

Clinical Observation of 63 Suspected Cases of Novel Coronavirus Pneumonia Treated with Traditional Chinese Medicine Lianhuaqingwen Capsules

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[Abstract] Objective: Retrospectively evaluating the clinical efficacy of Lianhuaqingwen in treating suspected cases of novel coronavirus pneumonia. **Method** Collecting 101 patients who was suspected cases and admitted to the CR&WISCO General Hospital of Wuhan University of Science and Technology and was suspected of meeting the diagnostic criteria for the new coronavirus pneumonia from Jan 1th to Jan 27th. Among the 101 patients, 63 cases in the treatment group were treated with a combination of conventional therapy (nutritional support therapy, symptomatic therapy, antiviral and antimicrobial therapy), taking traditional Chinese medicine Lianhuaqingwen Capsules. In the control group, 38 cases were only given conventional treatment. Clinical data were collected after 10 days of treatment, and the main symptoms (fever and cough) of the two groups were compared, disappearance rate, duration of fever, disappearance rates of other single symptom and sign. **Results** Compared with the control group, the disappearance rate of fever, cough and fatigue symptoms of the treatment group was 86.7%、55.6%、82.5% respectively, which were significantly better than the control group (67.7%、30.6%、58.6%) ($P<0.05$). The median fever duration was 6 days in the treatment group and 7 days in the control group. There was no statistical significance for the differences between the two groups ($P=0.171$). The disappearance rate of disappearance of tachypnea and moist rales in the treatment group (68.2% and 56.0% respectively) were significantly higher than control group (20.0% and 20.0% respectively) ($P<0.05$). The treatment group was aggravated in 4 cases (6.4%) and control group in 6 cases (15.8%). There was no statistical significance for the differences ($P>0.05$), but the trend was obviously lower than that of the control group. **Conclusion** The traditional Chinese medicine Lianhuaqingwen can significantly relieve symptoms in suspected patients by inhibiting fever, cough, asthenia and chest congestion as well as reduce the proportion of cases turning to severe.

[Keywords] Lianhuaqingwen; novel coronavirus pneumonia; suspected cases; clinical study;

On January 31th 2020, the World Health Organization stated that the novel type coronavirus pneumonia, (NCP) Rapid global dissemination has constituted a global emergency, and listed it as a public health emergency of international concern. For one of the major outbreaks of seriously harm to human health and public safety. Data released by the National Health and Health Commission^[2], as of February 7 at 24: 00, 31 provinces and municipalities had 34,546 confirmed cases, there was 27,657 suspected cases, with a cumulative follow-up of 345498 cases. There are still 18960 people under medical observation. Calculating the confirmed cases, the confirmed rate of suspected cases is 12.9%. Suspected disease, according to Xinhua News Agency disclosure on January 27th, 2020, The confirmed rate can reach to 45%^[3], which become a potential hazard factor. The positive nucleic acid test of pharyngeal test was used as the diagnostic criteria, but in the early stage, the outbreak of the epidemic situation, there was insufficient supply of the kit, low daily inspection quantity and detection knot is inaccurate, all of this contribute to a large number of suspected cases were not diagnosed in time. And this has make it to fail to control quickly for the novel coronary pneumonia in the early stage, disease inflection point fail to be found in time. Therefore, nucleic acid increased for suspected cases. Detection, accelerate clinical diagnosis, quickly take isolation measures^[4], and apply traditional Chinese medicine to participate in the treatment process of suspected cases in time^[5], which is of great significance for epidemic prevention and control.

Traditional Chinese medicine has played an important role and attracted much attention during the plague and epidemic disease broken out time, as a representative traditional Chinese medicine in respiratory system public health events^[6], Lianhuaqingwen Capsules (Granules) were recommended for medical observation period in <Pneumonia Diagnosis and Treatment of New Coronary Virus Infection> (Trial Editions 4 and 5)^[5,7] by National Health Commission of the People's Republic of China. Meanwhile, Health Commission of the People's Republic of Wuhan <The Therapeutic Regimen for Novel Coronavirus Infection Recommended Scheme for Home-Based Prevention Of Pneumonia>^[8] recommend the people who are usually prone to inflammation and sore throat, and also used in children's medical observation period treatment^[9]. So since the outbreak of the epidemic, I suspected the NCP case, the combination of Lianhuaqingwen Granules combined with routine treatment received good therapeutic effect, the clinical data of the cases are summarized as follows with a view to provide clinical basis for the treatment of suspected patients.

1 Clinical Information

1.1 Diagnostic Criteria

Refer to the guidelines for the diagnosis of suspected cases of <Diagnosis and Treatment of Pneumonia with Novel Coronavirus Infection> (Trial Version 4)^[7]. Any one item of the epidemic history including tourism, residence, contact, aggregation, any two items of the clinical

manifestations including fever and/or respiratory symptoms, early leukocyte total normal/decreased/decreased lymphocyte count and NCP image can be identified as suspected cases.

1.2 Inclusion Criteria

Meet the above diagnostic criteria for suspected cases aged 18 above, inpatients with NCP imaging features.

1.3 Exclusion criteria

Severe, critical NCP diagnosed patients; bronchial asthma, the chest X-ray computerized tomography apparatus (CT) confirms there are serious pulmonary interstitial lesions, bronchiectasis and other basic lung patients with disease; associated with severe immunodeficiency disease, congenital respiratory tract malformation, congenital heart disease, abnormal lung development and other basic diseases.

1.4 General Information

101 suspected NCP patients who were treated at CR&WISCO General Hospital of Wuhan University of Science and Technology from January 1th to January 27th, 2020 were collected. Among them, 38 cases were given routine western medicine as control group. The treatment group consisted of 63 cases of treatment combined with Lianhuaqingwen Granules. There was no statistical significance for the differences in baseline data including age, sex, body temperature, blood pressure, heart rate, respiration, past History, fever, fatigue, cough and routine treatment, major laboratory Inspection indicators and so on between the two groups ($P > 0.05$), they are comparable. See Table 1.

Table 1 Comparison of general data between the two groups ($\bar{x} \pm s$)

Items	Treatment group (63 cases)	Control group (38 cases)	t/χ^2	P
Age ($\bar{x} \pm s$)	59.1±16.56	60.2±17.01	-0.309	0.758
Male [cases (%)]	28 (44.4)	18 (47.4)	0.082	0.775
Temperature [$^{\circ}\text{C}$, ($\bar{x} \pm s$)]	38.08±0.63	38.08±0.67	0.318	0.751
Heart rate [Times/min, ($\bar{x} \pm s$)]	88.5±15.43	87.6 ± 13.13	0.305	0761
Breath [Times/min, ($\bar{x} \pm s$)]	19.4±2.03	18.8±1.65	1.315	0.192
Anamnesis [cases (%)]	42 (66.7)	28 (73.7)	-	0.628
Hypertension	21 (33.3)	11 (28.9)	0.211	0.646

Coronary heart disease	8 (12.7)	3 (7.9)	-	0.528
Diabetes	5 (7.9)	6 (15.8)	-	0.323
Cerebral infarction	10 (15.9)	5 (13.2)	0.138	0.710
Fever	60 (95.2)	34 (89.5)	-	0.421
Fatigue	40 (63.5)	29 (76.3)	1.801	0.180
Cough	54 (85.7)	36 (94.7)	-	0.201
Routine treatment [cases(%)]				
Antibiotics	55 (87.3)	34 (89.5)	-	1.000
Antivirus	54 (85.7)	32 (84.2)	0.042	0.837
Antipyretic analgesia	31 (49.2)	17 (44.7)	0.190	0.663
Immunoglobulin	33 (52.4)	19 (50.0)	0.054	0.817
Expectorant	54 (85.7)	32 (84.2)	0.042	0.837
Antiasthmatic Drugs	35 (55.6)	22 (57.9)	0.053	0.818
Glucocorticoid	23 (36.5)	13 (34.2)	0.055	0.815
Blood white blood cells [$\times 10^9/L$, ($\bar{x} \pm s$)]	4.62 \pm 2.14	4.42 \pm 2.32	-0.441	0.330
Neutrophil [%, ($\bar{x} \pm s$)]	67.09 \pm 14.08	65.52 \pm 14.8	-0.524	0.301
Lymphocytes [%, ($\bar{x} \pm s$)]	22.28 \pm 11.15	20.12 \pm 12.65	-0.896	0.186
C-reactive protein [mg/L, ($\bar{x} \pm s$)]	51.50 \pm 46.05	50.41 \pm 45.27	-0.116	0.454

2 Method

2.1 Treatment

Both groups were given nutritional support, symptomatic treatment and antivirus and antimicrobial therapy. The main treatment drug is moxifloxacin hydrochloride sodium injection (**250 ml:0/4 g**, which is produced by Chengdu Zhengkang Pharmaceutical Co., Ltd , lot number is **3419111102**) **0.4 g, once a day**; ganciclovir injection (**5 ml: 250 mg** per dose which is produced by Hubei Keyi Pharmaceutical Co., Ltd. Production, lot number **191003**) **0.5g, once a day**, Intravenous injection of human immunoglobulin (**2.5 g/bottle**, Guizhou Tai Bong Biological Products Co., Ltd., lot number **201906026**) **2.5 g, once a day**; ambroxol hydrochloride injection (**2 ml: 15mg/pill**, Tianjin Pharmaceutical Group Co., Ltd., lot number **1906116**) **30 mg, twice a day**; doxothephylline for injection (**0.2 g/bottle**, Ruiyang Pharmaceutical Co., Ltd., lot number **19082116**) **0.2 g , once a day**; methylprednisolone sodium succinate for injection (**40mg/bottle**, produced by Liaoning Haiske Pharmaceutical Co., Ltd, lot number **20191027**)**40 mg, once a day**.

Control group: simply given the above treatment.

Treatment group: on the basis of the above treatment combined with Lianhuaqingwen granules (6 g per bag, including forsythia, honeysuckle, flax, fried almonds, Gypsum, Radix Isatidis, Cotton Horse, Houத்துynia, Patchouli, Rhubarb, Rhodiola, etc., equivalent to 8,064 g of raw medicine, produced by Yiling Pharmaceutical Co., Ltd, lot number 1812017), **one bag once time, three times a day.**

Collect the clinical data.

2.2 Observation Indicators and Methods

2.2.1 Compare the disappearance of major symptoms in the two groups (fever, fatigue, cough) disappearance rate, fever disappearance time and other single symptom and signs (myalgia, expectoration, snuffles, runny nose, sore throat, tachypnea, chest congestion, dyspnea, headache, nausea, vomiting, anorexia, diarrhea, moist rales), treatment aggravated condition during the treatment.

2.2.2 Security assessment Check blood routine, routine urine, conventional stool, urine liver function and kidney function before and after treatment.

2.3 Statistical methods

Software of SAS9-4 was used for statistical analysis. All the statistical tests were tested bilaterally, and the counting data of descriptive analysis were counted and the ratio of composition to describe, the measurement data was described by mean \pm standard deviation to describe. T was used for the comparison of the measurement data and the chi-square test or exact probability method was used for the counting data. Survival analysis method was used for fever duration. $P \leq 0.05$ indicates that it has statistically significant.

3 results

3.1 Comparison of the rate of disappearance of main symptoms between two groups

Table 2 shows that the symptoms of fever, cough and fatigue in the treatment group were significantly better than those in the control group ($P < 0.05$).

Table 2 Comparison of disappearance situation of primary symptoms between two groups [cases (%)]

Groups	Fever		Cough		Fatigue	
	Cases	Disappearance	Cases	Disappearance	Cases	Disappearance
Treatment Group	60	52 (86.7)	54	30 (55.6)	40	33 (82.5)
Control Group	34	23 (67.6)	36	11 (30.6)	29	17 (58.6)
χ^2	4.868		5.443		4.804	
P	0.027		0.020		0.028	

3.2 Comparison of fever duration between two groups

There were 52 patients with fever in the treatment group and the median fever duration is 6 days; there were 23 patients with fever in the control group and the median fever duration is 7 days. There was no statistical significance for the differences between the two groups ($P = 0.171$).

3.3 Comparison of other symptoms and disappearance of vital signs between the two groups

Table 3 shows that the rate of disappearance of tachypnea and moist rales in the treatment group is significantly higher than that in the control group ($\chi^2 = 9.817, 4.972$), and there was statistical significance for the differences between the two groups ($P < 0.05$); There was no statistical significance for the differences of other symptoms between the two groups ($P > 0.05$)

3.4 Aggravation of illness during the treatment of the two groups

During the treatment, there were 4 patients (6.3%) with advanced disease in the treatment group (63 cases), and 6 patients (15.8%) with advanced disease in the control group (63 cases). There was no statistical significance for the differences between the two groups ($P > 0.05$).

Table 3 Comparison of other symptoms and disappearance of vital signs between the two groups

Items	Treatment Group		Control Group		χ^2	P
	Cases	Disappearance	Cases	Disappearance		
Myalgia	9	7 (77.8)	7	4 (57.1)	-	0.596
Expectoration	42	24 (57.1)	23	11 (47.8)	0.519	0.471
Snuffles	3	2 (66.7)	4	3 (75.0)	-	1.000
Runny Nose	6	5 (83.3)	3	3 (100.0)	-	1.000

Sore Throat	3	2 (66.7)	3	1 (33.3)	-	1.000
Tachypnea	22	15 (68.2)	20	4 (20.0)	9.817	0.002
Chest Congestion	24	17 (70.8)	19	12 (63.2)	0.285	0.594
Dyspnea	12	6 (50.0)	9	1 (11.1)	-	0.159
Headaches	6	5 (83.3)	6	4 (66.7)	-	1.000
Nausea	11	10 (90.9)	6	3 (50.0)	-	0.099
Vomiting	4	3 (75.0)	3	1 (33.3)	-	0.486
Anorexia	48	36 (75.0)	30	19 (63.3)	1.209	0.272
Diarrhea	8	4 (50.0)	3	1 (33.3)	-	1.000
Moist Rales	25	14 (56.0)	15	3 (20.0)	4.972	0.026

3.5 Security Analysis

During the treatment, it did not show any abnormal condition about the blood routine, liver and kidney function in the treatment group related to Lianhuaqingwen Granules, and no adverse reaction of Lianhuaqingwen Granules was found. The safety of clinical application is good.

4 Discussions

Coronaviruses have caused two large scale infections in the past 20 years, they are SARS-CoV^[10] and MERS-CoV^[11] respectively, infecting ten thousands of patients. The pathogen of the outbreak at the end of 2019 was 2019-nCoV (2019-nCoV), some studies indicated that the similarity between the virus and SARSs was 89.1%^[12], it was also found that the sequence similarity of 2019-nCoV and SARS-CoV BJ01 were 79.5%, and they have the same pathogenesis. The incubation time from entering the body to becoming ill for "2019-nCoV" is 1 ~ 14 days^[5], in the early stages of the outbreak, the supply of test kits at the end of the outbreak was insufficient and there was difficulties for patients to be diagnosed^[14]. Until to February 7th, 2020, there was still a gap in the sampling facilities and personnel^[15]. A large number of suspected cases cannot be confirmed due to the lack of etiological support. Recently, the number of suspected cases has increased to more than 20,000, and close contacts have reached 280 thousand, with 180 thousand people are being monitored^[2]. At present, there have no effective drugs for suspected and close contact cases, and home observation and clinical symptomatic supportive treatment are usually used in clinic^[5], and this has become an important invisible source of infection and potential risk factor, which make the prevention and

control of epidemic situation in China face great challenges, and the effective prevention and control measures and drugs for suspected cases should be the primary task of clinical and scientific research.

There is a history of thousands of years in preventing and treating "epidemic diseases" by traditional Chinese medicine. As early as in the Spring and Autumn Period and the Warring States period, it was recorded in the < Plain Question • Chapter of Cifa > "Five pestilence come, all phase infection easily, regardless of size, similar symptoms", there was also record that "Less than a decade has passed since the first year of Jian'an, and two-thirds have died of disease, seven-tenths of them are from typhoid" in the < Treatise on Cold Damage Diseases > Zhongjing Zhang in Han Dynasty created a series of classic formulas including Maxing Shigan Decoction for the treatment of typhoid disease. In the Ming Dynasty, the < treatise on pestilence > of Youke Wu discussed the prevention and control of pestilence, it is believed that the disease is caused by "epidemic pathogenic factors" and is transmitted through the mouth and nose, and the disease is specific, Wu creates Dayuan Drink for the treatment of such diseases, and applies the rule of "Rhubarb drive away its evil". In the Qing Dynasty, Tianshi Ye established the rule of the blood transmission of defense qi and nutrient qi and different stages of the prevention and treatment of Exogenous Febrile Diseases, Jutong Wu in the Qing Dynasty established the treatment method of syndrome differentiation of triple energizer for Exogenous Febrile Diseases, this shows that traditional Chinese medicine has made great contributions in the prevention and treatment of "epidemic disease" to ensure the prosperity of the Chinese nation. The whole course of the epidemic was mainly dampness-heat and toxic-stasis, and most of the suspected cases were accompanied by fever and/or respiratory symptoms, which coincided with the records and knowledge of the disease in traditional Chinese medicine.

Lianhuaqingwen formula, applying for the theory of collateral disease in Traditional Chinese Medicine to reveal the rule of the transmission of respiratory system is caused by virus, and put forward the treatment strategy of "active intervention", which included defense qi with the same method, expelling pathogens from both interior and superficies, medicated before having any symptoms, cut off the disease potential, overall regulation, multi-target treatment, the treatment of "heat-clearing and detoxifying and discharge heat by ventilating the lungs" was Established^[16]. The formula is based on Maxing Shigan Decoction in the < Treatise on Cold Damage Diseases > of Zhang Zhongjing in Han Dynasty, and Yinqiao powder in the < Item Differentiation of Warm Febrile Diseases > of Jutong Wu in Qing Dynasty, defense qi with the same method, discharge heat by ventilating the lungs, at the same time, it also draw from the the experience of treatment of rhubarb from Youke Wu's < treatise on pestilence > in Ming Dynasty, medicated before having any symptoms, discharge heat by ventilating the lungs, resolving dampness with aromatics by

pogostemon cablin, wake up the spleen and the brain, clear the Lungs and resolve stasis with rhodiola rosea, regulate immune, the formula is to clear the toxic heat in the lung, diffuse the lung, cut off the disease potential, it embodies the experience of ancient prescriptions in the three dynasties in the treatment of exogenous pestilence. The drug composition of Lianhuaqingwen is coincident with the pathogenesis of the disease, It embodies the active therapeutic principle of “heat-clearing and detoxifying, discharge heat by ventilating the lungs, resolving dampness with aromatics”^[17]. Previous pharmacodynamic studies have shown that Lianhuaqingwen Capsules can inhibit the expression of SARS-CoV in cultured cells in vitro^[18], at the same time, H1N1, H3N2, H7N9 and other influenza viruses were inhibited significantly^[19-20]. During the outbreak of H1N1 virus, a randomized, double blind, multicenter clinical study was conducted in nine hospitals, led by You An Hospital affiliated to Capital Medical University, it was confirmed that there was no difference between Lianhuaqingwen Capsules and Oseltamivir Phosphate in the time of virus nucleic acid turning negative and influenza symptom relieving, But Lianhuaqingwen Capsules significantly reduced the severity of the disease and the duration of symptoms, including fever and relief of cough, myalgia, fatigue. The completed clinical trial of randomized, open and positive controlled of Lianhuaqingwen Capsules in the treatment of Influenza A H1N1^[22] indicated that The time of virus turning negative in Lianhuaqingwen Capsules was similar to that in Oseltamivir, symptoms such as cough, sore throat, fatigue and myalgia were relieved more quickly than Oseltamivir, The above-mentioned clinical trials confirmed that Lianhuaqingwen in the treatment and control of Influenza epidemic has a definite effect.

In this study, 101 patients from January 1th to 27th, in 2020 were admitted to the hospital as suspected cases according to the <diagnosis and treatment of pneumonia due to 2019-ncov infection (fourth edition)>^[7], chest radiographic examination showed the imaging features of pneumonia, which is now clinically diagnosed according to <diagnosis and treatment of pneumonia due to 2019-ncov infection (fifth edition)>^[5], after treatment, the imaging data of some patients were missing. During treatment, 68 patients in two groups were tested for nucleic acid. However, due to the supply of reagent kits and other problems, all patients could not be tested for nucleic acid in time, therefore, nucleic acid detection was not included in the evaluation index of curative effect. The results showed that Lianhuaqingwen Granules could obviously improve the clinical symptoms and signs related to the disease, such as fever, cough, fatigue, tachypnea and moist rales; At the same time, the proportion of severe cases in the treatment group also showed a significant decline, showing that Lianhuaqingwen Granules have a good clinical efficacy for suspected cases to improve clinical symptoms, ease the severity of disease and so on. The results showed that the duration of fever in the treatment group was 1 day shorter than that in the control group, although there was no statistical difference, the trend of time shortening was obvious, at the same time it showed a good trend in the relief of myalgia, expectoration, Chest congestion, Dyspnea and other

symptoms. It reveals the characteristic advantage of "overall regulation, multi-target treatment" of compound Chinese medicine, and suggests that Lianhuaqingwen Granules have important clinical value in suspected cases.

It should be noted that this study was a retrospective clinical study of patients collected and included according to the <diagnosis and treatment of pneumonia due to 2019-ncov infection (fourth edition)>^[7]. The sample size was small, the exact clinical efficacy needs to be evaluated in large-scale, prospective, randomized controlled clinical trials.

References

- [1] World Health Organization, Statement of the Second Meeting of the Emergency Committee of the 2019-nCoV on the International Health Regulations (2005) concerning the 2019 pandemic, 2020-01-30. [https:// www.who.int/zh/news-room/](https://www.who.int/zh/news-room/).
- [2] Health Emergency Office of National Health Commission of the People's Republic of China. Update on the latest situation of pneumonia associated with 2019-nCoV as of 24:00 am on 7 February, 2020-02-08. [http:// www.nhc.gov.cn/xcs/yqfkdt/202002/6c305f6d70f545d59548ba17d79b8229.shtml](http://www.nhc.gov.cn/xcs/yqfkdt/202002/6c305f6d70f545d59548ba17d79b8229.shtml).
- [3] Xinhua News Agency. At present, the virus detection technology has a relatively long time, and the diagnostic rate is about 4.5%-Wuhan is expected to add about 1000 confirmed cases. 2020-01-27. <http://bj.people.com.cn/n2/2020/0127/c14540-33745973.html>.
- [4] Global Times. Chaoliang Jiang, Secretary of the provincial Party Committee: All suspected patients in Wuhan have been tested in two days. Jan 9th, 2020. https://mbd.baidu.com/news-page/data/landingshare?pageType=1&isBdboxFrom=1&context=%7B%22nid%22%3A%22news_10556299211611717315%22%2C%22sourceFrom%22%3A%22bjh%22%7D.
- [5] General Office of National Health Commission of the People's Republic of China, General Office of State Administration of Traditional Chinese Medicine. Notification concerning issuance the < Protocol for the Diagnosis and Treatment of Pneumonia with Novel Coronavirus Infection > (Trial Version 5). 2020-02-05, [http:// www.nhc.gov.cn/yzygj/s7653p](http://www.nhc.gov.cn/yzygj/s7653p).
- [6] Kaitao Yao, Mingyu Liu, xin Li et al. Retrospective Clinical Analysis on Treatment of Novel Coronavirus-infected Pneumonia with Traditional Chinese Medicine Lianhuaqingwen. Chinese Journal of Experimental Pharmaceutics, 2020-02-06, <http://doi.org/10.13422/j.cnki.syfjx.20201099>.

- [7] General Office of National Health Commission of the People's Republic of China, General Office of State Administration of Traditional Chinese Medicine. Notification concerning issuance the < Protocol for the Diagnosis and Treatment of Pneumonia with Novel Coronavirus Infection> (Trial Version 4) 2020-1-27, [http:// www.nhc.gov.cn/yzygj/s7653p](http://www.nhc.gov.cn/yzygj/s7653p).
- [8] Health Commission of the People's Republic of Wuhan. The recommendation for home-based prevention of pneumonia of Novel coronavirus infection in Chinese medicine is issued by Wuhan City. <http://wjw.wuhan.gov.cn/front/web/showDetail/2020020109319,2020-02-01>.
- [9] Jiang Yi, Runming Jin, Yuejie Zheng, et al. Expert consensus on diagnosis, treatment and prevention of new type of coronavirus infection in children. (Version 1) [J]. Chinese Practical Pediatrics Clinical Journal, 2020, 35(2):8185.
- [10] DROSTEN C, GUNTHER S, PREISER W, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome [J]. N Engl J Med, 2003, 348 (20): 1967-1976. Doi: 10.1056/NEJMoa.030747.
- [11] KILLERBY ME, BIGGS HM, MIDGLEY CM, et al. Middle East Respiratory Syndrome Coronavirus Transmission [J]. Emerg Infect Dis, 2020, 26 (2): 191-198. Doi: 10.3201/eid2602.190697.
- [12] WU, F, ZHAO, S, YU, B. et al. A new coronavirus associated with human respiratory disease in China [J]. Nature, 2020-02-03. Doi: 10.1038/s41586-020-2008-3 (2020).
- [13] ZHOU P, YANG XL, WANG XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin [J]. nature, 2020-02-03. Doi: 1038/s41586-020-2012-7.
- [14] Sina Finance. Novel crown pneumonia kit was officially approved for hospital diagnosis The interval is expected to be shortened to 2 hours, 2020-01-27. <http://finance.sina.com.cn/wm/2020-01-27/doc iihnzahk6611465.shtml>.
- [15] Chinese News Network. The confirmation of suspected cases was accelerated and the detection ability of nucleic acid daily was improved in Hubei Province, 2020-02-07. <https://mbd.baidu.com/newspage/data/landingshare?1pageType=1&isBdboxFrom=1&context=%7B%22nid%22%3A%22news-9465728434148816188%22%7D>.
- [16] Zhenhua Jia, Yiling Wu. Theory of collateral disease guiding study of exogenous febrile diseases [J]. Global Chinese Medicine, 2010, 3(01):26-28.
- [17] Yiling Wu . Theory of Qi and collaterals [M]. Beijing: Science and Technology Literature Press, 20018:1327-1329.

[18] Shunya Zhu, Xiaoying Li, Yunling Wei, et al. Three Chinese medicine prescriptions for SARS phase Preliminary study on inhibition of coronavirus in vitro [J]. *Biotechnology Communications*,2003,14(5):390-392.

[19] Hongying Mo, Changwen Ke, Jinping Zheng, et al. Lianhuaqingwen Capsules Anti-A in vitro Experimental Study on Type A Influenza Virus [J]. *New Chinese Medicine and Clinical Pharmacology*, 2007,18(1):69.

[20] DING YW, ZENG LJ, LI RF , et al. The Chinese prescription lianhuaqingwen capsule exerts anti-influenza activity through the inhibition of viral propagation and impacts immune function [J]. *BMC Complement Altern Med*, 2017 , 17 (1) : 130. Doi: 10.1186/s12906-017-1585-7.

[21] DUAN ZP , JIA ZH , ZHANG J , et al. Natural herbal medicine Lianhuaqingwen capsule anti-influenza A (H1N1) trial: arandomized, double blind , positive controlled clinical trial [J] . *Chinese Medical Journal*, 2011, 124 (18) : 2925-2933.

[22] Gengxin Liu, Yanxia Zhang, Jiqing Yang, et al. Lianhuaqingwen Capsule for the Treatment of A H1N1 Randomized controlled clinical study [J]. *Journal of Difficult Diseases*,2010, 9(1):1416.

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