and adverse reaction were compared between two groups after four months intervention. After 4 months treatment, the rate of patients with CD₄⁺ lymphocyte >350/μl (60% vs. 6.67%, P<0.05), medication compliance (91.11% vs. 66.67%, P<0.05), dietary compliance (82.22% vs. 57.78%, P<0.05) and inspection compliance (73.33% vs. 42.22%, P<0.05) were significantly higher in the observation group than that in control group. Whereas the rate of patients with CD₄⁺ lymphocyte <300/μl (6.67% vs. 22.22%, P<0.05) and adverse reaction (17.78% vs. 60%, P<0.05) in the observation group were markedly lower. Programmatic intervention on patients with HIV/TB dual infection can improve the patients' treatment compliance and CD₄⁺ T lymphocyte levels. It is worth popularized in clinic to improve life quality.

Keywords: HIV/TB dual infection, programmatic intervention, treatment compliance

Introduction

In recent years, AIDS patients and patients with human immunodeficiency virus (HIV) infection increased significantly and they drew numerous physicians' attention. AIDS is a kind of dangerous infectious disease, and it is caused by infection with HIV [1-3]. HIV mainly caused human immune system defects and make human body easy to be infected by various diseases including malignant tumor, resulting in high fatality rate [4, 5]. TB is a type of intracellular infection bacteria that is generally inhaled through respiratory tract and infected alveolar macrophage [6-8]. As shown in many studies, TB infection is the most common opportunistic infections in patients with HIV and AIDS. Furthermore, it is the leading lethal factor to such patients [8-10]. Some investigators reported that 23% to 64% HIV and AIDS patients complicated by TB infection. Though most simple tuberculosis patients can be cured, patients combined with HIV infection had higher incidence of adverse reactions and fatality rate,

while the cure rate is lower [10-12]. Several reports indicated that the main reason of TB patients' chemotherapy failure is irregular chemotherapy or premature discontinuation. Therefore, medication compliance is crucial in treating HIV/TB dual infection patients [13, 14].

Materials and methods

Clinical information

90 HIV/TB dual infection patients from Shanghai Pulmonary Hospital between January 2013 and July 2015 were enrolled. Exclusion criteria: (1) Mental illness history. (2) Disturbance of consciousness. (3) Unwilling to participate in. 61 cases were male and 29 were female with average 42.1±13.7 years old (ranged 17-67). Route of HIV infection: 35 cases by sexual transmission, 26 cases by intravenous drug abuse, 13 cases by both, and 16 cases by blood transfusion. The protocol of this study was approved by Shanghai Pulmonary Hospital. Informed consents were obtained from all subjects.

Methods

Observation group were treated by programmatic intervention treatment, while control group followed conventional treatment. Conventional treatment includes dietary intervention, psychological intervention, life intervention, and disinfection and isolation. All of the patients adopt anti-mycobacterium tuberculosis treatment and antiviral treatment.

Anti-mycobacterium tuberculosis treatment

In the 1st-2nd months (reinforcement phase, daily medication), isoniazid (before breakfast), rifampicin (before supper), ethambutol (before breakfast) were taken 1 time a day and 3 pieces per time; Pyrazinamide for 3 times a day and 2 pieces per time; Biphenyl double lipid for 3 times a day and 5 granules per time; Liver-protecting tablet for 3 times a day and 3 pieces per time. In the 3rd-12th months (consolidation phase, medicine every other day), isoniazid (before breakfast) for 1 piece every other day; Rifampicin (before supper) for 4 pieces every other day; Biphenyl double lipid and liver-protecting tablet for three times a day and 5 or 3 pieces each time, respectively.

Antiviral treatment

The treatment of patients with HIV/TB dual infection process is quite complex, which needing the coordinate function of anti-TB drugs and antiviral drugs. Antiviral drugs include protease inhibitors, nucleosides and non-nucleoside drugs. Combined drugs were selected for three types of drugs.

Programmatic intervention

(1) Evaluation: evaluation sheet was established, evaluation content includes basic condition, patients awareness to tuberculosis and HIV/AIDS, transmission route, prevention measures, treatment methods, and psychological reaction, etc. (2) Develop treatment interventions: develop the intervention program according to the different physiological condition and assessment of the patients as follows. ① Strengthen the training of medical personnel. Improve the previous treatment defects, standard medical personnel's behavior to ensure that treatment intervention put in place in a better way, and to improve patients' foundation treatment quality and service satisfaction. ②

Psychological intervention. Patients may be affected by the negative in life for infected by HIV, such as losing job, friends, and even family members which may result in depression, guilt or other mental state. Health care workers, therefore, should abandon discriminatory and maintain moderate attitude to close to patients, and encourage them face reality bravely. TB curative effect tends to be poor and prone to adverse when combined with HIV infection, whereas simultaneous treatment is likely to bring great economic burden. Therefore, encouraging patients' families to give spiritual and financial support, help patients overcome the difficulties is also important. ③ Health education. Provide the information about the development, treatment measure and its possible adverse reaction of TB and HIV/AIDS to the patients and their families. If possible, let the patients that have good treatment effect preach to relieve the patient's concerns and enhance their psychological acceptance. ④ Anti-TB treatment intervention. It is important to let the patient understand the necessity of taking anti-TB drugs united, early, right amount and regularly since anti-TB treatment can positively reduce the patient's clinical symptoms. Furthermore, stress the patients for sputum smear or sputum culture at least once a month, in order to ensure the correctness of the test. ⑤ Antiviral intervention. Inform patients that some adverse reaction is normal since most of the antiviral drug taking gastrointestinal adverse reactions, such as nausea, vomiting, etc. Also, inform the patients that these phenomena will slowly get better following their frequently use that can enhance patients confidence. (3) Implementation. Establishing a good doctor-patient relationship is the basis of the treatment interventions implementation. Medical staff should win the trust and cooperate of patients at first, and then put into plan according to the patients evaluation. (4) Evaluation. Constantly evaluate whether the treatment intervention was suitable through intervention-evaluation-feedback-intervene process so that the medical staff may modify the treatment plan on time. Evaluating intervention effect is not only an assessment of the medical staff work, more important is to evaluate patients to achieve actual effect.

Observation indexes and evaluation

CD₄⁺ T lymphocyte level, treatment compliance and the occurrence of adverse reaction were

Table 1. Treatment compliance between two groups (n %)

Group	Case number	Medication compliance	Dietary compliance	Inspection compliance
Observation group	45	41 (91.11)	37 (82.22)	33 (73.33)
Control group	45	30 (66.67)	26 (57.78)	19 (42.22)
χ^2		8.073	6.402	8.927
<i>P</i>		<0.05	<0.05	<0.05

(91.11% vs. 66.67%), dietary compliance (82.22% vs. 57.78%), and inspection compliance (73.33% vs. 42.22%) were significantly better than the control group (**Table 1**).

CD₄⁺ T lymphocyte level comparative analysis in two groups

After programmatic intervention, clinical symptoms improved significantly in the observation group. CD₄⁺ T lymphocyte level also had obviously difference. As shown in the **Table 2**, the rate of patients with CD₄⁺ T lymphocyte level >300/ μ l in observation group was markedly higher than control group (*P*<0.05).

Table 2. Comparative analysis of CD₄⁺ T lymphocyte level between two groups (n %)

Group	Case number	<300/ μ l	300-350/ μ l	>350/ μ l
Observation group	45	3 (6.67)	13 (28.89)	27 (60.00)
Control group	45	10 (22.22)	23 (51.11)	12 (26.67)
χ^2		4.406	4.630	10.181
<i>P</i>		<0.05	<0.05	<0.05

observed after four months. Compliance indicator was designed according to the requirement of the HIV/AIDS and tuberculosis prevention and control guidelines. Let patients answer the questionnaire one by one, "yes" means the poor compliance, while "no" is considered better compliance. CD₄⁺ T lymphocyte level is the best indicator to provide HIV immune damage condition, the lower the level of it showed the worse prognosis.

Statistical analysis

Experimental data was analyzed by SPSS13.0 software. Enumeration data was expressed as a percentage or rate, and analyzed using χ^2 tests. *P*<0.05 was considered statistically significant.

Results

In present study, treatment compliance of the patients from two groups changed significant changes, and the CD₄⁺ T lymphocyte levels increased markedly. Totally, 35 cases appeared adverse reactions, accounted for 38.89%. Among them, 15 cases were with nausea and vomiting, 13 cases with diarrhea, 7 cases with liver function damage. TB in 83 patients was cured, and sputum bacteria in 51 patients became negative.

Treatment compliance comparative analysis between two groups

After four months of treatment intervention, the observation group of medication compliance

Adverse reaction comparative analysis between groups

Totally 8 cases appeared adverse reactions in the observation group, accounted for 17.78%. There were 4 cases of nausea and vomiting, 3 cases of diarrhea, and 1 case of liver function damage. In contrast, there were 27 cases of adverse reactions observed in 2 control group (60.00%), including 11 cases of diarrhea, 10 cases of nausea and vomiting, 6 cases of liver damage (**Figure 1**).

Discussion

AIDS is a kind of dangerous infectious disease caused by HIV. TB infection is the most common type in patients with HIV and AIDS patients to infection, and its infection mechanism is complex [15, 16]. Due to the continuous decrease of CD₄⁺ T cells in the body and the immunity function weaken, HIV infection promoted the latent tuberculosis activation or reinfection. On the other hand, TB can activate macrophages and T lymphocyte resulting in accelerated replicates of CD₄⁺ T and HIV in the macrophage with CD4 protein expression [17-19]. Most simple tuberculosis patients can be healed; however, when combined incidence of HIV infection, rate of adverse reactions and fatality were higher and the cure rate was lower. Several researches have shown that medication compliance to treatment plays an important role in the treatment of HIV/TB dual infection.

Programmatic intervention on patients with HIV/TB dual infection

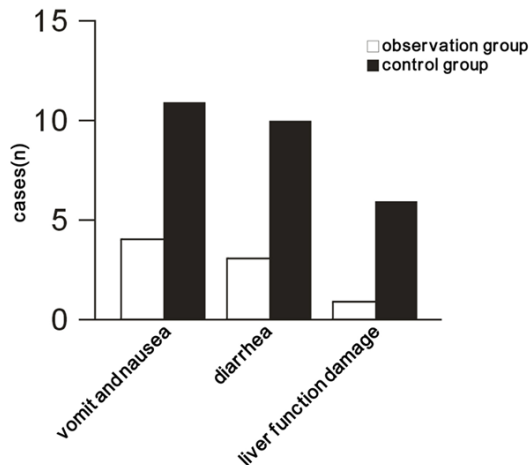


Figure 1. Adverse reaction comparison between two groups. The occurrence rate of vomit and nausea, diarrhea, and liver function damage in the observation group were significantly lower than the control group ($P=0.048, 0.036, 0.049$, respectively).

The reason of the poor treatment compliance according to condition assessment can be learned: (1) Some patients misunderstand that mistaken or fail to take medicine on time will not affect the treatment effect. (2) Some patients take the initiative to stop treatment due to the adverse reaction. (3) Some patients with HIV infection become depressed and inferiority complex that resulting in abandon treatment. (4) Some patients are very low awareness of the disease. (5) Some bad attitude of medical personnel or low level of management. Programmatic management is needed to solve these problems.

In the present result, all of the treatment compliance, CD_4^+ T lymphocyte level and adverse reaction were significantly better in the observation group after four months intervention compared with the control group. All of these indicated that programmatic intervention can obviously improve patient compliance to treatment, elevate CD_4^+ T lymphocyte level, and reduce the occurrence of adverse reactions. Programmatic interventions can improve patient compliance from the following aspects: (1) Busza found that only the medical staff master HIV relevant knowledge can reduce the medical staff discrimination against HIV patients [20]. Therefore, strengthen medical staff training can not only ensure the accurate measures put in place, but also further improve the quality of foundation treatment and patients

satisfaction. (2) Psychological intervention not only gives the patients psychological comfort and reduces the patient's psychological burden, but also lit up patient's hope. (3) Health education lets patients more fully understand HIV/TB dual infection, and it can enhance patients' confidence [21-23]. (4) Anti-TB treatment and antiviral intervention can improve the life quality greatly.

Currently, most TB can be cured, but no specific drugs had been found for HIV/AIDS. Insist on taking antiviral drugs and periodic inspection can reduce the fatality rate effectively [24, 25]. Through this study, we found that programmatic intervention can improve the patients' treatment compliance, elevate CD_4^+ T lymphocyte level, improve the clinical symptoms, and reduce incidence of adverse reactions. It is worth of practical in clinic.

Disclosure of conflict of interest

None.

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References

- [1] Vincenti D, Carrara S, Butera O, Bizzoni F, Casetti R, Girardi E, Goletti D. Response to region of difference 1 (RDI) epitopes in human immunodeficiency virus (HIV)-infected individuals enrolled with suspected active tuberculosis: a pilot study. *Clin Exp Immunol* 2007; 150: 91-98.
- [2] Idh J, Abate E, Westman A, Elias D, Janols H, Gelaw A, Getachew A, Alemu S, Aseffa A, Britton S, Stendahl O, Schön T. Kinetics of the QuantiFERON-TB Gold In-Tube test during treatment of patients with sputum smear-positive tuberculosis in relation to initial TST result and severity of disease. *Scand J Infect Dis* 2010; 42: 650-657.
- [3] Zhang F, Dou Z, Yu L, Xu J, Jiao JH, Wang N, Ma Y, Zhao Y, Zhao H, Chen RY. The effect of highly active antiretroviral therapy on mortality among HIV-infected former plasma donors in China. *Clin Infect Dis* 2011; 47: 825-833.
- [4] Lagrange PH and Herrmann JL. Diagnosing latent tuberculosis infection in the hiv era. *Open Respir Med J* 2010; 2: 52-59.

- [5] Glynn JR, Murray J, Bester A, Nelson G, Shearer S, Sonnenberg P. Effects of duration of HIV infection and secondary tuberculosis transmission on tuberculosis incidence in the South African gold mines. *AIDS* 2012; 22: 1859-1867.
- [6] Chee CB, KhinMar KW, Gan SH, Barkham TM, Koh CK, Shen L, Wang YT. Tuberculosis treatment effect on T-cell interferon gamma responses to *Mycobacterium tuberculosis*-specific antigens (HI V-negative). *Eur Respir J* 2010; 36: 355-361.
- [7] Patel NR, Zhu J, Tachado SD, Zhang J, Wan Z, Saukkonen J, Koziel H. HIV impairs TNF-alpha-mediated macrophage apoptotic response to *Mycobacterium tuberculosis*. *Immunol* 2010; 179: 6973-6980.
- [8] Adetifa IM, Ota MO, Walther B, Hammond AS, Lugos MD, Jeffries DJ, Donkor SA, Adegbola RA, Hill PC. Decay kinetics of an interferon gamma release assay with anti-tuberculosis therapy in newly diagnosed tuberculosis cases *PLoS One* 2010; 5.
- [9] Marra F, Marra CA, Bruchet N, Richardson K, Moadebi S, Elwood RK, FitzGerald JM. Adverse drug reactions associated with first-line anti-tuberculosis drug regimens. *Int J Tuberc Lung Dis* 2010; 11: 868-875.
- [10] Sonnenberg P, Murray J, Glynn JR, Shearer S, Kambashi B, Godfrey-Faussett P. HIV-1 and recurrence, relapse, and reinfection of tuberculosis after cure: a cohort study in South African mineworkers. *Lancet* 2010; 358: 1687-1693.
- [11] Havlir DV, Barnes PF. Tuberculosis in patients with human immunodeficiency virus infection. *N Engl J Med* 2010; 340: 367-373.
- [12] Protopopescu C, Marcellin F, Spire B, Préau M, Verdon R, Peyramond D, Raffi F, Chêne G, Lepout C, Carrieri MP. Health-related quality of life in HIV-1-infected patients HAART: a five-year longitudinal analysis accounting for dropout in the APROCO-COPILOTE cohort (ANRS CO-8). *Qual Life Res* 2010; 16: 577-591.
- [13] Liu H, Li X, Stanton B, Liu H, Liang G, Chen X, Yang H, Hong Y. Risk factors for sexually transmitted disease among rural-to-urban migrants in China: implication for HIV/Sexually transmitted disease prevention. *AIDS Patient Care STDS* 2011; 19: 49-57.
- [14] Bangsberg DR, Perry S, Charlebois ED, Clark RA, Roberston M, Zolopa AR, Moss A. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS* 2012; 15: 1181-1183.
- [15] Zhao Y, Xu S, Wang L, Chin DP, Wang S, Jiang G, Xia H, Zhou Y, Li Q, Ou X, Pang Y, Song Y, Zhao B, Zhang H, He G, Guo J, Wang Y. National survey of drug-resistant tuberculosis in china. *N Engl J Med* 2012; 366: 2161-2170.
- [16] Kuritzkes DR. Preventing and managing antiretroviral drug resistance. *AIDS Patient Care STDS* 2010; 18: 259-273.
- [17] Park-Wyllie LY, Strike CS, Antoniou T, Bayoumi AM. Adverse quality of life consequences of antiretroviral medications. *AIDS Care* 2011; 19: 252.
- [18] Gao X, Nau DP, Rosenbluth SA, Scott V, Woodward C. The relationship of disease severity, health beliefs and medication adherence among HIV patients. *AIDS Care* 2011; 12: 387-398.
- [19] Williams AB. Adherence to HIV regimens: 10 vital lessons. *Am J Nurs* 2010; 101: 37-43.
- [20] Busza JR. Promoting the positive responses to stigma and discrimination in Southeast Asia. *AIDS Care* 2011; 13: 441-456.
- [21] Gunneberg C, Reid A, Williams BG, Floyd K, Nun NP. Global monitoring of collaborative TB-HIV activities. *Int J Tuberc Lung Dis* 2008; 12 Suppl 1: 2-7.
- [22] Cain KP, Kanara N, Laserson KF, Vannarith C, Sameourn K, Samnang K, Qualls ML, Wells CD, Varma JK. The epidemiology of HIV-associated tuberculosis in rural Cambodia. *Int J Tuberc Lung Dis* 2012; 11: 1008-1013.
- [23] Sharma SK, Mohan A, Kadiravan T. HIV-TB coinfection: epidemiology, diagnosis and management. *Indian J Med Res* 2010; 121: 550-567.
- [24] Carrara S, Vincenti D, Petrosillo N, Amicosante M, Girardi E, Goletti D. Use of a T cell-based assay for monitoring efficacy of antituberculosis therapy. *Clin Infect Dis* 2010; 38: 754-756.
- [25] Harrington M. From HIV to tuberculosis and back again: a tale of activism in 2 pandemics. *Clin Infect Dis* 2010; 50 Suppl 3: 260-266.