



中国实验方剂学杂志

Chinese Journal of Experimental Traditional Medical Formulae

ISSN 1005-9903, CN 11-3495/R



《中国实验方剂学杂志》网络首发论文

题目: 祛肺毒一号方治疗新型冠状病毒肺炎重型/危重型患者临床疗效分析
作者: 李素云, 李高阳, 张华茹, 李彬, 刘易斯·霍夫曼, 慈中华
DOI: 10.13422/j.cnki.syfjx.20200843
收稿日期: 2020-03-03
网络首发日期: 2020-03-04
引用格式: 李素云, 李高阳, 张华茹, 李彬, 刘易斯·霍夫曼, 慈中华, 祛肺毒一号方治疗新型冠状病毒肺炎重型/危重型患者临床疗效分析. 中国实验方剂学杂志. <https://doi.org/10.13422/j.cnki.syfjx.20200843>



网络首发:在编辑部工作流程中,稿件从录用到出版要经历录用定稿、排版定稿、整期汇编定稿等阶段。录用定稿指内容已经确定,且通过同行评议、主编终审同意刊用的稿件。排版定稿指录用定稿按照期刊特定版式(包括网络呈现版式)排版后的稿件,可暂不确定出版年、卷、期和页码。整期汇编定稿指出版年、卷、期、页码均已确定的印刷或数字出版的整期汇编稿件。录用定稿网络首发稿件内容必须符合《出版管理条例》和《期刊出版管理规定》的有关规定;学术研究成果具有创新性、科学性和先进性,符合编辑部对刊文的录用要求,不存在学术不端行为及其他侵权行为;稿件内容应基本符合国家有关书刊编辑、出版的技术标准,正确使用和统一规范语言文字、符号、数字、外文字母、法定计量单位及地图标注等。为确保录用定稿网络首发的严肃性,录用定稿一经发布,不得修改论文题目、作者、机构名称和学术内容,只可基于编辑规范进行少量文字的修改。

出版确认:纸质期刊编辑部通过与《中国学术期刊(光盘版)》电子杂志社有限公司签约,在《中国学术期刊(网络版)》出版传播平台上创办与纸质期刊内容一致的网络版,以单篇或整期出版形式,在印刷出版之前刊发论文的录用定稿、排版定稿、整期汇编定稿。因为《中国学术期刊(网络版)》是国家新闻出版广电总局批准的网络连续型出版物(ISSN 2096-4188, CN 11-6037/Z),所以签约期刊的网络版上网络首发论文视为正式出版。

[收稿日期]2020-03-03

[基金项目]河南省 2020 年新型冠状病毒肺炎防控应急攻关项目(201100310400, 201100310500); 中医药传承与创新“百千万”人才工程(岐黄工程)项目(国中医药人教发[2017]9 号); 中原学者项目(ZYQR201912002)

[通信作者]李素云, 教授, 主任医师, 博士生导师, 从事中医药防治呼吸疾病临床与基础研究, Email:lisuyun2000@126.com

祛肺毒一号方治疗新型冠状病毒肺炎重型/危重型患者临床疗效分析

李素云^{1*}, 李高阳¹, 张华茹², 李彬¹, 刘易斯·霍夫曼³, 慈中华³

(1.河南中医药大学 第一附属医院, 郑州 450000; 2.驻马店市中心医院, 河南 驻马店 100191;

3.世界健康科学组织, 弗吉尼亚州 利斯堡 20176)

[摘要] **目的:**观察祛肺毒一号方治疗新型冠状病毒肺炎重型/危重型患者的临床疗效, 总结诊治经验。**方法:**收集 2020 年 1 月 31 日至 2020 年 2 月 27 日在驻马店市中心医院、河南中医药大学第一附属医院救治定点医院收治的使用祛肺毒一号方的重型/危重型新冠肺炎患者临床资料, 并进行分析。**结果:**患者均有明确流行病学史, 以发热、咳嗽、呼吸急促、乏力、肌肉酸痛等征状为主, 部分兼有食欲不振、腹泻征状, 患者平均年龄 59 岁, 从发病到病情加重的中位时间是 9 d, 双肺多发磨玻璃状、斑片状、结节状高密度影, 病灶进展较快, 经祛肺毒一号方联合西医治疗后, 患者病毒核酸检测转阴平均时间为 16 d, 平均住院天数为 20 d, 均痊愈出院。**结论:**祛肺毒一号方治疗新型冠状病毒肺炎重型/危重型患者具有一定临床疗效, 建议进一步开展大样本临床验证和推广。

[关键词] 新型冠状病毒肺炎; 重型; 危重型; 证候; 祛肺毒一号方

[中图分类号] R2-0; R254.3; R373.1; R511 **[文献标识码]** A

[doi] 10.13422/j.cnki.syfx.20200843

Clinical Efficacy and Experiences of Lung-toxin Dispelling Formula No.1 Treating Patients of Corona Virus Disease 2019 Type severe/Type Extremely Severe

Li Su-yun^{1*}, Li Gao-yang¹, ZHANG Hua-ru², Li Bin¹,

LEWIS A.Hofmann³, CI Zhong-hua³

(1.The First Affiliated Hospital of Henan University of Traditional Chinese Medicine, Zhengzhou 450000, China; 2.Central Hospital in Zhumadian, Zhumadian 100191, China; 3.World Health Science Organization, Virginia Leesburg 20176, USA)

[Abstract] **Objective:**To observe clinical efficacy of Lung-toxin dispelling formula No.1 treating patients of corona virus disease 2019(COVID-19) type severe/type extremely severe, and summarize experiences of diagnosis and treatment.**Method:**We collected and analyzed clinical informations of patients of COVID-19 type severe/type extremely severe, treated with Lung-toxin Dispelling Formula No.1, who were hospitalized in Central hospital in Zhumadian and the First affiliated hospital of Henan University of traditional Chinese medicine from 31st January to 27th February. **Result:** All patients had positive epidemiological history, major symptoms were fever, cough, tachypnea, weakness and sore heavy muscles, combined with bad appetite and diarrhea. The average age was 59y, median time from onset to getting worse was 9 days, ground glass opacity, lamellar, nodular high density shadow were mostly displayed in both lungs. Lesions progressed faster. After treatment with Lung-toxin Dispelling Formula No.1 combined with western medicine, the average time of PCR-NAD-test from positive to negative was 16 days, the average hospitalization days were 20 days, all patients were cured and discharged. **Conclusion:** Lung-toxin Dispelling Formula No.1 had certain clinical efficiency in treating patients of COVID-19 type severe/type extremely severe, further large sample clinical verification is needed.

**Clinical efficacy and experiences of Lung-toxin Dispelling Formula
No.1 treating patients of corona virus disease 2019(COVID-19)
type severe/type extremely severe**

**LI Su-yun¹, LI Gao-yang¹, ZHANG Hua-ru², LI Bin¹, LEWIS A.Hofmann³,
CI Zhong-hua³**

(1.The First affiliated hospital of Henan University of T.C.M., Zhengzhou 450000

2.Central hospital in Zhu Madian, Zhu Madian 100191

3.World Health Science Organization, Leesburg, Virginia, U.S.A. 20176)

[Abstract] Objective: To observe clinical efficacy of Lung-toxin dispelling formula No.1 treating patients with corona virus disease 2019(COVID-19) type severe/type extremely severe, and summarize experiences of diagnosis and treatment.

Methods: We collected and analyzed clinical information on patients with COVID-19 type severe/type extremely severe, treated with Lung-toxin Dispelling Formula No.1, who were hospitalized at Zhumadian Central hospital and the First affiliated hospital of Henan University of T.C.M. from January 31st to February 27th. **Results:** All six patients had explicit epidemiological history, major symptoms were fever, cough, tachypnea, weakness and sore heavy muscles, combined with inappetence and diarrhea. The average age of the patients was 59-year old and the median time from onset to getting worse was 9 days, and ground glass opacity, lamellar, nodular high density shadow were mostly displayed in both lungs. Lesions progressed rapidly. After treatment with Lung-toxin Dispelling Formula No.1 combined with western medicine, the average time of PCR-NAD-test from positive to negative was 16 days, the average hospitalization days were 20 days, and all patients were cured and discharged. **Conclusion:** Lung-toxin Dispelling Formula No.1 had certain clinical efficiency in treating patients of COVID-19 type severe/type extremely severe, further large sample clinical verification is needed.

[Key words]: corona virus disease 2019(COVID-19); type severe; type extremely severe; TCM syndromes; Lung-toxin Dispelling Formula No.1

Since December 2019, a new type of coronavirus pneumonia (coronavirus disease, COVID-19), which has emerged in Wuhan, Hubei province, has spread rapidly and caused serious consequences. It has become a serious public health emergency^[1-3]. Global researches focus on the prevention and treatment of coronavirus disease, especially researches on preventive and therapeutic drugs and methods have been accelerated for the purpose of preventing disease progression, improving curative ratio, and reducing mortality^[4,5]. Due to the severity of the disease, COVID-19 is clinically divided into four types: mild, general, severe, and extremely severe^[6-7]. At present, there are no specific medicine for the treatment of patients with type severe and type extremely severe, and the prognosis is poor^[8]. The national health authority has specially issued *Diagnosis and Treatment Program for type severe and type extremely severe of COVID-19 Pneumonia(Trial Version Second)*^[9]. In order to speed up the rate of improvement and cure rate of patients of type severe. Traditional Chinese medicine has certain advantages in the treatment of patients of type extremely severe, but there is shortage of certain clinical evidence^[10,11]. Therefore, this article studies the clinical data of 6 patients with coronavirus pneumonia type severe / type extremely severe treated by Lung-toxin Dispelling Formula No.1, analyzes the clinical efficacy, summarizes the experiences of diagnosis and treatment, and provides theoretical references for improving the therapeutic effect of TCM syndrome differentiation on patients of type extremely severe.

1 Materials and methods

1.1 Cases Source Selected patients of COVID-19 type severe/type extremely severe, treated with Lung-toxin Dispelling Formula No.1, who were hospitalized from 31st, January, 2020 to 27th, February, 2020 in Central Hospital in Zhumadian and the First Affiliated Hospital of Henan University of Traditional Chinese Medicine.

1.2 Diagnostic Criteria Based on Western medicine diagnostic criteria, clinical classification and TCM syndrome differentiation diagnostic criteria, which are issued by the Office of the National Health Commission and the Office of the State Administration of Traditional Chinese Medicine, which are *Diagnosis and Treatment Scheme for COVID-19 Pneumonia (Trial Implementation edition Fourth)*^[6] and

Diagnosis and Treatment Scheme for COVID-19 Pneumonia (Trial Implementation edition Fifth Revised edition) ^[7] .

Diagnostic criteria: Suspected cases have one of the following pathogenic evidences: 1) To detect coronavirus nucleic acid positive of Real-time fluorescent RT-PCR of respiratory specimens or blood specimens; 2) To sequence the viral genes of respiratory specimens or blood specimens and if highly homologous with known coronaviruse.

The diagnostic evidences for type severe/type extremely severe are: 1) Type severe: Matched with any one of the items: (1) Respiratory stress, respiratory rate (RR) ≥ 30 beats/min; (2) In resting state, finger oxygen saturation $\leq 93\%$; (3) Arterial blood oxygen partial pressure (PaO₂) / oxygen concentration (FiO₂) ≤ 300 mmHg (1mmHg =0.133kPa) 2) Type extremely severe: Matched with any one of the following conditions: (1) Respiratory failure occur and machinery ventilation is required; (2) Coma; (3) Combined with other organ failure and ICU monitoring treatment is required.

TCM diagnostic criteria: 1) Syndrome of pestilence-toxin blocking the lung: high fever, persistent fever or alternating chills and fever, cough and little sputum, or yellow phlegm, irritability, chest tightness, shortness of breath, dark purple face and lips, bloating, and constipation. The tongue is red or dark purple, the tongue fur is yellow and dry, and the pulse is slippery and rapid. 2) Syndrome of internal block and external collapse: dyspnea, asthma, even assisted ventilation is needed, chest tightness and distress, pale face, dark purple lips, sputum, great dripping sweat, cold limbs, abnormal consciousness(apathy, nagging, irritability, drowsiness, coma). The tongue is pale or dark purple, the tongue fur is thick sticky or dry, or yellow or white fur, and the pulses are weak and faint or racing and skipping or floating without roots.

1.3 Clinical treatment According to the protocols from *Diagnosis and Treatment Scheme for COVID-19 Pneumonia (Trial Implementation edition Fourth)*, *Diagnosis and Treatment Scheme for COVID-19 Pneumonia (Trial Implementation edition Fifth Revised edition)* and *Diagnosis and Treatment Program for type severe and type extremely severe of COVID-19 Pneumonia(Trial Version Second)*.

Western medicine treatment mainly includes symptomatic supportive treatment, maintaining water, electrolyte and acid-alkaline balance, oxygen therapy and respiratory support, circulation monitoring and support, nutrition support treatment, antiviral treatment, antibacterial treatment, etc.

Traditional Chinese medicine treatment is mainly Chinese medicine decoction/granules and Chinese patent medicine, which all patients were treated with Lung-toxin Dispelling Formula No.1: Ginseng 30g, Schizonepeta 15g, Honeysuckle 15g, Scrophulariaceae 15g, and others. Decoction of Chinese herbal medicine (Chinese medicine granules are prepared in water), 2 doses in a day. The prescription is provided by the World Health Science Organization (WHSO), according to the actual clinical situation of patients, to add or subtract on the basis of the original prescription with the syndromes differentiation.

1.4 Clinical information collection The basic data such as gender, age, contact history of the epidemic area, and past medical history during the hospitalization of patients with type extremely severe were collected. Clinical symptoms such as fever, cough, fatigue, shortness of breath, tongue, pulse, etc, clinical treatment, time of virus test from positive to negative, imaging and laboratory indicators, etc.

1.5 Statistical analysis SPSS 20.0 statistical software is applied. Measurement data are described by mean \pm standard deviation or median (interquartile range). Count data are described by frequency (ratio).

2 results

2.1 General clinical features 6 patients were 3 males, 3 females, ratio of gender is 1:1. The average age is 59 years. Six patients had clear epidemiological histories, which one had a history of residence in Wuhan, four had a history of close contact with suspected Wuhan patients, and one had no clear epidemiological history. On admission, the first symptoms are fever, cough, shortness of breath, fatigue, heavy and sore muscles, etc. At the same time, they often have digestive symptoms such as loss of appetite and diarrhea. The basic syndrome is the epidemic-toxin blocked lung. See Tables 1 and 2.

2.2 The main efficacy indicators The average time from the onset of the patient to the first visit was 6 days, the average time from onset to diagnosis was 8 days, and the average time from the onset of the disease to type severe or type extremely severe was 9 days. After treatment, the average time for Nucleic acid detection(NAD) converted to negative was 16 days, and the average days of hospitalization was 20 days. All patients were recovered and discharged. See Table 3.

Table 3 Main indicators of efficacy

Patient number	Time from onset to first hospitalization	Time from onset to diagnosis	Time for converting to type severe/extremely severe	Time of NAD converted to negative	Days in hospital	Outcome
1	7	8	7	17	20.00	cured
2	7	10	3	9	14.00	cured
3	8	12	8	19	26.00	cured
4	1	8	9	10	17.00	cured
5	5	6	7	17	25.00	cured
6	1	4	7	10	19.00	cured

2.3 Therapeutic medications Patients of type severe/type extremely severe were treated with Chinese and western medicines which are mainly antiviral drugs, anti-infective drugs, and drugs that enhance human immunity. 6 cases of NCP type severe/type extremely severe were applied with herbs decoction; Xuebijing injection, Reduning injection which were two kinds of higher frequency applied Chinese medicine injections in NCP type severe/type extremely severe. See Tables 4 and 5.

Table1 Basic information of patients

PN	Gender	Age	Clinical types	Epidemiological history	Past history	BT (°C)	Pulse (beats/m)	Breathe (times/m)	Heart rate (beats/m)	High BP (mmHg)	Low BP (mmHg)
1	female	42	extremely severe	Close contact	none	39	100	23	100	125	67
2	male	79	extremely severe	Close contact	High BP	36.3	100	19	100	180	96
3	male	64	extremely severe	Wuhan resident	High BP	36.5	100	24	100	109	76
4	male	43	severe	Close contact	none	37	68	32	68	138	85
5	female	79	severe	Close contact	none	38.8	88	22	88	159	80
6	female	47	extremely severe	Close contact	Preexcitation syndrome	36	90	24	90	124	74

Table2 Common clinical symptoms and syndromes of patients

PN	Skin cyanosis	Lip aster	Shortness of breath	fever	dyspnea	Fatigue	Cough	Sore muscle	Digestive system	Tongue	Pulse	Syndromes
1	no	no	no	yes	yes	yes	yes	yes	yes	Red tongue, yellow thick coating	Slippery rapid	Epidemic-toxin blocked lung
2	no	no	no	Yes	no	no	yes	No	Yes	Dark red tongue, yellow greasy fur	Slippery rapid	Epidemic-toxin blocked lung
3	no	no	Yes	Yes	Yes	yes	no	No	yes	Red tongue, yellow thin coating	Slippery rapid	Epidemic-toxin blocked lung
4	no	no	Yes	Yes	yes	No	Yes	No	No	red in tip and sides of tongue, yellow greasy fur	Slippery rapid	Epidemic-toxin blocked lung
5	no	no	No	Yes	no	No	Yes	No	Ye	Red tongue, little coating	Slippery rapid	Epidemic-toxin blocked lung
6	no	no	no	yes	yes	no	yes	no	no	Red tongue, yellow thick greasy coating	Slippery	Epidemic-toxin blocked lung

Table 4 Analysis on the Use of Western Medicine in Patients

Western medicine	Specific usage
Recombinant human interferon alpha-2b	
injection	6
Immunoglobulin	6
Ribavirin injection	5
Piperacillin sodium / tazobactam sodium	
injection	5
Ulinastatin injection	5
Lopinavir/Litonavir tablets	4
Moxifloxacin	4
Albumin	4
Oseltamivir capsule	3
Levofloxacin sodium chloride injection	3
Abidol	3
Meropenem	2
Abidol	2
Cefoperazone sulbactam injection	2
Linezolid	2
Methylprednisolone sodium succinate	2

Table 5 Analysis of the use of TCM for patients

Chinese medicine	Specific usage
Herb decoction (including granules)	6
Xuebijing injection	5
Lianhua qingwen granules	4
Reduning injection	3
Xiyanping injection	1
Suhuangzhike granules	1
Chaihu oral solution	1

2.4 Pulmonary CT manifestations Patients of type severe/type extremely severe whose manifestations were scattered or multiple pulmonary fluff, cable strip and frosted glass opacities high density shadows, accompanied by bilateral pleural localized thickening, enlarged lymph nodes were often seen in the mediastinum. There are cases of pleural effusion in individual patients. See Table 6.

Table 6 CT status of patients' lungs

Lung condition	distribution
Double lung disease	6
Multiple ground-like, patchy, nodular high density shadows	5
Localized pleural thickening	5
Slightly larger lymph nodes in Mediastinal	2
Pleural effusion	1

2.5 Laboratory indicators The absolute value and percentage of lymphocytes in most patients were lower than the normal range upon admission; the combined application of a large number of antivirals and other drugs had a certain effect on liver function in patients of type severe/type extremely severe; the COVID-19 disease itself and process of treatment, which may affect the body's function of coagulation, especially in patients of type severe /extremely severe, elevated D-dimer may occur; other indicators are basically within the normal range. Abnormal indicators returned to normal when discharged. See Table 7.

Table 7 Laboratory indicators

Indicators	Normal range	1	2	3	4	5	6
WBC($\times 10^9/L$)	3.5-9.5	6.11	5.07	2.28	7.09	6.57	6.7
RBC($\times 10^{12}/L$)	4.3-5.8	3.47	4.51	5.02	4.57	3.56	
Neu ($\times 10^9/L$)	1.8-6.3	5.45	4.44	1.48	6.64	5.07	
Ly ($\times 10^9/L$)	1.1-3.2	0.58	0.51	0.63	0.26	1.17	0.5
%NEU (%)	50-70	89.21	87.50	64.90	93.70	77.10	89.70

%Ly (%)	20-40	9.52	10.10	27.60	3.70	17.80	
Calcitonin (pg/mL)	0-0.046	0.075	0.052		0.169	0.061	
Hs-CRP (mg/L)	0-5		47.2	44			
urea (mmol/L)	2.2-8.2	3.33	5.75	5.47	4.07	1.87	
urea (umol/L)	20-115	56.70	61.00	90.10	67.00	58.90	
uric acid (umol/L)	200-440	221	93	269	201	89	
ALT (U/L)	0-40	42	31.00	68	45	29	108
AST (U/L)	0-40	72	37	56	21	44	85.3
LDH (U/L)	109-245	364	432	231	357	324	
PT (s)	9-14	10.70	11.00	9.90	11.00	10.80	9.70
INR	0.8-1.2	0.94	0.97	0.87	0.97	0.95	
TT	14-21	17.40	18.50	16.70	17.80	17.50	
APTT (s)	22.2-32.5	47.50	32.30	26.10	25.50	43.50	21.40
Contractinogen (g/L)	2-4	4.86	5.91	5.35	6.23	4.86	4.88
D- dimer (mg/L)	0-0.55	0.64	1.16	8.33	0.29	0.64	4

3 Discussions

3.1 Clinical characteristics of COVID-19 pneumonia type severe and type extremely severe

Patients with type severe and type extremely severe are the main types of death. The *Diagnosis and Treatment Scheme for COVID-19 Pneumonia (Trial Implementation edition Sixth)* [12] states that: fever, dry cough, weakness is the main manifestations, and a few patients have symptoms such as nasal congestion, running nose, sore throat, myalgia and diarrhea. In severe cases, dyspnea and / or hypoxemia occurred more than one week after the onset, and the most severe cases progressed rapidly to acute respiratory distress syndrome and septic shock. The main symptoms of the 6 patients treated by the authors : fever, dyspnea, short of breath, fatigue, occasional dry cough, a few accompanied by gastrointestinal symptoms such as diarrhea; the patient's chest CT showed diversity and multifocal characteristics at the onset of the

disease, with flaky ground glass shadows, consolidation shadows, involving both sides pulmonary lung field, Grinding Glass Shadow and Real Change Shadow, Grinding Glass Shadow and Mesh Shadow, which matched with the theory of traditional Chinese medicine" Lung were attacked first by the epidemic-warm pathogen"; the courses are suddenly worsened when occurred within 7 days of the disease process , the lymphocyte counts of patients with exacerbations all decreased significantly, the lowest was $0.13 \times 10^9/L$, albumin was decreased, suggesting that patients were deficient in Qi, and should be strengthened during treatment.

3.2 Treatment of patients COVID-19 type severe and type extremely severe should focus on strengthening Qi and dispelling toxin

There were signs of difficulty in breathing, shortness of breath, and blood oxygen saturation continued to decline, decreased lymphocyte count, persistent fever or fever again, the increase of D-dimers and the decrease of albumin are the most obvious characteristics. They belong to the traditional Chinese medicine epidemic-toxin blocked lung syndrome, which is a manifestation of deficiency of Qi and too much toxin. This formula replenishes qi and nourish yin, clears heat and detoxifies, relieves cough, expectorant and relieves asthma, which ginseng is to replenish qi of lung, benefit qi and regenerate fluid, which is matched with the idea of plague's " focus on kidney qi, save fluid " , and promotes righteousness to fight against evil qi, *Compendium of Materia Medica*: " Ginseng, slightly cold, sweet, non-toxic, Nourishing the five internal organs, restoring spirits, calming souls, stopping trembling, removing evil qi, ... Belongs with the Taiyin Lung Meridian, which is sweet and non-toxic with flavor of earthy and belongs to spleen meridian. The lung is the lead of the five internal organs, the ancestors of the hundred veins, the transport of Qi, ... Ginseng Qi is cold to clear the lungs, which is vigorous to the five internal organs"; Honeysuckle clears heat and detoxifies, *Compendium of Materia Medica*: " Honeysuckle, good at cure poison, to cure gangrene, swollen poison, sore addiction, "the two drugs played a vital role in reinforcing lung qi, antipyretic toxin, a total of king medicine. Schizonepeta has the ability to relieve sweat and make the disease out of sweat. "*Compendium of Materia Medica*": "The temperature of Schizonepeta, warm, non-toxic, used in cold and hot rat scrofula, sores, the

accumulation of gas, blood stasis, dehumidification gangrene, which intrinsic days of spring rising, wood element, into the gallbladder foot meridian, foot liver Meridian, spicy non-toxic, have to be gold element of the West, belonged to lung meridian, warm feasible gas, spicy breaks the blood, so the blood stasis can also be treated.. ... Schizonepeta can moisturize the lungs, and the lungs rule the water channels " ; Forsythia is bitterly cold, helps honeysuckle clear heat and detoxify. In short, the prescription is to remedy the symptoms of rectifying the evil, replenishing qi and nourishing yin, clearing heat and detoxifying, relieving cough, expectorant and relieving asthma; after taking the medicine, the patient showed perspiration on the back, vomiting more white foam, sputum, and fatigue. In order to cut the pathogenesis, the plague toxicant emerges from sweat, the pathological products are excreted from sputum, and from the stool. At the same time, the peripheral blood lymphocyte count has increased significantly, breathing difficulties have improved, and the oxygenation index has increased significantly.

3.3 The treatment of patients with type severe and extremely severe should pay attention to lung management and sputum discharge. The severe manifestations of novel pneumonia are shortness of breath, $RR \geq 30$ times / minute; in the resting state, finger oxygen saturation $\leq 93\%$; oxygenation index $\leq 300\text{mmHg}$; type extremely severe manifestations include respiratory failure, shock, combined with other organs failure. Wang Fusheng's autopsy revealed the pathological manifestations of pulmonary edema with hyaline membrane formation, shedding of lung cells, and hyaline membrane formation. Both lungs showed pathological manifestations such as inflammatory infiltration of interstitial monocytes, mainly lymphocytes, the predominant inflammatory response was shown ^[13]. We also found that peripheral blood lymphocytopenia is a common feature of patients with novel coronavirus pneumonia, and may be a key factor related to the severity and mortality of the disease. It is speculated that due to pulmonary inflammation, peripheral blood lymphocytes are recruited into the lung. This herbs prescription could help lung secretion discharge, pulmonary edema was reduced, lung ventilation and ventilation function improved, inflammation was reduced, lymphocytes recruited in the lungs returned to peripheral

blood, inhibited excessively activated lymph cell.

4 Classic medical records

4.1 Medical Record No.1: patient of COVID-19 type extremely severe, male, 43 years old, long-term resident in Zhumadian City, 19th Jan,2020 contacted with Wuhan returnees (diagnosed novel coronavirus pneumonia COVID-19), 29th Jan,2020 got fever without significant reasons, body temperature 38.5 °C, with cough, small amount of white sticky phlegm, treated in local hospital, symptomatic treatment of 8 days (specific treatment is unknown), ineffective. 5th Feb,2020 went to County people's hospital for treatment, his chest CT showed pneumonia in both lungs, ceftazidime (2.0, q8h), levofloxacin (0.5, qd, intravenous), methylprednisolone (40mg, qd , intravenous), treated for 5 days, the patient was still got intermittent fever, cough with sputum, 6th Feb,2020 22:00 County CDC notified the novel coronavirus nucleic acid testing is positive, the second chest CT showed significantly worse, so added with lopinavir / ritonavir (2pills, q12h, oral), Lee ribavirin (0.5g , q8h), Abidor (0.2g, Bid), Xuebijing (100ml, q12h), cefoperazone sodium and sulbactam sodium (4g , q12h),anti-infection treatment were ineffective, the patient's condition was worsening, 7th Feb, 2020 difficulty in breathing after movement was occurred, the third CT showed significantly worse than the second time, transferred into the central hospital.

Admission examination: body temperature 37.0°C, pulse rate 68 beats/min, breathing 32 beats/min, blood pressure 130/85mmHg, patient's consciousness is good, moderate nutrition, painful expression, shortness of breath, low breathing sounds in both lungs, unheard of dry and wet rales, poor sleep, normal urinary and bowel movements. Examination: blood routine: WBC:7.09, N:6.64, L:0.26, E:0, CRP39.09mg /L, arterial blood gas (non-invasive ventilator assisted breathing T 37 °C) PH 7.456 , PCO₂ 34.6mmHg, PO₂ 60.8mmHg , HCO₃ 23.8mmol/L, SO₂ 92.3%, Lac 2.3mmol/L , blood biochemistry (County People's Hospital 2020.02.09) : ALT 73U/L, AST 29U/ L, GGT 165U/L, TP 55.1g/L, ALB 30.1g/L, prealbumin 79mg/L, potassium 2.95mmol/L , chest CT (County People's Hospital 2020.02.09) : inflammation of both lungs, which was significantly worse than before. Pathogenic examination: novel coronavirus nucleic acid testing positive (6th Feb,2020, 22:00 from County CDC).

Admission diagnosis: 1. Novel coronavirus pneumonia COVID-19 (Type extremely severe), 2. Hepatic insufficiency. 3. Electrolyte disorders, hypokalemia. After admission, he was given non-invasive ventilator-assisted ventilation, adjusted the antibiotics to be imipenem, cilastatin, and linezolid for anti-infection, lopinavir / ritonavir, and interferon A-2B in aerosol inhalation. Xuebijing, Ambroxol, rabeprazole and sucralfate stomach protection, immunoglobulin (25g, qd), albumin (20g, qd), adjust electrolyte disorders and other symptomatic supportive treatment.

10th, Feb, 2020: the WBC: $7.09 \times 10^9/L$, N: $6.64 \times 10^9/L$, L: $0.26 \times 10^9/L$, E: $0 \times 10^9/L$, CRP 39.09 mg/L; 11th, Feb, 2020 WBC: $12.06 \times 10^9/L$, N: $11.37 \times 10^9/L$, L: $0.37 \times 10^9/L$, E: $00 \times 10^9/L$, CRP 14.96 mg/L, ESR 67 mm/h

11th, Feb, 2020 first diagnosis by TCM: Morning measure of patient's temperature is normal, difficulty breathing after movement, chest tightness, shortness of breath, fatigue, loose stools, cough small amount of white sputum, red in tip and sides of tongue, white greasy tongue fur, syndrome of hot and humid toxin blocked the lung, prescription: Ginseng 30g, Nepeta 15g, Honeysuckle 15g, Forsythia 30g, and others. Decoction, 1.5 doses daily, divided into 3 times. 12th, Feb, 2020 after taking the herb medicine, dyspnea and cough were reduced, coughing with more frothy sputum, frequency of stool was increased, suspend the use of hormones and for prevention of oral fungal infection, Nystatin and sodium bicarbonate were applied for mouthwash, patient got intermittent fever, Body temperature 37.2°C-38.3°C, after antipyretic medication for symptomatic treatment, which returned to normal. WBC: $11.08 \times 10^9/L$, N: $10.03 \times 10^9/L$, L: $0.31 \times 10^9/L$, E: $00 \times 10^9/L$, CRP 1.88 mg/L, ESR 52 mm/h;

13th, Feb, 2020, WBC: $10.27 \times 10^9/L$, N: $10.00 \times 10^9/L$, L: $0.13 \times 10^9/L$, E: $00 \times 10^9/L$, CRP 26 mg/L, ESR 57 mm/h; 14th, Feb, 2020, WBC: $11.5 \times 10^9/L$, N: $10.00 \times 10^9/L$, L: $0.69 \times 10^9/L$, E: $08 \times 10^9/L$, CRP 25 mg/L, ESR 58 mm/h;

16th, Feb, 2020, the spirit was improved, symptoms of dyspnea and cough sputum were reduced compared before, but still intermittent fever, non-invasive mechanical ventilation showed oxygen saturation at 96%, lung imaging was no significant improved, WBC: $6.17 \times 10^9/L$, N: $5.06 \times 10^9/L$, L: $0.61 \times 10^9/L$, E: $0.21 \times 10^9/L$, CRP 25 mg/L, ESR 51 mm/h; Add 15g of Bupleurum into original traditional Chinese

medicine and continue for 2 doses.

18th Feb, 2020 third time: the patient is in stable condition, the temperature dropped to 36.7 deg.] C, the pulse 94 times/min, breathing 20 times/min, blood pressure 130/60mmHg , refers to an oxygen saturation 97%, a sense of fatigue, anorexia, occasional cough, phlegm transparent white, pink tongue, greasy tongue coating; prescription: ginseng 30g, nepeta 15g, honeysuckle 15g, forsythia 30g, scrophulariaceae 15g, and others. Decoction, one dose daily, divided into two servings.

20th,Feb,2020 patient was better after symptomatic and supportive treatment by traditional Chinese medicine and anti-virus, liver protection, anti-inflammatory, anticoagulant and all symptoms were disappeared, his condition was improved, the recheck of lung CT showed: viral pneumonia in both lungs were better. Patients did the novel coronavirus nucleic acid tests twice in 17th and 19th,Feb,2020, both were negative, 20th,Feb,2020 the patient was qualified to discharge criteria, and continued to take the herb medicine after discharge.

4.2 Medical Records No.2: patient of type severe of COVID-19 pneumonia, female, 42 years old, 26th,Jan,2020 got fever with no obvious reason, the highest temperature 39.5 °C , accompanied by fatigue, itchy throat, body aches, no anorexia, no nausea, no vomiting, no diarrhea, no chest tightness, no chest pain, treated at a local clinic with amoxicillin and other drugs (specifically unknown), but ineffective, she felt worse , 1st,Feb,2020 she went to Central hospital, chest CT showed: two Pulmonary multiple focal infections ,then she was hospitalized in the outpatient clinic with " fever to be checked " and temporarily given cefoperazone/sulbactam sodium (4g q12h, intravenous drip), levofloxacin (0.5g qd , intravenous drip), and heat-detoxin (20ml qd, intravenous drip), a- interferon (5 million u bid, compressed nebulized inhalation) , in purpose of anti-infective, anti-viral treatment.

Admission examination: body temperature 39°C, pulse 100beats/ min, breathing 23beats / min, blood pressure 125/67mmHg. The patient was clear-minded, poor in spirit, wasted, slightly short of breath, thick breathing in both lungs, smell of wet rales, poor appetite, and normal urinary and stool. Laboratory examinations: blood routine showed: WBC $6.87 \times 10^9/L$, RBC $3.62 \times 10^{12}/L$, hemoglobin 111g/L, the percentage of

neutrophils 74.9%, lymphocyte count $1.22 \times 10^9/L$. Chest CT showed multiple flaky infections in both lungs. During the treatment, the patient still had intermittent fever, cough, fatigue, and difficulty breathing. 3rd,Feb,2020, body temperature of the patient 38 °C, pulse rate 124 times/min, breathing 28 times/min, blood pressure 108/ 64mmHg , oxygen saturation 95% (oxygen-flow), respiratory distress remains; novel coronavirus nucleic acid test was positive. Diagnosed as: novel coronavirus pneumonia COVID-19(Type severe) with respiratory failure. Transfer to RICU to continue treatment, monitoring vital signs changes, and add lopinavir/ritonavir (2tablets,bid,oral), immunoglobulin (4.5g, q8h intravenous), methylprednisolone injection (40mg, q12h), Xuebijing (100ml, q12h) and ambroxol, symptomatic treatment, non-invasive ventilator assisted ventilation.

3rd,Feb,2020, first time for TCM diagnosis: Patient got fever, body temperature 38 °C, dry cough with little phlegm, shortness of breath, difficulty in breathing, irritability, panic, poor appetite, lassitude, red tongue, yellow thick coating, slippery rapid pulse, the syndrome was wet-heat epidemic-toxin blocked the lung, treated with improving qi and yin, detoxification, relieving cough and asthma, prescription: ginseng 30g, nepeta 15g, honeysuckle 15g, forsythia 30g, scrophulariaceae 15g, and others. Three doses, 1.5 doses daily ,warn decoction both in morning and evening. 5th,Feb,2020 after taking the herb medicine, her temperature drops, 36.8 °C, heart rate 60 times/min, diarrhea for 2-4 times a day, emotional stability, breathing difficulties slightly better, dry cough, shortness of breath, with more sticky white foam phlegm, non-invasive mechanical ventilation to maintain a stable blood oxygen saturation of 90%-95%, Chinese medicine were continued as before. 6th,Feb,2020 patients with clear consciousness, the spirit was poor, respiratory distress, when coughing with phlegm white foam, anorexia, diarrhea for 3 times a day, at night there were yellow watery stools, continue the herb medicine, and the addition of methylprednisolone 40mg, bid for 2 days. 7th,Feb,2020, patient was with clear consciousness, the spirit was improved, better appetite, relieved diarrhea, respiratory distress was reduced. Laboratory tests: white blood cells $7.21 \times 10^9/L$, red blood cells $2.91 \times 10^{12}/L$, hemoglobin 90g/L, blood oxygen saturation after non-invasive assisted ventilation is 90% -95%.

8th,Feb,2020 second time of traditional Chinese medicine, the patient is currently in stable condition, a little diarrhea, red tongue, thin white little coating, the syndrome is heat-toxic blocked the lung, prescription: ginseng 30g, nepeta 15g, honeysuckle 15g, even Alice 30g, scrophulariaceae 15g, and others. Three doses, one dose a day, warm decoction in both morning and evening, and stop using methylprednisolone injections. 9th,Feb,2020, after taking herb medicine, she had a clear mind, the spirit was improved, more white foam sticky phlegm, better emotions, improved appetite, diarrhea for 2 times, oxygen saturation was improved. Examination: body temperature 37°C , heart rate 69 beats / min, breathing 25 beats / min, blood pressure 110/65mmHg . Laboratory tests: white blood cells $7.84 \times 10^9/L$, red blood cells $3.13 \times 10^{12}/L$, hemoglobin 98g/L , and blood oxygen saturation after non-invasive assisted ventilation is 90% -97%.

11th,Feb,2020, third time of traditional Chinese medicine, patient with clear consciousness, the spirit was improved, non-invasive mechanical ventilation in patient with stable respiration, oxygen saturation at 90%-96%. Examination: body temperature 36.0 °C, heart rate 72 beats/min, blood pressure 105/67mmHg, no abdominal distension, no abdominal pain, still diarrhea, 5 loose yellow stools, red tongue without coating, American ginseng 30g, Nepeta 15g, Honeysuckle 15g, Forsythia 30g, Radix Ginseng 15g, Saponaria 10g, and others. 5 doses, a dose for a day, decoction. 13th,Feb,2020 results: normal body temperature, improved appetite, soft stools for three times , the noninvasive oxygen saturation assisted ventilation was 94% or so, blood routines: WBC $7.44 \times 10^9/L$, RBC $2.75 \times 10^{12}/L$, hemoglobin 83 g/L . The C-reactive protein was still high, 45.6 mg/L, and there was no significant change in the performance of the chest radiograph, suggested no progress. 14th, Feb. 2020 results: Patient with clear consciousness, the spirit was good, appetite improved, soft stool for 1 time, without bloating, no abdominal pain, no shortness of breath after mild activity, oxygen saturation with high flow oxygen was at 95% or so. Blood routines: WBC $6.21 \times 10^9/L$, RBC $2.83 \times 10^{12}/L$, hemoglobin 86g /L. The first viral nucleic acid test was negative. 15th,Feb,2020 results, improved mental emotions, active in treatment, oxygen saturation with high flow oxygen was at 95% or so, tests: WBC $5.76 \times 10^9/L$, hemoglobin 92g/L , C-reactive protein 41.2mg /L. 16th,February, 2020 results, the blood

oxygen saturation was around 95% under non-invasive ventilator-assisted ventilation .
Laboratory tests: white blood cells $4.58 \times 10^9/L$, red blood cells $2.65 \times 10^{12}/L$,
hemoglobin 80g/L , C- reactive protein 31.2mg /L . The second viral nucleic acid test
was negative. After the intervention of Chinese medicine, the conditions were gradually
improved. Chinese medicine treatment were continued as before.