

Integrated Scheme of Traditional Chinese Medicine for Delaying the Morbidity of HIV Infection: Study Protocol for a Multicentre, Randomised Controlled Trial

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Study protocol

Keywords: HIV&AIDS, complementary medicine, Clinical trials

Posted Date: June 30th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-652624/v1>

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Abstract

Background: Acquired Immune Deficiency Syndrome (AIDS) is caused by human immunodeficiency virus (HIV) infection, the incidence and mortality rates of which are high worldwide. In the late 1990s, highly active antiretroviral therapy (ART) emerged; although it has been a long time of research on AIDS, there is still no vaccine cure. Traditional Chinese Medicine (TCM) role in AIDS has been recognised and accepted by more patients, especially patients with asymptomatic HIV infection.

Methods/Design: This trial will be conducted to enrol 216 eligible patients who will be randomised into the treatment and control groups. After 18 months of intervention, the efficacy and safety of TCM in patients with AIDS will be acquired. The results include clinical symptoms, TCM syndromes, viral load, immunological indicators, safety indicators, and other biological indicators.

Discussion: This study aimed to compare the effectiveness and safety of TCM for asymptomatic AIDS and explore the plausible mechanism and provide reference for adopting this approach to retard the onset and control the progression of HIV/AIDS.

Trial registration: ChiCTR1800018365, 13 Sep, 2018.

Background

Approximately 38 million people live with the human immunodeficiency virus (HIV) worldwide, and 1.7 million people are newly infected yearly[1].The HIV/acquired immune deficiency syndrome (AIDS) pandemic is the most rigorous challenge in global public health[2].Antiretroviral therapy (ART) is the most effective method for HIV/AIDS, which decreases the mortality rate. However, ART is often limited by drug toxicity, poor therapeutic tolerance, and drug resistance[3].Many patients chose not to use combination ART; therefore, it is necessary to find new drugs or treatments, such as complementary and alternative medicine (CAM). CAM has been used to treat AIDS and its complications worldwide, including TCM, acupuncture, and Qigong. Several studies have shown that TCM can reduce drug side effects, improve the immune system, clinical symptoms, quality of life, and decrease mortality[4-5].Community-acquired pneumonia (CAP) is a major contributor to morbidity and mortality even in the current HIV treatment era, especially as patients age[6].Diarrhoea is one of the most common presenting complaints in HIV-infected patients. Since the first AIDS cases were described, a high prevalence of gastrointestinal disturbance has been reported [7-8].Meanwhile, TCM is effective and safe for the treatment of asymptomatic AIDS[9-13]. However, there is not enough evidence to show the efficacy of TCM on patients with AIDS. Hence, a more rigorously designed large-scale, multicentre, randomised trial is needed to assess the effectiveness of TCM on AIDS. In conclusion, we aim to conduct a multicentre, randomised, double-blind, placebo-controlled trial to evaluate the efficacy and safety of TCM on AIDS. The results of this trial will provide evidence that TCM is an effective prescription for patients with AIDS and evaluate the clinical efficacy of TCM in delaying the morbidity of AIDS. In this 3trial, the time and incidence of endpoint events were used

as the primary evaluation indices, and immune function, viral load, clinical symptoms, and TCM syndrome were used as the secondary effect indices.

Methods/design

Study design

This study is a multicentre, randomised, double-blind, simulant parallel-controlled clinical trial, with a total of 216 patients randomly assigned to the herbal treatment and control groups. The treatment group is divided into syndromes of Qi deficiency, stagnant and jamming dampness-heat, and spleen-kidney deficiency, and are administered Yi Aikang capsule, Tangcao tablet, and Jian Aikang concentrated pill according to the results of the symptom differentiation. Similarly, the control group is also divided on the same basis but are administered simulants of the above tablets according to the results of symptom differentiation. Patients' symptoms will be identified during the follow-up period, and pharmaceutical preparations corresponding to the syndrome type will be administered each month according to the symptom differentiation results. The clinical efficacy of TCM in delaying the onset of HIV infection in patients will be evaluated using the time to endpoint events and incidence rate as the primary evaluation indicators and the immune function, viral load, symptoms, and TCM symptoms of HIV/AIDS patients as secondary effect indicators.

During the follow-up period, subjects may develop common community-acquired pneumonia. Therefore, the treatment group will be divided into a syndrome of phlegm-heat obstructing the lung and syndrome of phlegm-damp obstructing the lung according to TCM symptoms and treated with Qing Fei Pei Yuan Granules and Wen Fei Pei Yuan Granules, respectively. The control group will also be divided into the syndrome of phlegm-heat obstructing the lung and syndrome of phlegm-damp obstructing the lung according to TCM symptoms and treated with simulants of Qing Fei Pei Yuan Granules and Wen Fei Pei Yuan Granules, respectively. CAP will undergo directly observed treatment for 14 days. Clinical symptoms, TCM symptoms, inflammation indices, C-reactive protein (CRP), procalcitonin (PCT), IL-17, CD4+ IL-17+Th17, CD4+IL-4+Th2, IFN- γ , and CD4+IFN- γ +Th1 will be used as observation indices to study the effect of Qing Fei Pei Yuan micro-pellets on reducing the morbidity and endpoint events as well as immune-enhancing effects in patients with AIDS lung infections.

During the follow-up period, the subjects may develop common diarrhoea, and the treatment group is diagnosed as a syndrome of dampness-heat blocking collaterals according to the TCM symptom differentiation and treated with Xielikang Capsules. The control group will be diagnosed as a syndrome of dampness-heat blocking collaterals according to the TCM symptom differentiation and treated with simulant of Xielikang capsules. Diarrhoea will be observed and treated for 7 days. The number of diarrhoeas, TCM symptoms, and stool routine will be used as observation indices to study the effects of Xielikang capsules in reducing the incidence of diarrhoea and endpoint events in patients with diarrhoea in AIDS.

As the leading unit of research, the First Affiliated Hospital of the Henan University of TCM is responsible for training the standard operating procedures and monitoring the progress of all clinical trials. Other participating units and recruitment allocations: Shanghai Public Health Clinical Centre (30 patients), Beijing Ditan Hospital Capital Medical University (16 patients), Sichuan Academy of Chinese Medical Sciences (50 patients), Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine (50 patients), Kunming Municipal Hospital of Traditional Chinese Medicine (30 patients), and the First Affiliated Hospital of Henan University of Chinese Medicine (40 patients). The flow chart is shown in Figure 1. This study protocol is registered with the China Clinical Trial Registry, Trial registration number: ChiCTR1800018365.

Participants

Patients with HIV/AIDS who chose not to use ART and patients with Qi deficiency, damp-heat, sleep, and kidney will be enrolled in this study. Referring to the "Diagnostic criteria for HIV/AIDS (WS293-2008)," "Clinic terminology of traditional Chinese medical diagnosis and treatment-Syndromes (2002)" [14] "TCM diagnosis and treatment criteria for HIV/AIDS (2016)" as follows[15]: (1) Syndrome of Qi deficiency or unidentifiable syndrome; the primary symptoms are fatigue, weakness, and disinclination to talk. Secondary symptoms are dizziness, dim-complexioned, palpitations, and spontaneous perspiration. The tongue is slightly pale or normal, and the pulse is either deficient or normal or there are no obvious clinical symptoms and TCM signs and symptoms, with normal signs of pulse and tongue colour. (2) Syndrome of stagnant and jamming dampness-heat; the primary symptoms are dizziness and sleepiness. The secondary symptoms are chest tightness, abdominal fullness, mucous mouth dullness, loose stools, and sticky and foul-smelling vaginal discharge in females. The tongue appears red, with a thick, greasy, or yellowish and greasy coating, or both yellowish and whitish. The pulse is soft or slippery. (3) Deficiency of the spleen and kidney; the primary symptoms are fatigue, soreness, and weakness of the waist and knees or lumbago. The secondary symptoms include abdominal fullness, loss of appetite, intolerance of cold, pale face, loose stools, frequent urination, and tinnitus. The tongue is pale or swollen, with a thin white or white smooth coating and a deep and faint pulse.

CAP in this study refers to the "Guidelines for the diagnosis and treatment of CAP in Chinese adults (2016)" and "TCM diagnosis and treatment of AIDS cough (CAP)." TCM differentiation criteria for community-acquired pneumonia are as follows: (1) Syndrome of phlegm-heat obstructing the lung; the primary symptoms are cough, fever, shortness of breath, and yellow and thick or white sticky sputum. Secondary symptoms include dry mouth, bitterness, dysphoria, constipation, short and red urine, persistent coughing and vomiting, or bloody sputum, as well as distension and fullness in the chest. The tongue is red with a yellow and greasy coating, and the pulse is slippery. (2) Syndrome of phlegm-dampness retention of the lung; the main symptom is a heavy, muddy cough with excessive phlegm, which is sticky and greasy or thickened into lumps. The secondary symptoms are chest tightness, abdominal fullness, vomiting, poor appetite, and fatigue. The tongue is pale, with white and greasy coating, and the pulse is soft and slow or slippery.

Diarrhoea is referred to “TCM diagnosis and treatment plan for AIDS (adult).” TCM differentiation criteria for diarrhoea; syndrome of dampness-heat blocking collaterals; the main symptoms are diarrhoea and abdominal pain, persistent diarrhoea, yellowish-brown faeces, foul odour, and driving discharge. The secondary symptoms are burning sensation in the anus, irritability and thirst, and short yellowish urine. In addition, the tongue is red with a yellowish and greasy coating, and the pulse is soft or slippery.

Inclusion criteria

Patients must meet all the following criteria: (1) HIV/AIDS diagnostic criteria; (2) the number of CD4+ T cells ranges from 250 to 500/ μ l; (3) comply with the criteria for TCM syndrome criteria; (4) age of 18-65years old, sex is not limited; (5) provision of signed, informed consent.

Exclusion criteria

Patients meeting the following criteria are excluded from the study: (1) patients who are participating in other clinical trials or have participated in other clinical trials within the past 3 months; (2) patients receiving HAART (Highly Active Antiviral Therapy); (3) patients with a combination of severe organic heart disease and severe arrhythmia, patients with abnormal liver function (alanine transaminase or aspartate transaminase greater than two times of the upper limit of normal value), patients with abnormal renal function (serum creatinine greater than 1.5 times the upper limit of normal value), patients with active tuberculosis or patients undergoing anti-tuberculosis treatment, patients with haematologic disorders; (4) patients with combined tumours; (5) patients with severe psychiatric and neurological disorders; (6) pregnant or lactating women, or women preparing for pregnancy; (7) patients with allergies and patients who are allergic to the test article; (8) patients with a history of alcoholism (drinking more than 150 mL of alcohol per day) or those with manifestations of alcohol dependence syndrome.

Sample size

According to our pre-experiment, the incidence of endpoint events in the control group was 35%; meanwhile, the incidence of endpoint events was 8% in the TCM group. Therefore, the required sample size was 33 cases in the control group and 66 cases in the treatment group. According to the situation of the existing subjects and the 10% shedding rate, the final sample size for the whole experiment is 216 cases.

Randomised

The statistical unit uses the central stratified block randomisation method for a randomised assignment using a central randomisation system. First, the investigators will obtain the randomisation numbers of the patients from the data management unit, the Institute of Basic Research in Clinical Medicine, China Academy Of Chinese Medical Sciences, via the internet. The seed number is set to any 6-digit number, and the length of the block is 6. Then, the subjects are randomised into treatment and control groups at a

1:1 ratio. Finally, the treatment code is generated and used by each clinical centre according to the assigned drug number and in the order of case enrolment.

Interventions

Programme description

Volunteers meeting the inclusion criteria will receive an information form and be required to provide written consent to participate in the trial. Physical screening tests will then be performed to determine if other comorbidities might affect the trial. After the successful screening, they will participate in the test and obtain the identification number for the test. Allocation to a group according to the random sequence number, baseline measurements will be performed for each participant, including clinical symptoms scores and TCM syndrome scores, CD4+, CD8+T, CD4+/CD8+, HIV viral load, blood, urine, stool routine, etc. The research scheme flow path is shown in Table 1. All outcome measures will be managed by experienced medical workers, but the group classification of the participating groups is blinded to them.

The treatment group received three different TCM drugs (YAK capsule, TCP tablets, JPYQF pills) according to different syndrome differentiation. The control group received three different TCM placebo drugs (YAK capsule placebo, TCP tablet placebo, JPYQ pill placebo) according to different syndrome differentiation. According to the monthly follow-up of TCM syndrome differentiation, the treatment group and the control group were given corresponding TCM drugs and placebo drugs. The total study period was 18 months.

If the subjects were infected with CPA during the trial, based on antibiotic treatment, the treatment group would receive different TCM drugs (QFPY capsule, WFPY capsule) according to different syndrome differentiation. The control group would receive different TCM placebo drugs (QFPY capsule placebo, WFPY capsule placebo) according to different syndrome differentiation. The trial cycle continued for 14 days. The research scheme flow path is shown in Table 2.

If the subjects were infected with diarrhoea during the trial, based on antibiotic treatment, the treatment group would receive TCM drugs (XLK capsule) according to syndrome differentiation. According to different syndrome differentiation, the control group would receive TCM placebo drugs (XLK capsule placebo); the trial cycle continued for 7 days. The research scheme flow path is shown in Table 3.

Treatment drugs

TCP tablets have been approved by CFDA (z20050291) and produced by Shanghai Hundreds Ace Herbal Pharmaceutical co., Ltd. However, the composition of the drug (YAK capsule, TCP tablets, JPYQF pills, QFPY capsule, WFPY capsule, XLK capsule, produced by the affiliated hospital of Henan Academy of Chinese Medicine) cannot be disclosed because the formula is patented.

Placebo drugs

Placebo drugs consist of 1/10 of the original drug and starch produced by the same manufacturer. Placebo matches the appearance and taste of the drugs and is consistent with directions in the treatment group.

Outcome measure

The major therapeutic index. In this trial, the time and incidence of endpoint events and clinical symptoms score as mentioned in Table 4 were used as the main evaluation indexes. In addition, a comparison of the difference between the treatment group and the control group and the incidence of observation indices were used as the basis for efficacy evaluation.

Endpoint event criteria refer to the “Chinese guidelines for the diagnosis and treatment of AIDS (2018).” Anyone with the following criteria can be diagnosed as AIDS[16]: (1) unexplained persistent irregular fever of 38°C or higher, >1 month; (2) diarrhoea (stool more than three times/day), >1 month; (3) weight loss of 10% or more within 6 months; (4) recurrent oral fungal infections; (5) recurrent herpes simplex virus infections or herpes zoster virus infections; (6) pneumocystis pneumonia (PCP); (7) recurrent bacterial pneumonia; (8) active tuberculosis or nontuberculous mycobacteriosis; (9) deep fungal infections; (10) space-occupying lesions of the central nervous system; (11) dementia in the middle-aged and young adults; (12) active cytomegalovirus infection; (13) toxoplasma encephalopathy; (14) *Talaromyces marneffe*i infection; (15) recurrent sepsis; (16) Kaposi's sarcoma, lymphoma of the skin mucosa or viscera.

TCM syndrome score

TCM syndrome refers to the “Guiding principles for clinical research of new drugs of TCM (Trial) (2002)”, “TCM diagnosis and treatment criteria for HIV/AIDS (2016).” We conducted a comprehensive evaluation on fatigue, mental fatigue, dizziness, palpitation, etc. The evaluation criteria of the TCM syndrome score are shown in Table 5. Efficacy index (n) = [(pre-intervention scores - post-intervention scores)/pre-intervention scores] × 100%.

Clinical recovery: TCM clinical symptoms and signs approximately disappeared; TCM syndrome scores decreased by ≥90%.

Markedly effective: TCM clinical symptoms and signs are significantly improved; TCM syndrome scores reduced by ≥70%.

Effective: TCM clinical symptoms and signs are improved; TCM syndrome scores reduced by ≥30%.

Invalid: TCM clinical symptoms or signs are not improved and even aggravated; TCM syndrome scores reduced by <30%.

Virological index

Effective: HIV load decreased >1 log/ml;

Invalid: HIV load increased >1 log/ml;

Steady: HIV load decreased or rose <1 log/ml;

Immunological index

Effective: CD4 cell count increased 50 cells/mm³ or $>30\%$.

Invalid: CD4 cell count decreased 50 cells/mm³ or $>30\%$.

Steady: CD4 cell count increased or decreased not up to 50 cells/mm³ or 30%.

Safety assessments

From baseline to the end of the study, routine blood, urine, stool, liver and kidney functions, electrocardiogram and chest X-ray were performed every 4 weeks. Any adverse events during the trial will be recorded in detail.

The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) figure of enrolment, interventions, and assessments is shown in Fig. 2. The SPIRIT checklist is provided as Additional file 1.

Quality control and data management

At the pre-clinical trial coordination meeting, the medical workers who participate in clic data acquisition system, and upload it to the central database. To maintain the quality of each sub-centre shall be trained before the clinical trial. The team leader unit of the subproject shall control the quality of each sub-centre to ensure the authenticity and specification of data. The case form and electronic case collection management system were used together. During the clinical follow-up, the visiting doctors fill in the case report form, then double input it in the clinical research electronic system. To ensure the objectivity of the data, we will ensure that observers and statisticians are blinded to the data. The whole process will be supervised by an independent quality inspector. Guangzhou Boji Pharmaceutical Biotechnology Co. Ltd is responsible for data management.

Serious adverse event reporting and monitoring

Any serious adverse events deemed to be related to the intervention or due to study participation will be reported to the chief investigator within 24 hours. The First Affiliated Hospital of Henan University of Chinese Medicine will be responsible for serious adverse events.

Compliance evaluation

Drug compliance was determined at each visit. Compliance evaluation index: 80-120% of the prescribed dosage is the standard of good compliance, otherwise it is poor compliance. The compliance was

calculated as follows: medication compliance = the total amount of drugs actually taken / the amount of drugs that should be taken × 100%.

Combined drugs

It means that during the trial period (including the screening period and the treatment period), the same or similar efficacy of traditional Chinese medicine can not be used at the same time. If patients have common complications during the trial, anti-symptomatic measures were only scheduled. In case of community-acquired pneumonia and diarrhea specified in the plan, traditional Chinese medicine preparation specified in the plan will be given on the basis of conventional western medicine treatment. All drugs used during the trial should be recorded in the case report form.

Statistical analysis

All statistical analyses will be performed using SAS 9.0. All statistical tests were performed using a two-sided test, and a p-value less than 0.05 will be considered statistically significant. Baseline information, such as mean, standard deviation, minimum, and maximum values, will be calculated to describe quantitative indicators. Categorical indicators will be described by frequency. For the analysis of efficacy and safety indicators, Cox survival analysis will be used to compare the time to endpoint events between the two groups, and Chinese medicine symptoms will be analysed using the chi-square test or rank-sum test.

Patient and public involvement

Patients and their families did not participate in the study design. However, the results of the study will be widely distributed to scientific reports and academic conferences for the benefit of policymakers, clinicians, and patients.

Ethics and communication

All volunteers will sign an informed consent form, and the study will follow the tenets of the Helsinki Declaration. This trial will follow the Chinese clinical trial research regulations and norms. Biological samples will be treated following the national guidelines for biological waste management and disposal. The results will be published in international peer-reviewed journals and academic conferences. The results will also be fed back to volunteers to ask about the patient's health during the follow-up period.

Discussion

Facing AIDS complex, difficult, severe damage of coexisting major infectious diseases, under the principle of syndrome differentiation of TCM, build based on evidence-based medicine HIV/AIDS diagnosis and treatment system of combined disease, to improve the level of TCM diagnosis and treatment of HIV/AIDS and improve the clinical curative effect is of great significance as a whole. A great number of studies show that TCM can reduce side effects of drugs, improve patients' immunity, improve clinical symptoms

and quality of life.⁴⁻⁵ Meanwhile, some clinical studies show that TCM is effective and safe in the treatment of AIDS, and it has a positive effect on improving the quality of life, prolonging life and improving symptoms of HIV/AIDS patients.⁹⁻¹⁰ However, lack of high-quality research hindered the development of evidence-based clinical research on HIV/AIDS, so we designed this clinical trial.

This trial has the following advantages: (1) This is one of the first trials that RCT design is implemented throughout the treatment of complications, and the whole process of the trial is designed as a randomised, double-blind, placebo-controlled study from the perspective of evidence-based medicine, which is considered the best evaluation method, leading to the high strength of the argument of the study results. (2) The design method is guided by the theory of treatment based on symptom differentiation of TCM, reflecting the characteristics of TCM clinical treatment from the perspective of treatment based on symptom differentiation of TCM. (3) The study subjects are selected from a region with a high prevalence of HIV infection in China, and the long-term follow-up ensured the compliance of the study cases. (4) There are also limitations in the protocol. For example, there are many kinds of common opportunistic infections of HIV/AIDS. Only CAP and diarrhoea may be a bit short in this trial.

During the study, the subjects can choose different therapeutic drugs at different treatment stages, reflecting the concept of adaptive design and individualised treatment design. However, the adaptive design here does not refer to the subject's own choice but the researcher's choice of different treatment methods based on the subject's symptom differentiation. Meanwhile, the protocol design also has potential limitations, such as the fact that common infections, such as oral ulcers, are not included in the treatment.

In conclusion, this study aimed to answer whether TCM can be a supplement to western medical treatment. If the trial is successful, a new option for patients and physicians will be provided to reduce the cost and burden of AIDS care.

Trial status

Patient recruitment started on 1 March 2020 and will be completed on 20 December 2021. Version number: 2.0.

Abbreviations

HIV :human immunodeficiency virus ;AIDS:Acquired Immune Deficiency Syndrome;ART:active antiretroviral therapy;TCM:Traditional Chinese Medicine;CAM:complementary and alternative medicine;CAP:Community-acquired pneumonia ;CRP: C-reactive protein ;PCT: procalcitonin;HAART:Highly Active Antiviral Therapy;YAK: Yi Aikangcapsule;TCP :Tang Caopian tablets;JPYQ: Jian piyiqi ;PCP: pneumocystis pneumonia

Declarations

Acknowledgements This trial is conducted in six hospitals: Shanghai Public Health Clinical Centre, Beijing Ditan Hospital Capital Medical University, Sichuan Academy of Chinese Medical Sciences, Ruikang Hospital Affiliated to the Guangxi University of Chinese Medicine, Kunming Municipal Hospital of Traditional Chinese Medicine, and the First Affiliated Hospital of Henan University of Chinese Medicine.

Guangzhou Boji Pharmaceutical Biotechnology Co. Ltd for data management and the affiliated hospital of Henan Academy of Chinese Medicine for produce and package of medicine. The authors would like to thank the patients and their family members and the nurses, pharmacy staff, fellows and clinicians of the intensive care units at the above hospitals for making this study possible.

Author Contributions XD, PM, XM, and LX designed this study; PM, XM and LX; XD, PM, XM wrote the bid for the research project and obtained permission from the ethics committees; designed the statistical analysis plan; JW, CS, BW, XC, CM carried out this trial; XD and LX drafted this manuscript; PM and XM carefully reviewed the manuscript, and all authors read and approved the final manuscript.

Funding This work was supported by Key Program for International Science and Technology Cooperation of China(No.2017ZX10205502) and Nation Natural Science Foundation of China(U1604287;U1904153),The foundations have reviewed and approved this project.

Data Statement The data that support the findings of this study are openly available in “Clinical evaluation center of Chinese Academy of traditional Chinese Medicine”, Data or code generated or used during the study are available from the corresponding author by request.

Conflict Interest Statement The authors declare that they have no conflicts of interest.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required

Ethics approval This study follows the principles of the Helsinki Declaration 2013. The entire protocol was reviewed and approved by Ethics Committee of the First Affiliated Hospital of Henan University of Chinese Medicine (identifier: Clinical Ethical Approval No. 2018HL-042). Written informed consent will be obtained from all participants who will be informed about the purpose, intervention and possible risks/benefits of the study.

Ethics and dissemination

No ethical concerns.

References

1. Dybul M, Attoye T, Baptiste S, et al. The case for an HIV cure and how to get there. *LANCET HIV* 2021;8(1):e51-58. doi: 10.1016/S2352-3018(20)30232-0 pmid:33271124.[Copyright (c) 2021 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license. Published by Elsevier Ltd.. All rights reserved.:*2021-01-01].
2. Margolis DM, Garcia JV, Hazuda DJ, B. F. Haynes. Latency reversal and viral clearance to cure HIV-1. *SCIENCE* 2016;353(6297):f6517. doi: 10.1126/science.aaf65172016-07-22].
3. Mark A, Wainberg GJ, Zaharatos BG. Brenner. Development of Antiretroviral Drug Resistance. *N Engl J Med.* 2011;365(7):637–46. doi: 10.1056/NEJMra1004180.[Massachusetts Medical Society:*2011-01-01].
4. Wang J, Liang B, Zhang X, et al. An 84-month observational study of the changes in CD4 T-lymphocyte cell count of 110 HIV/AIDS patients treated with traditional Chinese medicine. *FRONT MED-PRC.* 2014;8(3):362–67. doi:10.1007/s11684-014-0363-x.
5. Wen Zou J, Wang Y, Liu. Effect of traditional Chinese medicine for treating human immunodeficiency virus infections and acquired immune deficiency syndrome: Boosting immune and alleviating symptoms. *CHIN J INTEGR MED.* 2016;22(1):3–08. doi:10.1007/s11655-015-2122-5.
6. Akgun KM, Huang L, Morris A, et al. Critical Illness in HIV-Infected Patients in the Era of Combination Antiretroviral Therapy. *Proceedings of the American Thoracic Society* 2011;8(3):301-07. doi: 10.1513/pats.201009-060WR2011-06-01].
7. Feriyl Bhaijee C, Subramony S-J, Tang, Dominique J. Pepper. Human Immunodeficiency Virus-Associated Gastrointestinal Disease: Common Endoscopic Biopsy Diagnoses. *Pathology Research International.* 2011;2011:1–08. doi:10.4061/2011/2479232011-04-26].
8. Stark D, Barratt JLN, van Hal S, et al. Clinical Significance of Enteric Protozoa in the Immunosuppressed Human Population. *CLIN MICROBIOL REV.* 2009;22(4):634–50. doi:10.1128/CMR.00017-09.
9. Deng X, Jiang M, Zhao X, Liang J. Efficacy and safety of traditional Chinese medicine for the treatment of acquired immunodeficiency syndrome: a systematic review. *J TRADIT CHIN MED* 2014;34(1):1–09. doi: 10.1016/s0254-6272(14)60046-7 pmid:251026832014-02-01].
10. Liu Z-B, Yang J-P, Xu L-R. Effectiveness and safety of traditional Chinese medicine in treating acquired immune deficiency syndrome: 2004–2014. *INFECT DIS POVERTY* 2015;4(1) doi:10.1186/s40249-015-0093-6.
11. Xu LR, Wang DX, Guo JZ, et al. Research on Chinese medicine syndrome distribution of asymptomatic HIV infected patients. *Zhongguo Zhong Xi Yi Jie He Za Zhi.* 2013 Jul;33(7):896–900. Chinese. PMID: 24063208.
12. Xiumin C, Qingting Y, Zhibin L, et al. Asymptomatic stage of human immunodeficiency virus infection is the optimal timing for its management with Traditional Chinese Medicine. *J TRADIT CHIN MED* 2015;35(2):244–48. doi: 10.1016/s0254-6272(15)30036-4 pmid:259750612015-04-01].

13. Yantao Jin X, Wang Z, Li, et al. Survival of AIDS Patients Treated with Traditional Chinese Medicine in Rural Central China: A Retrospective Cohort Study, 2004–2012. EVID-BASED COMPL ALT. 2015;2015:1–07. doi:10.1155/2015/282819.
14. The Central People's Government of. the People's Republic of China: www.gov.cn/zhengce/zhengceku/2020-11/24/content_5563703.htm.
15. Nation Administration of Traditional Chinese Medicine. <http://www.satcm.gov.cn/yizhengsi/zhengcewenjian/2018-03-24/3159.html>.
16. AIDS and Hepatitis C Professional Group, Society of Infectious Diseases, Chinese Medical Association Chinese Center for Disease Control and Prevention. Guidelines for diagnosis and treatment of AIDS in China(2018).Zhonghua Nei Ke Za Zhi.2018;57(12):867–884. doi:10.3760/cma.j.issn.0578-1426.2018.12.002.

Tables

Due to technical limitations, table 1 to 5 is only available as a download in the Supplemental Files section.

Figures

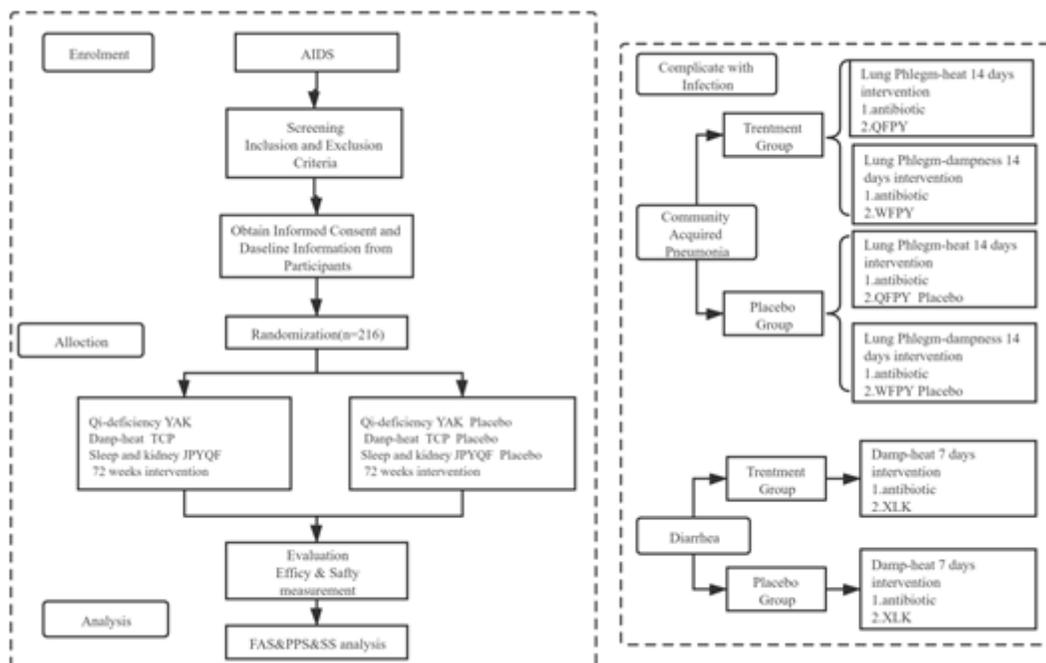


Figure 1

Trial flow chart AIDS, acquired immunodeficiency syndrome; YAK, Yi Ai Kang capsule; TCP, Tang Cao Pian Tablets; JPYQF, Jian Pi Yi Qi pills; QFPY, Qing Fei Pei Yuan capsule; WFPY, Wen Fei Pei Yuan capsule.

Supplementary Files

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