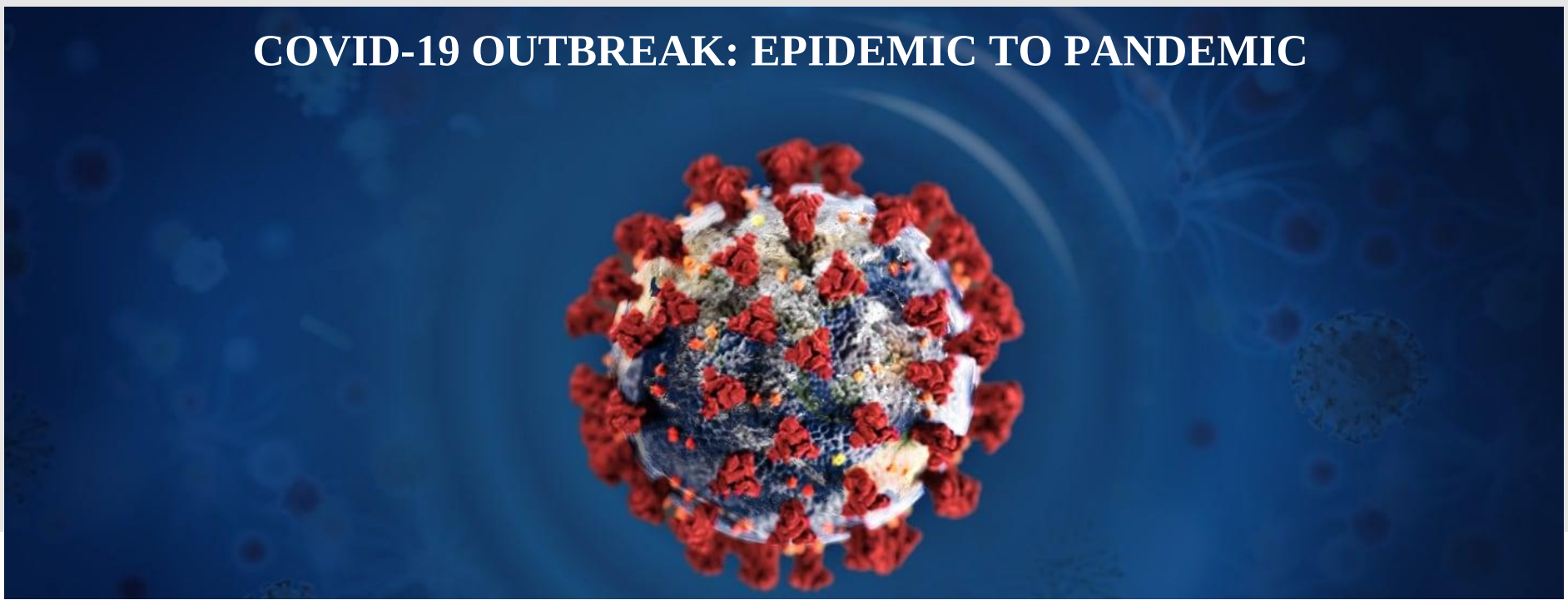

TREATMENT PROTOCOLS

-HARSHITA BALAMURUGAN

ABSTRACT

The outbreak of the novel coronavirus disease (COVID-19) in Wuhan, China was first identified in December 2019. Since then it has spread all around the world, becoming an emergency of major international concern. Similar to severe acute respiratory, SARS-CoV-2 infection results in clusters of severe respiratory illness. When a person with COVID-19 coughs or exhales, the disease spreads from person to individual by tiny droplets from the nose or mouth. In order to treat infected patients, early diagnosis, quarantine, and supportive care are very critical. Treatments include chloroquine and hydroxychloroquine, antiviral drugs, corticosteroids, antibodies, convalescent plasma transfusion, and vaccine therapy. The current treatment protocol includes real-time PCR test and Antigen test for its diagnosis.

INTRODUCTION

A novel coronavirus 2019-nCoV, emerged in Wuhan, China, at the end of 2019. More than half a million people have lost their lives to the killer disease. Research on various drugs took place that have been touted as a cure for COVID-19, but medical experts are yet to come up with the 'magic bullet' that can cure the killer disease and to make a decisive victory over the pandemic that has left a trail of destruction world over- emotional and financial.

There are currently no specific treatments for COVID-19. The treatments have been developed based on existing drugs for other diseases, or on techniques that have successfully produced as effective drugs for other diseases. Once a potential new drug has been developed it must be tested in clinical trials for safety and effectiveness.

Coronavirus is observed to be genetically very similar to the viruses that caused severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), so it is believed that the medications used to treat these infections might be effective against COVID-19 too. Other established antiviral drugs could also work and these could be used to treat COVID-19. Any new drug must be tested in clinical trials for checking its safety and efficacy in COVID-19 patients before it goes to market. These are some of the new methods taken to develop therapies and medications for the treatment of COVID-19.

THERAPIES AND MEDICATIONS

No specific treatments for COVID-19 exist as of now. Doctors and scientists are now scrambling to find treatments and drugs that can save the lives of COVID-19 affected people and to prevent the existing infection. Therapies and treatments that are under investigation includes drugs that have been used to treat malaria and autoimmune diseases, antiviral drugs that were developed for other viruses and antibodies from people who have recovered from COVID-19.

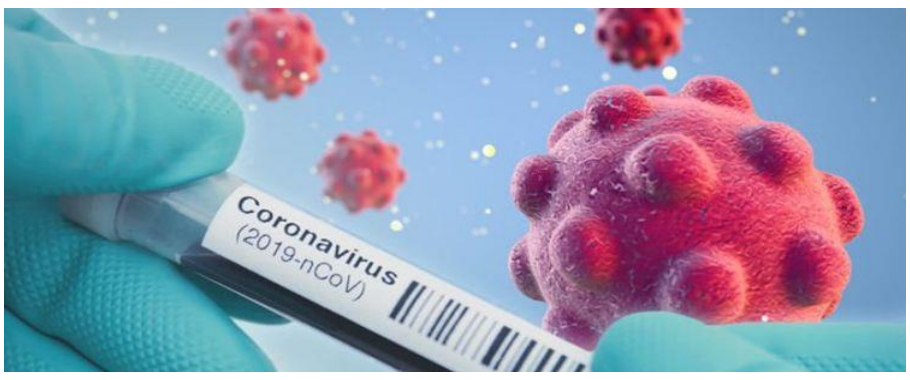

Fig. 1 Coronavirus (SARS-CoV-2)

Therapies and medications currently in use or under trial for the treatment of patients with COVID-19 are as follows:

- Supportive care is the treatment standard for COVID-19.
- While many therapies including antiviral and anti-inflammatory medications have been proposed to treat COVID-19, there is very little evidence to support the use of any therapy. Clinical trials to evaluate potential therapies are ongoing.

REMDESIVIR AND FAVIPIRAVIR

Remdesivir and Favipiravir have shown promise as stand-alone therapy in in-vitro models.

- Remdesivir prevents new virus copies from being produced by mimicking the genetic material of the coronavirus.
- Favipiravir is a flu drug that blocks the virus's ability to copy its genetic material.

Remdesivir (Veklury) is currently the only FDA approved medication to treat COVID-19 based on the findings that recovered faster in hospitalised patients who received Remdesivir (Veklury)

Fig. 2 Remdesivir and Favipiravir Antiviral drugs

LOPINAVIR-RITONAVIR

Lopinavir-Ritonavir (Not promising) Initially this combination of HIV drugs seemed to have prevented the replication of coronavirus, but clinical trials in patients proved disappointing and were suspended by the WHO. The drugs can still play a role as a preventive and in treating patients with mild symptoms. Clinical data have shown no benefit for lopinavir-ritonavir as stand-alone therapy.

Fig. 3 COVID-19 Therapy Combination Lopinavir/Ritonavir

HYDROXYCHLOROQUINE AND CHLOROQUINE

Hydroxychloroquine and Chloroquine (not promising)

During the start of the pandemic, researchers found that these old anti-malaria drugs could stop the replication of coronavirus in the cells. A few small studies on patients also offered hope that COVID-19 could be treated with hydroxychloroquine. However, clinical trials shows that hydroxychloroquine did not help people with COVID-19 to get better or prevent the virus from being contracted by healthy individuals.

Treating people with hydroxychloroquine after being diagnosed didn't reduce the severity of the disease. However, in the process of treating the disease the drug can cause serious side effects to the heart and other organs. Yet Chloroquine and Hydroxychloroquine have shown promise as effective therapy in limited clinical studies.

Fig. 4 Chloroquine and Hydroxychloroquine: Current evidence for their effectiveness in treating COVID-19

CONVALESCENT PLASMA THERAPY

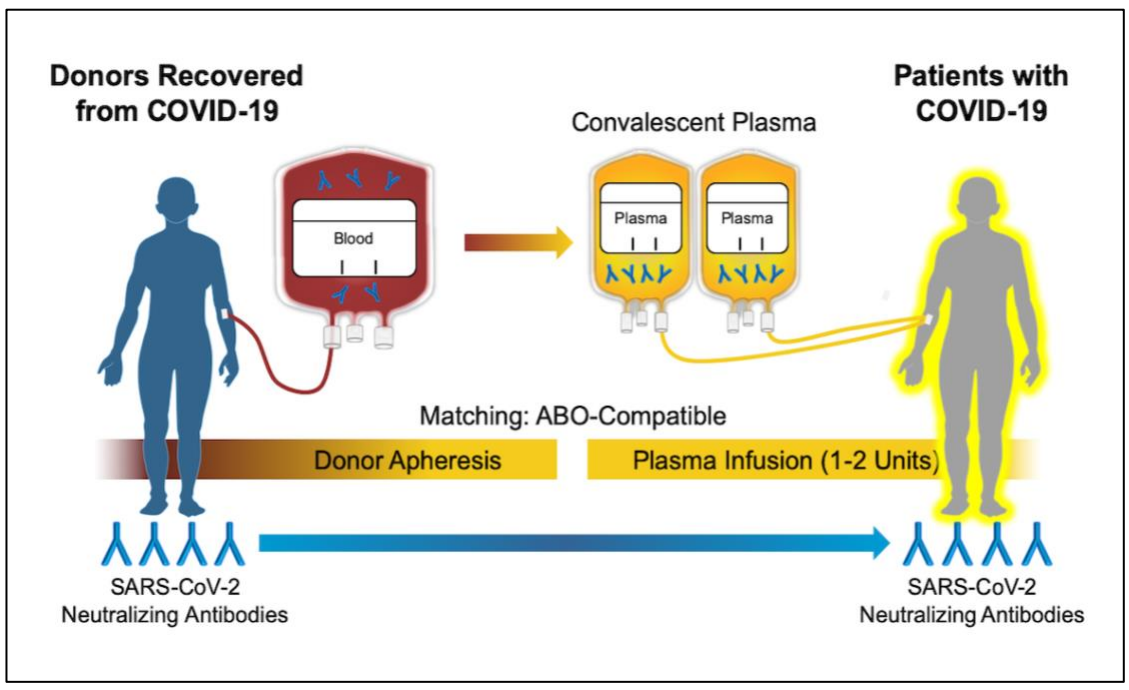

Fig.5 Concept of Using Convalescent Plasma to Treat COVID-19

Convalescent plasma has provided successful results with other viral infections. Plasma is the liquid part of blood which carries blood cells. Convalescent plasma is collected from individuals who have recovered from COVID-19 which is then transfused into someone with an active coronavirus infection. It is thought that antibodies found in the convalescent plasma can help prevent coronavirus infection.

Being approved as an "off-label" therapy it works best when given early on in the treatment cycle. Years back doctors used plasma from the blood of recovered flu patients to treat people sick with flu. The same treatment has been tried on severely ill COVID-19 patients and the early results seem to be promising. Hence, the FDA has authorised plasma therapy for very sick COVID-19 patients. Clinical trials are still ongoing to explore its efficacy in the treatment of COVID-19.

CORTICOSTEROIDS

Patients with severe COVID-19 can tend to develop a systemic inflammatory response that can lead to lung injury and multisystem organ dysfunction. It has been proposed that these deleterious effects can be prevented or mitigated by the potent anti-inflammatory effects of corticosteroids.

The corticosteroid drug dexamethasone has decreased the risk of dying in very ill hospitalized COVID-19 patients according to a recent report based on a clinical trial. Some of the less expensive and easily available potent anti-inflammatory drugs are Dexamethasone and other corticosteroids (prednisone, methylprednisolone). Several clinical trials to analyse corticosteroids for the treatment of COVID-19 are currently underway or in development.

Fig.6 Corticosteroids

MONOCLONAL ANTIBODIES

Two monoclonal antibody medications have received emergency use authorization from the FDA to treat COVID-19.

Monoclonal antibodies are artificially made proteins in a laboratory that can help the immune system fight off viruses. Two of the most common drugs used to treat mild to moderate COVID-19 in people who have a higher risk of developing serious illness due to COVID-19 are bamlanivimab, and a combination of two antibodies called casirivimab and imdevimab.

Treatment involves a single intravenous infusion given in an outpatient setting. It becomes more effective when these medications are given soon after COVID-19 symptoms start and prior to hospitalization.

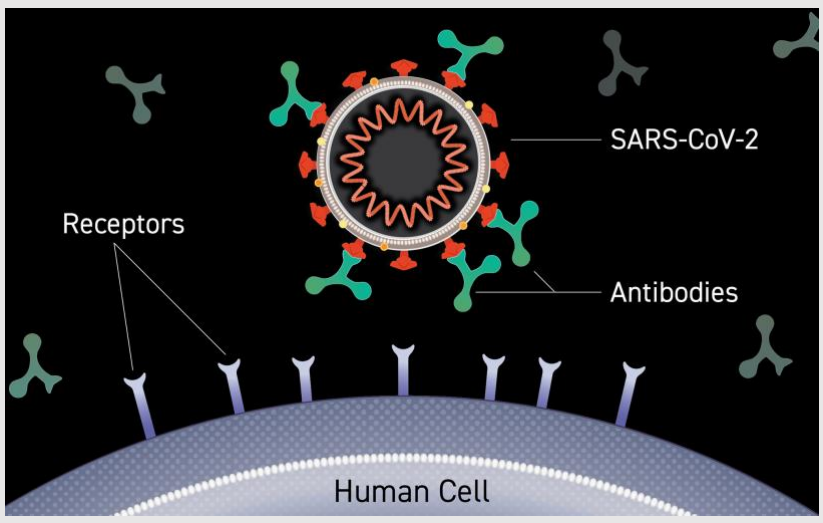

Fig.7 Monoclonal Antibodies for Treatment of COVID-19

At present there are many clinical trials in process to study about the other potential therapies for COVID-19. Researchers are also testing existing medications which has been typically used to treat other conditions to see if they are effective for treating COVID-19.

The FDA is carrying out ways to accelerate the development and availability of COVID-19 treatments during this unprecedented times of public health emergency. A new emergency program, Coronavirus Treatment Acceleration Program (CTAP), aimed at speeding up research for the development of COVID-19 treatments was implemented by FDA.

As of now, Remdesivir (Veklury) is the only medication approved by the FDA for the treatment of COVID-19, but it can only be used for certain hospitalized patients and is not 100% effective. Patients who are hospitalized can receive supportive care, participated in clinical trials, and be given medications off-label according to the conditions of the hospital guidelines and their doctors' clinical judgement. Patients with mild symptoms can be self-isolated in their respective places.

There isn't any cure or vaccine for COVID-19 at this time. More studies and research on this is needed to confirm if any of the potential treatments listed above will work for COVID-19. Research on COVID-19 is rapidly evolving and a numerous number of clinical trials are ongoing.

PRIORITY MEDICAL DEVICES FOR COVID PREVENTION, DIAGNOSTIC AND MANAGEMENT

In order to protect health care workers, diagnose and treat COVID-19, different types of medical devices including medical equipment, personal protective equipment (PPE), and other medical supplies are required for the management of COVID-19 patients.

COVID-19 diagnostic testing is done to find out if an individual is infected with SARS-CoV-2, which causes COVID-19. The FDA has approved the PCR test and Antigen test for the diagnosis of a COVID-19 infection.

PCR TEST

PCR test is also known as molecular test. The genetic material of the virus is detected using a lab technique called polymerase chain reaction. A fluid sample is collected by inserting a nasopharyngeal swab into the individual's nostril and the fluid is taken from the back of the nose. In some cases, a oropharyngeal swab is used.

The test results may be ready in few minutes if analysed onsite. However, in locations with test processing delays it might take longer. PCR tests are very accurate when performed by a qualified health care professional.

Fig. 8 Polymerase Chain Reaction COVID-19 Diagnostic Test

Fig. 9 COVID-19 Antigen Rapid Test

ANTIGEN TEST

Antigen test detects certain proteins in the virus. A long nasal swab is used to get a fluid sample and this test can produce results in minutes. Antigen test is faster and cheaper than a PCR test. As a result, antigen tests may be more practical to use for large numbers of people. When instructions are carefully followed, a positive antigen test result is considered accurate. However, there's an increased chance of false-negative results. This means that it is possible to be infected with the virus but have a negative result as well. The doctor may recommend a PCR test to confirm a negative antigen test result according to the situation.

Flu SC2 Multiplex Assay is a PCR test which can detect the COVID-19 virus, influenza A and influenza B at the same time. A single sample is only needed to check for all the three viruses, and this could be helpful particularly during the flu season. However, a negative result does not rule out the possibility of any of these infections. Depending on the symptoms, the possible exposures and the doctor's clinical judgment; the diagnostic process may include more steps.

PERSONAL PROTECTIVE EQUIPMENT

Given the threat of Covid-19, the need to emphasize on the usage of proper precautions for infection control in health care settings is important. The routes of transmission include direct contact —contact with the respiratory droplets and aerosols from an affected person — and indirect contact, such as contact with contaminated surfaces or supplies

The best way for health care workers to prevent infection is through training and demonstrated competency in putting on and removing, also known as donning and doffing, personal protective equipment (PPE). PPE is a personal protective equipment which includes gloves, a gown, a respirator with a rating of N95 or
higher, and a full-face shield or goggles. It protects the health care personnel by creating a barrier between them and infectious germs and also protects the patients by preventing the spreading of infections.

The types of PPE vary with the type of precautions that are required:

- Contact precautions require a gown and gloves.
- Droplet precautions require surgical masks.
- Airborne precautions require a particulate respirator.
- When eye protection is needed goggles are used.

Fig.10 COVID-19 Personal Protective Equipment

Fig. 11 Pulse oximeter

PULSE OXIMETER

During the Covid-19 pandemic, the pulse oximeter device has become something of a necessity for the mass. It is non-invasive, less expensive and easy to use. Pulse oximeters are effective at detecting hypoxemia or low blood oxygen levels which is one of the early signs of a Covid-19 infection.

The device is usually clipped onto the forefinger of the user. It consists of a monitor containing the batteries and a display; a probe consisting of light-emitting diodes or LEDs and a light detector called a photo-detector and senses the user's pulse. Two important readings are displayed:

1. Pulse rate which is recorded as beats per minute
2. Oxygen saturation of haemoglobin in arterial blood

OXYGEN CYLINDERS

Families of COVID-19 patients are receiving oxygen therapy at home due to scarcity of beds with oxygen facilities as they wait for a vacant spot in hospitals. However, the use of oxygen cylinders at home without medical supervision or prescription has been prohibited by the doctors. COVID-19's rising fear adds on to the panic and leads to stocking up of portable oxygen bottles at home. With inappropriate supply of oxygen a patient can even die from oxygen toxication.

Fig. 12 Oxygen Cylinder

THERMAL SCANNER

Among some Covid-19 common symptoms, fever is the most common symptom that confirms covid-19 followed by cough and fatigue. Thermal imaging scanner serves as a front line screening tool and helps to prevent the spread of the disease by detecting individuals with elevated body temperature in a high-traffic places at a point of entry such as airport, office building, supermarket, etc. It uses infrared for temperature detection and can tell us how much heat something has and give us information about the temperature.

This technology cannot directly identify Covid-19, but it helps to identify and filter out potential “high-risk” individuals. It is designed in such a way that it can accurately detect temperature from distance without any close human contact which can help to reduce the risk of Covid-19 transmission.

Fig. 13 Thermal Scanner

Fig. 14 Ventilator

VENTILATORS

There has been no specific treatment for COVID-19 patients. For the patients who develop respiratory failure and are unable to oxygenate with non-invasive methods, critical care doctors have been providing supportive therapy. Ever since the pandemic started, mechanical ventilation has been used to oxygenate seriously ill COVID-19 patients. When the disease causes the lungs to fail the ventilator takes over the body's breathing process. This extends the patient's time to fight off the infection and recover.

CPAP/BIPAP

BiPAP and CPAP machines are used to treat patients with sleep apnea and respiratory diseases. It is less invasive and less expensive than invasive ventilation.

Continuous positive airway pressure (CPAP) machines apply continuous pressure to the airways while on the other hand bi-level positive airway pressure (BiPAP) machines apply high pressure when the patients inhale and low pressure. They use a mask rather than intubating the patient like ventilators do.

These machines however cannot be used to treat patients with COVID-19 because they send the patient’s breath into the room, contaminating the area with virus droplets and putting medical staff at risk of exposure. A team of researchers developed pathogen management kits. The kits can be linked to the respiratory machines and can use UV to disable COVID-19 and other pathogens before a patient exhales and his/her breath is circulated back into the hospital room.

Fig. 15 CPAP Machine

CONCLUSION

At an increasingly alarming pace, the Covid-19 viral spectre outbreak is spreading across different. With hospitals overwhelmed with critically ill patients, there is a great need for treatment options for COVID-19. Rapid identification of such therapies is thus important, but it has been quite challenging. As the safety profile of these drugs are well known, a significant technique and an important strategy is repurposing of existing antiviral and immunomodulating drugs. However, the current outbreak of SARS-CoV-2 has once again highlighted the urgent need to develop broad-spectrum antiviral drugs, not just for coronaviruses, but also for other virus families that may also be the cause of future epidemics/pandemics.

There is not yet a therapeutic scheme of choice for this virus, and many of those mentioned, of which good preliminary results have been mentioned, are still in the experimental phase, so the use of these should be handled with caution. It is worth highlighting hand hygiene and the proper use of personal protective equipment. This use should always depend on the transmission mechanism, to optimize the use of health care costs, and maintain an adequate supply for health workers, especially in countries with the medium or low economy, government authorities should establish flows and protocols to establish the initiation of evidence-based therapeutic schemes.

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