Integrative Medicine Research 9 (2020) 100489

Contents lists available at ScienceDirect

Integrative Medicine Research

journal homepage: www.imr-journal.com

# Efficacy of herbal medicine (Xuanfei Baidu decoction) combined with conventional drug in treating COVID-19: a pilot randomized clinical trial

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ARTICLE INFO

*Article history:*
Received 13 June 2020
Received in revised form 20 July 2020
Accepted 20 July 2020
Available online 25 July 2020

*Keywords:*
COVID-19
Herbal medicine
Randomized controlled trial
Integrative medicine
Chinese medicine

ABSTRACT

*Background:* The aim of this study was to evaluate the clinical efficacy of Xuanfei Baidu Decoction (XBD) combined with conventional drug therapy compared with conventional medicine alone in patients with coronavirus disease 2019 (COVID-19).
*Methods:* Forty-two patients with COVID-19 were randomly assigned to XBD plus conventional medicine ($n = 22$) and conventional medicine alone ($n = 20$). Both groups were treated for 1 week. The primary endpoint was the disappearance rate of main symptoms (fever, cough, and fatigue).
*Results:* Compared with the conventional medicine, the disappearance rate of clinical symptoms such as fever, cough, fatigue and loss of appetite in the experimental group were significantly reduced ($P < 0.05$). The number of white blood cells and lymphocytes in the experimental group increased significantly ($P < 0.05$), which all returned to normal parameters. Meanwhile, the C-reactive protein and erythrocyte sedimentation rate in the experimental group were significantly reduced ($P < 0.05$).
*Conclusion:* XBD combined with conventional medicine may significantly improve patient's clinical symptoms, increase the number of white blood cells and lymphocytes to improve immunity, and also significantly reduce C-reactive protein and erythrocyte sedimentation rate to play an anti-inflammatory effect. However, it needs to be confirmed by a large sample study.
*Clinical trial registration:* China Clinical Trial Registry (ChiCTR2000034795).
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## 1. Introduction

At present, there is a lack of effective antiviral drugs, and vaccines are still being developed to treat coronavirus disease 2019 (COVID-19). China has been used integrated Chinese and Western medicine for treating patients with COVID-19. As the fourth version of the guideline (*Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia* released by National Health Commission and State Administration of Traditional Chinese Medicine)[1] clearly pointed out that blind use of antibacterial drugs should be avoided.

It is generally believed by traditional Chinese medicine experts that COVID-19 is the pestilence in view of its epidemic and infectious nature. Combined with the occurrence time and geographical environment, this epidemic has the characteristics of external evils such as toxin evil, wet evil and cold evil. Therefore, in Chinese medicine, COVID-19 is referred to as "wet toxin pestilence".[2,3] Based on the above pathogenic characteristics, Academician Boli Zhang and Professor Qingquan Liu created Xuanfei Baidu Decoction.[4] The aim of this study was to evaluate the efficacy Xuanfei Baidu Decoction (XBD) combined with conventional medicine for treating patients with COVID-19.

## 2. Methods

### 2.1. Type of study

This study was a pilot randomized controlled trial which has been registered with China Clinical Trial Registry (ChiCTR2000034795).

### 2.2. Inclusion criteria

The inclusion criteria for this trial were as follows:

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https://doi.org/10.1016/j.imr.2020.100489
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- Inpatients in Wuhan Pulmonary Hospital (from January 30 to February 10, 2020) who met the diagnostic criteria of COVID-19;
- Age of 18–75 years old;
- In the mild to severe stages according to the fourth edition of guideline;
- Agreed to participate in the trial;
- No antibiotics were used during one cycle of this treatment.

### 2.3. Exclusion criteria

The exclusion criteria for this trial were as follows:

- In the critical stage according to the fourth edition of guideline;
- Acute respiratory diseases not caused by 2019-nCoV;
- Asthma patients who needed daily treatment;
- Severe lung interstitial lesions, bronchiectasis and other basic lung disease patients;
- Accompanied by severe primary immunodeficiency disease, acquired immunodeficiency syndrome, congenital respiratory malformations, congenital heart disease, abnormal lung development and other basic diseases;
- Pregnant women.

### 2.4. Randomization and sample size calculation

According to the patient's hospitalization number, odd-numbered patients were allocated to group A, and even-numbered patients were allocated to group B. By tossing a coin, the two groups were randomly assigned to the experimental group and the control group. The head side represents group A, and the tail side with the national emblem represents group B. After tossing the coin, the one facing upward is the experimental group, and the one facing downward is the control group. For sample size calculation, the trial results in the early stage for the treatment of COVID-19 with integrated traditional Chinese and western medicine reported by the team of Zhang Boli was considered.[5] The study showed that the clinical cure rate of integrated traditional Chinese and western medicine group and simple western medicine group were 94.1% and 61.1%, respectively. Considering the clinical significance, the value of $\alpha$ is 0.05, power of test is 0.8, and SAS 9.4 software is used for sample estimation. The two groups both require a sample size of 24 cases. Since this trial is in a severe epidemic, the sample size of a single center that meets the inclusion criteria is 42 cases in total.

### 2.5. Intervention

For the experimental group, XBD (1 pouch of 200 ml each time, 2 times/day) was added on top of conventional medicine which were treated to the control group. The treatment time for both groups were 1 week. Antibiotics were disabled during the treatment of both groups, and other Chinese medicines were prohibited.

XBD was composed of the following herbs: Ephedrae Herba (Ma Huang) 8 g, Armeniacae Semen Amarum (Xing Ren) 15 g, Gypsum Fibrosum (Sheng Shi Gao) 30 g, Atractylodis Rhizoma (Cang Zhu) 10 g, Semen Coicis (Yi Yi Ren) 30 g, Agastachis Herba (Huo Xiang)15 g, Polygoni Cuspidati Rhizoma et Radix (Hu Zhang) 20 g, Lepidii seu Descurainiae Semen (Ting Li Zi) 15 g, Verbenae Herba (Ma Bian Cao) 30 g, Phragmitis Rhizoma (Lu Gen) 30 g, Artemisiae Annuae Herba (Qing Hao) 25 g, Citri Grandis Rubrum Exocarpium (Ju Hong) 20 g, Glycyrrhizae Radix et Rhizoma (Sheng Gan Cao) 10 g.

For the control group, conventional treatment was given, according to the treatment measures recommended by the "COVID-19 Prevention and Control Program (Trial)" issued by the National Health and Health Commission of China.

### 2.6. Outcome measures

#### 2.6.1. The primary endpoint

The primary endpoint was the disappearance rate of main symptoms of COVID-19. The disappearance rate of the main symptoms in the experimental group and the control group were compared by evaluating 3 symptoms, fever, fatigue, and cough, after 1 week of treatment.

#### 2.6.2. Secondary endpoints

The secondary endpoints were the disappearance rate of secondary symptoms, and the changes in white blood cells, lymphocytes, C-reactive protein, and erythrocyte sedimentation rate.

### 2.7. Safety monitoring

The occurrence of nausea, vomiting, diarrhea, rash and other adverse events after taking medicine were monitored and recorded.

### 2.8. Ethical concerns

This study followed and met the ethical requirements for conducting the clinical trial. The institute complies with the relevant regulations of the National Health Commission. The approval from the ethics committee was obtained from Wuhan Municipal Health Commission (approval number: 2020100).

### 2.9. Statistical analysis

For statistical analysis, SAS 9.4 software was used. All statistical tests used a two-sided test, with $P < 0.05$ indicating that the difference is statistically significant. The measurement data was described by $\bar{x} \pm s$. Quantitative data was compared using t test, and categorical data was compared using chi-square test or exact probability method.

## 3. Results

### 3.1. Patient characteristics

Of the 120 patients who were assessed for eligibility, 78 were excluded due to the lack of symptoms (not having fever, fatigue or coughing), SARS-CoV-2 assay findings, or radiologic abnormality on chest CT. Therefore, a total of 42 patients diagnosed with COVID-19 were included. The study flow chart is shown in Fig. 1.

There was no statistically significant difference between the two groups in terms of age, temperature, blood pressure, heart rate, blood oxygen saturation and other baseline data, and they were comparable (Table 1).

### 3.2. Outcome measures

The disappearance rates of major symptoms including fever, cough and fatigue were significantly high in XBD plus conventional medicine group compared with conventional medicine alone (Table 2).

There were a significant improvement in the disappearance rate of loss of appetite in XBD plus conventional medicine group, while there was no significant difference in other symptoms including shortness of breath, chest tightness, insomnia, pharyngalgia, chill, headache, nausea, vomiting and diarrhea between the two groups (Table 2).

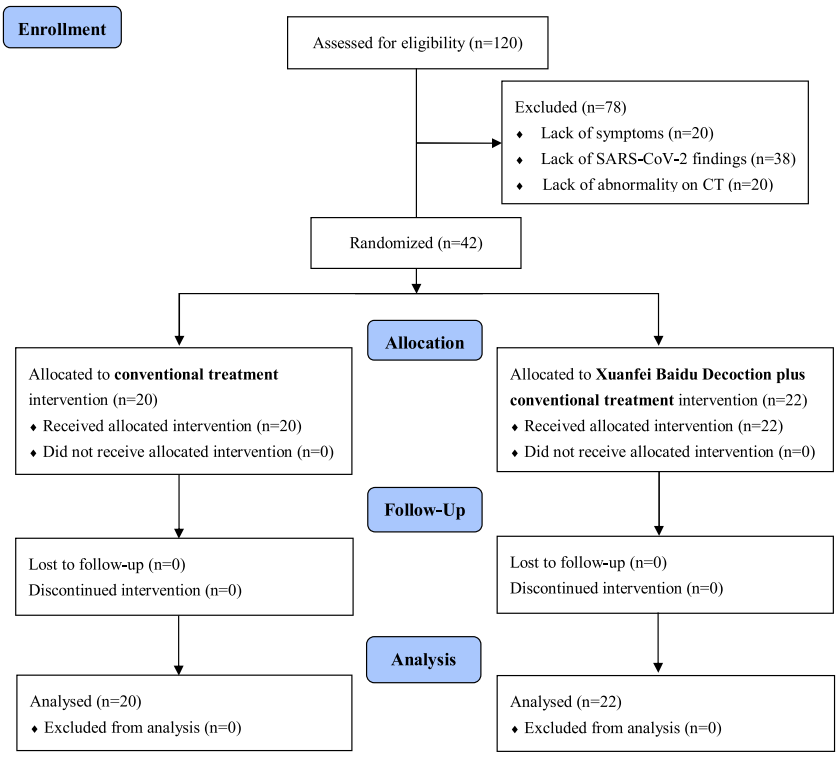


**Fig. 1.** Study flow chart.

**Table 1**
Demographic characteristics of participants

| | XBD plus conventional medicine ($n = 22$) | Conventional medicine ($n = 20$) | *P* value |
|---|---|---|---|
| Age, years | 57.10 ± 14.00 | 62.40 ± 12.30 | 0.202 |
| Temperature, °C | 38.56 ± 0.68 | 38.38 ± 0.63 | 0.383 |
| Systolic pressure, mmHg | 123.90 ± 12.90 | 119.30 ± 14.4 | 0.290 |
| Diastolic pressure, mmHg | 75.30 ± 10.20 | 72.40 ± 9.80 | 0.361 |
| Heart rate, number/min | 88.59 ± 10.80 | 88.40 ± 11.60 | 0.978 |
| Oxyhemoglobin saturation, % | 84.28 ± 7.23 | 85.26 ± 6.98 | 0.925 |

**Table 2**
Disappearance rate of outcomes.

| Outcomes | XBD plus conventional medicine | Conventional medicine | *P* value |
|---|---|---|---|
| *Major symptoms* | | | |
| Fever | 18/20 (90.0) | 11/18 (72.3) | 0.043 |
| Cough | 13/17 (76.5) | 7/18 (38.9) | 0.028 |
| Fatigue | 15/19 (78.9) | 6/14 (42.9) | 0.039 |
| *Other symptoms* | | | |
| Loss of appetite | 9/12 (75.0) | 2/9 (22.2) | 0.024 |
| Shortness of breath | 8/10 (80.0) | 4/8 (50.0) | 0.201 |
| Chest tightness | 7/11 (63.6) | 2/9 (22.2) | 0.080 |
| Insomnia | 4/9 (44.4) | 2/7 (28.6) | 0.451 |
| Pharyngalgia | 3/5 (50.0) | 3/5 (50.0) | 1 |
| Chill | 5/9 (55.5) | 5/9 (55.5) | 1 |
| Headache | 3/5 (50.0) | 2/4 (50.0) | 1 |
| Nausea | 4/6 (60.7) | 3/5 (60.0) | 1 |
| Vomiting | 2/3 (66.7) | 2/3 (66.6) | 1 |
| Diarrhea | 5/7 (71.4) | 5/7 (71.4) | 1 |
| *Biochemical parameters* | | | |
| White blood cell | 9/12 (75.0) | 3/11 (27.2) | 0.030 |
| Lymphocytes | 7/10 (70.0) | 2/10 (20.0) | 0.035 |
| C-reactive protein | 15/18 (83.3) | 5/17 (29.4) | 0.002 |
| Erythrocyte sedimentation rate. | 16/19 (84.2) | 6/16 (37.5) | 0.006 |

Regarding the main laboratory indicators, the increase rates of WBC and lymphocytes, the reduction rate of C-reactive protein, and erythrocyte sedimentation rate were favorable to XBD plus conventional medicine group (Table 2).

### 3.3. Safety monitoring

No obvious adverse reactions were seen in patients taking Chinese medicine.

## 4. Discussion

The results showed that the XBD combined with conventional medicine could significantly relieve clinical symptoms such as fever, cough, fatigue, loss of appetite, etc. From the laboratory data comparison results, this treatment can obviously increase the number of white blood cells and lymphocytes. Meanwhile, XBD may also significantly reduce C reactive protein and erythrocyte sedimentation rate, to play an obvious anti-inflammatory effect.

However, this study has several limitations. It had a small sample size, a short course of treatment, no strict random methods, and no blinding methods. Therefore, further exploration is needed in the future.

Chinese medicine participates in the treatment of this disease, paying more attention to the stage of the disease, and early treatment is a key period to reduce critical illness and mortality, and a large number of clinical literature is also proving that early use of Chinese medicine can improve the prognosis.[6,7] In the absence of effective antiviral drugs, use traditional Chinese medicine to treat patients with COVID -19 may be considered.

## Authors' contribution

Conceptualization: W-zX, GW; Methodology: W-zX, GW; Formal Analysis: JD, WA; Investigation: JD, WA; Data Curation: W-zX, GW; Writing–Original Draft: W-zX; Writing–Review & Editing: GW; Funding Acquisition: W-zX

## Conflict of interest

The authors declare no conflict of interest.

## Funding

None.

## Ethical statement

This research has been approved by Wuhan Municipal Health Commission (2020100).

## Data availability

The data will be made available upon request.

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