



MANAGEMENT STRATEGIES OF COVID-19

General Medicine

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ABSTRACT

The ongoing COVID-19 pandemic clearing the globe has caused incredible concern around the world. Because of the restricted proof accessible on the elements of the infection and viable treatment alternatives accessible, extreme intense respiratory condition Covid 2 (SARS-CoV-2) has had an immense effect regarding horribleness and mortality. The monetary effect is still to be surveyed.

The reason for this article is to survey the proof for the numerous treatment alternatives accessible, to think about the fate of this worldwide pandemic, and to distinguish some potential choices that could change the treatment of COVID-19. Also, this article underscores the sheer significance of repurposing a portion of the accessible antiviral and antimicrobial specialists that have for quite some time been being used in order to have a compelling and quick reaction to this inescapable pandemic and the need to direct a multicenter worldwide randomized controlled preliminary to locate a successful single antiviral operator or a mixed combination of accessible antimicrobial operators.

We are as of now confronting one of the most noticeably terrible pandemics ever. Even though the mortality rate of SARS CoV 2 is not that high, yet less knowledge regarding transmission and the fear of infectivity makes it something to be scared of. Sadly, no immunization against SARS-CoV-2 or successful medication routine for COVID-19 presently exists. Medication repurposing of accessible antiviral operators may give a relief; in addition, combinations of many of antivirals and antibiotics might be useful in treating this malady. Here, we have featured a couple of accessible treatments like HCQ, Macrolides, Protease inhibitors, Convalescent Plasma therapy and the much awaited vaccines that could be compelling in treating COVID-19; in fact, various preliminaries are in progress to distinguish and affirm the viability of these specialists.

KEYWORDS

SARS CoV-2 , viable treatments, anti microbial, anti viral, hydroxychloroquine, vaccine

INTRODUCTION

In the city of Wuhan, China there was an outbreak of this deadly COVID-19 virus which affected the world badly. This was declared as a global pandemic in March and the entire world was trying to deal with it in different hit and trials¹

The clinical features and radiological findings of COVID 19 are non specific and are not easily distinguishable with a variety of circulating respiratory viruses, particularly influenza, is very important and chiefly done using upper (nasopharyngeal) or lower (induced sputum, endotracheal aspirates, bronchoalveolar lavage) tract samples for reverse transcriptase-polymerase chain reaction and bacterial cultures. Rapid access to diagnostic testing results may be a public health and clinical priority, with efficient patient triage and implementation of infection control practice²

The treatment protocols are not yet specified. In this article we try to explore some treatment modalities which were proven successful. Several trials are still undergoing around the world and we are yet to reach a revolutionising treatment. A worldwide collaboration of prominent scientists, doctors, pharmaceutical companies and scientific bodies are working to find out treatment options by exploring existing drugs. It is called the solidarity trial. WHO has recommended four therapies. Remdesivir, a drug originally developed for Ebola, Chloroquine/Hydroxychloroquine used in treatment of Malaria/Arthritis, Lopinavir along with Ritonavir used in treatment of HIV and an anti inflammatory compound called Interferon Beta in combination with Lopinavir and Ritonavir¹. Other potential therapies that have proven to be successful are Convalescent Plasma Therapy which is giving patients plasma of people who have recovered from COVID-19 which might help produce antibodies that can fight against the virus. The main objective of these studies is to rule out if any of the mentioned drugs help to slow down progression of the disease, improves survival with less side effects and less chances of recurrence. All of these drugs are promising as they've been proven to be safe for human use under specific conditions.

AIIMS Protocol

A patient is said to be a suspect if they have an acute respiratory illness with fever, cough or shortness of breath and if they have travelled to high risk COVID-19 affected countries in the last 14 days or came in close contact with a confirmed positive case within 14 days. Any health care worker with symptoms is also said to be a suspect. Asymptomatic traveller or a person who had close contact with a confirmed case should be advised to self quarantine and check temperature twice. All other precautions like wearing a mask and sanitising everything is also advised.

We can consider a case as 'mild' if they have low grade fever, cough,

malaise, rhinorrhea, sore throat without shortness of breath. Mild cases can be treated by Tab Oseltamivir 75 mg BD (for high risk influenza suspects), antibiotics like azithromycin in combination of amox/clav can be used. Paracetamol 500mg SOS used in high fever. If the patient is tested positive home isolation is advised and patient is asked to monitor temperature all day.

Any patient who has any of the following symptoms will be considered as a 'moderate to severe case'- Respiratory rate >24pm, sPO₂ <94% in room air, confusion or drowsiness, SBP <90 mmHg DBP <60mmHg. These patients are to be admitted and tested. If they are tested positive-Oxygen is given to maintain sPO₂ >94%, Antipyretics, Antitussives, Antibiotics are indicated. MDI is preferred over nebulisation. We can also consider Hydroxychloroquine (400mg BDX1 day followed by 200 mg BD X 5 days). Protease inhibitors like Lopinavir/Ritonavir can be considered on case to case basis (within 10 days of symptom onset). In severe cases if patient's conditions are worsening they will have respiratory failure, hypotension, worsening mental status, MODS. These patients are supposed to be admitted to ICU. After shifting to ICU NIV/HFNC to be carefully used in view of risk of aerosol generation. According to ARDS protocol, ventilator management is done along with standard care.

Pharmacological management

HYDROXYCHLOROQUINE (HCQ)

HCQ is a drug used for management of malaria and rheumatoid arthritis. This drug is now used against Coronavirus due to its in vitro efficacy.

Indian Council for Medical Research, India has stated to use this drug as chemoprophylactic in high risk population, specially health care personnel.

Hydroxychloroquine has higher efficacy than chloroquine. Both of these drugs show an inhibitory effect on SARS-CoV mRNA production¹

The proposed component of activity of both CQ and HCQ in rheumatic diseases incorporates concealment of T-lymphocyte reactions to mitogens, hindrance of leukocyte chemotaxis, adjustment of lysosomal compounds, restraint of DNA and RNA combination and catching of free radicals. As an enemy of malarial specialist, CQ is a blood schizonticide, and acts by gathering in the parasite food vacuole, and forestalling biocrystallization. As an immunosuppressant, HCQ is proposed to stifle intracellular antigen handling and stacking of peptides onto MHC class II molecules. The function of HCQ in COVID-19 or other viral contaminations has been founded on its

mitigating and hostile to viral activities showed in before in vitro and in vivo studies³

The New England Journal Of Medicine published a study for which 821 adults who were in contact of a confirmed COVID-19 case were selected. Two groups were divided. In first group people were given HCQ and the other group people received a placebo. Out of these groups 11.8% of the group that received HCQ developed an illness similar to COVID-19 and 14.3% of the Placebo group developed respiratory symptoms. This study contradicts the claim of ICMR as patients who received HCQ developed COVID-19⁷.

Azithromycin

It is a macrolide with bacteriostatic properties. It inhibits protein synthesis and doesn't let the bacteria grow. It is also used to treat viral illness as it shows anti viral effects too. When azithromycin was given along with HCQ it proved to have demonstrable antiviral activity against SARS-CoV-2^{1,5}

Azithromycin is easily available and has an excellent safety profile. It has proven to be affected and is used as first line management in many hospitals in the country for covid-19⁵. According to two New York University researchers, Dr Jennifer Lighter and Dr Vanessa Raabe recommending Azithromycin is careless^{6,7}. There is no clinical evidence that can support the benefits of Azithromycin in treatment of COVID-19. Evidences say that mortality rates are higher in patients receiving both HCQ and Azithromycin in comparison with HCQ. It has been demonstrated that HCQ and azithromycin freely can initiate QT interval prolongation, torsades de pointes, and drug-actuated unexpected cardiovascular death. Thus, consolidating these drugs represents a significant danger. A major study containing 956 374 HCQ receiving patients, in which 323 122 utilized both HCQ and azithromycin, watched an expanded danger of 30-day cardiovascular mortality, chest pain/angina, and cardiovascular breakdown among the patients taking HCQ in addition to azithromycin contrasted and HCQ utilize alone. SARS-CoV-2 can legitimately taint the heart, which may autonomously additionally incline COVID-19 patients to arrhythmia improvement beside the dangers passed on by favorable to arrhythmogenic drug mixes⁸. The Infectious Diseases Society of America, Centers for Disease Control and Prevention, and National Institutes of Health suggest that treatment with HCQ and azithromycin just be recommended with regards to clinical preliminary use because of the potential risks associated with it.

Other drugs

Lopinavir along with Ritonavir (Kaletra: works against HIV) together (protease inhibitor) are used to upgrade lopinavir's bioavailability by restraining its metabolic inactivation. Lopinavir with Ritonavir is viewed as a profoundly powerful antiretroviral agent. According to few studies the utilization of monotherapy as a restorative alternative in certain HIV-infected patients. In patients with SARS related with SARS-CoV disease, the mix of lopinavir/ritonavir and ribavirin brought about a lower pace of intense respiratory distress disorder (ARDS) or demise at day 21.

Favipiravir is an antiviral drug mostly used for treating influenza but now proven to be effective for hospitalised covid patients.

Remdesivir (adenosine analog) disrupts formation of new viral DNA. It is used against RSV, SARS-CoV and MERS-CoV for its antiviral activity. It improves pulmonary function when received by a patient just after a day of onset of symptoms.¹

Interferon

Interferon may have the least foothold in the domain of treatment strategies yet studies have shown that it ends up being efficacious⁹. Interferon is a signalling protein. It belongs to the class of cytokines. It inhibits protein synthesis and inactivates viral RNA. It helps in enhancing phagocytes activity and can thus affect the immune system. Interferon has to be given intramuscularly (i.m.) and not per oral (p.o.) as it is generated by gastrointestinal enzymes. Some studies have shown when interferon is combined by corticosteroids patients have had better oxygen saturation and improved radiological findings. Whereas when given in combination with Ribavirin it has shown decrease in mortality in 30 days and no change in mortality in 90 days. So utility of this drug is a flimsy topic to talk on. Interferon has also shown many adverse effects like neuropsychiatric illnesses, autoimmune effects like SLE, ischemia, renal problems, dermatological problems etc¹

Convalescent plasma

Recently FDA stated after conducting many trials that blood plasma can be used specifically from patients who recently recovered from COVID-19.

Recovered patients develop circulating antibodies after few days of infection. These circulatory antibodies are detected by ELISA. Most studies have proven that CP therapy doesn't show side effects and is a relatively safe intervention. The protocol for potential donor includes a verified document of SARS-CoV-2 infection. They can either show nasopharyngeal swab or serologic positivity. Donor should be symptomless for more than 14 days and should meet standard blood donor eligibility^{1,8}

The utilization of CCP is an interval approach until there is endorsement and wide accessibility of elective medicines, for example, hyperimmune globulin, built monoclonal antibodies, as well as antiviral medications, and the advancement of viable immunizations. The coordinations of CCP acquirement are perplexing, requiring collaboration between numerous partners including recuperated patients (for example planned givers), blood focuses or other plasma assortment focuses, treating doctors and their patients, and medical services managers and controllers administering the security of each progression. Plasmapheresis is alluring as a way to gather huge volumes of plasma. There are various ELISA-based tests for immunizer recognition: it is essential to consider the measure stage just as the explicitness (for example responsive with spike protein versus nucleocapsid) and the class of neutralizer (IgG versus complete) while assessing titers⁹

Vaccines

Russia was one of the first countries to go ahead in vaccine research. Successful Clinical trials were also conducted in University of Oxford in England but had to be halted due to possible adverse effects. As of September 2020, 49 trials are going on. 24 are in phase 1, 14 are in phase 2, 9 are in phase 3. Phase 3 means that they are safe to test in humans, but we have to test in numbers as high as 200,000 to 400,000. Then we have to monitor the candidates for quite a span of time. Following here means we have to see if the vaccine is provoking an immune response which protects us from Covid-19.

AstraZeneca trial was paused as one person in Britain came back with inflammation of spinal cord. A lot of big pharmaceutical companies have decided to come together to ensure scientific standards and ethical treatment of people when it comes to actual administering of phase 3 trials and the concept of approving vaccines will be held to highest standards. Every country has a regulatory body which governs the approval of vaccines. For example Food and Drug Administration in United States Of America and HealthCanada in Canada and India Council of Medical Research in India. When the phase 3 trials began they are obligated to make information public. Apparently some scientists also believe that human challenge trials can be a quicker way of speeding up clinical trials⁹

WHO has declared there are around 169 candidates for COVID-19. Out of these 169, 26 are undergoing human trial phase. WHO chief Dr Tedros has assured there will be equitable access and distribution of vaccines. People that are at high risk for example Healthcare workers, Police, other frontline workers, neonates and infants and geriatric patients will be prioritised^{10,11}

CONCLUSION

Since SARS-CoV2 is a novel virus we are still learning and trying to figure out how it works and the making an attempt to work out absolute best possible treatments for the deadly virus. At the moment the most suitable and foremost appropriate treatment would be self quarantine and treatment of mild symptoms like cough with cough medicines and fever with antipyretics and sometimes antibiotics. In severe cases we can provide oxygen therapy and ventilator support for patients having low SPO2 and difficulty in breathing.

We can conclude that therapeutic and prophylactic role of HCQ/Chloroquine is not clear yet (1). But if these medicines used in conjunction with Azithromycin or Remdesivir can be considered promising treatment options for patients with mild and moderate COVID-19. Efficacy of interferon is still controversial. Convalescent plasma therapy is proven to be a safe option too with less side effects. Although there is still need for randomised trials to prove the potency

of these drugs. We still need to conduct trials for vaccines because we cant rush into making faulty vaccines and risking patients. We have to ensure that vaccine is not only safe but also elicit enough of immune response.

We can easily say due to the fast growing pandemic many mistakes are being made hence we cannot rely on a particular treatment regimen yet

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