Clinical Studies on the Treatment of Novel Coronavirus Pneumonia With Traditional Chinese Medicine—A Literature Analysis

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Objective: This study aims to analyze the current situation and characteristics of traditional Chinese medicine for treatment of novel coronavirus pneumonia, clarify its clinical advantages and provide a reference for clinical treatment.

Methods: Clinical randomized controlled trials, clinical control trials and case series research involving the use of Chinese medicine for novel coronavirus pneumonia treatment were selected from PubMed, Chinese Journal Service Platform of CNKI, VIP, and WanFang Data Knowledge Service Platform from the establishment of the library to 11:00 AM on April 15, 2020. The published information, research design, intervention measures and research observation index were statistically analyzed.

Results: Twenty studies were included. The research methods were mainly clinical controlled trials. The observation indicators were mostly fever improvement time, cough improvement time, shortness of breath improvement time, chest CT and CRP examination. Maxing Ganshi (Ephedrae Herba, Armeniacae Semen Amarum, Glycyrrhizae Radix Et Rhizoma, and Gypsum Fibrosum) decoction was the core prescription. The most frequently used drugs were Glycyrrhizae Radix Et Rhizoma (Gancao), Ephedrae Herba (Mahuang), Armeniacae Semen Amarum (Kuxingren), Atractylodis Rhizoma (Cangzhu), and Scutellariae Radix (Huangqin). The most frequently used drug combination was Ephedrae Herba (Mahuang)–Armeniacae Semen Amarum (Kuxingren). The most frequently used Chinese patent medicine was Lianhua Qingwen capsule/granule.

Conclusions: Traditional Chinese medicine has widely used for novel coronavirus pneumonia in China. It is worthy of global attention. Also, high-quality randomized controlled clinical trials on the effectiveness and safety of traditional Chinese medicine in the treatment of novel coronavirus pneumonia need to carry out.

Keywords: novel coronavirus pneumonia, traditional Chinese medicine, clinical research, Drug application rule, literature analysis
INTRODUCTION

Recently, new coronary pneumonia (NCP) outbreaks worldwide, according to the daily information released by the Chinese State and Regional Health Committees' daily information as of 21:31 on April 16, 2020, China has confirmed a total of 83,798 cases and 3,352 cumulative deaths; among the cumulative confirmed cases of 2,019,857 worldwide, 135,165 died and 1,422,853 remained infected (Dingxiangyuan, 2020). The epidemic trend in regions outside of China has greatly erupted, overseas outbreaks have escalated, and more than 20 countries and regions have been infected. Except for Antarctica, all continents have confirmed cases. How to effectively treat NCP remains a key problem. The Office of the State Administration of Traditional Chinese Medicine and the General Office of the National Health And Health Commission have issued seven editions of the “Diagnosis and Treatment Plan of Novel Coronavirus Infection Pneumonia”; each version of the diagnosis and treatment plan has always emphasized the active role of Chinese medicine in the treatment and the strengthening of its combination with Western medicine to promote medical treatment and achieve good results (National Health Commission of the People’s Republic of China, 2020). In an interview, Zhong Nanshan affirmed the role of Chinese medicine in treatment of NCP; Chinese medicine can effectively suppress inflammatory damages and can also be popularized in foreign countries (Tencent News, 2020a). The article aimed to systematically organize clinical research by literature metrology and data mining methods, analyze the current situation of clinical treatment research in Chinese medicine, explore the clinical treatment characteristics of Chinese medicine and provide a reference for global clinical treatment of NCP.

MATERIALS AND METHODS

Search Strategy

Two reviewers (ZZ and NG) independently isolated the useful information from the database. Studies that used Chinese medicine to treat NCP were selected from PubMed, Chinese Journal Service Platform of CNKI, VIP, and WanFang Data Knowledge Service Platform. Advanced search was conducted using the following terms: “NCP” or “Novel Coronavirus Infection” or “New Coronavirus” “2019-nCoV” “COVID-19” “SARS-CoV-2” containing “Chinese and Western medicine” or “Chinese medicine” or “Traditional Chinese medicine” or “prescription.” The search time was from the establishment of the library to 11:00 on 15 April 2020.

Inclusion and Exclusion Criteria

Inclusion criteria: All studies on clinical treatment of NCP in Chinese medicine that state complete treatment options and processes and are classified as clinical control trials (CCT), randomized controlled trials (RCT), and case series studies (CS) were included.

Exclusion criteria: Studies categorized as review, basic research, regional epidemiological research, experience summary, and syndrome analysis were excluded.

Data Extraction and Analysis

Noteexpress, a document management software program, was used to manage the studies obtained from different databases. An access database was established to extract information on the publication of the literature (author, time of issue, issue journal, type of fund), research design (number of cases, subject gender and age), intervention measures (prescription, traditional Chinese medicine), research observation indicators and other information for statistical analysis. For eligible studies, two review authors (ZZ, and GN) extracted the data independently. Disagreements were resolved through consultation with a third party (FS). The law of the prescription use of Chinese medicine was analyzed statistically through the “Traditional Chinese medicine inheritance auxiliary system.”

RESULTS

Description of Studies

We identified 757 potentially relevant articles. After removal of duplicates, 625 records remained. After going through the titles and abstracts, we exclude 605 papers. By reading the full text of the remaining 46 articles, 26 were exclude because they were case reports. Ultimately, 20 studies were included in present study (Bin et al., 2020; Cheng and Li, 2020; Cheng et al., 2020; Ding et al., 2020; Duan et al., 2020; Fang et al., 2020; Fu et al., 2020; Gong et al., 2020; Hu et al., 2020; Lv et al., 2020; Qu et al., 2020; Shi et al., 2020; Wang Y. et al., 2020; Wang T. et al., 2020; Xia et al., 2020; Xiao et al., 2020; Yang Q. et al., 2020; Yang Z. et al., 2020; Yao et al., 2020; Zhu et al., 2020). Among these studies, 2 RCTs, 10 CCTs and 8 CSs were included, which accounted for 10.00%, 50.00% and 40.00% of the total number of studies, respectively. The specific screening process is shown in Figure 1.

Basic Characteristics of the Literature

The basic characteristics of the 20 trials are summarized in Tables 1 and 2. The first study on clinical treatment involving Chinese medicine for treatment of NCP was published on February 6, 2020 (Gong et al., 2020). After February 15, the volume of studies published began to increase. By March 25, 19 articles were published. By April 4, the volume of literature published showed a downward trend. The total number of observations was 1,810, of which 1,021 and 789 were males and females, respectively. The age ranged from 0.6 to 95 y. The largest number of subjects in the study was 308 (Wang T. et al., 2020), and the minimum number of study cases was 13 (Cheng and Li, 2020). About the research areas, the worst-affected area, Hubei region, had the largest volume of studies, accounting for more than 50%, followed by Henan and Anhui regions. 12 trails were funded by research projects. All trials adopted decoction or patent medicine of traditional Chinese medicine (TCM) therapy.
combination with western treatment in the trial group for NCP. While the control group only adopted western treatment. For the severity of included subjects, most RCTs and CCTs included subjects who were the mild or common type, while the subjects in CS were common type and serious type. Three studies mentioned death cases (Bin et al., 2020; Xia et al., 2020; Yang Q. et al., 2020). One study mentioned there were no death cases (Wang T. et al., 2020). The other 16 studies did not mention the death condition. Adverse reactions were reported in eight studies, while no mention in the other studies. Specific research characteristics of RCTs and CCTs are shown in Table 1 and CSs are shown in Table 2.

Analysis of the Law of Prescription Use in TCM

Frequency Analysis of Single Chinese Herbal Medicine

The statistical analysis showed that 34 traditional Chinese medicine prescriptions, involving 106 traditional Chinese medicines, were used in 20 clinical studies. The frequency of traditional Chinese medicine use was sorted. The top three drugs are commonly used for cough and sputum and are also the basic components of Maxing Ganshi decoction in traditional Chinese medicine to treat cough and asthma. In the included prescriptions, 24 drugs were found with a frequency of ≥5 (Table 3). According to the traditional Chinese medicine category to sort out the 106 traditional Chinese medicines, the top 3 most frequently used are heat-clearing medicines, exterior syndrome-relieving medicines and phlegm-resolving and cough and asthma-relieving medicines, followed by damp-resolving medicines, tonify medicines, and damp-draining diuretic medicines. The details are presented in Table 4.

Analysis of the Association Rules of Traditional Chinese Herbal Medicine

The association rules of traditional Chinese medicine for the included prescriptions were analyzed. The support was set to 20%. The results showed 10 associations of traditional Chinese medicine with a confidence of above 0.8. The association of traditional Chinese medicine with a confidence of 1 was Gypsum Fibrosum (Shigao) -> Armeniacae Semen Amarum (Kuxingren), Tsuoko Fructus (Caoguo) -> Arecae Semen (Binglang). The association of traditional Chinese medicine with a confidence level of above 0.86 was Gypsum Fibrosum (Shigao) -> Ephedrae Herba (Mahuang), Gypsum Fibrosum (Shigao), Armeniacae Semen Amarum (Kuxingren) -> Ephedrae Herba (Mahuang), Ephedrae Herba (Mahuang), Arecae Semen (Binglang) -> Atractylodis Rhizoma (Gangzhu), Ephedrae Herba (Mahuang), Arecae Semen (Binglang) -> Armeniacae Semen Amarum (Kuxingren), Atractylodis Rhizoma (Gangzhu), Arecae Semen (Binglang) -> Ephedrae Herba (Mahuang). Table 5 presents the analysis of specific association rules.

Analysis of Chinese Herbal Medicine Combinations Network

The relationship among different drug combinations was visualized using the network display function of the traditional Chinese medicine inheritance auxiliary system. The results showed that Ephedrae Herba (Mahuang)-Armeniacae Semen Amarum (Kuxingren) had the highest support, as the most common core combination, followed by Pinelliae Rhizoma (Banxia)-Poria (Fuling), Ephedrae Herba (Mahuang)-Glycyrrhizae Radix Et Rhizoma (Gancao) and Ephedrae Herba (Mahuang)-Atractylodis Rhizoma (Cangzhu). This result indicates that commonly used clinical treatments for NCP involve depressing qi, relieving cough, eliminating dampness and eliminating phlegm. The Chinese herbal medicine combinations network is presented in Figure 2.

Analysis of Application of Classical Prescriptions of TCM

Studies involving the application of classical prescriptions of TCM were collected and summarized. Six studies were obtained. Among these classical prescriptions, Da Yuan decoction and Ganlu Xiaodou pill were created by doctors Wu Youke (Ming Dynasty and Ye Tianshi (Qing Dynasty) and who studied in epidemic exogenous febrile diseases, while Maxing Ganshi
| Included trials | Funding designs | Study region | Sample characteristics type; male/female; age(y) | Interventions | Duration | Fever improvement time(d) | Outcome index | Intergroup differences | Adverse reactions |
|-----------------|-----------------|--------------|---------------------------------------------------|---------------|---------|--------------------------|--------------|-----------------------|-----------------|
| YAO 0206 (Yao et al., 2020) | CCT | Hubei | CT: 21 M: 16; F: 5 57.1 ± 14.0 | Chinese patent drug +WT1.2.6.7 | T: 4.6 ± 3.2 C: 6.1 ± 3.1 | 1. Disappearance rate of fever and cough 2. Disappearance rate of fatigue 3. Fever improvement time 4. Disappearance rate of anhelation, expectoration 5. Disappearance rate of sore throat, choking sensation in chest, dyspnea, headache, nausea, anorexia, diarrhea, muscle pain |
| LV 0217 (Lv et al., 2020) | CCT | Hubei | MT, CT: 83 M: 28; F: 35 59.1 ± 15.61 | Chinese patent drug +WT1.2.3.5.7.8 | T: 6 (median) C: 7 (median) | 1. Disappearance rate of fever, fatigue, cough 2. Disappearance rate of anhelation, moist rale 3. Fever improvement time 4. Disappearance rate of muscle pain, expectoration, nasal obstruction, nasal discharge, sore throat, choking sensation in chest, dyspnea, headache, nausea, vomiting, anorexia, diarrhea 5. Aggravation rate 6. Death rate |
| XIA 0218 (Xia et al., 2020) | √ | CCT | Hubei | Decoction +WT1.2.7.8 | T: 2.84 ± 1.31 C: 4.38 ± 1.90 | 1. Fever improvement time 2. Recovery time of cough, fatigue, dyspnea, diarrhea 3. Score of TCM syndrome scale 4. Incidence of mild type to severe type 5. Improvement rate of lung |

(Continued)
| Included trials     | Funding designs | Study region | Sample characteristics type; male/female; age(y) | Interventions | Duration | Fever improvement time(d) | Outcome index                                                                 | Intergroup differences | Adverse reactions |
|---------------------|----------------|--------------|--------------------------------------------------|---------------|----------|---------------------------|--------------------------------------------------------------------------------|------------------------|--------------------|
| QU 0226 (Qu et al., 2020) | √  | CCT Anhui | MT, CT: 40 M: 25, F: 15 40.65 ± 8.23 | Chinese patent drug + WTI.2 | 10 d | T: 3.24 ± 0.89 C: 5.10 ± 1.40 | 1. Improvement time of temperature, dry cough, nasal obstruction, Fever improvement time, sore throat, fatigue, diarrhea 2. Dime of nucleic acid test turning negative 3. Death rate | 1. P<0.05 2. P<0.05 3. Not mentioned | Trial: 1 case of nausea; Control: 2 cases of nausea |
| DING 0303 (Ding et al., 2020) | RCT Hubei | MT: 10 CT: 36 ST: 5 M: 39, F: 12 54.7 ± 21.3 | decoction + WTI.2.6 | 10 d | T: 16 (4,42) C: 17.5 (8,42) | 1. Disappearance rate of fever, cough, choking sensation in chest and anhelation 2. Disappearance rate of nasal obstruction, abdominal pain, and diarrhea 3. Improvement rate of ESR 4. Improvement rate of CRP, IL-6 5. Improvement rate of TNF-α, TNF-γ 6. Improvement rate of lung CT 7. Liver function 8. Death rate | 1. P<0.05 2. P>0.05 3. P<0.01 4. P<0.05 5. P>0.05 6. P<0.05 7. P>0.05 8. Not mentioned | |
| SHI 0305 (Shi et al., 2020) | √  | CCT Shanghai | MT: 1 CT: 14 ST: 3 M: 26, F: 23 47.94 ± 14.46 | Chinese patent drug + decoction | 6 d | T: 16 (4,42) C: 17.5 (8,42) | 1. Clinical syndrome integral 2. Hospitalization time 3. Course of disease, fever improvement time 4. Improvement rate of lung CT 5. Death rate | 1. P<0.05 2. P<0.05 3. P>0.05 4. P>0.05 5. Not mentioned | |
| Included trials | Funding Study designs | Study region | Sample characteristics type; male/female; age(y) | Interventions | Duration | Fever improvement time(d) | Outcome index | Intergroup differences | Adverse reactions |
|-----------------|----------------------|--------------|------------------------------------------------|--------------|----------|--------------------------|--------------|----------------------|------------------|
| Trial | Control | Trial | Control | Trial | Control | | |
| XIAO 0310 (Xiao et al., 2020) | CCT | Hubei | MT: 100 | M: 64, F: 36 | 60.90 ± 8.70 | 2 w | Chinese patent drug+WT1 | T: 2.25 ± 1.12 | 1. Total effective rate | 1. P<0.05 |
| | | | MT: 100 | M: 66, F: 34 | 62.20 ± 7.50 | C: 3.08 ± 1.64 | 2. Lung CT | | 2. P<0.05 |
| | | | | | | | 3. Fever improvement time | | 3. P<0.05 |
| | | | | | | | 4. Disappearance time of cough, fatigue, dizziness, nasal discharge | | 4. P<0.05 |
| | | | | | | | 5. WBC, Lymph% | | 5. P<0.05 |
| | | | | | | | 6. Death rate | | 6. Not mentioned |
| | | | | | | | | Trail: 1 case of drug allergy; 2 cases of abdominal pain and diarrhea; | |
| CHENG 0311 (Cheng et al., 2020) | CCT | Hubei | CT: 51 | M: 26, F: 25 | 55.5 ± 12.3 | 7 d | Chinese patent drug+WT1.2.8 | T: 2.9 ± 1.7 | 1. Disappearance rate and time of fever, fatigue, cough | 1. P<0.05 |
| | | | CT: 51 | M: 27, F: 24 | 55.8 ± 11.6 | C: 3.9 ± 1.3 | 2. Effective rate of main symptoms | | 2. P<0.05 |
| | | | | | | | 3. Disappearance rate of expectoration, anhelation, choking sensation in chest, anorexia | | 3. P<0.05 |
| | | | | | | | 4. Disappearance rate of muscle pain, dyspnea, nausea | | 4. P>0.05 |
| | | | | | | | 5. Improvement rate of lung CT | | 5. P<0.05 |
| | | | | | | | 6. Rate of turn to severe type | | 6. P<0.05 |
| | | | | | | | 7. Death rate | | 7. Not mentioned |
| | | | | | | | | | Trail: 2 cases of drug allergy, 1 case of abdominal pain and diarrhea |
| FU 0320 (Fu et al., 2020) | √ | CCT | Hubei | CT: 37 | M: 19, F: 18 | 45.26 ± 7.25 | 10–15 d | Chinese patent drug+WT1.7 | T: 1.3 | 1. Accumulated points of fever, cough, dry throat and sore throat, choking sensation in chest and anhelation, fatigue | 1. P<0.05 |
| | | | CT: 36 | M: 19, F: 17 | 44.68 ± 7.45 | | 2. Effective rate, hospital discharge rate | | 2. P<0.05 |
| | | | | | | | 3. Absolute value of LYM, CRP | | 3. P<0.05 |
| | | | | | | | 4. WBC, LYM ratio | | 4. P>0.05 |
| | | | | | | | 5. Death rate | | 5. Not mentioned |
| | | | | | | | | Trail: No adverse response |
| WANG 0323 (Wang Y. et al., 2020) | √ | RCT | Hubei | MT, CT: 10 | M: 5, F: 5 | 54.90 ± 3.71 | 7 d | decoction, incense+WT1. | | 1. Clinical symptoms improved conditions (fatigue, cough, dry throat, short of breath) | 1. P<0.05 |

(Continued)
| Included trials | Funding Study designs | Study region | Sample characteristics type; male/female; age(y) | Interventions | Duration | Fever improvement time(d) | Outcome index | Intergroup differences | Adverse reactions |
|-----------------|-----------------------|--------------|---------------------------------------------------|----------------|----------|--------------------------|---------------|------------------------|------------------|
| DUAN 0324 (Duan et al., 2020) | √ OCT | Hubei | MT: 82 M: 39, F: 43; 51.99 ± 13.88 | Chinese patent drug +WT1.2.6.7 | WT1.2.6.7 | 5 d | 1. Disappearance condition of fever | 2. Lung CT | 2. P>0.05 | 4. Not mentioned |
|               |                      |              | MT: 41 M:23 F:18; 50.29 ± 13.17 |                |          |                          | 3. Nucleic acid test turning negative | 3. P>0.05 | |
| YANG 0414 (Yang Z. et al., 2020) | √ OCT | Hubei | ST: 51 M: 28, F: 23; 61.57 ± 1.84 | decoction +Chinese patent drug +WT1.2.6.7 | WT1.2.6.7 | 1. CRP | 1. P<0.01 | 1. Trial: 27 cases of diarrhea |
|               |                      |              | ST: 52 M: 24, F: 28; 66.35 ± 1.82 |                |          |                          | 2. Albumin | 2. P<0.05 | Control: no adverse response |

MT, mild type; CT, common type; ST, serious type; WT, western treatment.

WT: 1. antiviral; 2. anti-infection/anti-inflammatory/antibiotics; 3. immunoregulation; 4. gastrointestinal regulation; 5. relieving cough and asthma; 6. oxygen therapy; 7. glucocorticoid; 8. nutritional support; 9. nlgesics; 10. liver protection; 11. anti-anxiety.
| Included trials | Funding | Study region | Sample characteristics | Interventions | Duration | Fever improvement time (d) | Outcome index | Self before and after comparison | Adverse reactions |
|-----------------|---------|--------------|------------------------|---------------|----------|---------------------------|---------------|---------------------------------|-----------------|
| CHENG 0219      | Hubei   | CT:54        | M:29,F:25              | Chinese patent drug +WT1.3.2.7 | 7 d      | 3.6 ± 2.14                | 1. Disappearance rate of fever 1.80%, 2. Disappearance rate of fatigue, disappearance days of fatigue 3.76%, 3. Disappearance rate of cough, disappearance days of cough 4.84%, 4. Disappearance rate of choking sensation in chest 5. Disappearance rate of anhelation 6.40%, 6. Disappearance rate of anorexia 5.3 ± 2.63, 7. Disappearance rate of moist rale 8.81%, 8. Effective rate 9. Death rate 9. Not mentioned | No adverse response |
| WANG 0228       | Jilin   | MT,CT,ST:50  | M:30,F:20              | decoction +WT1.2.6.7 | 7 d      | 1. Total effective rate 1.98% 2. Disappearance rate of aversion to cold 2.10%, 3. Disappearance rate of thirst 3.100%, 4. Disappearance rate of fever 4.96.96%, 5. Disappearance rate of sweating 5.90.91%, 6. Disappearance rate of nasal obstruction 6.73.33%, 7. Disappearance rate of headache body ache 7.73.33%, 8. Disappearance rate of short of breath 8.72%, 9. Disappearance rate of nausea 9.64.54%, 10. Disappearance rate of choking sensation in chest 10.64%, 11. Disappearance rate of diarrhea 11.63.64%, 12. Disappearance rate of anorexia 12.55.56%, 13. Disappearance rate of expectoration 13.30.30%, 14. Disappearance rate of fatigue 14.25.93%, 15. Disappearance rate of cough 15.10.53%, 16. Death rate 16.0% | |
| BIN 0229 (Bin et al., 2020) | Hubei | MT,ST:10 | M:31,F:24              | Chinese patent drug +WT1.2.6.7 | 5.0 ± 3.8  | 1. Remaining proportion of fever 1.00% 2. Improvement time and remaining proportion of diarrhea 2.63 ± 3.8, 0% 3. Improvement time and remaining proportion of choking sensation in chest 3.85 ± 4.4,2.4% 4. Improvement time and remaining proportion of fatigue 4.71 ± 3.6,3.6% | 1. Gradually increase 2. Gradually increase 3. Drop to normal 4. Increase 5. Not mentioned |
| GONG 0309 (Gong et al., 2020) | Chongqing | CT:188 | ST:37 | decoction +WT1.2 | 5.0 ± 3.8 | 1. Remaining proportion of fever 1.00% 2. Improvement time and remaining proportion of diarrhea 2.63 ± 3.8, 0% 3. Improvement time and remaining proportion of choking sensation in chest 3.85 ± 4.4,2.4% 4. Improvement time and remaining proportion of fatigue 4.71 ± 3.6,3.6% | |
| FANG 0312 (Fang et al., 2020) | Hubei | MT:90 | CT:98, ST:120 | decoction, Chinese patent drug +WT1.2.7 | 5.0 ± 3.8 | 1. Remaining proportion of fever 1.00% 2. Improvement time and remaining proportion of diarrhea 2.63 ± 3.8, 0% 3. Improvement time and remaining proportion of choking sensation in chest 3.85 ± 4.4,2.4% 4. Improvement time and remaining proportion of fatigue 4.71 ± 3.6,3.6% | 1. Gradually increase 2. Gradually increase 3. Drop to normal 4. Increase 5. Not mentioned |
| Included trials | Funding region | Sample characteristics | Interventions | Duration | Fever improvement time(d) | Outcome index | Self before and after comparison | Adverse reactions |
|-----------------|----------------|------------------------|---------------|----------|---------------------------|---------------|----------------------------------|-----------------|
| ZHU 0319 (Zhu et al., 2020) | Jiangsu | CT:22 ST:1 M:10 F:13 50.0 ± 13.0 | Chinese patent drug + decoction + WT1.2.6.7 | 1.2.6 1.6 | 1. Not mentioned | 5. Improvement time and remaining proportion of cough | 5.10.4 ± 4.8,35.7% | 6. Not mentioned |
| HU 0320 (Hu et al., 2020) | Henan | CT:19 M:8 F:11 40.55 ± 10.59 | decoction+WT1.6 | 1.6 1.6 | 1. Not mentioned | 1. Obviously increase | 1.100% | 2. Obviously decline | 3.65.2% |
| YANG 0324 (Yang Z. et al., 2020) | Henan | MT, CT:13 M:10 F:3 41.31 ± 13.51 | decoction + WT1.2.3.4.5 | 3 ± 0.71 | 5. Obvious improvement | 5. Lung CT | 1.100% | 6. Not mentioned | 7.0% |

MT, mild type; CT, common type; ST, serious type; WT, western treatment; WT: 1. antiviral; 2. anti-infection/anti-inflammatory/antibiotics; 3. immunoregulation; 4. gastrointestinal regulation; 5. relieving cough and asthma; 6. oxygen therapy; 7. glucocorticoid; 8. nutritional support; 9. analgesics; 10. liver protection; 11. anti-anxiety.
Analysis of Application of Chinese Patent Medicine

Given its convenient application, Chinese patent medicine has gained increasing research attention. An analysis of the use of Chinese patent medicine in 20 clinical studies showed that Lianhua Qingwen capsules/granules are the most widely used. These capsules have been widely studied to verify their clinical efficacy. Lianhua Qingwen can act on coronavirus through multiple components, targets and pathways via their broad-spectrum antiviral, antibacterial and antipyretic; cough relief; sputum reduction and immune regulation effects (Ling et al., 2020). In the treatment of NCP, Xuebijing and other traditional Chinese medicine injections have been used several times. Xuebijing can antagonize endotoxins (Zhang, 2018; Wang, 2019) and inhibit the excessive release of inflammatory mediators, such as interferon and interleukin (Tian et al., 2019), thereby inhibiting inflammation and enhancing immunity (Diao et al., 2015). The academician Zhang Boli emphasized that the early application of traditional Chinese medicine injection can play a vital role in treating critical patients (Tencent news, 2020b).

The frequency of application of Glycyrrhizae Radix Et Rhizoma (gancao) has not been counted in the statistics, because of Glycyrrhizae Radix Et Rhizoma commonly used as harmonizing herb in TCM decoctions. Decoction was created by doctor Zhang Zhongjing (Han Dynasty) who researched on exogenous cold induced febrile diseases. Modern prescriptions are mostly added and subtracted by classical prescriptions. For example, the Qingfei Paidu decoction recommended by the State Administration of Traditional Chinese Medicine is based on Maxing Ganshi decoction, Shegan Mahuang decoction, Wuling powder and Xiao Chaihu decoction. The classical prescriptions with a literature frequency of ≥ 2 are presented in Table 6.

Investigation of the Observation Indicators

In 20 studies on the treatment of NCP, the most commonly used clinical observation and evaluation indices was fever improvement time, followed by cough improvement time, shortness of breath improvement time, chest CT, and TCM syndrome scale score. Some articles also used the disappearance rate of other accompanying symptoms as an evaluation index. The investigation of the observation indicators is shown in Table 7.

The commonly used Chinese patent medicine for NCP includes Lianhua Qingwen capsules/granules, Xuebijing capsules, and other traditional Chinese medicine injections. Among them, Lianhua Qingwen capsules/granules are the most widely used. Chinese patent medicine in 20 clinical studies showed that Chinese patent medicine is effective in improving clinical symptoms, such as fever, cough, shortness of breath, chest CT, and TCM syndrome scale score. Some articles also used the disappearance rate of other accompanying symptoms as an evaluation index.
Figure 2 | Commonly used Chinese herbal medicine combinations network diagram for NCP with different support rate. Support rate was (A) ≥20%, (B) ≥25%, and (C) ≥30%.

Table 6 | The commonly used classical prescriptions of TCM for NCP.

| No. | Classical Prescriptions of TCM | Components Latin name (Chinese name) | Source (year of completion) | Freq. | Application of cases |
|-----|--------------------------------|--------------------------------------|-----------------------------|-------|----------------------|
| 1   | Ganlu Xiaodu Pill             | Amomi Fructus Rotundus (Doukou), Pogostemonis Herba (Guanghuoxiang), Acori Tatarinowii Rhizoma (Shichangpu), Betelamomum Amurensis Radix (Lianqiao), Scutellariae Radix (Huangqin), Fritillariae Cirrhosae Bulbus (Chuanbeimu), Forsythiae Fructus (Lianqiao), Arunci Rhizoma (Shicangpu), Pogostemonis Herba (Guanghuoxiang), Acori Tatarinowii Rhizoma (Shichangpu), Betelamomum Amurensis Radix (Lianqiao), Scutellariae Radix (Huangqin), Fritillariae Cirrhosae Bulbus (Chuanbeimu), Forsythiae Fructus (Lianqiao), Arunci Rhizoma (Shicangpu) | Secret of Medical Efficacy AD 1831 | 3     | 40                   |
| 2   | Maxing Ganshi Decoction       | Ephedrae Herba (Mahuang), Armeniacae Semen Amarum (Kuxingren), Gypsum Fibrosum (Shigao), Glycyrrhizae Radix Et Rhizoma (Gancao) | Treatise on Febrile Diseases AD 200 | 2     | 80                   |
| 3   | Huopo Xialing Decoction       | Pogostemonis Herba (Guanghuoxiang), Sciae Semen Praeparatum (Dandouch), Amomi Fructus Rotundus (Doukou), Magnoliae Officinalis Cortex (Houpo), Pinelliae Rhizoma (Banxia), Armeniacae Semen Amarum (Kuxingren), Poria (Fuling), Polyporus (Zhiying), Alismatis Rhizoma (Xiaomai) | Original Medical Theory AD 1861 | 2     | 45                   |
| 4   | Da Yuan Decoction             | Arecae Semen (Binglang), Magnoliae Officinalis Cortex (Houpo), Tsaoko Fructus (Caoci), Anemarrhenae Rhizoma (Zhimu), Paeoniae Radix Alba (Baishao), Scutellariae Radix (Huangqin), Glycyrrhizae Radix Et Rhizoma (Gancao) | Treatise on Acute Epidemic Febrile Diseases AD 1642 | 2     | 42                   |
| 5   | Haoqin Qianlong Decoction     | Artemisiae Annuae Herba (Qinghao), Bambusae Caulis In Taenias (Zhuwu), Pinelliae Rhizoma (Banxia), Poria (Fuling), Scutellariae Radix (Huangqin), Aurantii Fructus (Zhiqiao), Citri Reticulatae Pericarpium (Chenpi), Talcum (Huashi), Indigo Naturalis (Qingdai), Glycyrrhizae Radix Et Rhizoma (Gancao) | Revisiting of Treatise on Acute Epidemic Febrile Diseases AD 1956 | 2     | 25                   |
| 6   | Xinian Chengqi Decoction      | Gypsum Fibrosum (Shigao), Rhei Radix Et Rhizoma (Dahuang), Armeniacae Semen Amarum (Kuxingren), Trichosanthis Fructus (Gualou) | Item Differentiation of Warm Febrile Diseases AD 1798 | 2     | 18                   |
| 7   | Tingli Dazao Xiefei Decoction | Descurainiae Semen Lepidii Semen (Tinglizi), Jujubae Fructus (Dazao), Scutellariae Radix (Huangqin) | Synopsis of Golden Chamber AD 200 | 2     | 18                   |

Table 7 | The commonly used Chinese patent medicine for NCP.

| No. | Chinese patent medicine | Components Latin name (Chinese name) | Freq. | Prop. |
|-----|-------------------------|--------------------------------------|-------|------|
| 1   | Lianhua Qingwen capsule/ granule | Forsythiae Fructus (Lianqiao), Lonicerae Japonicae Flos (Jinyinhua), Ephedrae Herba (Mahuang), Armeniacae Semen Amarum (Kuxingren), Gypsum Fibrosum (Shigao), Isatidis Radix (Banlange), Dryopteridis Crassirhizomatis Rhizoma (Mianma Guanzhong), Houttuyniae Herba (Yuxingcao), Pogostemonis Herba (Guanghuoxiang), Paeoniae Radix Alba (Baishao), Scutellariae Radix (Huangqin) | 7     | 35.00% |
| 2   | Xue Bi Jing Injection     | Carthami Flos (Honghua), Paeonae Radix Rubra (Chishao), Chuanxiong Rhizoma (Chuanxiong), Salviae Miltiorrhizae Radix Et Rhizoma (Danshen), Angelicae Sinensis Radix Et Rhizoma (Danggui) | 3     | 15.00% |
| 3   | Shufeng Jiedu Capsule     | Polygoni Cuspidati Rhizoma Et Radix (Huzhang), Forsythiae Fructus (Lianqiao), Isatidis Radix (Banlange), Bupleuri Radix (Chaihu), Herba Patriniae (Baijia) | 3     | 15.00% |
symptoms and CRP examination as observation indices. From Table 1, we can see the fever improvement time in the trial group was significantly shorter than that in the control group. In Table 8, we listed the Chinese name, Latin name in Chinese pharmacopeia, and Name in Medicinal Plant Names Services.

**DISCUSSION**

On the discussion of epidemic, the ancient Chinese doctor Wu Youke from the Ming Dynasty pointed out it was caused by epidemic pathogenic evils. Given its strong infectivity,
disease location and clinical characteristics, NCP can be named “pulmonary epidemic disease” (Guo and Wan, 2020). The main consensus regarding its pathogenesis is that the virus invades the lungs and causes vital qi deficiency. The pathological nature is dampness, heat, toxin, deficiency, and stasis.

This study mainly uses bibliometrics and data mining methods to obtain a systematic summary of clinical studies published at this stage and systematically analyses the published information, research design, intervention measures and observation indicators. A summary of the research methods indicates that only 2 RCTs were conducted. Most of the studies were CCTs and CSs. Considering the large number of patients and the rapid spread of the epidemic, the shortage of medical resources has led to the unconditional implementation of RCT research. The treatment of patients is the first priority at this time.

Regarding the time distribution of publications, the time that research on traditional Chinese medicine treatment of NCP was conducted synchronized with the epidemic. Furthermore, the symptom improvement rate and symptom scores in the observation and evaluation indicators fully reflect the characteristics of the judgment standard of clinical efficacy of traditional Chinese medicine. The total number of observation cases also reflects the high participation of traditional Chinese medicine in this anti-epidemic treatment. A clear understanding of Chinese herbal medicines use has been achieved through the data mining and analysis of prescriptions for treatment of NCP. In addition to Glycyrrhiza Radix Et Rhizoma (Gancao), Ephedrae Herba (Mahuang), Armeniacae Semen Amarum (Kuxingren) Atractylodis Rhizoma (Cang Zhu) and Scutellariae Radix (Huang Qin) are frequently used. An analysis of drug categories showed that heat-clearing medicine, exterior syndrome-relieving medicines, phlegm-resolving and cough and asthma-relieving medicines, and humidifying drugs are frequently used. This finding suggests that dampness and toxin accumulating in the lung are the main pathogenesis of NCP. Ephedrae Herba (Mahuang)-Armeniacae Semen Amarum (Kuxingren) had the highest support and high confidence in the association rules, which reflects the classic compatibility of Maxing Shigan
decotion. About the high frequency Chinese herbal medicines, most of it enters the lung meridian or spleen meridian. Chinese medicine recognizes that NCP mainly involves the lung. The spleen is the source of phlegm, and the lung is the sputum storage position, phlegm and dampness caused by lung and spleen disease. The results of clinical application analysis of Chinese patent medicines reflect the participation in clinical treatment. Given their wide range of applications and convenient application, Chinese patent medicines play an important role in clinical treatment of the epidemic in China. Traditional Chinese medicine for treatment of NCP is worthy of global attention.

Our study has several limitations. Randomized controlled trials are the most commonly used to judge the effectiveness of interventions. This review only included two RCTs. And they did not mention blinding method. In addition, the interventions, treatment courses, and observation indicators of each study were quite different, so meta-analysis cannot be done. High-quality RCTs on the effectiveness and safety of traditional Chinese medicine in the treatment of new coronary pneumonia need further study.

**AUTHOR CONTRIBUTIONS**

ZZ conceived and wrote the manuscript draft. SF designed the study and revised the manuscript. NG drafted the manuscript. YW was responsible for data collection. PC helped data management. YT was in charge of statistical analysis of data. All authors contributed to the article and approved the submitted version.

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**SUPPLEMENTARY MATERIAL**

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.