



Contents

- 1.COVID-19: An Update on the Epidemiological, Clinical, Preventive and Therapeutic Evidence and Guidelines of Integrative Chinese-Western Medicine for the Management of 2019 Novel Coronavirus Disease**
- 2. Can Chinese Medicine Be Used for Prevention of Corona Virus Disease 2019 (COVID-19)? A Review of Historical Classics, Research Evidence and Current Prevention Programs**
- 3. Case Report : Clinical Characteristics and Therapeutic Procedure for Four Cases With 2019 Novel Coronavirus Pneumonia Receiving Combined Chinese and Western Medicine Treatment**
- 4. Analysis of Medication Characteristics of Traditional Chinese Medicine in Treating Coronavirus disease-19 Based on Data Mining**
- 5. Treatment Efficacy Analysis of Traditional Chinese Medicine for Novel Coronavirus Pneumonia (COVID-19): An Empirical Study From Wuhan, Hubei Province, China**

6. Analysis of Property and Efficacy of Traditional Chinese Medicine in Staging Revention and Treatment of Coronavirus Disease 2019

7. Chinese Medicine for COVID-19: A Protocol for Systematic Review and Meta-Analysis

8. Highlights of Traditional Chinese Medicine Frontline Expert Advice in the China National Guideline for COVID-19

9. Traditional Chinese Medicine in Emergency Treatment Mechanism and Application

10. Network Pharmacology in Research of Chinese Medicine Formula: Methodology, Application and Prospective

1. COVID-19: An Update on the Epidemiological, Clinical, Preventive and Therapeutic Evidence and Guidelines of Integrative Chinese-Western Medicine for the Management of 2019 Novel Coronavirus Disease

Keywords: 2019-nCoV; COVID-19; Chinese Medicine; Guideline; Integrative Medicine; Review

Kam Wa Chan; Vivian Taam Wong; Chi Wai Tang et al. *Am J Chin Med.* 2020;48(3):737-762.

Abstract

As of 22 February 2020, more than 77662 cases of confirmed COVID-19 have been documented globally with over 2360 deaths. Common presentations of confirmed cases include fever, fatigue, dry cough, upper airway congestion, sputum production, shortness of breath, myalgia/arthritis with lymphopenia, prolonged prothrombin time,

elevated C-reactive protein, and elevated lactate dehydrogenase. The reported severe/critical case ratio is approximately 7-10% and median time to intensive care admission is 9.5-10.5 days with mortality of around 1-2% varied geographically. Similar to outbreaks of other newly identified virus, there is no proven regimen from conventional medicine and most reports managed the patients with lopinavir/ritonavir, ribavirin, beta-interferon, glucocorticoid and supportive treatment with remdesivir undergoing clinical trial. In China, Chinese medicine is proposed as a treatment option by national and provincial guidelines with substantial utilization. We reviewed the latest national and provincial clinical guidelines, retrospective cohort studies, and case series regarding the treatment of COVID-19 by add-on Chinese medicine. We have also reviewed the clinical evidence generated from SARS and H1N1 management with hypothesized mechanisms and latest *in silico* findings to identify candidate Chinese medicines for the consideration of possible trials and management. Given the paucity of strongly evidence-based regimens, the available data suggest that Chinese medicine could be considered as an adjunctive therapeutic option in the management of COVID-19.

2. Can Chinese Medicine Be Used for Prevention of Corona Virus Disease 2019 (COVID-19)? A Review of Historical Classics, Research Evidence and Current Prevention Programs

Keywords: Chinese medicine; clinical evidence; corona virus disease 2019 (COVID-19); prevention program; review.

Hui Luo; Qiao-Ling Tand; Ta-Xi Shang et al. *Chin J Integr Med.* 2020 Apr;26(4):243-250

Abstract

Objective: Since December 2019, an outbreak of corona virus disease 2019 (COVID-19) occurred in Wuhan, and rapidly spread to almost all parts of China. This was followed by prevention programs recommending Chinese medicine (CM) for the

prevention. In order to provide evidence for CM recommendations, we reviewed ancient classics and human studies.

Methods: Historical records on prevention and treatment of infections in CM classics, clinical evidence of CM on the prevention of severe acute respiratory syndrome (SARS) and H1N1 influenza, and CM prevention programs issued by health authorities in China since the COVID-19 outbreak were retrieved from different databases and websites till 12 February, 2020. Research evidence included data from clinical trials, cohort or other population studies using CM for preventing contagious respiratory virus diseases.

Results: The use of CM to prevent epidemics of infectious diseases was traced back to ancient Chinese practice cited in Huangdi's Internal Classic (Huang Di Nei Jing) where preventive effects were recorded. There were 3 studies using CM for prevention of SARS and 4 studies for H1N1 influenza. None of the participants who took CM contracted SARS in the 3 studies. The infection rate of H1N1 influenza in the CM group was significantly lower than the non-CM group (relative risk 0.36, 95% confidence interval 0.24-0.52; n=4). For prevention of COVID-19, 23 provinces in China issued CM programs. The main principles of CM use were to tonify qi to protect from external pathogens, disperse wind and discharge heat, and resolve dampness. The most frequently used herbs included Radix astragali (Huangqi), Radix glycyrrhizae (Gancao), Radix saposhnikoviae (Fangfeng), Rhizoma Atractylodis Macrocephalae (Baizhu), Lonicerae Japonicae Flos (Jinyinhua), and Fructus forsythia (Lianqiao).

Conclusions: Based on historical records and human evidence of SARS and H1N1 influenza prevention, Chinese herbal formula could be an alternative approach for prevention of COVID-19 in high-risk population. Prospective, rigorous population studies are warranted to confirm the potential preventive effect of CM.

3. Case Report : Clinical Characteristics and Therapeutic Procedure for Four Cases With 2019 Novel Coronavirus Pneumonia Receiving Combined Chinese and Western Medicine Treatment

Keywords: 2019-nCoV; Shufeng Jiedu Capsule; arbidol; lopinavir; ritonavir.

Zhenwei Wang ; Xiaorong Chen; Yunfei Lu et al. Biosci Trends. 2020 Mar 16;14(1):64-68

Abstract

Pneumonia associated with the 2019 novel coronavirus (2019-nCoV) is continuously and rapidly circulating at present. No effective antiviral treatment has been verified thus far. We report here the clinical characteristics and therapeutic procedure for four patients with mild or severe 2019-nCoV pneumonia admitted to Shanghai Public Health Clinical Center. All the patients were given antiviral treatment including lopinavir/ritonavir (Kaletra®), arbidol, and Shufeng Jiedu Capsule (SFJDC, a traditional Chinese medicine) and other necessary support care. After treatment, three patients gained significant improvement in pneumonia associated symptoms, two of whom were confirmed 2019-nCoV negative and discharged, and one of whom was virus negative at the first test. The remaining patient with severe pneumonia had shown signs of improvement by the cutoff date for data collection. Results obtained in the current study may provide clues for treatment of 2019-nCoV pneumonia. The efficacy of antiviral treatment including lopinavir/ritonavir, arbidol, and SFJDC warrants further verification in future study.

4. Analysis of Medication Characteristics of Traditional Chinese Medicine in Treating Coronavirus disease-19 Based on Data Mining

Tiantian Fan ; Yongcan Chen ; Yu Bai et al. Zhejiang Da Xue Xue Bao Yi Xue Ban. 2020 May 25;49(1):0.

Abstract

Objective: To analysis the medication characteristics of the prescriptions issued via open channel by the National and Provincial Health Committee and the State

Administration of Traditional Chinese Medicine in treating coronavirus disease 2019 (COVID-19).

Methods: We collected the data of traditional Chinese medicine related to treatment plans published by the National and Provincial Health Committee and the State Administration of Traditional Chinese Medicine from the start of COVID-19 outbreak in Wuhan to February 19, 2020. The frequency analysis, cluster analysis and correlation analysis were performed.

Results: The study collected 4 national and 34 regional prevention and treatment plans, 578 items, 84 traditional Chinese formulations, 60 Chinese patent medicines, and 230 Chinese herbs. The high frequently used herbs were *Liquorice*, *Scutellariabaicalensis*, *Semen armeniacaeamarae*, and *Gypsum*. The commonly used traditional formulations included *Maxing Shigan* Decoction, *Yin Qiao* Powder, and *Xuanbai Chengqi* Decoction. The Chinese patent drugs included *Angong Niu Huang* Pill, *Xuebijing* Injection, and *Lianhua Qingwen* Capsule. The most common paired medications were *Ephedra* and *Semen armeniacaeamarae*, *Fructusforsythiae* and *Liquorice*. Two core combinations and one novel formula were discovered in the study.

Conclusions: *Yin Qiao* Powder and *Huopo Xialing* Decoction are the basic formulations for *Weifensyndrome* of COVID-19. In addition, *Maxing Shigan* Decoction, *Liang Ge* Powder, *Qingwen Baidu* Decoction and *Da Yuan* Decoction are the basic formulations for *Qifen* syndrome of COVID-19. The main medication characteristics are clearing heat, entilating lung, removing toxicity and removing turbidity. It shows that removing toxicity and eliminating evil are the prescription thought in treating epidemic disease of traditional Chinese medicine.

5. Treatment Efficacy Analysis of Traditional Chinese Medicine for Novel Coronavirus Pneumonia (COVID-19): An Empirical Study From Wuhan, Hubei Province, China

Keywords: Empirical study; Novel coronavirus pneumonia; Traditional Chinese Medicine; Treatment efficacy; Wuhan China.

Erdan Luo ; Daiyan Zhang ; Hua Luo et al. *Chin Med.* 2020 Apr 15;15:34.

Abstract

Background: A novel coronavirus was identified in December, 2019 in Wuhan, China, and traditional Chinese medicine (TCM) played an active role in combating the novel coronavirus pneumonia (NCP) caused by this fast-spreading virus COVID-19. Thus, we aimed to explore TCM characteristics of clinical efficacy to NCP, as well as to optimize Qingfei Paidu decoction (QFPDD) and the recommended formulas to NCP by National Health Commission (NHC).

Methods: Chinese medical sciences theory and clinical application of TCM were analyzed. A total of 54 NCP patients were observed in a hospital from Wuhan, whose clinical characteristics and utilization of Chinese Medicines (CMs) were described. Paired t test was used to measure the change of patients' hemogram during hospitalization period, indicating the effect of CMs. Multiple linear regression analysis was applied to explore the factors affecting the length of hospital stay. Network pharmacology analysis was applied to figure out the performance of NHC-recommended formulas of five disease stages at levels of compounds, targets and pathways.

Result: The average length of hospital stay was 8.96 days. Patients over 45 stayed 9.79 days in hospital in average, longer than 7.64 days of patients under 45. Comparing the hemograms between admission and discharge of hospital, the number of leukocytes, neutrophil, lymphocyte and platelet increased, while the numbers of erythrocytes, hemoglobin concentration and hematocrit decreased. According to the standard coefficients of regression, the factor affecting the length of stay for the most

was CMs in category of invigorating spleen and removing dampness (ISR), followed by administering CMs, male, and cough. Thirty-two CMs were screened after deleting duplication from QFPDD and NHC-recommended formulas. Compound quercetin, luteolin, kaempferol, acacetin etc., were all involved in the treatment of various disease stages on the compound level both in generality and individuality.

Conclusion: TCM has a systemic theoretical understanding on the pathological evolution and a positive clinical efficacy on NCP. The CMs of ISR improved patients' recovery, suggesting the importance of regulating intestinal function and keeping microenvironmental balance in TCM treatment of NCP. The active compounds from QFPDD and NHC-recommended formulas contribute to recovery of varied disease progresses during TCM treating NCP.

6. Analysis of Property and Efficacy of Traditional Chinese Medicine in Staging Revention and Treatment of Coronavirus Disease 2019

Keywords: 2019-nCoV; characteristics of medicinal properties; coronavirus disease 2019(COVID-19); efficacy distribution; prevention and treatment of traditional Chinese medicine.

Min Gu; Jiao Liu; Nan-Nan Shi et al. *Zhongguo Zhong Yao Za Zhi*. 2020 Mar;45(6):1253-1258.

Abstract

Coronavirus disease 2019(COVID-19) triggered a severe and complicated epidemic situation, and it is of great significance to discuss the rules and characteristics of the prescription of COVID-19 in traditional Chinese medicine. This study collected prevention and treatment approaches of traditional Chinese medicine for COVID-19 released from the National Health Committee of China, 7 provinces and municipal health committees, the Chinese Medicine Administration and Handbook of Traditional Chinese Medicine Diagnosis and Treatment of COVID-19 between January 1 and February 18, 2020, and prescriptions prepared by 3 masters of Chinese medicine and

4 well-known Chinese medicine experts. These information were selected according to the inclusion and exclusion criteria, and EpiData 3.0 software was used to establish the "Traditional Chinese Medicine Prescription Library for the Prevention and Treatment of COVID-19" and the "Common Database of Traditional Chinese Medicine for the Prevention and Treatment of COVID-19". A total of 93 effective Chinese medicine prescriptions and a total of 157 kinds of constituent medicines were collected. Data analysis was performed by SPSS 18.0 software. The results showed that: ①most of the medicines are with cold and warm properties, 69 with cold medicines, accounting for 43.95%, 57 with warm medicines, accounting for 36.31%, and less with hot medicines, taking up 1.27%; ②there are many pungent, bitter and sweet medicines, and the distribution of medicinal flavors is different at different disease stage. The pungent medicines are mostly found in the early stage, the bitter drugs are the main flavor in the middle and severe stage, and the sweet medicines are mostly used in the recovery stage; ③the meridian of the drug is more concentrated at the lung, stomach, and heart, and most of drugs are into the lung meridian, accounting for 24.55%; these medicines are mostly into the lungs and stomach in the initial and middle stages, and into the heart and kidney in severe stages; ④oral drugs are mostly non-toxic, among which only 6 kinds are toxic, namely *Armeniacae Semen Amarum*, *Dryopteridis Crassirhizomatis Rhizoma*, *Paridis Rhizoma*, *Pinelliae Rhizoma*, *Aconiti Lateralis Radix Praeparata*; ⑤most of the drugs have five types of functions: treating exterior syndromes, resolving dampness, clearing heat, replenishing deficiency, resolving phlegm, cough, and asthma. In the early stage, both drugs for treating exterior syndromes and heat clearing drugs were equally used, accounting for 18.81% each. In the middle stage, drugs resolving phlegm, cough, and asthma drugs are more often used, accounting for 29.61%. In the severe stage, heat clearing drugs are mostly used, accounting for 33.33%. During the recovery period, tonic deficiency drugs are used the most, accounting for 36.47%. The medical characteristics and efficacy of Chinese medicine in preventing and treating COVID-19 are closely related to the understanding of the etiology of Chinese medicine and the location and pathogenesis of the disease. Staged medication and local conditions need attention during the identification and treatment of COVID-19 clinical syndromes.

7. Chinese Medicine for COVID-19: A Protocol for Systematic Review and Meta-Analysis

Huizhen Chen , Ziyan Xie , Yuxia Zhu et al. *Medicine (Baltimore)*. 2020 Jun 19;99(25):e20660.

Abstract

Background: Coronavirus disease 2019 (COVID-19) is a respiratory illness that can spread from person to person. The virus that causes COVID-19 is a novel coronavirus that was first identified during an investigation into an outbreak in Wuhan, China. The clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death, with many patients being hospitalised with pneumonia. In China and East Asia, Chinese medicine has been widely used to treat diverse diseases for thousands of years. As an important means of treatment now, Chinese medicine plays a significant role in the treatment of respiratory diseases in China. The aim of this study is to assess the efficacy and safety of Chinese medicine for COVID-19.

Methods: We will search the following sources for the identification of trials: The Cochrane Library, PubMed, EMBASE, Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure Database (CNKI), Chinese Science and Technique Journals Database (VIP), and the Wanfang Database. All the above databases will be searched from the available date of inception until the latest issue. No language or publication restriction will be used. Randomized controlled trials will be included if they recruited participants with COVID-19 for assessing the effect of Chinese medicine vs control (placebo, no treatment, and other therapeutic agents). Primary outcomes will include chest CT and nucleic acid detection of respiratory samples. Two authors will independently scan the articles searched, extract the data from articles included, and assess the risk of bias by Cochrane tool of risk of bias. Disagreements will be resolved by consensus or the involvement of a third party. All analysis will be performed based on the Cochrane Handbook for Systematic Reviews

of Interventions. Dichotomous variables will be reported as risk ratio or odds ratio with 95% confidence intervals (CIs) and continuous variables will be summarized as mean difference or standard mean difference with 95% CIs.

Results and conclusion: The available evidence of the treatment of COVID-19 with traditional Chinese medicine will be summarized, and evaluation of the efficacy and the adverse effects of these treatments will be made. This review will be disseminated in print by peer-review.

8. Highlights of Traditional Chinese Medicine Frontline Expert Advice in the China National Guideline for COVID-19

Keywords: COVID-19; Chinese herbal medicines; Guideline; Traditional Chinese medicine

Leonard T F Ho; Karina K H Chan; Vincent C H Chung et al. *Eur J Integr Med.* 2020 Apr 3;36:101116.

Abstract

Introduction: The World Health Organization has declared the coronavirus disease (COVID-19) as a pandemic on 11 March 2020, after the number of confirmed cases outside China increased 13-fold. As the epicentre of the initial outbreak, China has been updating the National COVID-19 Diagnostic and Treatment Guideline with up-to-date information about the disease. To facilitate the implementation of integrative Chinese-Western Medicine in COVID-19 management, Traditional Chinese medicine (TCM) has been recommended in recent editions of the national guideline.

Methods: The national guideline summarised the opinions and frontline experience of medical experts across the country to provide by far the best management for COVID-19. We extracted the case definition and clinical classifications of COVID-19 in China along with relevant TCM treatments cited in the seventh edition of the guideline, with

an intend to disseminate practical information to TCM practitioners and researchers around the world.

Results: We presented the most recent case definition, clinical classifications, and relevant TCM treatments of COVID-19 in accordance to recommendations of the Chinese guideline. TCM treatments are stratified into two groups based on patients' disease status. Four types of Chinese patent medicines are recommended for suspected COVID-19 cases. Several herbal formulae are recommended for confirmed COVID-19 cases according to their clinical classification and TCM pattern diagnoses. Two herbal formulae are also recommended for rehabilitation of recovering cases.

Conclusion: To control the waves of COVID-19 outbreak, countries must ensure the adherence of their citizens to local public health measures. Medical professionals should diagnose and treat patients according to up-to-date guidelines. Future evaluation of the outcomes of implementing TCM recommendations will strengthen the evidence base for COVID-19 management for the sake of public health and the internationalisation of TCM

9. Traditional Chinese Medicine in Emergency Treatment Mechanism and Application

Keywords: acupuncture; ear blowing; first-aid; moxibustion; nose insufflating therapy; traditional Chinese medicine

Yu Meng ; Toby M Michelena ; Fangfang Cai et al. *Open Access Emerg Med.* . 2020 Apr 30;12:111-119.

Abstract

Traditional Chinese medicine has usually been recognized to be efficacious to treat chronic diseases from the western point-of-view. However, there is a long history in China of applying traditional Chinese medicine in many acute and urgent medical conditions. In this review, selected methods documented in traditional Chinese

medicine including blowing air to ear, nose insufflating therapy, acupuncture and moxibustion were presented as the common practices to promote consciousness recovery from coma. We aimed to explore the mechanism of these four methods with current scientific evidence, further discuss the potential of traditional Chinese medicine to be applied in emergency medicine and provide a path forward to more rigorously validate these procedures. The development of the integrated traditional Chinese medicine and western medicines provides a new therapeutic direction for the new first-aid treatment.

10. Network Pharmacology in Research of Chinese Medicine Formula: Methodology, Application and Prospective

Keywords: Chinese medicine formula; mechanism research; network pharmacology; quality control research; targets discovery.

Ting-Ting Luo ; Yuan Lu ; Shi-Kai Yan et al. *Chin J Integr Med*. 2020 Jan;26(1):72-80.

Abstract

Chinese medicine (CM) is usually prescribed as CM formula to treat disease. The lack of effective research approach makes it difficult to elucidate the molecular mechanisms of CM formula owing to its complicated chemical compounds. Network pharmacology is increasingly applied in CM formula research in recent years, which is identified suitable for the study of CM formula. In this review, we summarized the methodology of network pharmacology, including network construction, network analysis and network verification. The aim of constructing a network is to achieve the interaction between the bioactive compounds and targets and the interaction between various targets, and then find out and validate the key nodes via network analysis and network verification. Besides, we reviewed the application in CM formula research, mainly including targets discovery, bioactive compounds screening, toxicity evaluation, mechanism research and quality control research. Finally, we proposed prospective

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in the future and limitations of network pharmacology, expecting to provide new strategy and thinking on study for CM formula.

