DIRECT TRANSLATION OF SHANHGAI MANAGEMENT GUIDELINE FOR COVID-19

Consensus and guidelines · New coronavirus infections •

Expert consensus on comprehensive treatment of coronavirus disease in Shanghai 2019

Shanghai Coronavirus Disease Clinical Treatment Expert Group

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Summary

With the deepening of the understanding of coronavirus disease 2019 (COVID-19), the Shanghai New Coronavirus Disease Clinical Treatment Expert Group followed the National New Coronarvirus Pneumonia Diagnosis and Treatment Program, and fully absorbed the foundation of domestic and foreign counterparts' experience in treatment In the past, the treatment plan was continuously optimized and refined, and expert consensus was formed from the three aspects of etiology and epidemiological characteristics, clinical characteristics and diagnosis, and treatment plan.

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Corona virus disease 2019 (COVID-19) was first reported in Wuhan, Hubei Province on December 31, 2019 [1,2]. COVID-19, as a respiratory infectious disease, has been included in the Class B infectious diseases stipulated in the Law of the People's Republic of China on the Prevention and Control of Infectious Diseases and managed as a Class A infectious disease.

With the deepening of understanding of the disease, COVID-19 has accumulated a certain amount of experience in the prevention and control of COVID-19. The Shanghai New Coronavirus Disease Clinical Treatment Expert Team follows the National New Coronavirus Pneumonia Diagnosis and Treatment Program [3], and fully absorbs domestic and foreign counterparts' experience in treatment, in order to improve the success rate of clinical treatment and reduce the patient's mortality rate, prevent the progress of the disease, and gradually It reduces the proportion of patients with severe illness and improves their clinical prognosis. Based on the continuous optimization and refinement of the treatment plan, expert consensus has been formed on the relevant clinical diagnosis and treatment.

I. Etiology and epidemiological characteristics

2019 novel coronavirus (2019-nCoV) is a new coronavirus belonging to the genus β. On February 11, 2020, the International Committee on Taxonomy of Viruses (ICTV) named the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [4]. Patients with COVID-19 and asymptomatic

infection can transmit 2019-nCoV. Respiratory droplet transmission is the main route of transmission and can also be transmitted through contact. There is also the risk of aerosol transmission in confined enclosed spaces. COVID-19 patients can detect 2019-nCoV in stool, urine, and blood; some patients can still test positive for fecal pathogenic nucleic acid after the pathogenic nucleic acid test of respiratory specimens is negative. The crowd is generally susceptible. Children, infants, and young children also develop disease, but the condition is relatively mild.

Clinical characteristics and diagnosis

(A) clinical characteristics

The incubation period is 1 to 14 d, mostly 3 to 7 d, with an average of 6.4 d. Main symptoms are fever, fatigue, and dry cough. May be accompanied by runny nose, sore throat, chest tightness, vomiting and diarrhea. Some patients have mild symptoms, and a few patients have no symptoms or pneumonia.

The elderly and those suffering from basic diseases such as diabetes, hypertension, coronary atherosclerotic heart disease, and extreme obesity tend to develop severe illness after infection. Some patients develop symptoms such as dyspnea within one week after the onset of the disease. In severe cases, they can progress to acute respiratory distress syndrome (ARDS) and multiple organ damage. The time to progression to severe illness was approximately 8.5 days. It is worth noting that in the course of severe and critically ill patients, there may be moderate to low fever, even without obvious fever. Most patients have a good prognosis, and deaths are more common in the elderly and those with chronic underlying disease.

The early CT examination showed multiple small patches or ground glass shadows, and the internal texture of the CT scans was thickened in the form of grid cables, which was obvious in the outer lung zone. A few days later, the lesions increased and the scope expanded, showing extensive lungs, multiple ground glass shadows, or infiltrating lesions, some of which showed consolidation of the lungs, often with bronchial inflation signs, and pleural effusions were rare. A small number of patients progressed rapidly, with imaging changes reaching a peak on days 7 to 10 of the course. Typical "white lung" performance is rare. After entering the recovery period, the lesions are reduced, the scope is narrowed, the exudative lesions are absorbed, part of the fiber cable shadow appears, and some patients' lesions can be completely absorbed.

In the early stage of the disease, the total number of white blood cells in the peripheral blood was normal or decreased, and the lymphocyte count was reduced. Some patients may have abnormal liver function, and the levels of lactate dehydrogenase, muscle enzyme, and myoglobin increased; Most patients had elevated CRP and ESR levels and normal procalcitonin levels. In severe cases, D-dimer levels are elevated, other coagulation indicators are abnormal, lactic acid levels are elevated, peripheral blood lymphocytes and CD4 + T lymphocytes are progressively reduced, and electrolyte disorders and acid-base imbalances are caused by metabolic alkalosis See more. Elevated levels of inflammatory cytokines (such as IL-6, IL-8, etc.) can occur during the disease progression stage [5].

B) Diagnostic criteria

1. Suspected cases:

Combined with the following epidemiological history and clinical manifestations. Suspected cases were diagnosed as having any one of epidemiological history and meeting any two of the clinical manifestations, or having no clear epidemiological history but meeting three of the clinical manifestations. ① Epidemiological history: Travel history or residence history of Wuhan and surrounding areas or other communities with case reports within 14 days before the onset; history of contact with 2019-nCoV infection (positive nucleic acid test) within 14 days before the onset ; Patients with fever or respiratory symptoms from Wuhan and surrounding areas or from communities with case reports within 14 days before the onset of the disease; cluster onset. ② Clinical manifestations: fever and / or respiratory symptoms; with the above-mentioned imaging features of the new coronavirus pneumonia; the total number of white blood cells was normal or decreased in the early stage of onset, and the lymphocyte count decreased.

2. Confirmed cases:

A confirmed case is diagnosed with one of the following pathogenic evidence. ① Real-time fluorescent reverse transcription PCR detected 2019-nCoV nucleic acid positive. ② Viral gene sequencing revealed high homology with the known 2019-nCoV. ③ Except for nasopharyngeal swabs, it is recommended to take as much sputum as possible. Patients undergoing tracheal intubation can collect lower respiratory tract secretions for viral nucleic acid testing.

3. Differential diagnosis

It is mainly distinguished from other known viral pneumonias such as influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, severe acute respiratory syndrome (SARS) coronavirus, etc. , Different from Mycoplasma pneumoniae, Chlamydia pneumonia and bacterial pneumonia. In addition, it should be distinguished from non-infectious diseases, such as pulmonary interstitial lesions and organizing pneumonia caused by connective tissue diseases such as vasculitis and dermatomyositis [6,7].

4. Clinical typing

1. Lightweight:

The clinical symptoms were mild, and no pneumonia manifested on imaging examination.

2. Normal type:

With fever, respiratory tract and other symptoms, imaging examination showed pneumonia.

3. Heavy:

Meet any of the following. ① Shortness of breath, respiratory rate ≥ 30 times / min; ② In resting state, arterial oxygen saturation (SaO_2) ≤ 93%; ③ arterial partial pressure of oxygen, PaO_2) / fraction of inspired oxygen (FiO_2) ≤300 mmHg (1 mmHg = 0.133 kPa). At high altitudes (above 1 000 m), PaO_2 / FiO_2 should be corrected according to the following formula: PaO_2 / FiO_2 × [Atmospheric Pressure (mmHg) / 760].

Pulmonary imaging examination showed that the lesions progressed significantly within 24 to 48 hours, and those with more than 50% of the lesions were managed as severe.

4. Dangerous:

Those who meet any of the following can be judged as critical. ①Respiratory failure occurs and requires mechanical ventilation; ②Shock occurs; ③Combination with other organ failure requires ICU monitoring and treatment.

Early warning of severe cases of common patients should be strengthened. Based on current clinical studies, elderly (age> 65 years) with underlying diseases, CD4 + T lymphocyte count <250 / μL, blood IL-6 levels have significantly increased, and lesions were found on lung imaging on 2 to 3 days Significant progress> 50%, lactic dehydrogenase (LDH)> 2 times the upper limit of normal value, blood lactic acid ≥ 3 mmol / L, metabolic alkalosis, etc. are all early warning indicators of severe disease [8].

(5) Clinical monitoring

The patient's clinical manifestations, vital signs, fluid volume, gastrointestinal function and mental state are monitored daily.

All patients were dynamically monitored for terminal blood oxygen saturation. For critically ill and critically ill patients, timely blood gas analysis is performed according to the changes in the condition; blood routine, electrolytes, CRP, procalcitonin, LDH, blood coagulation function indicators, blood lactic acid, etc. are tested at least once every 2 days; liver function, kidney function , ESR, IL-6, IL-8, lymphocyte subsets, at least once every 3 days; chest imaging examination, usually every 2 days. For patients with ARDS, routine ultrasound examination of the heart and lungs at the bedside is recommended to observe extravascular lung water and cardiac parameters. For monitoring of extracorporeal membrane oxygenation (ECMO) patients, refer to the implementation section of ECMO.

Treatment plan

(A) Antiviral treatment

Try hydroxychloroquine sulfate or chloroquine phosphate, or abidol for oral administration, interferon atomization and inhalation, interferon κ is preferred. It is not recommended to use 3 or more antivirals at the same time. The viral nucleic acid should be stopped in time after it becomes negative. The efficacy of all antiviral drugs remains to be evaluated in further clinical studies.

For patients with severe and critical viral nucleic acid positives, recovery patients can be tested for recovery plasma. For detailed operation and management of adverse reactions, please refer to the "Clinical Treatment Program for Recovery of New Coronavirus Pneumonia Patients in Recovery Period" (trial version) [3]. Infusion within 14 days of the onset may be more effective. If the viral nucleic acid is continuously detected at the later stage of the disease, the recovery period of plasma treatment can also be tried.

B) Treatment of light and ordinary patients

Supportive treatment needs to be strengthened to ensure sufficient heat; pay attention to water and electrolyte balance to maintain internal environment stability; closely monitor patient vital signs and finger oxygen saturation. Give effective oxygen therapy in time. Antibacterials and glucocorticoids are not used in principle. The patient's condition needs to be closely monitored. If the disease progresses significantly and there is a risk of turning into severe, it is recommended to take comprehensive measures to prevent the disease from progressing to severe. Low-dose short-course glucocorticoids can be used with caution (see the application section of glucocorticoids for specific protocols)). Heparin anticoagulation and **high-dose vitamin C treatment are recommended [9,10].** Low-molecular-weight heparin 1 to 2 per day, continued until the patient's D-dimer level returned to normal. Once fibrinogen degradation product (FDP) ≥10 μg / mL and / or D-dimer ≥5 μg / mL, switch to unfractionated heparin. Vitamin C is administered at a dose of 50 to 100 mg / kg per day, and the continuous use time is aimed at a significant improvement in the oxygenation index. If lung lesions progress, it is recommended to apply large doses of broad-spectrum protease inhibitors from 600 to 1 million units / day until the pulmonary imaging examination improves. Once a "cytokine storm" occurs, intermittent short veno-venuous hemofiltration (ISVVH) is recommended [11].

???? ROLE OF PLASMA EXCHANGE FOR CYTOKINE STORM OR HLH PICTURE.

(III) Organ function supportive treatment for severe and critically ill patients

1. Protection and maintenance of cyclic functions:

Implement the principle of early active controlled fluid replacement. It is recommended to evaluate the effective volume and initiate fluid therapy as soon as possible after admission. Severe patients can choose intravenous or transcolonic fluid resuscitation depending on the conditions. The preferred supplement is lactated Ringer's solution. Regarding vasoactive drugs, noradrenaline and dopamine are recommended to maintain vascular tone and increase cardiac output. For patients with shock, norepinephrine is the first choice. It is recommended to start low-dose vasoactive drugs at the same time as fluid resuscitation to maintain circulation stability and avoid excessive fluid infusion. Cardioprotective drugs are recommended for severe and critically ill patients, and sedative drugs that inhibit the heart are avoided as much as possible. For patients with sinus bradycardia, isoprenaline can be used. For patients with sinus rhythm, heart rate <50 beats / min and hemodynamic instability, intravenous pumping of small doses of isoproterenol or dopamine is recommended to maintain heart rate at about 80 beats / min.

2. Reduce pulmonary interstitial inflammation:

2019-nCoV causes severe pulmonary interstitial lesions that can cause pulmonary function deterioration, and high-dose broad-spectrum protease inhibitors are recommended.

3. Protection of kidney function:

It is recommended to use reasonable anticoagulant therapy and proper fluid therapy as soon as possible. See the "Cytokine Storm" chapter for prevention and protection of circulatory function.

4. Protection of intestinal function:

Prebiotics can be used to improve the patient's intestinal microecology. Use raw rhubarb (made with 15-20 g plus 150 ml warm water) or Dachengqi decoction orally or enema (would not do this).

5. Nutritional support:

Enteral nutrition is preferred, either via nasal feeding or via jejunal route. The whole protein nutrient preparation is preferred, and the energy is 25-35 kcal / kg (1 kcal = 4.184 kJ) per day.

6. Prevention and treatment of "cytokine storm":

Large doses of vitamin C and unfractionated heparin are recommended. **Large doses of vitamin C are administered intravenously at a dose of 100 to 200 mg / kg daily**. Continuous use time is aimed at a significant improvement in the oxygenation index. It is recommended to use a large-dose broad-spectrum protease inhibitor, given 1.6 million units, once every 8 h. Under mechanical ventilation, when the oxygenation index> 300 mmHg can be reduced to 1 million units / d. Anticoagulation therapy can be used to protect endothelial cells and reduce cytokine release. Anticoagulation with unfractionated heparin (3-15 IU / kg per hour) when FDP ≥10 μg / mL and / or D-dimer ≥5 μg / mL . The patient's coagulation function and platelets must be re-examined 4 h after the first use of heparin. With ISVVH, 6 to 10 hours per day.

7. Sedation and Artificial Hibernation:

Patients undergoing mechanical ventilation or receiving ECMO need to be sedated on the basis of analgesia. For patients with severe man-machine confrontation during the establishment of an artificial airway, short-term application of low-dose muscle relaxants is recommended. Hibernation therapy is recommended for severe patients with oxygenation index <200 mmHg. Artificial hibernation therapy can reduce the body's metabolism and oxygen consumption, and at the same time dilate the pulmonary blood vessels to significantly improve oxygenation. It is recommended to use continuous intravenous bolus medication, and the patient's blood pressure should be closely monitored. Use opioids and dexmedetomidine with caution. Severe patients often have abnormal levels of IL-6 and are prone to cause abdominal distension, and opioids should be avoided; 2019-nCoV can still inhibit sinus node function and cause sinus bradycardia, so it should be used with caution to inhibit the heart Effect of sedative drugs. In order to prevent the occurrence and exacerbation of lung infections, and to avoid prolonged excessive sedation, try to withdraw muscle relaxants as soon as possible. It is recommended to monitor the depth of sedation closely.

8. Oxygen therapy and respiratory support:

① Oxygen therapy with nasal cannula or mask, SaO2 ≤93% under resting air, or SaO2 <90% after exercise, or oxygenation index (PaO2 / FiO2) 200-300 mmHg; with or without respiratory distress; both Continuous oxygen therapy is recommended. ② Transnasal high-flow nasal cannula oxygen therapy (HFNC), receiving nasal cannula or mask oxygen therapy for 1 to 2 hours, oxygenation fails to meet treatment requirements, and respiratory distress does not improve; or hypoxemia during treatment And

/ or exacerbation of respiratory distress; or an oxygenation index of 150 to 200 mmHg; HFNC is recommended. ③ Noninvasive positive pressure ventilation (NPPV), receiving 1 to 2 h of HFNC oxygenation does not achieve the treatment effect, and there is no improvement in respiratory distress; or hypoxemia and / or exacerbation of respiratory distress during treatment; or When the oxygenation index is 150 ～ 200 mmHg; NPPV can be selected. ④ Invasive mechanical ventilation, HFNC or NPPV treatment for 1 to 2 hours oxygenation can not meet the treatment requirements, no improvement in respiratory distress; or hypoxemia and / or exacerbation of respiratory distress during treatment; or oxygenation index <150 mmHg; invasive ventilation should be considered. Protective ventilation strategies with a small tidal volume (4-8 mL / kg ideal body mass) as the core are preferred.

9. ECMO implementation:

Those who meet one of the following conditions may consider implementing ECMO. ① PaO2 / FiO2 <50 mmHg for more than 1 h; ② PaO2 / FiO2 <80 mmHg for more than 2 h; ③ Arterial blood pH <7.25 with PaCO2> 60 mmHg for more than 6 h. ECMO mode is preferred for intravenous-venous ECMO.

4. Special problems and treatment in treatment

1. Application of glucocorticoids:

Use glucocorticoids with caution. Imaging showed significant progress in pneumonia. Patients with SaO2 ≤ 93% or shortness of breath (respiratory frequency ≥ 30 breaths / min) or oxygenation index ≤ 300 mmHg in the state of no oxygen inhalation. Glucocorticoids can be added at the risk of intubation. Patients are advised to withdraw promptly from glucocorticoid use when intubation or ECMO support can maintain effective blood oxygen concentrations. For non-severe patients using methylprednisolone, the recommended dose is controlled at 20 to 40 mg / d, severe patients are controlled at 40 to 80 mg / d, and the course of treatment is generally 3 to 6 days. Can be increased or decreased according to the body weight [12].

2. Use of immunomodulatory drugs:

Injecting thymosin subcutaneously twice a week has certain effects on improving patients' immune function, preventing the disease from becoming worse, and shortening the time of detoxification. Due to the lack of specific antibodies, high-dose intravenous immunoglobulin therapy is currently not supported. However, some patients have low levels of lymphocytes and the risk of co-infection with other viruses. Human immunoglobulin can be infused intravenously at 10 g / d for 3 to 5 days.

3. Accurate diagnosis and treatment of bacterial and fungal infections:

Clinical microbiological monitoring of all critically and critically ill patients. The sputum and urine of the patients are kept daily for culture, and the patients with high fever should be cultured in time. All patients with suspected sepsis who have indwelling vascular catheters should be sent for peripheral venous blood culture and catheter blood culture at the same time. All patients with suspected sepsis

may consider collecting peripheral blood for molecular diagnostic tests for etiology, including PCR-based molecular biology testing and next-generation sequencing.

Elevated procalcitonin levels have implications for the diagnosis of sepsis / septic shock. When patients with new type of coronavirus pneumonia get worse, there is an increase in the level of CRP, which is not specific for the diagnosis of sepsis caused by bacterial and fungal infections.

Critically ill patients with open airways are often prone to bacterial and fungal infections at a later stage. If sepsis occurs, empirical anti-infective treatment should be given as soon as possible. For patients with septic shock, empirical antibacterial drugs can be used in combination before obtaining an etiological diagnosis, while covering the most common Enterobacteriaceae, Staphylococcus and Enterococcus infections. Patients with infection after hospitalization can choose β-lactamase inhibitor complex. If the treatment effect is not good, or the patient has severe septic shock, it can be replaced with carbapenem drugs. If considering enterococci and staphylococcal infections, glycopeptide drugs (vancomycin) can be added for empirical treatment. Daptomycin can be used for bloodstream infections, and linezolid can be used for lung infections. Attention should be paid to catheter-related infections in critically ill patients, and treatment should be empirically covered with methicillin-resistant staphylococci. Glycopeptide drugs (vancomycin) can be used for empirical treatment. Candida infection is also more common in critically ill patients. Candida should be covered empirically when necessary. Echinocin drugs can be added. With the length of hospitalization of critically ill patients, drug-resistant infections have gradually increased. At this time, the use of antibacterial drugs must be adjusted according to drug sensitivity tests.

4. Nosocomial infection prevention and control:

① According to the Basic System for Infection Prevention and Control of Medical Institutions (Trial) [13] of the National Health and Health Commission in 2019, actively implement evidence-based infection prevention and control clustering intervention strategies to effectively prevent ventilator-associated pneumonia and intravascular catheter-related blood flow Infections, urinary tract-associated urinary tract infections, multi-resistant bacteria and fungal infections such as carbapenem-resistant gram-negative bacilli. ② Strictly follow the National Health and Health Commission's "Technical Guidelines for the Prevention and Control of New Coronavirus Infection in Medical Institutions (First Edition)", "Guidelines for the Use of Common Medical Protective Products in the Prevention and Control of Pneumonia of New Coronavirus Infection (Trial)" and "New Coronary Pneumonia" During the epidemic, the requirements of Technical Guidelines for Protecting Medical Staff (Trial) [14,15,16], strengthened process management, and correctly selected and used personal protective equipment such as masks, gowns, protective clothing, eye masks, protective masks, gloves, etc. The implementation of this disinfection and quarantine measure minimized the risk of nosocomial infections and eliminated 2019-nCoV infections in hospitals by medical staff.

5. Treatment of infants and young children:

Mild children need only symptomatic oral administration. In addition to symptomatic oral administration for children with common type, treatment with syndrome differentiation can be considered. If combined with bacterial infection, antibacterial drugs can be added. Severely ill children

are mainly symptomatic and supportive treatment. Ribavirin injection is given antiviral therapy empirically at 15 mg / kg (2 times / day).

6) Discharge standards

At the same time, those who meet the following conditions can be considered for discharge: ①The body temperature returns to normal> 3 d; ②Respiratory symptoms have improved significantly; ③Imaging examination of the lungs shows a significant improvement of acute exudative lesions; ④Two consecutive negative airway nucleic acid tests (sampling time At least 1 d); ⑤ After the nucleic acid test of the respiratory specimen is negative, the fecal pathogenic nucleic acid test is also negative; ⑥ The total disease course exceeds 2 weeks.

7) Health management of discharged patients

1. For discharged patients, close follow-up is still required. Follow-up is recommended from 2 weeks and 4 weeks after discharge to the designated follow-up clinic.

2. When a patient is discharged from the hospital, his place of residence and address in the city should be specified.

3. Patients should rest at home for 2 weeks after leaving the hospital, avoid activities in public places, and must wear masks when going out.

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