

Knowledgeable Research ISSN 2583-6633 Vol.02, No.08, March, 2024

Effective Strategies for Preventing and Treating Coronavirus

Dr. Abnish Kumar Gautam^{1,} Pooja Agarwal², Abhisek Agarwal³ and Dr. Jyoti⁴ Associate professor, Mahamaya Government Degree College, Mahona, Lucknow¹, Assistant professor, Maharaja Agarsen Mahavidhaya, Bareilly² Assistant professor, Government Medical College, Badaun³ Assistant professor, NSCB Govt girls PG College, Aliganj, Lucknow⁴ Email: <u>abnishcdri@gmail.com</u>

Abstract:

The coronavirus disease 2019 (COVID-19) spread has developed into a worldwide health disaster and achieved pandemic status. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) stands as a substantial international danger with more than 8 million infections and 425,000 fatalities reported during its first six months of global transmission. Highly pathogenic strains such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have caused human coronaviruses (HCoVs) to attract growing attention during the last 14 years. Doctors and scientists have yet to discover a definitive cure or vaccine for COVID-19. A number of vaccines and treatments remain in preclinical or early-stage clinical trials but several have demonstrated potential in managing the infection. This article explores prevention methods and treatment strategies for human coronaviruses along with promising vaccines and their therapeutic options while examining challenges and alternative COVID-19 treatment strategies.

Keywords: COVID-19, Strategies, Treatment, Prevention

Introduction

Coronaviruses are a large family of viruses that can cause illness in both humans and animals. In rare cases, animal coronaviruses can evolve to infect humans and then spread between individuals, as seen with Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). COVID-19 is a severe respiratory illness caused by the novel coronavirus, SARS-CoV-2 (Munster et.al., 2020 & Shetty, 2020). As of June 16, 2020, COVID-19 has become a serious global threat, leading over million infections 400,000 deaths to 8 and more than (https://www.worldometers.info/coronavirus/). The emergence of SARS-CoV-2 was first identified in

Vol.02, No.08, March, 2024

An International Peer-Reviewed Multidisciplinary Journal

Wuhan, China, in December 2019. In a short span of time, infections spread rapidly worldwide, causing widespread distress and significant loss of life.

Current evidence suggests that SARS-CoV-2, the causative virus of COVID-19, likely has a zoonotic origin closely related to bat-derived SARS-like coronaviruses. Like the Severe Acute Respiratory Syndrome (SARS) virus, it is an enveloped RNA beta coronavirus that enters human cells through the angiotensin-converting enzyme 2 (ACE2) receptor. The major way that the disease is communicated from person to person is through respiratory droplets that are emitted when an infected person coughs, sneezes, or speaks. If a person contacts a contaminated surface and subsequently touches their mouth, nose, or eyes, they could become infected. These droplets can also land on surfaces where the virus may still be active.

The virus's typical incubation time falls between 2 and 14 days, at around 5.1 days. Although the exact window of infectiousness is yet unknown, present data points to infectivity starting two days before symptom start and lasting up to eight days. Pre-symptomatic or asymptomatic transmission is still under research (Ministry of Health and Family Welfare, 2020). Acute respiratory distress, brought on by a cytokine storm that results in elevated plasma concentrations of proinflammatory cytokines, including IL-2, IL-7, IL-10, IL-17, GM-CSF, interferon-inducible protein 10, MCP-1, macrophage inflammatory protein-1 alpha, and TNF-alpha (Mehta et.al., 2020) is the main cause of the great morbidity in SARS-CoV-2 patients. The precise route of SARS-CoV-2 infection is unknown yet. Our content is based on few instances and insights gained from related coronavirus illnesses like SARS-CoV and MERS-CoV. (Gu & Korteweg, 2007, Ng et.al., 2016 & Xu et.al., 2020)

Mode of Transmission

For contagious diseases it is usually easy to comprehend how a sick person can pass on pathogens to a healthy person in the vicinity (Lal et.al., 2019). Close or direct contact with infected secretions or large respiratory droplets is the primary method of transmission of COVID-19 (Yang et. al., 2020). However, fecal-oral route of transmission raises certain doubts regarding the spread of SARS-CoV2 (Zhang & Gao et. al., 2020). This concern stems from the fact that the ACE-2 receptor protein, which the virus uses to enter into human cells, abundant in epithelial cells of the intestinal lining. Concerning vertical transmission (mother to child) in pregnant women, current analyses during pregnancy with COVID-19 have not shown any evidence for such transmission. Viral shedding hasn't been observed in vaginal secretions and SARS-CoV-2 has not been detected in breast milk. (Lal et. al., 2019, Liang & Acharya, 2020 & Favre et.al. 2020).

Diagnosis

Confirmatory diagnosis of COVID-19 can be established clinically by performing molecular tests of respiratory specimens which include: throat swabs, nasopharyngeal swabs, sputum, endotracheal aspirates, bronchoalvelolar lavage. The virus can also be recorded in feces and, in extreme situations, the blood. It is important to remember that SARS-CoV-2 is absent in the current multiplex PCR panel. In the suspected cases commercial tests weren't available in the beginning and the samples had to be sent to reference laboratories or National Institute of Virology at Pune. With the progression of the pandemic commercial tests are bound to be easily available. COVID-19 diagnosis is established with the use of imaging tests which is very important. The typical findings on a Chest X-ray CXR is bilateral

Vol.02, No.08, March, 2024

An International Peer-Reviewed Multidisciplinary Journal

infiltrates, but there are cases where the X-ray shows a normal appearance in the initial weeks of the disease. Infiltrates, ground glass opacities with sub segmental consolidations are usually found in abnormal CT scans. They are however much more sensitive and specific. It is worthy noting that even among those who are asymptomatic, or appearing to have no clinical signs to suggest active lower respiratory disease, abnormal CT changes have been noticed. Indeed, COVID-19 has been diagnosed on the basis of abnormal chest CT scans in persons suspected of having COVID-19 who had negative PCR tests, later these patients tested positive molecular testing (Huang et.al., 2019).

Prevention and Treatment

Treatment for COVID-19 is primarily supportive and symptomatic. The first critical step is ensuring adequate isolation to prevent the spread of infection to others, including patients, contacts, and healthcare workers. General hygiene measures should be followed rigorously, including:

- 1. Washing hands frequently with soap and water or using an alcohol-based hand sanitizer.
- 2. Following proper cough or sneeze etiquette, such as covering the mouth.
- 3. Avoiding touching the eyes, nose, and mouth with unclean hands.
- 4. Avoiding close contact with sick individuals.
- 5. Not sharing dishes, glasses, bedding, or other household items with infected people.
- 6. Regularly cleaning and disinfecting frequently touched surfaces.
- 7. Staying home from work, school, and public areas when feeling unwell.

In general, patients with mild cases can be managed at home, usually with some counseling on warning signs. The basic principles involve maintaining adequate hydration, nutrition, and fever or cough control. Routinely prescribing antivirals like oseltamivir and antibiotics should not be done in confirmed cases of COVID-19 unless there is strong suspicion of a secondary infection.

For patients with hypoxia, oxygen may be necessary by way of nasal prongs, face masks, high flow nasal cannula (HFNC), or non-invasive ventilation. In extreme cases patients may need to be placed on a ventilator or ECMO machine. Some may need dialysis. Hydration is important, and antibiotics, as well as antifungals, should only be started if a secondary infection is likely or known.

Information from the World Health Organization (WHO) states that there are well developed guidelines for the critical care management of COVID-19 patients.

Earlier Drug development against Corona virus

The drug development process is lengthy, requiring extensive safety assessments and clinical trials. However, several existing antivirals, antiparasitic, antihypertensive, and cholesterol-lowering drugs have shown some success in preclinical evaluations and early clinical trials when repurposed for potential use against coronavirus. The primary goals of these repurposed therapeutic interventions are to control viral infection and reduce the severity of the disease. As a result, certain drugs have been used to treat COVID-19 patients, with promising results in some cases.

Chloroquine

Chloroquine is a known drug used to treat malaria and certain autoimmune disorders and had shown antiviral activity against several viruses including HIV, Zika virus and coronaviruses (Taherian et. al.,

Vol.02, No.08, March, 2024

An International Peer-Reviewed Multidisciplinary Journal

2013, Savarino et. al., 2006 & Delvecchio et. al., 2016). It also hinders terminal glycosylation of the ACE2 receptor on host cells, which is necessary for virus-cell fusion. These in vitro findings were promising and indicated that chloroquine might potentially be a medication for COVID-19. Numerous clinical trials of chloroquine have been undertaken in a variety of designs studying chloroquine alone or in combination with other agents, both randomized and non-randomized (with and without placebo), (Chowdhury et. al., 2020). However, one study of 14 patients reported superior viral clearance in the combination group [6/6, 100% compared with hydroxychloroquine alone 8/14 (57%)]

Randomized controlled trials (RCTs) of the chloroquine and hydroxychloroquine for COVID-19 treatment are under way. Other studies to evaluate chloroquine prophylaxis in health care workers (NCT04303507) and hydroxychloroquine for post-exposure prophylaxis following high-risk exposures (NCT04308668) are also ongoing.

Remdesivir

Remdesivir is a broad-spectrum antiviral agent with activity against a number of RNA viruses, including SARS-CoV and MERS-CoV, in cultured cells, mouse, and in nonhuman primate studies. an adenosine analogue activating nucleoside triphosphate metabolites to inhibit viral RNA polymerases. In early clinical trials, remdesivir was shown to improve recovery time in COVID-19 patients (Chu et. al., 2004, Wilde et. al., 2014 & Cao et. al., 2020), with FDA approval for use in critically ill patients. Yet, even with its use, the high mortality rate we have seen in COVID-19 patients indicates that remdesivir alone may not be a cure."

To improve patient outcomes, researchers are currently exploring the combination of remdesivir with other medications in ongoing clinical trials. Since a hyperactive immune response, often referred to as a "cytokine storm," is linked to greater disease severity and higher mortality rates, the addition of the anti-inflammatory drug baricitinib to the remdesivir treatment is being investigated. This combination is being assessed in clinical trials (NCT04401579) to evaluate its potential for enhancing mortality outcomes.

There are several clinical trials currently in progress to evaluate the safety and antiviral effects of remdesivir in patients suffering from mild to moderate or severe COVID-19 (NCT04292899, NCT04292730, NCT04257656, NCT04252664, NCT04280705). Notably, the National Institutes of Health (NIH) is funding an adaptive, randomized, double-blind, placebo-controlled trial (NCT04280705) to further assess how effective remdesivir is in comparison to supportive care.

Favipiravir

Favipiravir, previously referred to as T-705, is a prodrug that converts into favipiravir ribofuranosyl-5'-triphosphate, a purine nucleotide. The active form of favipiravir works by inhibiting RNA polymerase, which effectively stops viral replication. Although most of the preclinical data on favipiravir comes from its effects on influenza and Ebola, the drug has also demonstrated broadspectrum effectiveness against various RNA viruses (Furuta et al., 2017). In vitro studies have shown that favipiravir has an EC50 of 61.88 μ M/L against SARS-CoV-2 in Vero E6 cells. (Wang et. al., 2020).

Lopinavir/Ritonavir and Other Antiretrovirals

Lopinavir/ritonavir is an oral combination medication approved by the US Food and Drug Administration (FDA) for the treatment of HIV. It has shown in vitro activity against novel coronaviruses by inhibiting 3-chymotrypsin-like protease (Gautret et al., 2020 & Chu et al., 2024). However, there are no published in vitro studies specifically assessing the effectiveness of lopinavir/ritonavir against SARS-CoV-2 (Dong et al., 2019). Recently, Cao and colleagues published findings from an open-label randomized controlled trial (RCT) that compared the efficacy of lopinavir/ritonavir to standard care in patients with COVID-19 (Wilde et al., 2014). Other antiretroviral drugs, including protease inhibitors and integrase strand transfer inhibitors, have also been identified as potentially effective against SARS-CoV-2 through enzyme activity screening (Dong et al., 2019). Importantly, in vitro studies indicate that darunavir has activity against SARS-CoV-2; however, there is currently no clinical data available on the use of these medications for treating COVID-19.

Ribavirin

Ribavirin, which is a guanine analogue, works by inhibiting viral RNA-dependent RNA polymerase, making it a potential treatment option for COVID-19 because of its effects on other coronaviruses. However, its effectiveness against SARS-CoV in laboratory settings was limited, as it required high concentrations to effectively inhibit viral replication. In the case of MERS, ribavirin—usually administered alongside interferons—did not show a significant effect on clinical outcomes or viral clearance (Morra et al., 2018 & Arabi et al., 2020). Since there is a lack of clinical data specifically addressing ribavirin's effectiveness for SARS-CoV-2, its potential role in treating COVID-19 must be inferred from studies on other coronaviruses.

Aldehyde based indole-2-carboxamide compounds

The structure-based design of antiviral drug candidates 11a and 11b, which are aldehyde-based indole-2-carboxamide compounds, has recently shown promising in vitro antiviral activity and favorable pharmacokinetic properties in vivo (Dai et al., 2020). These results indicate that they could be strong candidates for treating COVID-19. Although the in vivo pharmacokinetics and toxicity studies for these two new compounds have produced positive outcomes, their effectiveness against viral infections still needs to be confirmed in suitable experimental infection models before moving on to clinical trials.

Tocilizumab

Tocilizumab is a monoclonal antibody that specifically targets the interleukin-6 (IL-6) receptor. It has demonstrated a good safety profile and encouraging clinical results in the treatment of COVID-19. This medication can help mitigate cytokine storms, enhance respiratory function, and bring body temperature back to normal (Fu et al., 2020).

Tocilizumab is a monoclonal antibody that specifically targets the interleukin-6 (IL-6) receptor. It has demonstrated a good safety profile and encouraging clinical results in the treatment of COVID-19.

Vol.02, No.08, March, 2024

An International Peer-Reviewed Multidisciplinary Journal

This medication can help mitigate cytokine storms, enhance respiratory function, and bring body temperature back to normal (Fu et al., 2020).

Steroids

Low-dose steroids like prednisolone and the immunosuppressant tacrolimus have been found to reduce pro-inflammatory cytokines that worsen lung issues (Yamano et al., 2018). Since pneumonia can arise from a damaging inflammatory response during COVID-19 progression, administering prednisolone and/or tacrolimus to patients with severe lung injuries related to COVID-19 might lead to better clinical outcomes. Clinical trials are currently in progress to assess the effectiveness of these two immunosuppressive medications in alleviating the secondary lung pneumonia complications in COVID-19 patients (NCT04341038) (Stockman et al., 2006).

Hypertension drugs

Hypertension medications like lisinopril, an ACE inhibitor, and losartan, an angiotensin II receptor blocker (ARB), may lead to an increase in ACE2 receptor expression, raising concerns about the potential for higher viral loads in cells. However, some research suggests that ACE inhibitors and ARBs might actually be beneficial for patients with COVID-19. This is due to the role of ACE2 in converting angiotensin II into angiotensin, which may have vasodilatory and anti-inflammatory effects that could help mitigate some of the severe complications associated with the virus (Li et al., 2020).

Miscellaneous Agents

New version: Interferon- α and - β have been studied for their effects on novel coronaviruses, with interferon- β showing effectiveness against MERS (Stockman et al., 2006 & Morra et al., 2018). Several other immunomodulatory agents, typically used for non-infectious conditions, exhibit in vitro activity or mechanisms that may inhibit SARS-CoV-2. These include, but are not limited to, baricitinib, imatinib, dasatinib, and cyclosporine (Li et al., 2020, Coleman et al., 2016, Dyall et al., 2017, Pfefferle et al., 2011 & Wilde et al., 2011). However, there is currently no animal or human data to support their use specifically for COVID-19, and it remains uncertain whether they offer any additional protection for patients already taking them for other conditions.

Nitazoxanide, traditionally an antihelminthic agent, has broad antiviral activity and a relatively favorable safety profile. It has shown in vitro antiviral activity against both MERS and SARS-CoV-2 (Wang et al., 2020 & Rossignol et al., 2016). Camostat mesilate, primarily used for treating postoperative reflux esophagitis and acute exacerbations of chronic pancreatitis, has demonstrated potential in blocking the spread and pathogenesis of SARS-CoV in pathogenic mouse models. It inhibits the host serine protease TMPRSS2, which primes the spike protein of highly pathogenic human coronaviruses (Rabaan, 2017).

Oseltamivir, a neuraminidase inhibitor approved for influenza treatment, has no documented in vitro activity against SARS-CoV-2. During the initial COVID-19 outbreak in China, which coincided with peak influenza season, many patients received empirical oseltamivir therapy until SARS-CoV-2 was identified as the cause of COVID-19 (Wang et al., 2020). In contrast, umifenovir (also known as

Vol.02, No.08, March, 2024

An International Peer-Reviewed Multidisciplinary Journal

Arbidol) is a promising repurposed antiviral agent with a unique mechanism of action that targets the S protein/ACE2 interaction, inhibiting the membrane fusion of the viral envelope (Kadam et al., 2017).

Promising therapies against Corona virus

There are numerous therapies currently under investigation for the treatment of coronavirus infections, but some promising options include the following:

Convalescent Plasma (CP) Therapy

Convalescent plasma (CP) has been used for over a century as a form of passive immunotherapy to help improve survival rates in patients suffering from infectious diseases (Zhang et al., 2020). Studies have shown that administering CP can lower mortality rates and reduce the length of hospital stays for patients with SARS. In the case of COVID-19, CP from individuals who have recovered is utilized to treat those infected with SARS-CoV-2. The IgG antibodies specific to SARS-CoV-2 found in the plasma of recovered patients are transferred to those currently infected, where they work to neutralize the virus and activate the complement system, aiding in the elimination of the virus (Soo et al., 2004). To optimize CP therapy, it is essential to define key parameters such as the correlation between the reduction of SARS-CoV-2 RNA and CP treatment, the ideal concentration of neutralizing antibodies needed for effective therapy, and the changes in various cytokines throughout the treatment process. By addressing these factors, we can potentially improve the effectiveness of this therapeutic approach.

Stem Cell Therapy

A few decades ago, researchers found that stem cells, including pluripotent and multipotent types, show resistance to viral infections due to the expression of certain genes, such as those stimulated by interferon-gamma (Langhi et al., 2020). Mesenchymal stromal cells (MSCs) have attracted considerable interest because they can be sourced easily, collected through minimally invasive procedures, proliferate rapidly, and raise no ethical issues. MSCs can be obtained from various tissues, including adipose tissue, bone marrow, peripheral blood, cord blood, dental pulp, menstrual blood, Wharton's jelly, buccal fat pad, and fetal liver, and they can be preserved for future therapies.

While many clinical trials are investigating the use of MSCs for different diseases, none have been specifically designed for treating COVID-19. During SARS-CoV-2 infections, the host immune system ramps up the production of inflammatory factors, resulting in a cytokine storm marked by an overproduction of immune cells and cytokines (Mehta et al., 2020). MSC therapy might help curb the release of pro-inflammatory cytokines and, thanks to the regenerative capabilities of stem cells, support the natural repair of damaged tissues. Recent research has also indicated that MSCs can help reduce lung fibrosis, a significant pathological factor in COVID-19 (Li et al., 2017). Furthermore, MSCs are recognized for their strong antimicrobial properties, attributed to the secretion of antimicrobial peptides and proteins (such as LL-37, defensins, hepcidin, and lipocalins), which could aid in lowering viral loads during the course of COVID-19 (Miranda et al., 2017 & Sutton et al., 2016).

Chimeric Antigen Receptor T-Cell (CAR-T) Therapy

Research teams are exploring the potential of CAR-T-based immunotherapy as a treatment for COVID-19. CAR-T therapy is an innovative approach that involves reprogramming T cells to express

Vol.02, No.08, March, 2024

An International Peer-Reviewed Multidisciplinary Journal

synthetic receptors aimed at specific antigens, which allows for the destruction of virus-infected or cancerous cells and aids in managing disease progression (Mandini et al., 2018). Early studies indicate that engineered T cells designed to target SARS-CoV-specific antigens show a functional profile similar to that of SARS-specific memory CD8 T cells found in patients who had previously been infected with SARS-CoV. This initial evidence points to the possibility that CAR-T cells could serve as an effective treatment for SARS-CoV-2, the virus that causes COVID-19.

Vaccine Development against Coronavirus

Vaccination against COVID-19 began in India on January 16, 2021 (Kumar et al., 2021). The Indian government, along with various states, initiated a comprehensive vaccination campaign aimed at reaching 300 million people in priority groups, including healthcare and frontline workers, as well as individuals over the age of 50 (Ministry of Health and Family Welfare, 2021).

Types of COVID-19 vaccines

As of now, several COVID-19 vaccines have been approved and are in use worldwide. Here are some of the key vaccines:

- 1. **Pfizer-BioNTech (Comirnaty)**: An mRNA vaccine that has been widely used for its efficacy in preventing COVID-19 and its variants.
- 2. **Moderna (Spikevax)**: Another mRNA vaccine, similar to Pfizer-BioNTech, known for its strong immune response.
- 3. **AstraZeneca (Vaxzevria)**: A viral vector vaccine that has been widely distributed, particularly in Europe and low- and middle-income countries.
- 4. **Johnson & Johnson (Janssen)**: A viral vector vaccine that is administered as a single dose, providing a convenient option for vaccination.
- 5. **Sinopharm** (**BBIBP-CorV**): An inactivated virus vaccine developed in China, which has been used in many countries, particularly in the Middle East and Africa.
- 6. **Sinovac** (**CoronaVac**): Another inactivated virus vaccine from China that has been widely used in several countries.
- 7. **Novavax** (**Nuvaxovid**): A protein subunit vaccine that has shown good efficacy in trials and has been approved in several regions.
- 8. **Sputnik V**: A viral vector vaccine developed in Russia, which has been used in various countries.
- 9. **Covovax**: A version of the Novavax vaccine produced by the Serum Institute of India, primarily for use in India and neighbouring countries.

Covaxin: An inactivated virus vaccine developed by Bharat Biotech in India, which has received emergency use authorization in several countries (World Health Organization).

COVID-19 Vaccine Technology:

You've given an excellent summary of various vaccine technologies and their mechanisms! Here's a recap along with some additional details on each type you discussed:

1. mRNA Vaccines (Pfizer-BioNTech and Moderna):

- Mechanism: These vaccines utilize messenger RNA (mRNA) to direct cells in the body to create a harmless fragment of the spike protein present on the surface of the SARS-CoV-2 virus. This protein stimulates an immune response, resulting in the production of antibodies and preparing the immune system to identify and combat the virus if it is encountered later on.
- **Technology**: Although mRNA vaccines are a recent development, they have been researched for many years and have demonstrated strong effectiveness and safety in preventing COVID-19.

2. Viral Vector Vaccines (Covishield/AstraZeneca):

- **Mechanism**: These vaccines utilize a harmless virus, specifically an adenovirus, which has been genetically altered to transport a segment of the coronavirus's genetic material. After entering the body, this vector virus can replicate and stimulate the immune system to generate antibodies against the coronavirus.
- **Technology**: This approach is a proven method that has been employed in vaccines for various other diseases, such as Ebola and certain flu vaccines.

3. Inactivated Virus Vaccines (Covaxin):

- **Mechanism**: These vaccines include virus particles that have been killed or inactivated, ensuring they cannot cause disease. When given, they prompt the immune system to generate antibodies without leading to illness.
- **Technology**: Inactivated virus vaccines have a long history of use, being employed in vaccines for diseases such as polio, hepatitis A, and influenza (Centers for Disease Control and Prevention).

COVID-19 Vaccine efficacy:

The Pfizer vaccine boasts an efficacy rate of 95% and is administered in two doses, spaced 21 days apart. It is authorized for individuals aged 16 and older. The Moderna COVID-19 vaccine has an effectiveness of 94.1%, requiring two doses given 28 days apart, and is intended for those 18 and older. The Oxford vaccine shows a 62% efficacy after two full doses, with a notable 90% effectiveness observed in a small group that received a half dose followed by a full dose.

Vaccine Efficacies and Dosing

1. **Pfizer-BioNTech** (Comirnaty)

An International Peer-Reviewed Multidisciplinary Journal

- Efficacy: 95%
- Dosing Schedule: Two doses administered 21 days apart.
- Age Approval: Approved for individuals aged 16 and older (Baden et. al., 2021 & Pfizer-BroNTech)

2. Moderna (Spikevax)

- Efficacy: 94.1%
- Dosing Schedule: Two doses administered 28 days apart.
- Age Approval: Approved for individuals aged 18 and older (Polack et. al., 2020 & CDC)

3. AstraZeneca (Oxford)

- Efficacy: Typically about 62%, with effectiveness increasing to 90% in a limited group that received a half dose followed by a full dose.
- Dosing Schedule: Administered in two doses, with the timing differing by study, usually between 4 to 12 weeks.
- Age Approval: Authorized for use in individuals aged 18 and older in numerous countries (Voysey et al., 2021 & CDC)

4. Covaxin (Bharat Biotech)

- Efficacy has been reported at around 77.8% for symptomatic COVID-19 following two doses.
- The efficacy against severe disease is generally higher, though exact percentages can differ depending on the circulating variants.
- o Dosing Schedule: Two doses given 28 days apart.
- $\circ~$ Approved for use in individuals aged 18 and older in India.

COVID-19 Vaccine Storage Requirements

1. Pfizer-BioNTech (Comirnaty)

- Storage Temperature: Requires ultra-cold storage at approximately -94°F (-70°C).
- Special Requirements: Must be kept in specialized freezers designed for ultra-cold temperatures to maintain efficacy.

2. Moderna (Spikevax)

- \circ Storage Temperature: Can be stored in a conventional freezer at -4°F (-20°C).
- Shelf Life: Can also be stored in a refrigerator at 36°F to 46°F (2°C to 8°C) for a limited time before administration.

3. AstraZeneca (Oxford)

- $\circ~$ Storage Temperature: Can be stored in a normal refrigerator at 2°C to 8°C (36°F to 46°F).
- Advantages: This temperature stability makes it easier to distribute and store in various healthcare settings, especially in low-resource areas.

The different storage needs of these vaccines underscore the logistical hurdles faced in vaccination campaigns. The Pfizer vaccine requires ultra-cold storage, demanding specialized equipment, whereas the Moderna and AstraZeneca vaccines provide more adaptable storage solutions, making it easier to distribute and increase access.

Conclusions

The approach to preventing and treating COVID-19 shows that relying on just one method isn't enough. We need a mix of vaccination, public health measures, treatments, and community involvement to truly manage the pandemic. Staying alert and adjusting our strategies will be crucial as circumstances change and new variants come up. Working together—governments, health organizations, and communities—will be key to tackling the challenges that COVID-19 and future pandemics present.

Reference

- 1. Alcayaga-Miranda, F., Cuenca, J., & Khoury, M. (2017). Antimicrobial activity of mesenchymal stem cells: current status and new perspectives of antimicrobial peptide-based therapies. *Frontiers in immunology*, *8*, 339.
- 2. Arabi, Y. M., Shalhoub, S., Mandourah, Y., Al-Hameed, F., Al-Omari, A., Al Qasim, E., ... & Fowler, R. (2020). Ribavirin and interferon therapy for critically ill patients with middle east respiratory syndrome: a multicenter observational study. *Clinical infectious diseases*, 70(9), 1837-1844.
- 3. AstraZeneca COVID-19 Vaccine. CDC Website.
- 4. Baden, L. R., et al. (2021). Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. New England Journal of Medicine, 384(5), 403-416.
- Cao, B., Wang, Y., Wen, D., Liu, W., Wang, J., Fan, G., ... & Wang, C. (2020). A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. *New England journal of medicine*, 382(19), 1787-1799.
- 6. Centers for Disease Control and Prevention (CDC). How COVID-19 Vaccines Works https://www.cdc.gov/covid/vaccines/how-they-work.

- 7. Chowdhury, M. S., Rathod, J., & Gernsheimer, J. (2020). A rapid systematic review of clinical trials utilizing chloroquine and hydroxychloroquine as a treatment for COVID-19. *Academic Emergency Medicine*, 27(6), 493-504.
- 8. Chu, C. M., Cheng, V. C. C., Hung, I. F. N., Wong, M. M. L., Chan, K. H., Chan, K. S., ... & Yuen, K. Y. (2004). Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax*, *59*(3), 252-256.
- Coleman, C. M., Sisk, J. M., Mingo, R. M., Nelson, E. A., White, J. M., & Frieman, M. B. (2016). Abelson kinase inhibitors are potent inhibitors of severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus fusion. *Journal of virology*, 90(19), 8924-8933.
- 10. Dai, W., Zhang, B., Jiang, X. M., Su, H., Li, J., Zhao, Y., ... & Liu, H. (2020). Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease. *Science*, *368*(6497), 1331-1335.
- De Wilde, A. H., Jochmans, D., Posthuma, C. C., Zevenhoven-Dobbe, J. C., Van Nieuwkoop, S., Bestebroer, T. M., ... & Snijder, E. J. (2014). Screening of an FDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture. *Antimicrobial agents and chemotherapy*, 58(8), 4875-4884.
- 12. Delvecchio, R., Higa, L. M., Pezzuto, P., Valadão, A. L., Garcez, P. P., Monteiro, F. L., ... & Tanuri, A. (2016). Chloroquine, an endocytosis blocking agent, inhibits Zika virus infection in different cell models. *Viruses*, 8(12), 322.
- 13. Dong L, Hu S, Gao J. (2019). Discovering drugs to treat coronavirus disease (COVID-19). Drug Discov Ther. 2020;14(1):58-60.
- Dyall, J., Gross, R., Kindrachuk, J., Johnson, R. F., Olinger Jr, G. G., Hensley, L. E., ... & Jahrling, P. B. (2017). Middle East respiratory syndrome and severe acute respiratory syndrome: current therapeutic options and potential targets for novel therapies. *Drugs*, 77(18), 1935-1966.
- 15. Favre G, Pomar L, Musso D, Baud D. (2020) 2019-nCoV epidemic: what about pregnancies? Lancet 2020;395:e40.
- 16. Fu, B., Xu, X., & Wei, H. (2020). Why tocilizumab could be an effective treatment for severe COVID-19?. *Journal of translational medicine*, *18*(1), 164.
- 17. Furuta, Y., Komeno, T., & Nakamura, T. (2017). Favipiravir (T-705), a broad-spectrum inhibitor of viral RNA polymerase. *Proceedings of the Japan Academy, Series B*, 93(7), 449-463.

- 18. Gao, Q. Y., Chen, Y. X., & Fang, J. Y. (2020). 2019 Novel coronavirus infection and gastrointestinal tract. *Journal of digestive diseases*, 21(3), 125.
- 19. Gautret, P., Lagier, J. C., Parola, P., Meddeb, L., Mailhe, M., Doudier, B., ... & Raoult, D. (2020). Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *International journal of antimicrobial agents*, *56*(1), 105949.
- 20. Government of India, Ministry of Health and Family Welfare, Directorate General of Health Services (EMR Division). (2020, June 13). *Clinical management protocol: COVID-19* (Version 3).
- 21. Gu, J., & Korteweg, C. (2007). Pathology and pathogenesis of severe acute respiratory syndrome. The American journal of pathology, 170(4), 1136-1147.
- 22. Huang P, Liu T, Huang L, et al. Use of chest CTin combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology. 2020.
- 23. Kadam, R. U., & Wilson, I. A. (2017). Structural basis of influenza virus fusion inhibition by the antiviral drug Arbidol. *Proceedings of the National Academy of Sciences*, *114*(2), 206-214.
- 24. Kumar, V. M., Pandi-Perumal, S. R., Trakht, I., & Thyagarajan, S. P. (2021). Strategy for COVID-19 vaccination in India: the country with the second highest population and number of cases. *npj Vaccines*, *6*(1), 60.
- 25. Lal A, Davaro R, Mishra AK, et al. (2019). Detection of coexisting toxigenic Clostridium difficile and nontyphoidal Salmonella in healthcare worker with diarrhea: A therapeutic dilemma. J Family Med Prim Care;8:2724-7.
- 26. Lal, A., Al Hammadi, A., & Rapose, A. (2019). Latent tuberculosis infection: treatment initiation and completion rates in persons seeking immigration and health care workers. *The American journal of medicine*, *132*(11), 1353-1355.
- 27. Langhi, D. M., Santis, G. C. D., & Bordin, J. O. (2020). COVID-19 convalescent plasma transfusion. *Hematology, transfusion and cell therapy*, 42(2), 113-115.
- 28. Li, G., & De Clercq, E. (2020). Therapeutic options for the 2019 novel coronavirus (2019nCoV). *Nature reviews Drug discovery*, *19*(3), 149-150.
- 29. Li, G., Hu, R., & Zhang, X. (2020). Antihypertensive treatment with ACEI/ARB of patients with COVID-19 complicated by hypertension. *Hypertension Research*, *43*(6), 588-590.
- 30. Li, X., Yue, S., & Luo, Z. (2017). Mesenchymal stem cells in idiopathic pulmonary fibrosis. *Oncotarget*, 8(60), 102600.

An International Peer-Reviewed Multidisciplinary Journal

- Liang H, Acharya G. (2020). Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow? Acta Obstet Gynecol Scand;99:439-42. doi: 10.1111/ aogs.13836.
- 32. Maldini, C. R., Ellis, G. I., & Riley, J. L. (2018). CAR T cells for infection, autoimmunity and allotransplantation. *Nature Reviews Immunology*, *18*(10), 605-616.
- 33. Mehta, P., McAuley, D. F., Brown, M., Sanchez, E., Tattersall, R. S., & Manson, J. J. (2020). COVID-19: consider cytokine storm syndromes and immunosuppression. *The lancet*, 395(10229), 1033-1034.
- 34. Ministry of Health and Family Welfare, Government of India. COVID-19 vaccine operational guidelines. [accessed on December 20, 2021]. Available from: https://main.mohfw.gov.in/sites/default/files/COVID19VaccineOG111Chapter16.pdf .
- 35. Moderna COVID-19 Vaccine. CDC Website.
- 36. Morra, M. E., Van Thanh, L., Kamel, M. G., Ghazy, A. A., Altibi, A. M., Dat, L. M., ... & Huy, N. T. (2018). Clinical outcomes of current medical approaches for Middle East respiratory syndrome: a systematic review and meta-analysis. *Reviews in medical virology*, 28(3), e1977.
- Munster, V. J., Koopmans, M., Van Doremalen, N., Van Riel, D., & de Wit, E. (2020). A novel coronavirus emerging in China—key questions for impact assessment. *New England Journal* of *Medicine*, 382(8), 692-694.
- 38. Ng, D. L., Al Hosani, F., Keating, M. K., Gerber, S. I., Jones, T. L., Metcalfe, M. G., ... & Zaki, S. R. (2016). Clinicopathologic, immunohistochemical, and ultrastructural findings of a fatal case of Middle East respiratory syndrome coronavirus infection in the United Arab Emirates, April 2014. *The American journal of pathology*, 186(3), 652-658.
- 39. Pfefferle, S., Schöpf, J., Kögl, M., Friedel, C. C., Müller, M. A., Carbajo-Lozoya, J., ... & von Brunn, A. (2011). The SARS-coronavirus-host interactome: identification of cyclophilins as target for pan-coronavirus inhibitors. *PLoS pathogens*, 7(10), e1002331.
- 40. Pfizer-BioNTech COVID-19 Vaccine. CDC Website.
- 41. Polack, F. P., et al. (2020). Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine. New England Journal of Medicine, 383(27), 2603-2615.
- 42. Rabaan, A. A. (2017). Middle East respiratory syndrome coronavirus: five years later. *Expert Review of Respiratory Medicine*, 11(11), 901-912.
- 43. Rossignol, J. F. (2016). Nitazoxanide, a new drug candidate for the treatment of Middle East respiratory syndrome coronavirus. *Journal of infection and public health*, 9(3), 227-230.

- 44. Savarino, A., Di Trani, L., Donatelli, I., Cauda, R., & Cassone, A. (2006). New insights into the antiviral effects of chloroquine. *The Lancet infectious diseases*, 6(2), 67-69.
- 45. Shetty, A. K. (2020). Mesenchymal stem cell infusion shows promise for combating coronavirus (COVID-19)-induced pneumonia. *Aging and disease*, 11(2), 462.
- 46. Soo, Y. O. Y., Cheng, Y., Wong, R., Hui, D. S., Lee, C. K., Tsang, K. K. S., ... & Sung, J. J. Y. (2004). Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. *Clinical microbiology and infection*, 10(7), 676-678.
- 47. Stockman, L. J., Bellamy, R., & Garner, P. (2006). SARS: systematic review of treatment effects. *PLoS medicine*, *3*(9), e343.
- 48. Sutton, M. T., Fletcher, D., Ghosh, S. K., Weinberg, A., van Heeckeren, R., Kaur, S., ... & Bonfield, T. L. (2016). Antimicrobial properties of mesenchymal stem cells: therapeutic potential for cystic fibrosis infection, and treatment. *Stem cells international*, 2016(1), 5303048.
- 49. Taherian, E., Rao, A., Malemud, C. J., & Askari, A. D. (2013). The biological and clinical activity of anti-malarial drugs in autoimmune disorders. *Current Rheumatology Reviews*, 9(1), 45-62.
- 50. Voysey, M., et al. (2021). Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet, 397(10269), 99-111.
- 51. Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., ... & Peng, Z. (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *jama*, *323*(11), 1061-1069.
- 52. Wang, M., Cao, R., Zhang, L., Yang, X., Liu, J., Xu, M., ... & Xiao, G. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell research*, *30*(3), 269-271.
- 53. World Health Organization (WHO). COVID-19 Vaccines: Overview and Information. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines.
- 54. World Health Organization. (2020). Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance, 28 January 2020 (No. WHO/nCoV/Clinical/2020.3). World Health Organization.

- 55. Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., ... & Wang, F. S. (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *The Lancet respiratory medicine*, 8(4), 420-422.
- 56. Yamano, Y., Taniguchi, H., Kondoh, Y., Ando, M., Kataoka, K., Furukawa, T., ... & Hasegawa, Y. (2018). Multidimensional improvement in connective tissue disease-associated interstitial lung disease: Two courses of pulse dose methylprednisolone followed by low-dose prednisone and tacrolimus. *Respirology*, 23(11), 1041-1048.
- 57. Yang, H. Y., & Duan, G. C. (2020). Analysis on the epidemic factors for COVID-19. Zhonghua yu Fang yi xue za zhi [Chinese Journal of Preventive Medicine], 54(6), 608-613.
- 58. Zhang, L., & Liu, Y. (2020). Potential interventions for novel coronavirus in China: A systematic review. *Journal of medical virology*, 92(5), 479-490.
- 59. Zhang, W., Du, R. H., Li, B., Zheng, X. S., Yang, X. L., Hu, B., ... & Zhou, P. (2020). Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerging microbes & infections*, 9(1), 386-389.