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Current knowledge on the treatment of COVID-19

Abstract

COVID-19 is a novel infectious disease that has spread over the world, causing severe morbidity and mortality. Coronavirus-2 (SARS-CoV-2) causes this severe acute respiratory disease. Corona viruses are primarily transmitted from person to person through inhaled or deposited respiratory droplets on the mucosal surfaces, such as aerosols produced during coughing and speaking. COVID-19 and its therapeutic management were poorly understood early in the pandemic, forcing a rush to create experimental medicines, and repurposed pharmaceuticals to combat this unique viral disease. Treatment options include antiviral pharmaceuticals, anti-SARS-CoV-2 monoclonal antibodies, anti-inflammatory drugs, and immunomodulator agents.

This mini review focuses on the current developments in the treatment of COVID-19 that has seriously affected the developed as well as developing nations of the world.

Keywords: anti-inflammatory drugs, anti-SARS-CoV-2 monoclonal antibodies, antiviral drugs, covid-19, immunomodulators agents

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Introduction

SARS-CoV-2 causes Corona virus disease 2019 (COVID-19), which is a life-threatening new disease.[1] SARS-CoV-2 is a novel corona virus that can spread to other people by respiratory particles causing fever, dry cough, shortness of breath, anorexia, drowsiness, and sore throat in afflicted patients. COVID-19 is difficult to detect in its early stages because it has a wide range of clinical symptoms that are frequently confused with other respiratory disorders. COVID-19 is currently being diagnosed using molecular methods all around the world.[2]

Early on in the pandemic, there was a rush to develop experimental therapies and repurpose medications to combat this new unique viral disease due to a lack of understanding of COVID-19 and its curative management. Significant progress has been made thanks to the dedicated work of clinical researchers all around the world, leading in a better understanding of not just COVID-19 and its management, but also the quick development of novel medications and vaccines.[3] Antiviral medicines, anti-SARS-CoV-2 monoclonal antibodies, anti-inflammatory pharmaceuticals, and immunomodulators substances are already available or being researched for COVID-19 care under FDA Emergency Use Authorization (EUA).[4]

The treatments' therapeutic value varies depending on the severity of the infection and the existence of certain risk factors. SARS-CoV-2 replication is at its greatest before or shortly after the onset of symptoms in the early phase of COVID-19 infection, and it is at its lowest in the late phase. During this stage of viral replication, antiviral medicines and antibody-based treatments are expected to be more successful. The synthesis of cytokines and the activation of the coagulation system cause a hyper-inflammatory condition in the later stages of the infection, resulting in a prothrombotic state. Anti-inflammatory medications, such as corticosteroids, immunomodulating therapies, or a combination of these therapies may be more effective in addressing this hyper-inflammatory condition than antiviral therapies.[5] The objective of this brief review is an attempt to bring existing COVID-19 therapeutic knowledge up to date.

Antiviral therapies

Remdesivir is a broad-spectrum antiviral medication that has been found to be effective against a variety of viruses in vitro, including the Nipah virus,[6] hepatitis C,[7] and Marburg,[8] as well as SARS-CoV-2. The US Food and Drug Administration (FDA) approved Remdesivir for clinical use in COVID-19-positive adults and children (over the age of 12 and weighing at least 40 kilos).[9,10] However, in October 2020, the WHO removed it off the list of effective drugs for the treatment of COVID-19 patients.[11] Molnupiravir is the first oral, direct-acting antiviral that has been shown to reduce nasopharyngeal SARS-CoV-2 infection while also having an excellent safety and tolerability profile. A Phase III clinical trial is now underway for the treatment of non-hospitalized people with laboratory-confirmed COVID-19 infections.[12]

Antiviral therapies such as hydroxychloroquine and chloroquine were proposed during the pandemic. These medications, on the other hand, do not appear to be therapeutic and should not be used to treat COVID-19.[13] Typical AIDS medicine lopinavir/ritonavir was suggested as an antiviral therapy against COVID-19 during the early phases of the pandemic.[14] In contrast, lopinavir/ritonavir is not currently licensed for the treatment of COVID-19.[3,15] Ivermectin is an antiparasitic medication used to treat a variety of tropical parasitic infections.[16] Ivermectin has been shown to inhibit SARS-CoV-2 replication in cell cultures.[17] There is inadequate data to support or oppose the use of ivermectin for COVID-19 therapy. Results from suitably powered, well-designed, and well-conducted clinical trials are needed to provide more detailed, evidence-based guidance on the function of ivermectin in the treatment of COVID-19.[18]

Anti-sars-cov-2 neutralizing antibody products

Individuals who recover from COVID-19 develop SARS-CoV-2 neutralizing antibodies, albeit the duration of this immunity is unknown. Nonetheless, their potential as COVID-19 therapeutic agents is being studied in a number of clinical trials.[3] Convalescent plasma therapy was tested during the SARS, MERS, and Ebola epidemics.[19] Convalescent plasma has been issued an Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) for the treatment of COVID-19 in selected hospitalized patients. Using low-titer COVID-19 convalescent plasma in mechanically ventilated patients or high-titer COVID-19 convalescent plasma in hospitalized patients who do not require mechanical ventilation is not recommended unless in a clinical trial.[18]

REGN-COV2 is a cocktail of two noncompeting, neutralizing human IgG1 antibodies (casirivimab and imdevimab) that target the

receptor-binding region of the SARS-CoV-2 spike protein, preventing viral entry into human cells via the ACE2 receptor.[20,21] It has been shown to lower viral load in vivo.[20] According to preliminary findings from a phase-III trial of REGN-COV,[22] it reduced hospitalization or death in non-hospitalized individuals by 70%. The REGN-COV2 antibody combination reduced viral load, with a higher effect in patients with a delayed immune response or a high viral load at baseline.[23]

Bamlanivimab and Etesevimab (LY-CoV555 or LY3819253 and LY-CoV016 or LY3832479), anti-spike neutralizing monoclonal antibodies, have been shown to neutralize SARS-CoV-2 and restrict viral replication in non-human primates.[24] The results of BLAZE-1's phase III trial are still being disclosed, although preliminary data suggests the medication reduced hospitalization and mortality by 87%.[22] Sotrovimab (VIR-7831) is a powerful anti-spike neutralizing monoclonal antibody that is effective in vitro against all four VOCs: Alpha (B.1.1.7), Beta (B.1.351), Gamma (P1), and Delta (P1) (B.1.617.2). REGN-COV2, bamlanivimab/etesevimab, and sotrovimab were approved by the FDA for clinical use, but only in non-hospitalized patients (aged 12 years and weighing 40 kg) with laboratory-confirmed SARS-CoV-2 infection and mild to moderate COVID-19 who are at high risk of developing severe disease and/or hospitalization.[3]

Immunomodulatory agents

The severity of COVID-19 is characterized by the immune system's hyperactivity. As a result, immunosuppressive therapy has been suggested as a potential COVID-19 treatment.[25] Corticosteroids have a powerful anti-inflammatory effect and are currently being utilized to treat autoimmune diseases with an inflammatory response that is out of control. Inhaled corticosteroids inhibited SARS-CoV-2 ribonucleic acid (RNA) replication in COVID-19 by targeting the viral replication-transcription complex.[26] Dexamethasone is now considered routine therapy in hospitalized patients who require supplemental oxygen or non-invasive or invasive mechanical breathing, either alone or in combination with remdesivir, depending on the severity of illness.[3]

Janus kinase (JAK) inhibitors like Baricitinib were considered a potential treatment for COVID-19 because of their inhibitory effect on SARS-CoV-2 endocytosis in vitro and on the intracellular signaling pathway of cytokines that cause the late-onset hyper-inflammatory state that leads to severe illness.[24,26] Baricitinib improved time to recovery when compared to remdesivir alone, and, more intriguingly, the combination was linked with less serious side events, such as infections and thrombosis.[27] It has been cleared for clinical use in COVID-19-positive hospitalized patients under EUA issued by the FDA.[3] Ruxolitinib is an oral selective Janus kinase inhibitor that is thought to impair the intracellular signaling route of cytokines, making it a potential COVID-19 treatment. The efficacy and safety of ruxolitinib in individuals with severe COVID-19 are now being studied in a large randomized trial.[27]

Interleukin (IL) inhibitors may help to minimize the significant damage to lung tissue caused by cytokine production in people with severe COVID-19 infections.[28] Endogenous IL-1 levels are higher in people with COVID-19 and other diseases, such as severe cell–mediated cytokine–release syndrome. According to the National Institutes of Health, there is insufficient evidence to recommend whether or not to use IL-1 inhibitors.[29] The recombinant interleukin-7 inhibitor CYT107 (RevImmune) stimulates T-cell production and relieves immunological fatigue. It was used to assess immune reconstitution in lymphopenic patients in several phase II clinical trials.[30] The European Union has approved tocilizumab, an interleukin-6 inhibitor, for the treatment of coronavirus disease 2019 (COVID-19) in hospitalized adults and pediatric patients (aged >2 years) who needed supplemental oxygen, noninvasive or invasive mechanical ventilation, or systemic corticosteroids.[28]

Acalabrutinib, ibrutinib, and rilzabrutinib are Bruton's tyrosine kinase inhibitors that modulate macrophage signaling and activation. Macrophage activation is thought to happen during the hyperinflammatory immune response seen in severe COVID-19. Clinical trials are currently underway to confirm the medications' true efficacy in severe COVID-19 sickness.[31] Due to their reported significance in COVID-19 pathogenesis, several novel immunologic targets, such as tumor necrosis factor (TNF) inhibitors, retinoic acid-inducible gene I-like receptor (RLR) and mTOR inhibitors, NLRP3 inflammasome inhibitors, complement inhibitors, toll-like receptor modulators, IL-18 inhibitors, and possibly mesenchymal stem-cell secretome, may be tested in the future.[25]

Conclusion

SARS-CoV-2 causes COVID-19, a highly contagious respiratory disease. The current state of COVID-19 treatment is discussed in this review. At this moment, there is no cure for COVID-19, though therapy can help with symptoms and breathing. Vaccines are becoming more widely available. Meanwhile, keep a safe distance from others, use hand sanitizers or soap and water to wash your hands frequently, avoid touching your face, and cover your face in public. More efforts should be made to produce a safe, effective, and low-cost chemotherapeutic drug that may be used broadly, even in poor resource countries, to treat COVID-19. This would undoubtedly reduce the morbidity and mortality associated with this new viral disease of global significance.

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Contribution of authors

During the writing of the manuscript, all of the authors contributed equally. They read the final manuscript and gave it their approval for publishing.

Conflicts of interest

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