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A mini-review on the current COVID-19 therapeutic strategies

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ABSTRACT

The coronavirus outbreak (COVID-19) started in china, on 31 December 2019. COVID-19 is a severe acute respiratory syndrome. Research on COVID-19 treatment strategies for development of an effective drug therapy has attracted worldwide attention recently. So far, no certain cure or specific vaccine has been suggested by Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) to fight this deadly disease. However, several different treatment protocols have been proposed based on older drugs. Researchers around the world still attempt to evaluate them in clinical trials. In this mini review, we summarize the available drugs that have been used in the treatment of COVID-19 based on the existing guidelines.

1. Introduction

The COVID-19 is spreading rapidly all over the world [1]. Furthermore, people of any age are at risk for coronavirus disease, but those with underlying disease such as high blood pressure, diabetes, and cardiovascular disease are at high risk [2, 3].

1.1. Virology and Symptoms of COVID-19

Coronaviruses (CoVs), which are enveloped positive-sense RNA viruses, appear as crown-shaped viruses when observed by electron microscope [4, 5]. They are categorized into four subtypes: alpha CoV, beta CoV, delta CoV, and gamma CoV[5]. Coronavirus disease originates from a betacoronaviruse (β-CoVs or Beta-CoVs) which is known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [6]. Infected people may experience fever ≥38C°, cough, and shortness of breath [6]. The incubation period is not exactly clear, but depending on the age and more importantly the immune system status of patients, differs from 6-41 days post-infection. Besides, the symptoms reveal within 5.2 days after infection [7]. However, coronavirus involves human strains that are related with approximately 15% of common cold symptoms, its development may appear with variable intensity from mild to severe illness and even death [8].

1.2. Transmission of COVID-19

It is little known about COVID-19 transmission, but it is concluded to be spread from infected people to other people through virus-contaminated droplets such as sneeze and cough [9].

1.3. General medications

Scheme 1 shows general medications for viral infection including nutritional interventions which may be effective by strengthening the immune system. Clearly, micronutrients including vitamins A, B, C, D, E, some minerals, and fatty acid may be beneficial elements to fight different viruses [10].

2. Therapeutic procedures of COVID-19

Possible therapeutic strategies which are already recommended for SARS-CoV-2 is shown in scheme 2 [6, 10, 11].

2.1. Care procedures

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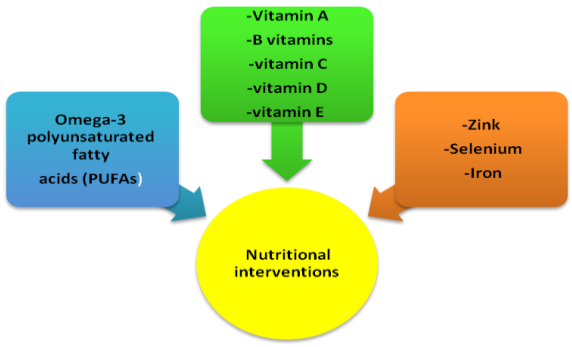
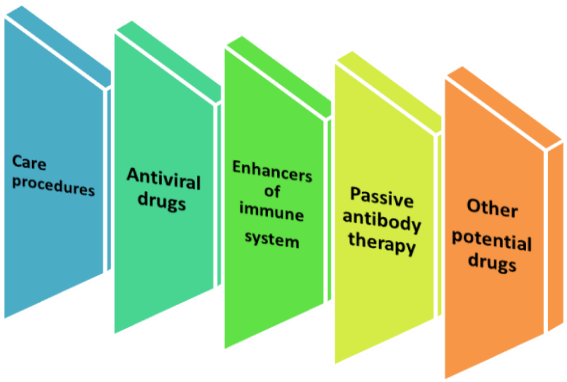
First-line COVID-19 treatments are paracetamol and expectorants like guaifenesin for fever and non-productive cough, respectively [6].



Scheme 1. General medications for viral infections [10]



Scheme 2. Possible therapeutic strategies for SARS-CoV-2 [6, 10, 11]

Guaifenesin is used in reducing congestion of chest in some disorders including allergies, common cold, and infection.

Paracetamol, also known as APAP/acetaminophen, is a drug used to cure mild to moderate pain and fever. The care-related procedures for COVID-19 initially include oxygen therapy when is required and other supportive strategies [6, 11].

2.2. Potential medicines to treat COVID-19

Various antiviral agents have been showed in-vivo anti-SARS-CoV-2 activity and have potential for drug repurposing (also called drug repositioning, re-tasking or reprofiling). Drug repurposing is an approach for identifying new application of investigational or approved of existing drugs. So far, no specific drug or vaccine is available to treat COVID-19 [6].

Several international and national scientific teams are endeavoring to discover certain cure or vaccine against this disease [12]. According to the existing researches there are some approaches to achieve effective drugs against COVID-19 such as in silico methods [13, 14]. In silico predictions/methods are computational approaches that provide innovative candidates testable [12]. Drug repurposing [13, 15, 16] or drug repositioning [17, 18], and pathogenic mechanisms of the virus [10, 12] can be also fruitful in distinguishing accurate therapeutic targets to synthesize specific antivirals against this novel virus [19].

2.2.1. Antiviral drugs

Some of the antiviral drugs are specific for COVID-19 such as protease inhibitors including chymotrypsin-like (3C-like) and papain-like protease (PLP) which were synthesized in the past. Diarylheptanoids belong to the papain-like protease inhibitors while cinanserin and flavonoids are associated with chymotrypsin-like (3C-like). Another specific antivirals for cronavirus are spike (S) protein-angiotensin-converting enzyme 2 (ACE2) blockers which include, human monoclonal antibody, chloroquine, emodin, promazine, and nicotianamine [10].

Apart from specific antivirals, one of the best strategies in the field of cronavirus disease treatment is the utilization of existing broad-spectrum antiviral drugs such as protease inhibitors of HIV and hepatitis C antivrals till the discovery of specific drug or vaccine [7, 20]. So, it is a promising approach since drug information including interactions, adverse effects, and therapeutic effects are available [21]. Among the researches, one in vitro screening model followed by a clinical investigation showed that remdesivir, which is an inhibitor of viral protein as the analogue of adenosine, has been effective in treating a cronavirus patient [22]. Acorrding to Kim et al. success in treating MERS-CoV disease using triple combination treatment consisting of LPV/RTV, ribavirin, and IFN-alpha 2a in South Korea , this therapeutic strategy can be followed and evaluated [10]. Currently, several approved old antiviral drugs are being used in different countries around the world including ribavirin , lopinavir/ritonavir (kaletra), remdesivir, nelfinavir, [10], and arbidol (an antiviral drug available in Russia and China) [23]. Favipiravir is also undergoing clinic trials to combat COVID-19 [27].

2.2.2. Enhancers of Immune system

Interferons, thymosin α-1 (Ta1), thymopentin (TP5, munox), levamisole, cyclosporine-A are able to combat with SARS-CoV-2 by enhancing the immune system [10]. Chloroquine is a malarial drug that reflected reliable activity in pneumonia caused by COVID-19 in several clinical trials [21, 23]. More importantly, in vitro evaluation of hydroxychloroquine as the chloroquine

analogue indicated potential anti-COVID-19 effectiveness. Moreover, it showed better saftey compred with chloroquine which is suitable for constant using and highly-dose recommendation, as well [21]. Intravenous immunoglobulin (IVIG) is one of the proposed treatment for patients with severe intensity of COVID-19 [23, 24].

2.2.3. Passive antibody therapy

WHO has invited doctors from all around the world to a clinical research to compare therapeutic approaches. One of these researches is analyzing the plasma gained from patients who have recovered from COVID-19 that is enriched with antibody [25], and have tested negative for covid-19 within the last 14 days [26]. Since the success of monoclonal antibody therapy has been proved in treating many diseases, exsiting studies about neutralizing monoclonal antibodies against similar coronaviruses such as SARS-CoV and MERS-CoV propose potential therapy against COVID-19 [19]. In addition, due to the emergency needs , the FDA said it was preparing urgent access to convalescent plasma for patients who are in critical conditions [26].

2.2.4. Other potential drugs

Another drugs from different classifications are speculated to be potential candidates to cure COVID-19 including α-lipoic acid, estradiol and phytoestrogen, mucroporin-M1 ,and nitric oxide [10]. Imatinib is also effective against COVID-19 due to the inhibition of virions fusion with the endosomal membrane [27].
In a published article in International Journal of Antimicrobial Agents, it was mentioned that the combination of azithromycin and hydroxychloroquine in clinical trial indicated viral clearance within 6 days [28].
Moreover, adding azithromycin to Hydroxychloroquine has showed great effectiveness to eliminate COVID-19 [21]. Ivermectin as an anti-parasitic compound has showed in vitro effectiveness against COVID-19 [29].

3. Conclusion

As a global concern of COVID-19 outbreak worldwide, there is an urgent need to find efficient therapeutic strategies against it. Therefore, studies confirm to evaluate all the poposed therapeutic protocles in clincal trials and record the results to check whether they are efficient. It is also suggested that studying the plasma of recovered patients may pave the way to find the accurate and certain drug or vaccine.

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