



Therapeutic options for Covid - 19 : Pandemic - A Review

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ABSTRACT

Covid-19 is an outbreak of a severe acute respiratory disorder which emerged in December 2019 in Wuhan, China. Since then the virus has spread to many countries and has become a pandemic. The mortality rate of the disease is very high but it varies from country to country depending on the medical facilities and the observance of isolation among the population. As the disease is very contagious many different treatment modalities have been tried. The therapeutic methods which are used are Ayurvedic and homeopathic along with that some Allopathic drugs are also used. Ayurvedic and homeopathy were found to be useful in asymptomatic patients rather than symptomatic patients. The drug which is used for treatment is antiviral drugs, protease inhibitors, antimalarial drugs, and neuraminidase inhibitors. But most promising results were obtained by using hydroxychloroquine, thus many countries are using this drug for treatment. Research related to vaccine development is still in progress. but there is still an absence of data regarding the effectiveness of these methods. Clinical trials need to be performed to prove the drug or the measure effective. While the search for a vaccine is still underway, preventive measures should be taken to curb the chain of infection. This includes the use of face mask, washing hands frequently, at least 1 meter distance while in public places. This Literature review summarizes all the measures that have been used for the treatment of COVID 19 pandemic all around the world.

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INTRODUCTION

History

The first evidence of coronavirus dated back in 1965 when it was in people suffering from a common cold which was HCoV-229E. Then it was seen that about 5 to 30% of respiratory infections are due to HCoV-OC43. In 2002 it was found that SARS-CoV was responsible for causing severe acute respiratory syndrome and it was described as a worldwide threat by WHO (V *et al.*, 2020). MERS-CoV was discovered in 2012 in the middle east Asian region (Saudi Arabia) and was named Middle East Respiratory Syndrome (MERS-CoV, 2020). In early December 2019, an epidemic was observed in Wuhan province in China. The symptoms of the patients were similar to pneumonia and the virus resembled the SARS-CoV and it was called Covid-19 (V *et al.*,

2020).

Epidemiology of Coronavirus

An outbreak of an acute respiratory disease occurs first in Wuhan province of China supposedly from the seafood market. Bats are the home reservoir for the coronavirus including SARS and MERS (Guo *et al.*, 2020). On December 31 2019 a clump of patients was observed by the Chinese center for disease control and prevention and Wuhan health authorities with pneumonia of unknown origin. China CDC observed coronavirus on 7th January 2020 and the genomic sequence on January 11 (Park, 2020). It was found that 31.3% of patients had traveled to Wuhan and 72.3% of patients had come in contact with non-residents of Wuhan. 3.8% of the transmission occurs between health care professionals according to the National Health Commission of China (Guo *et al.*, 2020). It was found that Covid19 has inflated spreading risk and have a reproductive rate of 2.9 with an average incubation period of 2 -14 days (Hamid *et al.*, 2020). On 11 March 2020 WHO declared it as pandemic with 13 fold increased in patients outside China (Cucinotta and Vanelli, 2020). As of May 2020, the total number of confirmed cases is 4.53 million with deaths of about 307,000 patients all-around the world due to Covid19. Out of which 1.63 million cases are recover (COVID-19, 2020).

Introduction to Coronavirus

Coronavirus is single-stranded RNA viruses which are 80 -220nm in diameter. It belongs to the sub-family coronavirinae family coronaviridae and order nidovirales (Park, 2020). There are 4 classes of coronavirus alpha, delta, gamma, and betacoronavirus. SARS and MERS are associated with beta coronavirus (Liu *et al.*, 2020). 6-10 open reading frames or ORFs are present in Covid19 of which first contains 2/3rd of the genome and replicas proteins, structural proteins are arranged in sequence in the last third of ORFs (Belouzard *et al.*, 2012). The genome of Covid-19 encodes structural proteins, non-structural proteins, and accessory proteins. It includes glycosylated spikes(S) proteins that induce host immune response. It binds to a receptor protein called angiotensin-converting enzyme -2 (ACE2). Several non-structural proteins RNA dependent RNA Polymerase, Coronavirus main protease, and papain-like protease are present. Infections start when S proteins and ACE2 interact (Liu *et al.*, 2020). The structure of Covid-19 is similar to SARS and MERS (Li and Clercq, 2020).

The genomic sequence of SARS CoV 2 was found to be 96.2% identical to bat CoV. Though SARS CoV2 shows similarity with SARS CoV but the dif-

ference is the absence of amino acid substitution on non-structural proteins 7 and 13, envelope, and accessory proteins. Research had suggested that non-structural proteins 2 and 3 have an important role in the infectious capability of SARS CoV2. The S-glycoprotein attaches to the ACE2 receptor on human cells and has two subunits S1 and S2. S1 governs the virus-host scope and cellular tropism and S2 mediates virus-cell membrane fusion(yu2020). As the membrane fusion happens, viral RNA is freed into the cytoplasm, this RNA then translates two polyproteins pp1a and p1ab. These proteins encode non-structural proteins and shape the replication transcription complex(RTC). Constant replication of RTC leads to the synthesis of subgenomic RNAs that encode structural and accessory proteins. Virus buds are formed after assembling of endoplasmic reticulum, Golgi, new RNA, nucleocapsid protein and glycoproteins. Finally, the vesicles which contain viruses fuse with the plasma membrane and are released.

Transmission and Signs of Coronavirus Infection

Respiratory secretions, droplet spread, and direct contact are the major means of the spread of Covid-19 (Guo *et al.*, 2020). The period between the arrival of symptoms and morbidity ranges from 6 - 41 days with an average 14 days. But this period varies according to the host immune system (Hamid *et al.*, 2020). Out of the confirmed cases, 77.8% were aged between 30-69 years out of which 51.1 % were male with 80% without pneumonia, 15% with pneumonia, up to 6% were under ICU due respiratory failure, shock, and multiple organ failure (Park, 2020).

The initial symptoms present at onset were fatigue, cough, and fever, and other symptoms such as sore throat, dyspnea and headache were present. The patients with mild symptoms were able to recover but with moderate to severe symptoms suffer respiratory failure. Deaths due to COVID 19 are common among patients with preexisting diseases (Hamid *et al.*, 2020). The confirmation of COVID 19 case is done by examining the sample collected from the upper and lower respiratory tract. These samples are stored at 4 degrees centigrade. The probes that are used to compare are the gene sequencing released by China (Cascella *et al.*, 2020). Bilateral effusion was seen in both lungs in pneumonia (Singhal, 2008). Pandemic preparation by country includes creating awareness among people, preventive measures, keeping stock of diagnostic kits, and proper measures to reduce the effect of pandemic (Jain and Sharma, 2017).

This review aimed at finding pieces of evidence for the therapeutic management of Covid19 patients.

For this review search for literature was performed using Pubmed and Google Scholars.

Preventive Measure

1. Quarantine / Stay home: Quarantine is the oldest and effective way of arresting the spread of infectious disease. It is a procedure that is performed to restrict the people that might have come in contact with the infectious agent and they are monitored for any early signs and symptoms. Quarantine of people may reduce the infected cases by 44 to 81% and deaths by 31 to 63%.
2. Social Distancing: The coronavirus spreads droplets so a certain distance should be maintained to reduce the spread of the virus. It is usually done in areas where community transmission had occurred. This is practiced in public markets and work areas.
3. Use Of Personal Protective Equipment: Use of masks in public places is highly recommended. It should be considered while going to closed space areas such as grocery shops, shopping, or while using public transport. The reason for using a face mask is to contain the secretion and prevent the transmission.
4. Hand hygiene: According to WHO hands play an important role in the transmission of coronavirus. According to WHO hands should be frequently cleaned with alcohol-based solutions or soap.

Curative measures for Covid-19

Curative measures include the use of allopathy, homeopathy, and ayurvedic medicine. Literature was searched in favor of each of the fraternity and evaluation was done.

Ayurvedic and Homeopathy medicine in treating Covid19

This is the prophylactic measures that are taken to improve and boost the immune system in an asymptomatic patient. India has vast knowledge in the medical field one of the oldest begins Ayurveda. Sahaja Yoga can be performed to increase the capacity of the lungs (Yunati *et al.*, 2017). In Ayurveda respiratory diseases are treated with steam inhalation, consumption of hot water, gargling with medicated water (Golechha, 2020). Ministry of AYUSH had set up guidelines for boosting immunity in COVID 19 crises. Ayush guidelines are based on dietary management and change in lifestyle. The Ayush management of Covid19 has been grouped as follows:

Preventive and prophylactic :

Ayurvedic: Samshamani Vati 500mg BD with warm water for 15 days. This preparation has *Tinospora cordifolia*.

Siddha: An extract of *Andrograhis paniculate* called nilavembu kudineer 60ml decoction BD for 14 days.

Unani: The mixture that is prepared by boiling Behidana 3gm, Unnab 5 in number, Sapistan 9 in no. in water. This preparation has been found to have antioxidant, immune-modulatory, and anti-influenza activity. It has to be taken BD for 14 days.

Homeopathy: Arsenicum album 30 empty stomach OD for 3 days. It is the common constituent in treatment for a respiratory infection. This dose should be continued for one month till coronavirus infection subsides from the community.

Symptomatic management

Ayurvedic

1. AYUSH-64: 02 tablets BD
2. Agasthya Hareetaki: 05 gm BD with warm water
3. Anuthaila/Sesame oil 02 drops in each nostril daily in the morning.

Siddha

1. Nilavembu Kudineer/Kaba Sura Kudineer—decoction 60ml BD
2. Adathodai Manapagu — Syrup 10 ml BD

Homeopathy

Arsenicum album, Bryonia alba, Rhus toxicodendron, Belladonna Gelsemium Eupatorium perfoliatum these are the drugs that had shown good response in treating flu-like illness.

Intervention to general care

Ayurvedic

1. AYUSH-64: 02 tablets BD
2. Agastya Hareetaki: 05 gm BD with warm water

Siddha

1. Vishasur Kudineer: decoction 60ml BD
2. Kaba Sura Kudineer — decoction 60ml BD

Homeopathy: Those medicines which are mentioned under symptomatic management are to be used in the intervention.

AYUSH had mentioned that these medicines to be taken only after consulting the physician. Detailed information can be obtained from the AYUSH website.

Therapeutic Drugs used for treating COVID 19

Antimalarial Drugs

Chloroquine in which an antimalarial drug was found to be effective against the spreading of SARS CoV. The drug affects the replication of the virus. Hydroxychloroquine has invitro action in response to SARS COV-2. It also impedes the terminal glycosylation in receptor cells (Vincent and Joseph, 2017). Hydroxychloroquine antiviral activity inhibits the growth of many viruses including SARS COVID 19. Inhibition of viral DNA and RNA Polymerase, viral protein glycosylation, and ACE2 cellular receptor inhibition. Studies carried out show that on day 6, 70% of the hydroxychloroquine treated were virologically cured compared to 12.5% in the untreated group (Smith et al., 2020). Due to antiviral activity against COVID -19 it has now been used in the treatment of Covid-19.

Antiviral drugs

Lopinavir/ Ripinavir

An antiretroviral drug use mainly in the treatment of HIV. It is a protease inhibitor (Lu, 2019). Ripinavir and corticosteroid use in combination treating SARS Covid-19. Many patients are being treated with this combination as animal trails were showing effect (Medhi et al., 2020). These drugs' mechanism of action is on the replication enzyme M^{pro} . No specific evidence is available in favor of ripinavir. Besides the use of ripinavir have its side effects (Smith et al., 2020).

Remdesivir

It is a broad spectrum antiretroviral drug. It is a monophosphoramidate prodrug of remdesivir triphosphate, which acts on the RNA Dependent RNA Polymerase. In vitro data suggest that it shows potent antiviral activity against COVID -19 virus (Smith et al., 2020). It effectively reduces the virus titer in mice infected with MERS- Covid-19. And also improves the condition of the lung (Lu, 2019). It has been used in several patients in the United States, Europe, and Japan in confirmed cases of SARS- COVID 19.

Neuraminidase Inhibitors

It has been used in treatment for influenza. Drugs such as oseltamivir, zanamivir are recommended as

antiviral drugs in COVID- 19 patients (Lu, 2019). In Paris from 2013-2016 MERS COVID -19 had been treated with oseltamivir (Medhi et al., 2020).

Protease Inhibitor

There are two types of protease in coronavirus i.e. papain-like protease and non-structural proteins. These proteins have a vital role in Covid19 infection to the host. Some of the protease inhibitors are lopinavir and saquinavir. Among these lopinavir has been found to have the most inhibitory action. But there is no presence of sufficient evidence for the use of protease inhibitors (Smith et al., 2020).

Vaccines for Covid19

Vaccines provide acquired immunity against particular diseases. These are prepared from dead or attenuated organisms or refine products derived from specific organisms. Novavax has been producing a recombinant vaccine (Hemilä, 2003). For this genetic code for spike present on the SARC-Cov2 had been isolated and a large quantity of it is produced by sticking it to the genome of a bacterium. National Institute of Allergy And Infectious Disease produced mRNA - 1273 in opposition to SARC- Cov2. This vaccine is currently in phase 1 of clinical trials (coronavirus vaccine, 2020). BNT162 which nearly like the mRNA-1273 vaccine has been produced by BioNTech and Pfizer. ChAdOx1 nCov-19 vaccine developed by Oxford University (V et al., 2020). Few of the vaccines have shown good results and they are undergoing trials on humans. With these noticeable results soon the production of the vaccine will be started.

CONCLUSIONS

Covid19 has been a fatal respiratory infection since it was discovered in early Dec.2019, which lead researchers to find out modalities to treat this infection. Since the last 50 years when the virus was first found to infect humans, the treatment strategy had changed. But with the knowledge that had been gained during these have been useful in treating patients but no specific drug has been mentioned for Covid-19. Therapeutic drugs such as hydroxychloroquine have shown some promising results and thus it has been extended around the world in treating this pandemic. 70% of patients get virologically cured due to hydroxychloroquine. This has been extensively carried out for symptomatic patients. Ayush project a mission by the Ministry of AYUSH has been shown to be effective in asymptomatic patients. The missions help in building immunity and boosting the health of individuals by some dietary management and ayurvedic drugs.

Some pharmaceutical companies with the help of research institutions are building vaccines for treating Covid19. Some of them have shown effective results and tried on humans.

At times there is no specific drug available for Covid19, the search is still going on. But the best way to stop transmission of coronavirus is by carrying out the preventive measures.

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Conflict of Interest

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