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A SYSTEMIC REVIEW- UPDATE ON TREATMENT OF COVID-19

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Abstract

With over 4,441,874 cases and 298,296 deaths globally, COVID-19 is one of the worst infectious disease outbreaks in history. The objective of this paper is to review the available evidence regarding the prevention and management of COVID-19.The management of COVID-19 includes rapid sequencing of the virus for preparation of the testing kits, quarantine measures and in absence of a vaccine, use of supportive therapies such as antivirals, high flow oxygen, mechanical ventilation, corticosteroids, hydroxychloroquine, interferons, intravenous immunoglobulin and convalescent plasma infusions. These measures appeared to provide only moderate success. While some measures and their effectiveness is still under clinical trials, only the enforcement of drastic quarantine measures can stop the SARS-CoV-2 from spreading. The earlier the implementation, the less likely resources will be depleted. The most critical factors in stopping a pandemic are early recognition of infected individuals, carriers and contacts, and early implementation of quarantine measures with an organized, proactive and unified strategy at a national level. Delays result in significantly higher death tolls.

Keywords: COVID-19, SARS-CoV-2, anti -viral, corticosteroids, intravenous immunoglobulin, hydroxychloroquine, mechanical ventilation, cardiac complications

Introduction

Since mid-December 2019, there has been a worldwide outbreak of Coronavirus disease (COVID)-19, caused by SARS-CoV-2first detected in Wuhan, China. The incubation period is 1 to 14 days in most cases, but can be as long as 24 days. The Chinese chrysanthemum bat is thought to be the origin of SARS-CoV-2 based on the sequence homology, the pangolin has been proposed as an intermediate host. Human-to-human transmission of SARS-CoV-2 occurs mainly via respiratory droplets, direct contact, asymptomatic transmission, and interfamilial transmission.

SARS-CoV-2 can affect any demographic, including senior citizens, children and pregnant women. As of May 14, 2020, there have been over 4,441,874 cases of COVID-19 worldwide, with 2,475,513 active cases (45,932 active severe cases) 298,296 deaths (mortality rate: 15%), and 1,668,065 recovered cases (recovered

rate: 85%).

On March 2, the European Centres for Disease Control and Prevention (CDC) raised the SARS-CoV-2 risk level from moderate to high. On March 11, 2020, WHO declared COVID-19 a pandemic and recommended aggressive action by all countries in the world, warning that most countries were not prepared to handle the spread of SARS-CoV-2. As of April 12, 2020, SARS-CoV-2 has infected 1,770,469 people outside of China, causing 110,867 deaths (mortality rate: 6.27%). It has been found in 6 continents including 212 of 233 (91.0%) countries and international conveyances. The United States (560,402 cases), Spain (166,831 cases), Italy (156,363 cases), Germany (127,854 cases), and Iran (71,686 cases) are among the hardest hit, but cases in other countries are increasing rapidly.

To stop transmission of the virus and save lives, most of the countries adopted strategies and tactics including a nationwide free testing (nucleic acid assay, gene sequencing and IgM-IgG serology), free treatment, travel restrictions, etc.

Managing the spread of the epidemic

The most important strategy to combat a pandemic is to prevent it from even happening. This means that the spread of a virus needs to be countered as early as possible.

1. Quarantine strategies

Quarantine and surveillance are still the most effective means of controlling the spread of infectious diseases. Some of the strategies and tactics are described below:

a) Limit migration

b) Designated hospitals

c)Community isolation

d)Maintaining adequate supply of essential items

e)Testing

f) Tracking

g)Temperature screening

h) Personal protection

i) Control cross-infection

2.Managing human and equipment resources

Treatment of COVID-19

1. General Treatment

Symptomatic and supportive treatment is essential and main treatment for COVID-19. General supportive measures for SARS-CoV-2 infected patients include bed rest, adequate nutrition, water and electrolyte balance and intensively monitoring vital signs (blood pressure, respiratory rate, heart rate and oxygen saturation). Laboratory markers of disease progression and clinical outcomes, such as C-reactive protein (CRP), neutrophil count, lymphocyte count and inflammatory cytokines were monitored.

2. Symptomatic Therapy

Fever is the most common symptom of SARS-CoV-2 infection. Continuous high fever may cause metabolic

disorders and system dysfunction. Therefore, WHO guidance advocates the use of antipyretics and cooling measures. Multiple studies have shown that COVID-19 patients having underlying diseases, including hypertension and diabetes, leading to higher mortality. For these patients, blood pressure and blood sugar must be monitored and if abnormal, should be promptly treated. The onset of severe disease leading to liver, kidney, or cardiac injury should be anticipated and treated appropriately.

i)Respiratory Support

a)Supplemental oxygen –In a study of 1099 patients in China, 41.3% of COVID-19 confirmed patients and 35.7% of non-severe patients received oxygen therapy. WHO guidelines recommend that supplemental oxygen therapy be given to patients with severe acute respiratory infection (SARI), respiratory distress, hypoxemia or shock

b) HFNC and NIPPV – High-flow nasal cannula oxygen therapy (HFNC) and non-invasive positive pressure ventilation (NIPPV) was used as step-up therapy in patients who failed to improve on supplemental oxygen. A Chinese expert consensus released in 2019 recommend that physicians can consider providing HFNC to mild or moderately ill patients (100 mmHg≤Pa02/Fi02<300 mmHg). The clinical application of NIPPV on hypoxemic respiratory failure caused by severe pneumonia has long been controversial. WHOguidelines recommend using HFNC and NIPPV with extreme care and closely monitoring the condition of patients treated with HFNC or NIPPV for deterioration.

c) Invasive mechanical ventilation – According to Guan et al, 14.5% of severe patients received invasive mechanical ventilation, but 32.4% patients received non-invasive mechanical ventilation. If standard oxygen therapy fails WHO guidelines recommend escalating to invasive mechanical ventilation. It is generally accepted that timely use of invasive mechanical ventilation is an important component of the treatment of severe respiratory failure and acute respiratory distress syndrome (ARDS).

d) Extracorporeal membrane oxygenation – Extracorporeal membrane oxygenation (ECMO) is a form of extracorporeal life support that circulates blood flow through an artificial lung for gas exchange and then back into the bloodstream of very ill patients. It provides a period of pulmonary rest, and artificially supports critical ill patients while their heart and/or lungs recover, and plays a role in the care of heart or lung transplant patients. ECMO has rarely been used due to limited resources.

ii) Pharmacologic agents

According to literature from an article by Guan et al and Liu et al a study was done on 327 pooled cases of severe infection with COVID-19, in severe cases 87.3% (254/291) patients received antibiotic treatment, 61.5% (201/327) patients received antiviral treatment, 53.8% (176/327) received corticosteroid treatment, and 41.0%

(114/278) received intravenous immunoglobulin. Only 8.4% (23/274) patients received continuous renal replacement therapy. The mortality rate of the 327 pooled severe cases was 25.4% (83/327). However, because of the wide-spread use of the medications, ongoing trials are being conducted to clarify which medications may or may not be helpful in treating COVID-19

Despite the use of various medications, the consensus of Chinese experts is that neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc.) and ganciclovir are not generally recommended. Routine prophylactic antibiotics, especially combined wide-spectrum antibiotics, are also not typically recommended.

iii) Antiviral treatment

The guidelines of the NHC recommended interferon-α2b inhalation, lopinavir/ritonavir, ribavirin, chloroquine, and arbidol as antiviral therapy, and does not recommend using three or more antiviral drugs at the same time

According to Chen et al the duration of antiviral treatment was 3-14 days. However, the results of a clinical trial of lopinavir/ritonavir in China showed no clear benefit with lopinavir/ritonavir treatment beyond standard care in hospitalized adult patients with severe COVID-19. According to Wang et al, Remdesivir may have the greatest potential for the successful treatment of SARS-CoV-2. Remdesivir has been studied in clinical trials to treat COVID-19

Favipiravir was approved for treatment of influenza and is being studied in COVID-19 clinical trials. The preliminary results indicate that favipiravir has significantly more potent antiviral action and fewer adverse effects than that of lopinavir/ritonavir. One of the clinical trials was conducted in Shenzhen and the results showed that the median time to viral clearance was 4 days in the favipiravir treatment group compared with 11 days in the lopinavir/ritonavir treatment group. In terms of chest imaging, the improvement rates of the favipiravir treatment group and the lopinavir/ritonavir treatment group were 91.4% and 62.2%, respectively. According to China National Health Commission, no significant adverse reactions were noted in the favipiravir treatment group, and there were significantly fewer adverse effects than in the lopinavir/ritonavir group.

According to Liu et al, in the early *in vitro* studies, chloroquine and hydroxychloroquine were found to inhibit SARS-CoV-2 infection efficiently, and several clinical trials have been conducted to evaluate the efficacy and safety of chloroquine or hydroxychloroquine. Gao et al summarized that compared with the control treatment, chloroquine phosphate was effective in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course.The expert consensus on chloroquine phosphate recommends 500mg twice per day for 10 days for patients

diagnosed with COVID-19.Zhonghua et al summarised that the adverse effects of chloroquine and hydroxychloroquine must be carefully monitored.

Zhou et al proposed that hydroxychloroquine could serve as a better therapeutic agent than chloroquine due to reduced toxicity, fewer side effects, lower cost and relative safety in pregnancy. Yao et al used physiologically-based pharmacokinetic (PBPK) models and found that hydroxychloroquine was more potent than chloroquine at inhibiting SARS-CoV-2 *in vitro*. They recommended hydroxychloroquine sulfate 400 mg twice daily for 1 day, followed by 200 mg twice daily for 4 days to treat SARS-CoV-2 infection.

Safety concerns:Chloroquine and hydroxychloroquine are extremely toxic in overdose, sharing several manifestations in common with cyclic antidepressant poisoning. Deliberate or inadvertent overdose leads to rapid onset of central nervous system toxicity,cardiovascular collapse and hypokalemia resulting from intracellular shifting.

iv) Convalescent plasma

Previous studiespublished in Public Health England in Middle East Respiratory Syndrome (MERS) suggested that convalescent plasma may be effective.Donors and recipients should be carefully selected, and serum specific IgG antibodies for SARS-CoV-2 should be tested to guarantee the quality of convalescent plasma. Critical patients who received convalescent plasma showed significant improvement in clinical symptoms and laboratory findings.

v)Intravenous immunoglobulin treatment (IVIG)

IVIG was considered as a potential therapy for immunologic injury in COVID-19 in clinical practice by virtue of its anti-inflammatory action in treating conditions such as Hemophagocytic Lymphohistiocytosis (HLH) and cytokine storm. Similarly, two reviewsbyLin et al andFu Y et al also recommended IVIG based on mechanisms of SARS-CoV-2-mediated inflammatory responses. However, further investigation and more clinical studies are needed.

vi)Other treatment methods under clinical trials:

a) Cell Therapy

Four of six critically ill COVID-19 patients significantly improved after receiving an experimental therapeutic designed to reduce inflammation, a major cause of death from this disease, according to a case series published by Cedars-Sinai and Capricor Therapeutics.The therapeutic, known as CAP-1002, contains cardio sphere-derived cells (CDCs) that are grown in the laboratory from human heart tissues. Previous preclinical and clinical research showed that the CDCs, originally created by a process developed to treat heart failure, can help the whole body.

b) Antibody treatment methods

ULTOMIRIS is a monoclonal antibody. ULTOMIRIS is used to treat adults with a disease called Paroxysmal Nocturnal Hemoglobinuria. ULTOMIRIS is the first and only long-acting C5 complement inhibitor. The medication works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. When activated in an uncontrolled manner, the complement cascade over -responds, leading the body to attack its own healthy cells.

c) Vaccine

Vaccine safety is a priority. Currently, strategies for Coronavirus vaccine development include recombinant proteins, DNA vaccines, mRNA vaccines, traditional live vaccines and recombinant adenovirus vaccines.

Conclusion

Viral epidemics need to be countered with a unified national strategy that can be implemented quickly on a very large scale. The ability to mobilize and to stay nimble in adapting to these challenges is paramount. Public buy-in is crucial for all citizens to abide by the rules and recommendations. Rules must be mandatory and cannot be simply recommended and voluntary. Designated officers must be deployed to enforce these rules. The negative short-term public and economic consequences that may result from shutting down services, restricting travel and aggressive quarantining must be accepted or the virus will keep spreading. Collaboration and sharing among countries are imperative to establish more effective policies to control the spread of future epidemics and minimize mortality and morbidity.

BIBLIOGRAPHY

1.Guan W.-J., Ni Z.-Y., Hu Y. Clinical Characteristics of Coronavirus Disease 2019 in China. The New England journal of medicine. 2020 doi: 10.1056/NEJMoa2002032. [CrossRef] [Google Scholar]

.Liu Y, Sun W, Li J, et al. Clinical features and progression of acute respiratory distress syndrome in coronavirus disease 2019. medRxiv. 2020:2020.2002.2017.20024166.

3. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet (London, England). 2020:S0140 -6736(0120)30211-30217.

4. Wang M., Cao R., Zhang L. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell research. 2020 doi: 10.1038/s41422-41020-40282-41420.

5. China NHCo. Press Conference of the Joint Prevention and Control Mechanism of the State Council.(Mar-17-2020).

6.Liu J., Cao R., Xu M. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. Cell Discovery. 2020;6:16. [PMC free article] [PubMed] [Google Scholar]

7. Gao J., Tian Z., Breakthrough Yang X.

Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends. 2020;14:72–73. [PubMed] [Google Scholar]

8. multicenter collaboration group of Department of S, Technology of Guangdong P Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus p. [Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia] Zhonghua Jie He He Hu Xi Za Zhi. 2020;43:185–188. [PubMed] [Google Scholar]

9.England PH. Treatment of MERS-CoV: information for clinicians: Public Health England; 2014

10.Lin L., Lu L., Cao W., Li T. Hypothesis for potential pathogenesis of SARS-CoV-2 infection-a review of immune changes in patients with viral pneumonia. Emerg Microbes Infect. 2020;9:727–732. [PMC free article] [PubMed] [Google Scholar]

11. Fu Y., Cheng Y., Wu Y. Understanding SARS-CoV-2-Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools. Virol Sin. 2020 [Google Scholar]