Novel Coronavirus Pneumonia Diagnosis and Treatment Scheme for Severe and Critical Cases

（Trial Version 3, Mar.14, 2020）

Novel coronavirus infections most often affect the respiratory system and cause pneumonia. Multiple organs such as the heart, kidneys, and intestines of severe and critically ill patients can also be affected. Therefore, new coronavirus pneumonia needs comprehensive prevention and treatment for multiple organs.

1. Applicable people

Patients who have been diagnosed as severe and critically ill according to the National Health Commission's "Novel Coronavirus Infected Pneumonia Diagnosis and Treatment Scheme (Trial Version 7)".

1.1 Server case

Conform to any of the followings:

1.1.1 Respiratory distress, respiratory rate (RR) ≥30 beats / min;

1.1.2 In resting state, and fingerless pulse oxygen saturation ≤93% without oxygen;

Arterial blood oxygen partial pressure (PaO2) / oxygen concentration (FiO2) ≤300mmHg;

1.1.3 Meet any of the above, managed as the server case; or, although the above-mentioned severe diagnostic criteria have not been met, the following cases are also managed as severe cases: pulmonary imaging shows that within 24-48 hours the lesions progress significantly > 50%; age > 70 years old, combined with severe chronic diseases including hypertension, diabetes, coronary heart disease, malignant tumors, structural lung disease, pulmonary heart disease, and immunosuppressed populations.

1.2 Critical case

Conform to any of the followings:

1.2.1 Respiratory failure occurs and requires mechanical ventilation;

1.2.2 Shock occurs;

1.2.3 Combining other organ failures requires ICU treatment.

2. Diagnosis and treatment of severe patients

2.1 Clinical warning indicators

In severe cases, assessment of the vital signs, blood oxygen saturation (SpO2), state of consciousness and routine clinical organ function is required. Monitoring content according to the condition include: blood routine, urine routine, biochemical indicators (liver and kidney function, lactic acid, blood glucose, electrolyte, lactate dehydrogenase, etc.), myocardial injury markers, C-reactive protein, procalcitonin, coagulation function, arteries Blood gas analysis, electrocardiogram and chest imaging.

Besides, the following changes of indicators should be vigilant as worthening condition:

2.1.1 Progressive decrease of peripheral blood lymphocyte count;

2.1.2 Peripheral blood inflammatory factors such as IL-6 and C-reactive protein are increasing;

2.1.3 Tissue oxygenation index deteriorates or lactic acid increases progressively;

2.1.4 Chest CT shows obvious progression of lung lesions.

2.2 Treatment

2.2.1 Treatment Principles

Stay in bed, sustain treatment, ensure sufficient warmth; maintain balance of water, electrolyte and acid-base; perform life support measures such as oxygen therapy and mechanical ventilation in time, prevent and treat the complications; treat underlying diseases; prevent secondary infections. In a word, to enable patients to survive the critical illness under the most likely effective state of life support.

2.2.2 Antiviral treatment

Currently there are no specific antiviral drugs. For cases within 10 days of onset, try lopinavir / ritonavir, ribavirin, chloroquine phosphate, arbidol, etc. During the medication, adverse drug reactions and interactions with other drugs should be closely monitored.

2.3 Oxygen therapy and respiratory support

2.3.1 Hypoxic patients, PaO2 / FiO2 at 200-300mmHg

2.3.1.1 A nasal cannula or oxygen mask should be used for oxygen inhalation, assess in time if the respiratory distress and / or hypoxemia has been remitted. The oxygen flow of the nasal cannula is suggested not exceed 5L / min in general; the oxygen flow of the mask oxygen therapy is suggested to be 5-10L / min.

2.3.1.2 Transnasal high-flow oxygen therapy (HFNC): When patient has received nasal cannula or mask for 2 hours, no improvement in respiratory distress and / or hypoxemia, transnasal high-flow oxygen therapy should be used.

When performing HFNC treatment, it is necessary to closely observe the patient's symptoms and signs. If the patient's hypoxemia cannot be improved (SPO2 <93%), or RR ≥35 times / minute, obvious inhalation effort occurs, suggesting that HFNC treatment is not effective, the patient should be promptly switched to use respiratory support treatment. Those with conditions can use inhalation treatment with hydrogen / oxygen mixture (H2 / O2: 66.7% / 33.3%) to improve respiratory distress.

2.3.2 Patients with hypoxemia, PaO2 / FiO2 at 150-200mmHg.

Non-invasive mechanical ventilation (NIV) treatment is preferred. The failure rate of such patients with noninvasive mechanical ventilation is high and should be closely monitored. If the condition does not improve or worsens in a short period of time (1-2 hours), invasive mechanical ventilation should be treated in time.

During the implementation of NIV, the patient's symptoms and signs need to be closely observed. If the patient cannot improve hypoxemia (SPO2 <93%), or RR≥35 beats / min, has excessive tidal volume, or excessive inspiratory negative pressure, etc., it is often suggested that NIV treatment is not effective, and invasive mechanical ventilation should be promptly switched into use.

2.3.3 Patients with hypoxemia, PaO2 / FiO2 is less than 150mmHg

2.3.3.1 Invasive mechanical ventilation

Early and appropriate invasive mechanical ventilation is an important treatment for critically ill patients. A lung protective mechanical ventilation strategy was implemented with an initial tidal volume of 6 ml / kg ideal body weight. If the platform pressure exceeds 30cmH2O or the driving pressure exceeds 15cmH2O, the tidal volume should be further lowered to reduce the risk of ventilator-related lung injury.

When setting the PEEP, both the platform pressure and / or the driving pressure must be considered. When the PEEP is set according to the FiO2-PEEP correspondence table (the low PEEP setting method of ARDSnet), the platform pressure or driving pressure is often too high. PEEP can be set according to the best oxygenation or the best compliance method.

2.3.3.2 Lung recruitment

For moderate to severe ARDS patients, or when the invasive mechanical ventilation FiO2 is higher than 0.5, lung recruitment can be used. Based on the responsiveness of the lung re-expansion, to decide whether to repeat the lung recruitment technique.

2.3.3.3 Prone ventilation

Most patients with moderate to severe ARDS have significantly improved oxygenation when adopt prone ventilation. If PaO2 / FiO2 is consistently below 150mmHg, prone ventilation (more than 12 hours per day) is recommended. Some patients may consider adopting prone ventilation and lung recruitment simultaneously.

2.3.3.4 Invasive mechanical ventilation evacuation

If the patient's oxygenation improves after treatment (PaO2 / FiO2 continues to be greater than 200mmHg), and the patient is conscious with stable circulation, he/she can be considered to start an assessment for the evacuation of invasive mechanical ventilation.

2.3.4 Extracorporeal Membrane Oxygenation (ECMO)

2.3.4.1 Timing of ECMO

When protective ventilation and prone ventilation are not effective, and the following conditions are met, early evaluation and implementation of ECMO should be considered:

Under optimal ventilation conditions (FiO2 ≥ 0.8, tidal volume of 6 ml / kg ideal body weight, PEEP ≥ 10 cmH2O, and no contraindications), and prone ventilation has been implemented, and meet one of the following:

(a) PaO2 / FiO2 <50 mmHg for more than 3 hours;

(b) PaO2 / FiO2 <80 mmHg for more than 6 hours;

(c) FiO2 1.0, PaO2 / FiO2 <100 mmHg;

(d) Arterial blood pH <7.25 and PaCO2> 60 mmHg for more than 6 hours, and RR> 35 times / minute;

(e) Arterial blood pH <7.2 and plateau pressure> 30 cmH2O when RR> 35 times / minute;

(f) Concomitant cardiogenic shock or cardiac arrest.

2.3.4.2 ECMO contraindications

Combined with unrecoverable primary disease; anticoagulation contraindications exist; mechanical ventilation is taken over 7 days under higher mechanical ventilation settings (FiO2> 0.9, plateau pressure> 30 cmH2O); age older than 70 years; immunosuppression; presence of large peripheral vascular anatomy or vascular disease.

2.3.4.3 Choice of ECMO treatment mode

VV-ECMO mode is recommended. When circulatory failure occurs, the cause should be judged for whether there is cardiogenic shock, in order to determine whether the VA-ECMO mode is needed.

2.4 Drainage of Airway secretions

Drainage of airway secretions is an important treatment for patients with pneumonia. Airway humidification should be strengthened in conventional treatment measures, and phlegm-reducing drugs (ambroxol, N-acetylcysteine, etc.) should be added.

2.5 Cycle monitoring and support

2.5.1 When patients have significant increase of myocardial enzymes (especially troponin) and / or BNP, cardiac function needs to be closely monitored.

Severe conditions are prone to acute pulmonary heart disease (ACP), and right cardiac function should be closely monitored.

2.5.2 Follow the principle of tissue perfusion-oriented hemodynamic therapy, closely monitor the patient's circulation status, when appear hemodynamic instability (shock, systolic blood pressure <90mmHg or 40mmHg lower than the basic blood pressure, or need to use vasoconstriction drugs, severe arrhythmia etc.), the cause should be carefully identified, different types of shocks should be properly handled, tissue perfusion should be improved, and severe arrhythmias should be actively managed.

2.5.3 Hemodynamic monitoring technology that is simple and easy to maintain and manage should be selected. Invasive hemodynamic monitoring need bedside implementation with complicated techniques is not recommended. When conditions permit, ultrasound Doppler monitoring is a non-invasive and convenient monitoring method and should be actively adopted.

2.5.4 When hemodynamic instability occurs, firstly assess the volume status, maintain effective tissue perfusion, avoid volume overload; vasoactive drugs such as noradrenaline can be used if necessary.

2.6 Nutrition support treatment

Patients with severe and critical novel coronavirus pneumonia often have inadequate nutrition intake and high catabolic status, leading to rapid consumption of patients, occur anemia and hypoproteinemia. Malnutrition becomes a prominent problem for these patients. Earlier nutritional support may help reversing the status of malnutrition.

2.6.1 Patients with severe novel coronavirus pneumonia should take nutritional risk assessment.

2.6.2 Start enteral nutrition (EN) earlier. Early use of parenteral nutrition (PN) alone, or supplemental PN in combination with EN, is not recommended.

2.6.3 For patients with unstable hemodynamics, nutritional support should be started as soon as possible after the fluid resuscitation is completed and the hemodynamics is basically stable. Delayed initiation of nutritional support is not recommended for non-life-threatening, controllable hypoxemia or compensatory / permissive hypercapnia, even during prone position ventilation or ECMO.

2.6.4 It is recommended to indwell the nasogastric tube for gastric nutrition in severe patients. For patients who are not suitable for gastric nutrition, use the pyloric feeding route, such as nasointestinal tube.

2.6.5 For severe patients, the target feeding amount is 25-30 kcal // kg / d, and feeding shall be started at a low dose. For feeding intolerance conditions, nourishing feeding shall be considered (Infusion rate 10-20kcal / h or 10-30ml / h).

2.6.6 Strengthen the protein supply, the target required amount of protein is 1.5-2.0g / kg / d.

2.6.7 Severe patients can use enteral nutrition rich in omega-3 fatty acids. Lipid emulsion rich in EPA and DHA components can be added into parenteral nutrition.

2.6.8 Take appropriate measures for patients with EN to prevent vomiting and reflux.

2.6.9 If feeding-related diarrhea occurs, it is recommended to change the nutrient solution infusion method or formula composition.

2.7 Glucocorticoid

There is no evidence-based medical evidence to support the use of glucocorticoids to improve the prognosis of critically ill patients. Routine use of glucocorticoids is not recommended. For patients with progressive deterioration of oxygenation indicators, rapid imaging progress, and over activated body inflammatory response, short-term treatment with Methylprednisolone at 40mg q 12h, for 5 days can be considered. Patients should be tested for contraindications of hormone before use.

2.8 Antimicrobial treatment

Routine use of antimicrobials is not recommended without clear evidence of bacterial infection. It should be noted that severe patients often have a disease course of more than 5-7 days, and there are many manifestations of cellular immunosuppression. Particularly, for patients who require invasive mechanical ventilation in the ICU, secondary bacterial or fungal infections should be aware of.

If conditions permit, respiratory pathogens should be actively monitored for targeted anti-infective treatment. Patients with antimicrobial use history within 90 days, or hospital stay of more than 72 hours, or previous structural lung disease, antibiotic selection should be considered as drugs that can cover resistant bacteria.

2.9 Anticoagulant therapy

Obvious endothelial cell damage, microthrombosis and focal necrosis in lung tissue and other organs suggest that anticoagulation therapy may be beneficial. For patients with both DIC and hypercoagulability, a therapeutic dose of unfractionated or low molecular weight heparin shall be given. Patients' coagulation function indexes and bleeding should be monitored during the treatment.

2.10 Prevention and treatment of VTE

Due to prolonged bed rest and frequent coagulation abnormalities, the risk of VTE in severe and critically ill patients needs to be assessed. For patients at high risk of VTE, DVT ultrasound screening can be performed conditionally. Early postoperative mobilization is encouraged to prevent DVT. For patients without anticoagulation contraindications such as severe active bleeding or bleeding in important areas, it is recommended to use common heparin or low molecular weight heparin for preventive treatment. For patients with anticoagulation contraindications, limb compression therapy should be applied.

2.11 Analgesia

Patients with heavy mechanical ventilation should be given appropriate analgesia and sedation. For patients with tachypnoea, excessive tidal volume, or obvious man-machine confrontation, short-term use of muscle relaxants should be considered. Set analgesia and sedation goals according to the patient's condition and treatment. Humanistic care must be valued for severe patients.

2.12 Acute kidney injury (AKI) and Renal replacement therapy (RRT)

AKI appears in some severe patients, and the patient's capacity status and renal function should be fully evaluated. In general, in the second stage of the KDIGO standard, which is 2-2.9 times the baseline value of creatinine increase, urine output lasting more than 12 hours and less than 0.5 ml / kg / h, renal replacement therapy should be used.

2.13 Other medications

2.13.1 IVIG. At present, the efficacy of IVIG for coronavirus has is not fully supported by medical evidence. It can be used for severe conditions.

2.13.2 Convalescent plasma. The use of human convalescent plasma

containing a novel coronavirus antibody in patients with early symptoms may be an option for specific treatment. If used, the protective antibody titer in the plasma should be measured. Plasma should be infused slowly, and transfusion reactions and respiratory function changes should be closely observed.

2.13.3 Thymosin α1. Consider the use of thymosin α1 in patients with severely reduced lymphocyte counts.

2.13.4 Intestinal microecological regulator. Intestinal microecological regulator can be used to maintain intestinal micro-ecological balance.

2.13.5 XUEBIJING Injections. TCM XUEBIJING injections can be used.

2.14 TCM treatments

Different regions can refer to the following plans for dialectical treatment according to the disease, local climate characteristics, and different physical conditions. When overdose is involved, it should be used under the guidance of a physician.

2.14.1 Qingfei Paidu Soup (Soup for lung catharsis and body detox)

Can be used in severe conditions, according to patients' physical status.

Substantial formula：Ma Huang (Herba Ephedrae) 9g，Zhigancao（baked Radix et Rhizoma Glycyrrhizae)）6g， almond 9g， gypsum 15-30g（decocted first），Gui Zhi (Ramulus Cinnamomi) 9g, Ze Xie(alisma rhizome)9g, Zhu Ling (Polyporus)9g, Bai Shu(atractylodes macrocephala) 9g, Poria 15g,Chai Hu (Radix Bupleuri) 16g, Huang Qin(Radix Scutellariae) 6g, Jiang Ban Xia 9g, ginger 9g, Zi Wan(aster root) 9g, Dong Hua 5g, She Gan (Rhizoma Belamcandae)9g, Xi Xin(Herba Asari) 6g, Shan Yao(Yam) 12g， Zhi Shi(immature bitter orange) 6g, Chen Pi (Pericarpium Citri Reticulatae) 6g, Huo Xiang(agastache) 9g.

How to take：TCM herbs，drink after decocted. One dose per day (drink by twice, in the morning & evening, 40min after meal). 3 doses for one treatment.

Patients can have half to one bowl of rice soup after taking the TCM soup. (Patients without fever should control the use of gypsum. Patients with higher temperature, more gypsum should be used). If the symptoms improve but do not heal, then take the second course of treatment. If the

patient has special conditions or other underlying diseases, the prescription can be modified according to the actual situation, and the symptoms should be discontinued.

2.14.2 Lung Closure by Coronavirus

Clinical manifestation: fever blush, cough, yellow & stick & small amount of sputum or Blood in sputum; panting, tiredness, dry mouth, nausea, constipation, short urine. Red tongue, yellow tongue coating, slippery pulse.

Prescription recommended: Huashi Paidu therapy

Substantial formula: Sheng Ma Huang(Herba Ephedrae) 6g, almond 9g, gypsum 15g（decocted first）, Gan Cao(liquorice) 3g, Huo Xiang(agastache) 10g(lastly be added), Hou Pu (magnolia bark)10g, Cang Shu(atractylodes rhizome) 15g, Cao Guo(tsaoko) 10g, Fa Ban Xia(prepared pinellia) 9g, Fu Ling(Poria) 15g, Sheng Da Huang (raw rhubarb root)5g (lastly be added), Sheng Huang Qi (raw milkvetch root), Ting Li Zi(lepidium seed) 10g, Chi Shao(unoeeled root of herbaceous peony) 10g.

How to Take: one-two doses per day, decocted in hot water. 100-200ml per each time, 2-4 times a day. Orally or nasally.

2.14.3 Qiying Liangfan Symptom

Clinical manifestation: high fever, thirsty, short of breath, delirious, blurred vision， macula, convulsion of the limbs. Dark tongue and small amount of tongue coating, heavy pulse.

Prescription recommended: Qingyun Paidudu Drink

Substantial formula: gypsum 30-60g （ decocted first ） , Zhi Mu(anemarrhena) 30g, Sheng Di(dried rehmannia root) 30-60g, cornu bubali 30g, Chi Shao(unoeeled root of herbaceous peony) 30g, Xuan Shen(figwirt root) 30g, Lianqiao (Fructus forsythia)15g, Dan Pi(moutan bark) 15g, Huang Lian (Rhizoma Coptidis) 6g, Zhu Ye (Herba Lophatheri) 12g, Ting Li Zi(lepidium seed) 15g, Gan Cao(Radix glycyrrhizae) 6g.

How to Take: One dose per day, decocted in hot water. 100-200ml per each time, 2-4 times a day. Orally or nasally.

2.14.4 Neibi Waituo Symptom

Clinical manifestation: short of breath, delirious, dysphoria, perspiration, thick tongue coating, impractical pulse.

Prescription recommended: Shen Fu Soup

Substantial formula: ginseng 15g, Hei Shun Pian 10g (decocted first), Shan Zhu Yu(fruit of asiatic cornelian cherry) 15g. Su He Xiang Wan(storax pill) and An Gong Niu Huang Wan(Cow-bezoar Bolus for Resurrection) be taken together.

How to Take: One to two doses per day, decocted in hot water. 100-200ml per each time, 2-4 times a day. Orally or nasally.

2.14.5 TCM injections

Medicines recommended: XUEBIJING, XIYANPING, REDUNING, TANREQING, XINGNAOJING, SHENFUZHU, SHENGMAI, SHENMAI. Drugs with similar efficacy can be selected according to individual conditions, or can be used in combination according to clinical symptoms. Traditional Chinese medicine injection can be used in combination with traditional Chinese medicine decoction.

Recommended usage：The use of traditional Chinese medicine injections should be in accordance with the drug instructions, as follows:

2.14.5.1 basic medication: 0.9% Sodium chloride injection 250ml + XUEBIJING 100ml bid, 5% Glucose injection 250ml + SHENMAI injection 100ml or SHENGMAI Injection 20-60ml bid.

2.14.5.2 fever: 0.9% Sodium chloride injection 250ml + XIYANPING Injection 100mg bid. Or 0.9% Sodium chloride injection 250ml + REDUNING Injection 20ml. Or 0.9% Sodium chloride injection 250ml + TANREAING Injection 40ml bid.

2.14.5.3 Unconsciousness: 0.9% Sodium chloride injection 250ml + XINGNAOJING Injection 20ml bid.

2.14.5.4 Shock: 5% Glucose injection 250ml + SHENFU Injection 40-100ml bid.

2.14.6 Other conditions

2.14.6.1 Unstable blood oxygen saturation: Ginseng，decocted by hot water 200ml, drink frequently.

2.14.6.2 Bloating constipation or out of sync: Sheng Da Huang(raw

rhubarb root) 5-10 g, decocted by hot water 200ml, drink frequently, or add Mang Xiao(Glauber salt) 15g in aviation therapy, twice per day.

2.14.6.3 Long-lasting high fever: Angong Niuhuang Wan(Cow-bezoar Bolus for Resurrection), 1 dose each time, twice a day. Or Zi Xue San(anti-pestilence and fever powde) 3g, twice a day. Nasally.

3. Criteria for transfer out of ICU

When severe patients are stable, oxygenation is improved, and life support is not needed, they should be transferred out of the intensive care unit as soon as possible. Criteria is (should be all met)

3.1 Conscious. Analgesic sedatives and / or muscle relaxants have been discontinued as instructed.

3.2 Have withdrawn from mechanical ventilation. When inhaling air or low-flow oxygen (nasal catheter or ordinary mask), RR <30 times / min, and SpO2> 93%.

3.3 The cycle is stable. No need for boosters and fluid resuscitation.

3.4 No other acute progressive organ dysfunction. No supportive treatment measures are needed, such as blood purification.

Provided By:

COVID-19 Medical Treat & Cure Team

Central Directive Group of China