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Treatment Effects of Integrated TCM and Western Medicine Treatment Scheme on COVID-19: A Single-armed Clinical Trial

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ABSTRACT

Background: The outbreak of COVID-19 has brought unprecedented perils to human health and raised public health concerns in more than two hundred countries. Safe and effective treatment scheme is needed urgently.
Objective: To evaluate the effects of integratedTCM and western medicine treatment scheme on COVID-19.
Methods: A single-armed clinical trial was carried out in Hangzhou Xixi Hospital, an affiliated hospital with Zhejiang Chinese Medical University. 102 confirmed cases were screened out from 725 suspected cases and 93 of them were treated with integrated TCM and western medicine treatment scheme.
Results: 83 cases were cured, 5 cases deteriorated, and 5 cases withdrew from the study. No deaths were reported. The mean relief time of fever, cough, diarrhea, and fatigue were (4.78 ± 4.61) days, (7.22 ± 4.99) days, (5.28 ± 3.39) days, and (5.28 ± 3.39) days, respectively. It took (14.84 ± 5.50) days for SARS-CoV-2 by nucleic acid amplification-based testing to turn negative. Multivariable cox regression analysis revealed that age, BMI, PISCT, BPC, AST, CK, BS, and UPRO were independent risk factors for COVID-19 treatment.
Conclusion: Our study suggested that integrated TCM and western medicine treatment scheme was effective for COVID-19.

1. Introduction

COVID-19 (also named Novel Coronavirus Pneumonia, NCP) has continued to spread across the world and caused millions of deaths. Current studies have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has highly homologous with bat SARS-like coronavirus (Lai et al., 2020). The main clinical manifestations of patients with early-onset symptoms are fever, cough, and fatigue while patients with severe cases result in respiratory failure, multiple organ failure, and even death (Wu et al., 2020).

Traditional Chinese medicine (TCM) has been used in China with a long history for fighting serious plagues with success, including the most recently occurring Severe Acute Respiratory Syndrome (SARS) (Liu et al., 2004). Treatment of SARS with TCM has been efficacious in the alleviation of symptoms such as fever, cough, expectoration, and gasping; it also improved lung function by inhibiting lung inflammation (Junhui et al., 2003; Xiaolin et al., 2003; Min, 2003; Jin-pan et al., 2003; Hsu et al., 2006; Lau et al., 2005a, 2005b). Research showed that the combination of western medicine and TCM had better performance on reducing fatality, alleviating symptoms, and curtailing hospitalization. In this present study, a single-arm, open-label trial of COVID-19 therapy was carried out to evaluate both the efficacy and safety on the combined application of western medicine and TCM (Junhui et al., 2003; Xiaolin et al., 2003; Min, 2003; Jin-pan et al., 2003; Hsu et al., 2006; Lau et al., 2005a, 2005b).

2. Materials and Methods

2.1. Study design and patients

The single-armed, open-label study was conducted in Hangzhou Xixi Hospital, an affiliated hospital with Zhejiang Chinese Medical Univer-

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sity. This study was registered at the Chinese Clinical Trial Registry (Register NO. ChiCTR2000029578) and was approved by the Medical Ethics Committee of Hangzhou Xixi Hospital (Approval NO.2020- KLS-15).

By March 2nd, 2020, a total of 725 suspected patients of COVID-19, either exposed to the virus or with a history of fever were considered for the study. 105 among such suspects, whose respiratory or blood specimens were tested SARS-COV-2-positive consecutively twice by the nucleic acid amplification-based tests were diagnosed as confirmed cases. Among them, 12 cases declined to participate, therefore 93 cases were enrolled in the subsequent clinical trial. During the treatment and follow-up, 5 cases withdrew, and the symptoms of other 5 patients were exacerbated and transformed into critical pneumonia. Finally, 83 participants completed the full treatment scheme and the follow-up.

All the patients were provided with informed consent and signed agreement. Patients who met the criteria of the Diagnosis and Treatment Protocol for COVID-19 were included and assigned according to their symptoms as classified by the Protocol to mild, moderate, and severe groups, respectively (Tian et al., 2020). Mild group patients were characterized by mild respiratory symptoms with no imaging manifestations of pneumonia, the moderate group patients were characterized by clinical symptoms that included fever, respiratory symptoms, and imaging manifestations of pneumonia. The severe group patients should meet at least one of the following conditions:

(1) Respiratory distress (respiratory rate is ≥30 times/minute).
(2) Oxygen saturation under the resting state is ≤93%.
(3) Arterial blood oxygen partial pressure / oxygen concentration is ≤300 mmHg.

The exclusion criteria were 1) patients in critical stage; 2) patients with other serious organ diseases or mental diseases.

Standard of cure in this study was defined as follows: patients' body temperature returned to normal for >3d; respiratory symptoms were significantly alleviated; obvious absorption of inflammation from lung imaging was observed; two consecutive negative results of respiratory pathogen nucleic acid tests were obtained.

2.2. General treatment principle with western medicine

Patients were suggested to take bed rest and receive other support including strengthening treatments, balanced intake of water and electrolytes, and close monitoring of oxygen saturation.

All patients were treated with alpha-interferon nebulization (5 million units each time for adults, added to 2 ml of sterilized water for injection twice daily) or lopinavir (200 mg, two capsules each time, twice a day for 5 days). Inappropriate use of antibacterial drugs was avoided, in particular the combined use of broad-spectrum antibacterial drugs.

2.3. TCM treatment protocol

The prescription for patients in mild group included 9 g of Pogostemon cablin (Guang Huo Xiang), 9 g of Magnolia officinalis (Hou Pu), 9 g of Lonicera japonica (Jin Yin Hua), 9 g of Atractylodes lancea (Cang Zhu), 6 g of Periostracum cicada (Chan Tui), 6 g of Folium perillae (Su Ye), 15 g of Poria cocos (Fu Ling), and 15 g of Rhizoma Dioscoreae (Shan Yao). Prescription for patients in moderate group comprised of the following: 6 g of Ephedra sinica (Ma Huang), 9 g of Semen armeniacae amarae (Ku Xing Ren), 30 g of Semen coicis (Yi Ren), 3 g of Glycyrrhiza uralensis (Zhi Gan Cao), 9 g of Atractylodes lancea (Cang Zhu), 9 g of Magnolia officinalis (Hou Pu), 9 g of Rhizoma Pinelliae (Jiang Ban Xia), 15 g of Excrementum Bombycis Mori (Can Sha), 9 g of Forsythia suspensa (Lian Qiao), 15 g of French chalk (Hua Shi), 12 g of Dioscorea spongiosa (Bi Xie), and 6 g of Periostracum cicada (Chan Tui). For patients in severe group, the prescription consisted of 30 g of French chalk (Hua Shi), 15 g of Artemisia capillaris (Yin Chen), 12 g of Acorus tatarinowii (Shi Chang Pu), 9 g of Forsythia suspensa (Lian Qiao), 9 g of Amomum cardamomum (Bai Dou Kou), 9 g of Scutellaria baicalensis (Huang Qin), 15 g of Gypsum Fibrosum (Shi Gao), 12 g of Lepidium apetalum (Ting Li Zi), 9 g of Folium perillae (Su Ye), 9 g of Rhizoma Pinelliae (Jiang Ban Xia), 15 g of Artemisia apiacea (Qing Hao), and 15 g of Massa Medicata Fermentata (Shen Qu).

2.4. Statistical analysis

Continuous variables were expressed as mean±SD or median (IQR) and compared with the Paired *t*-test or one-way ANOVA, categorical variables were expressed as number (%) and compared by χ^2 test or Fisher's exact test or the Matching Rank Sum test. The comparison of grade variables was analyzed by Ridit analysis. The cure rate was analyzed with survival analysis-life tables, and factors affecting disease improvement were analyzed by multivariable cox regression model. Relief time of clinical symptoms and time of SARS-CoV-2 by nucleic acid amplification-based testing turning negative were analyzed with survival analysis-Kaplan Meier analysis. The statistical analysis was done using SPSS 20.0 (SPSS, Chicago, IL, USA) software. A two-sided P-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

According to the *Diagnosis and Treatment Protocol for COVID-19 (5th Trial Edition)* issued by the National Health Commission of People's Republic of China on February 4th, 2020 (http://www.gov.cn/zhengce/zhengceku/2020–02/05/content_5474791.htm), all the 105 participants shared the main symptoms, such as fever, cough, expectoration, diarrhea, and fatigue, were classified into the mild, moderate, and severe stages, respectively (Fig. 1A).

As shown in Tables 1 and 2, the levels of C reactive protein (CRP), lactate dehydrogenase (LDH), and urine protein (UPRO) were all raised, and the CRP levels in severe patients were significantly higher than those in the mild-type patients ($P < 0.05$), and Globulin (GLB) and Albumin (ALB) levels between moderate-type and severe-type patients were significantly different ($P < 0.05$). UPRO was found to be elevated in 41 cases (44.09%). Furthermore, according to Ridit analysis, we found that the pulmonary infiltration signs by computerized tomography (PISCT) were significantly different between mild, moderate, and severe COVID-19 participants ($P < 0.05$) (Table 2).

3.2. Efficacy

The participants with mild COVID-19 were all cured without exacerbation. As for the moderate patients, symptoms of two patients deteriorated into critical COVID-19, and five were transferred to other local hospitals for personal reasons and dropped out. Three cases in the severe group were cured, and symptoms of other three patients were exacerbated. The total exacerbation rate was 5.38%. There was no death reported (Table 3). The median cure time was 14.67 days, and the cure rate was 41.8% on day 14, 80.2% on day 21, and 98.1% on day 28, respectively (Fig. 1B).

As shown in Fig. 2, all clinical symptoms were improved after treatment. The mean relief times of fever, cough, diarrhea and fatigue of the total COVID-19 participators were (4.78 ± 4.61) days, (7.22 ± 4.99) days, (5.28 ± 3.39) days and (5.28 ± 3.39) days, respectively (Table 4), and the relief time of mild COVID-19 participators was shorter than other COVID-19 participates.

It took an average of (14.84 ± 5.50) days for the SARS-Cov-2-positive cases to turn negative, as indicated by the nucleic acid amplification-based testing. Specifically, the recovery time in mild, moderate, and severe groups participants were (14.44 ± 8.25) days, (14.86 ± 5.11) days, and (15.67 ± 5.11) days, respectively (Fig. 3A).

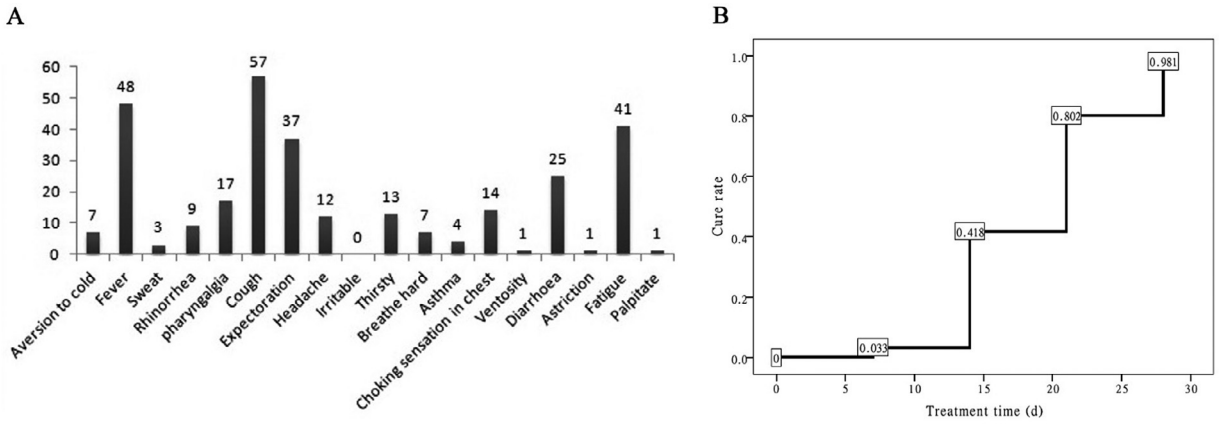

Fig. 1. Clinical symptoms of participants and cure rate of integrated TCM and western medicine treatment scheme across the time. **(A)** Distribution of clinical symptoms before treatment; **(B)** The median cure time was 14.67 days, and the cure rate was 41.8% on day 14, 80.2% on day 21 and 98.1% on day 28, respectively.

Table 1
Clinical baseline characteristic in 93 cases of NCP.

Indexes	Total($n = 93$)	Classification of NCP		
		Mild($n = 9$)	Moderate($n = 78$)	Severe($n = 6$)
Age (years)	45.06 ± 15.48	42.00 ± 19.19	45.10 ± 15.56	49.17 ± 7.22
Gender Men	42	4	34	4
BMI (Kg/m2)	22.70 ± 3.30	22.33 ± 3.20	22.59 ± 3.23	25.00 ± 4.36
WBC [M(IQR)]	5.24(4.28,6.74)	5.78(4.76,6.12)	5.09(4.21,6.74)	5.62(4.77,10.13)
LYMPH [M(IQR)]	1.21(0.86,1.85)	1.97(1.03,2.12)	1.20(0.86,1.74)	0.91(0.59,1.68)
CRP (mg/L)	17.01 ± 22.14	3.71 ± 4.11	17.25 ± 22.41	29.67 ± 25.36*
ALT (U/L)	32.97 ± 36.34	19.33 ± 9.85	32.57 ± 39.18	29.33 ± 18.78
AST (U/L)	30.27 ± 16.67	24.78 ± 9.08	29.66 ± 17.62	28.17 ± 12.92
GLB (g/L)	30.44 ± 4.33	32.38 ± 5.07	29.61 ± 3.72	34.60 ± 6.80△
ALB (g/L)	40.94 ± 4.33	42.13 ± 4.67	42.79 ± 8.84	35.00 ± 6.48△
Scr (μmol/L)	63.44 ± 17.50	65.33 ± 20.71	64.49 ± 17.43	64.83 ± 16.46
BUN (mmol/L)	5.09 ± 4.36	4.44 ± 1.67	4.73 ± 4.69	5.50 ± 2.07
LDH (U/L)	258.62 ± 4.36	220.38 ± 162.51	260.96 ± 171.49	297.4 ± 95.21
CK (U/L)	88.84 ± 156.03	75.33 ± 37.20	104.55 ± 169.69	62.33 ± 31.08
BS (mmol/L)	4.33 ± 0.94	5.63 ± 0.92	7.07 ± 3.00	8.40 ± 2.30

* $P < 0.05$ compared with mild NCP.
△ $P < 0.05$ compared with moderate NCP. BMI: Body Mass Index, WBC: White Blood Cell, LYMPH: Percentage of lymphocytes, CRP: c-reactive protein, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GLB: Globulin, ALB:Albumin, Src: serum creatinine, BUN: blood urea nitrogen, LDH: lactate dehydrogenase, CK: creatine kinase, BS: blood sugar.

Table 2
Comparison of PISCT in different classification of NCP by Ridit analysis.

Classification of NCP	n	PISCT [a]				UPRO				
		(-)	(1+)	(2+)	Ridit value	(-)	(1+)	(2+)	(3+)	Ridit value
Mild	9	2	6	1	0.28 ± 0.21	5	2	2	0	0.51 ± 0.29
Moderate	78	4	35	39	0.51 ± 0.25**	45	21	11	1	0.49 ± 0.26
Severe	6	0	0	6	0.75 ± 0.00△	2	2	2	0	0.63 ± 0.29

** $P < 0.01$ compared with mild NCP. △ $P < 0.05$ compared with moderate NCP.
[a] PISCT(pneumonia infiltration signs in CT); the grading criteria of PISCT as follows: Moderate(2+): grinding glass-like changes; Mild(+): focal infiltration; Normal(-): no infiltration.[b] Qualitative examination of urinary protein: Negative (-): < 0.1 g/L, (+): 0.2–1.0 g/L; (2+): 1.0–2.0 g/L, (3+):>2.0 g/L.

Table 3
Disease outcomes of all the NCP participators at post treatment.

Outcomes	Total	Classification of NCP		
		Mild($n = 9$)	Moderate($n = 78$)	Severe($n = 6$)
Cured	83 (89.25)	9(100.00)	71(91.03)	3(50.00)
Withdrawal for personal reason	5 (5.38)	0(0.00)	5(6.41)	0(0.00)
Exacerbated into critical	5 (5.38)	0(0.00)	2(2.56)	3(50.00)
Exacerbated into Fatality	0(0.00)	0(0.00)	0(0.00)	0(0.00)

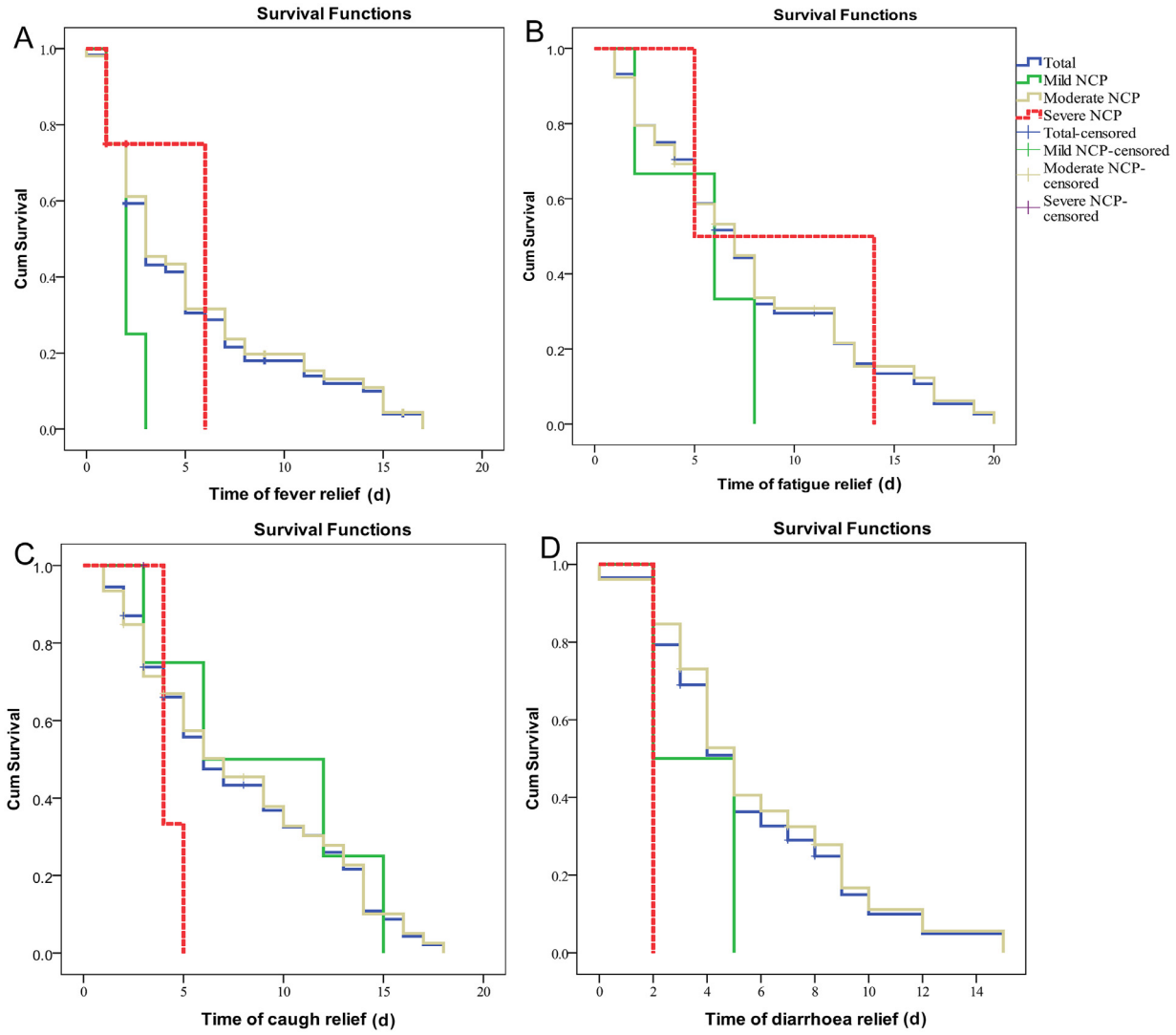

Fig. 2. Survival analysis for relief times of the main clinical symptoms. The blue line indicates the relief time of total COVID-19 participants, the green line indicates the relief time of mild COVID-19, the gray line indicates the relief time of moderate COVID-19, the red line indicates the deadline time of withdrawal cases.

Table 4
Relief time of clinical symptom in NCP.

Indexes	mean±SD	M(QTR)
Fever	4.78 ± 4.61	3 (1, 7)
Pharyngalgia	2.59 ± 1.91	2 (1, 3)
Caugh	7.22 ± 4.99	5.5 (3, 11.75)
Expectoration	8.00 ± 6.49	1 (2, 13)
choking sensation in chest	6.67 ± 5.47	4 (3, 10)
Headache	4.30 ± 3.53	4 (1.5, 4)
thirsty	7.33 ± 6.76	5 (1, 13)
diarrhea	5.28 ± 3.39	4 (3, 7)
Fatigue	7.60 ± 5.22	6 (4, 11.75)
Coatef tongue	12.18 ± 5.72	12 (7, 17)
Nature of tongue	11.84 ± 5.64	12 (8.5, 16.25)

As shown in Table 5 and Fig. 3B, all the participants' UPRO and PISCT were significantly improved ($P < 0.01$). As analyzed by the Matching Rank Sum test, the level of CRP, Aspartate Aminotransferase (AST), LDH, Blood Sugar (BS) of all the participants improved after treatment ($P < 0.05$).

Finally, we analyzed the prognostic factors for COVID-19 outcomes by using Cox regression analysis. As shown in Table 6, age, body mass index (BMI), PISCT, blood platelet count (BPC), AST, CK, BS, UPRO were included into the model equation and found that CK, BS, UPRO (+), and UPRO (2+) were the significant prognostic factors for COVID-19 outcomes ($P < 0.05$).

3.3. Safety

Fifteen participators' Alanine Aminotransferase (ALT) increased during the treatment. However, they all returned to normal after taking diammonium glycyrrhizinate capsules for liver protection treatment (Table 7).

4. Discussion

The outbreak of COVID-19 has brought unprecedented perils to human health and raised public health concerns in more than two hundred countries. In a study with western medicine intervention, 26% of COVID-19 patients received ICU care, with a fatality rate of 4.3%. After one month of treatment, 47 (34.1%) were discharged from the hospital, and the median hospitalization time of the 47 discharged patients was 10 (7.0 to 14.0) days (Wang et al., 2020). A clinical retrospective study of 34 cases COVID-19 treated with integrated TCM and western medicine showed that the clinical cure rate and exacerbation rate in the

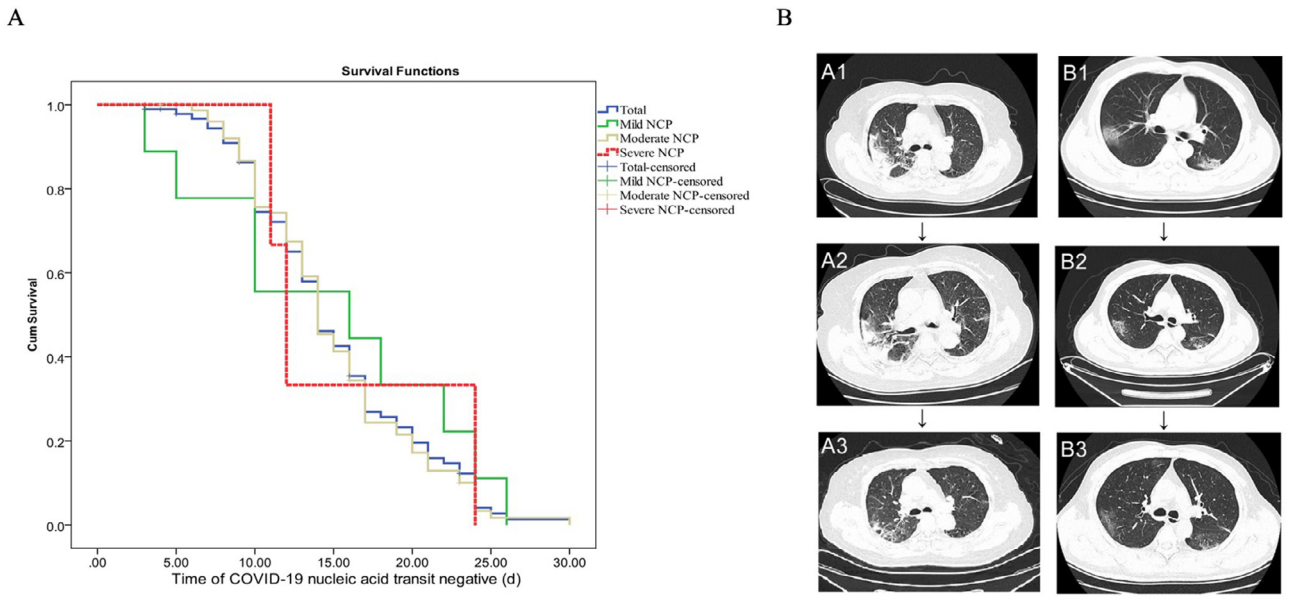

Fig. 3. SARS-CoV-2 nucleic acid and pneumonia infiltration. **(A)** The blue line indicates the relief time of total COVID-19 participants, the green line indicates the relief time of mild COVID-19, the gray line indicates the relief time of moderate COVID-19, the red line indicates the deadline time of withdrawal cases; **(B)** Comparison of pneumonia infiltration in CT of 2 cases in the treatment course. A1-A3, moderate COVID-19 cases at baseline, who exacerbated to severe COVID-19 during the treatment, recovered after treatment. B1-B3, severe COVID-19 cases at baseline, who improved to moderate COVID-19 during the treatment, recovered after treatment.

Table 5
Comparison of clinical indicators at prior and post treatment.

Indexes	prior treatment(n = 93)	post treatment(n = 93)	P
UPRO [a]	0.74 ± 0.81	0.35 ± 0.58	0.00
PISCT [a]	1.42 ± 0.61	1.12 ± 0.75	0.00
Leukocytosis[b]	16 (17.2%)	5 (5.38%)	0.004
Granulocytosis[b]	21 (22.58%)	7 (7.53%)	0.002
Lymphopenia [b]	42 (45.16%)	21 (22.58%)	0.003
Elevated CRP[b]	43 (46.24%)	23 (24.73%)	0.001
Elevated ALT [b]	17 (18.28%)	18 (19.35%)	1.000
Elevated AST [b]	24 (25.81%)	13 (13.98%)	0.031
Elevated Scr [b]	14 (15.05%)	13 (13.98%)	1.000
Elevated BUN [b]	4 (4.3%)	3 (3.23%)	1.000
Elevated LDH [b]	25 (26.88%)	6 (6.45%)	0.001
Elevated CK [b]	7 (7.53%)	3 (3.23%)	0.219
Elevated BS [b]	48 (51.61%)	47 (50.54%)	1.000

[a] Statistical analysis with paired t-test.
[b] Statistical analysis with Matching Rank Sum test. Leukocytosis (>9.5 × 10^9/L), Granulocytosis (>6.3 × 10^9/L), Lymphopenia (<1.1 × 10^9/L) Elevated CRP (>8 mg/L), Elevated ALT (>40 U/L), Elevated AST (>35 U/L), Elevated Scr (>81umol/L), Elevated BUN (>8.8 mmol/L), Elevated LDH (>250 U/L), Elevated CK (>170 U/L), Elevated BS(>6.1 mmol/L). UPRO: urine protein PISCT: pulmonary infiltration signs in computerized tomography, CRP: c-reactive protein, ALT: alanine aminotransferase, AST: aspartate aminotransferase, Src: serum creatinine, BUN: blood urea nitrogen, LDH: lactate dehydrogenase, CK: creatine kinase, BS: blood sugar.

Table 6
NCP prognostic factor analysis by survival analysis-Cox regression.

	Hazard ratio	95.0% CI(lower-upper)	P value
Age	0.91	0.8–1.04	0.16
BMI	1.14	0.6–2.15	0.69
PISCT	14.68	0.29–751.02	0.18
BPC	1.02	0.99–1.05	0.27
ALT	0.79	0.66–0.95	0.01
AST	1.26	0.93–1.71	0.14
CK	1.02	1–1.03	0.01
BS	4.65	2–10.81	0.00
UPRO(+)[a]	0.00	0–0.1	0.01
UPRO(2+) [a]	0.00	0–0.3	0.02

[a] Qualitative examination of UPRO(urinary protein): (+): 0.2–1.0 g/L; (2+): 1.0–2.0 g/L. BMI: Body Mass Index, PISCT: pulmonary infiltration signs in computerized tomography, BPC: blood platelets count, AST: aspartate aminotransferase, CK: creatine kinase, BS: blood sugar, UPRO: urine protein.

Table 7
Adverse event during the treatment.

	Baseline	Post treatment
ALT Total normal cases	76	65
Total abnormal cases	17	18
Normal turn to abnormal cases	–	7
Further exacerbation in abnormal cases	–	8
Improving in abnormal cases	–	3
Abnormal turn to normal cases	–	8
Nausea	–	33
alt	0.79	0.66–0.95
diarrhea	–	29

Note. abnormal ALT: ALT >40 U/L. ALT: alanine aminotransferase.

integrated TCM and Western Medicine group were significantly better than those in the western treatment group (94.1% vs 61.1% and 5.9% vs 33.3%, respectively) (Wen-guang et al., 2020).

This paper here reported a prospective study involving 105 COVID-19-positive patients, result of which revealed both efficacy and safety of the treatment scheme applied.

Symptoms of COVID-19 fitted well with the "cold-dampness epidemic disease (han-shi-yi)" in TCM theory. The formula "Chu-shi-tang" was used to protect mild-type patients with apparent signs of phlegm dampness symptoms. Ban Xia and Chen Pi were removed, and Jin Yin Hua and Chan Tui were added to prevent viral cold, while Shan Yao was added to strengthen the spleen and stomach. Most of the moderate patients had running fever, coughs, and subsequently developed appetite loss, fatigue, and gastrointestinal problems. Symptoms from coldness and dampness at this stage were equally important, therefore Ma-xing-

yi-gan-tang was used as a base formula. Atractylodes lancea (Cang Zhu), Magnolia officinalis (Hou Pu), Rhizoma Pinelliae (Jiang Ban Xia), and Excrementum Bombycis Mori (Can Sha) were used to eliminate dampness and activate the spleen. French chalk (Hua Shi) and Dioscorea spongiosa (Bi Xie) were used to induce diuresis and strengthen Qi transformation, while Forsythia suspensa (Lian Qiao) and Periostracum cicada (Chan Tui) were used to relieve exterior syndrome and clear heat toxins. Severe patients, the main clinical manifestations included chest tightness, shortness of breath and irritability which were in accordance with an accumulation of heat and toxin in lungs. Therefore Gan-lu-xiao-du-yin and Ting-li-da-zao-tang were used as the base formula. Bulbus fritillariae cirrhosae (Chuan Bei Mu), Akebia Stem Caulis Akebiae (Mu Tong), Pogostemon cablin (Huo Xiang), Mentha haplocalyx (Bo He), Rhizoma Belamcandae (She Gan), and Fructus Ziziphi Jujubae (Da Zao) were replaced with Gypsum Fibrosum (Shi Gao), Folium perillae (Su Ye), Rhizoma Pinelliae (Jiang Ban Xia), Artemisia apiacea (Qing Hao), Massa Medicata Fermentata (Shen Qu) to clear away lung heat, reduce phlegm and strengthen the spleen and stomach.

The clinical baseline characteristics of patients showed elevated levels of CRP, LDH and UPRO, as well as pneumonia infiltration with various degrees, which indicated the occurrence of pneumonia, cardiac and renal co-injury for patients with COVID-19 and was clinically worthy of further attention.

The median cure time was 14.67 days, and the cure rate was 41.8% on day 14, 80.2% on day 21, and 98.1% on day 28, respectively, and the total exacerbation rate was 5.38%. Fortunately, the fatality rate was 0%. Moreover, the 10 withdrawal cases were all recovered.

This study's cure rate, exacerbation rate, and fatality rate were better than the data reported by CCDC (98.10% vs 64.86%, 5.38% vs 7.39%, and 0% vs 3.74%). In addition, the total cure rate and exacerbation rate in this study were also better than those in the western medicine group reported in the clinical retrospective study (98.10% vs 61.1%, 5.38% vs 33.3%) (Wen-guang et al., 2020). The trial showed the efficacy and safety of western medicine combined with TCM in treating different stage COVID-19 patients.

It has been reported that SARS-CoV-2 utilized angiotensin-converting enzyme 2 as a cell receptor (Lan et al., 2020). During this process, spike protein (S protein) on the surface of the virus recognizes the host cell receptor and induces fusion of the virus membrane and the cell membrane. Based on the results of previous studies on SARS or other viruses treated by TCM, we speculated that the mechanism of TCM treatment on COVID-19 might be as follows. The TCM treatment scheme contains a variety of antiviral herbs, such as Flos Lonicerae (Jin Yin Hua), Forsythia suspensa (Lian Qiao), Scutellaria baicalensis (Huang Qin), which can inhibit the replication of SARS-Cov or other respiratory viruses (Dong et al., 2017; Huang et al., 2014; Lau et al., 2008; Poon et al., 2006). Based on the network pharmacology and molecular docking method, Zong et al. (Yang et al., 2020) found that quercetin, kaempferol, formononetin, and baicalein could bind to 2019-nCoV 3CL hydrolase and inhibit virus invasion. Moreover, Scutellaria baicalensis could inhibit the inflammatory reaction and reduce the damage of the human immune system (Yu-lu et al., 2018; Pei-ming et al., 2016).

During the study, liver damage and abnormal gastrointestinal activities occurred in some patients, which might be related to antiviral drugs (Han et al., 2017; Aboud et al., 2019). Nevertheless, these side-effects were slight and controllable.

5. Conclusion

In conclusion, results showed that the integrated TCM and western medicine treatment approach was effective and safe. Compared with conventional Western medicine treatment, integrated TCM and Western medicine treatment has shown to be more promising and worthy of further clinical reference and application. Our team plans for more in-depth research on the mechanism of TCM treatment of COVID-19 from the aspects of antiviral, regulation of microecology, and immunity.

Ethical approval

The study was approved by the ethical committee of Hangzhou Xixi Hospital affiliated to Zhejiang Chinese Medical University (2020- KLS-15).

Data availability

Additional data are available on reasonable request.

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Declaration of Competing Interest

All authors declare no competing interests.

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Supplementary Materials

Nil.

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