RECOMMENDED MEDICATIONS FOR N-COV DISEASE - A REVIEW

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ABSTRACT:
With the raising concerns on the mortality rate in the recent covid pandemic, the lacunae of proper treatment strategy plays a vital factor. Since there is no approved medication for COVID-19, medications involving hydroxychloroquine sulfate and chloroquine phosphate were recently recommended. The National Medical Products Administration of China has approved Favilavir, an antiviral medication, with minimal side effects and a moderate control on viral replication. Remdesvir, another antiviral, has drawn the attention of several researchers to treat the novel COVID-19 virus as COVID-19 is identical to SARS and MERS viruses. Remdesvir, was successful in the previous outbreaks of SARS and MERS. Some researchers also suggest high doses of vitamin C supplementation may improve the patient's condition. This review thus provides a basic overview on the recommended medication and urges the need to develop novel anti-covid drugs and vaccines.

KEYWORDS:
Antimalarial drug, Coronavirus, Hydroxychloroquine, Immunotherapy, Medication, Vaccine.

INTRODUCTION :

Coronaviruses in the Orthocoronavirinae subfamily, in the Coronaviridae family, the Nidovirales order, and the Ribovirus domain are viruses enveloped with a single-stranded positive-sense virus. They possess RNA genome and a helical symmetry nucleocapsid with distinctive club-shaped spikes that extend from their top, producing a picture of the solar corona from which their name derives in electron micrographs (Pongpirul et al. 2020). Coronavirus is a type of common virus that causes infection of your nose, sinus, or upper throat. Most coronaviruses don't cause harm.The World Health Organization described SARS-CoV-2 as a new form of coronavirus in early 2020, following an outbreak in China in December 2019 . The epidemic is spreading rapidly across the world(Wilson, Jenner, and Roberts 2020) . COVID-19 is a disease caused by SARS-CoV-2 which can cause respiratory disease. It can affect the upper respiratory tract (sinuses, nose, and throat) or lower respiratory tract (windpipe and lungs) (Yadav et al. 2020). It spreads in the same manner as other coronaviruses do, primarily by communication between persons. Infections range from mild to deadly. SARS-CoV-2 is one of seven types of coronavirus including those causing severe diseases such as respiratory syndrome in the Middle East (MERS) (SARS) (Liu, Lu, and Chen 2020).

The other coronaviruses cause most of the colds that affect us throughout the year but are not a serious threat to otherwise healthy people (Yang et al. 2020). With serious concerns from various outbreaks with

drug resistant strains, novel coronavirus (COVID-19) is an infectious condition that can spread directly or indirectly from person to person and causes respiratory diseases ranging from the common cold to acute respiratory syndrome. A total of 87,137 confirmed cases were registered worldwide until 3 March 2020. Of these, 2977 were fatal (3.42 percent) (Mathuria, Yadav, and Rajkumar 2020). Of all cases approximately 92 percent.The virus can lead to pneumonia, shortness of breath, septic shock, and death. Many complications of COVID-19 can result from a condition known as cytokine release syndrome or a cytokine storm .The exorbitant mortality rate is associated with the lack of proper medication. Recently WHO, and other national medical councils have recommended the administration of few medicines as a supportive therapy in the initial stage of the disease (Huang et al. 2020). This reivew thus throws an insight into that recommended medications, with its limitations and challenges to treat covid disease. That is when an infection causes the immune system to use inflammatory proteins called cytokines to invade the bloodstream (Sahni and Gupta 2020). They can kill tissue and damage your organs. The main transmission of this virus is through droplet transmission while talking and touching the objects used by the infected person, physical contact, etc (Malviya 2020). With no proper medications for covid, this review highlights the recommended medications available to treat the covid diseased patients.

Antiviral agents against SARS viruses - an overview:

Many antivirals were recommended for the potent viral diseases including SARS, with potent nucleoside and nucleotide inhibiting activities. Analogous to guanine, ribavirin inhibits RNA-dependent viral polymerase (Elhusseiny, Abd-Elshahed Abd-Elhay, and Kamel 2020). However, it is in vitro activity against SARS-CoV was limited, and high concentrations were required to inhibit viral replication, requiring high doses and combination therapy. In previous studies, patients were given either intravenous or enteral administration(Kulkarni and Jacobson 2009). There is no evidence for inhaled ribavirin for diagnosis with nCoV, and data with respiratory syncytial virus indicates inhaled administration does not offer any advantage over enteral or intravenous administration (Field 1988). Neuraminidase inhibitors are known to suppress viral shedding of respiratory secretions and are used for influenza prophylaxis (Yuan et al. 2020). In a Cochrane systematic review, Oseltamivir has shown a 55 percent reduction in symptomatic influenza and Zanamivir Oseltamivir is currently being tested as a treatment alternative but not specifically for coronary prophylaxis(Sharmeen et al. 2020) . However, it may also play a role in chemoprophylaxis in coronavirus disease, taking a cue from its prophylaxis properties against influenza viruses. Protease inhibitors such as Lopinavir are a powerful inhibitor of the SARS-CoV protease enzyme that is necessary for the life cycle function of this virus. Ritonavir was used in HIV patients to improve this function of Lopinavir. However, the largest study carried out in China on the use of Lopinavir plus Ritonavir for its effectiveness in patients infected with COVID-19 found no difference in the clinical outcome compared to standard care alone, as it also involves resistant forms too as seen in bacterial infections (Kesel 2012) . Currently, the NCT04304053 trial examines the effectiveness of Darunavir / Cobicistat plus chloroquine treatment in all those found to be effective in infected cases . There is currently no guideline about the use of antiviral agents for COVID-19 prophylaxis.The viral RNA was detected in urine samples of recovered patients (Girija et al. 2019),(Girija As and Priyadharsini J 2019),(Selvakumar and Np 2017),(Girija, Jayaseelan, and Arumugam 2018) . Personal hygiene and social distancing is important to prevent the entry of viruses.Herbal mouthwashes can be used to prevent oral entry of viruses(Shahana and Muralidharan 2016),(Shahzan et al. 2019),(Pratha, Ashwatha Pratha, and Geetha 2017). Patients with hypertension,cardiovascular disease, diabetes and immunocompromised patients are at higher risk of COVID-19 (Paramasivam, Vijayashree Priyadharsini, and Raghunandhakumar 2020) .

Chloroquine - hydroxy Chloroquine Sulphate:

Chloroquine has been commonly known for over 70 years, is readily available, and is an effective antimalarial agent with proven properties of chemoprophylaxis in malaria. Different mechanisms have

shown it also plays a role in infection with SARS CoV (Latif and Latif 2020). The SARS-CoV2 is known to be bound to human cells via the receptor Angiotensin-Converting Enzyme 2 (ACE 2) (Dongala, Ettaboina, and Katari n.d.). In vitro studies have shown that the ACE2 receptor glycosylation process is affected, causing the Vero cells pretreated with chloroquine to be refractory to SARS-CoV infection, which can be the mechanism by which even human cells can become refractory to this infection (Ahuja and Shashi Ahuja 2014). It was also found that chloroquine treatment avoids the spread of SARS-CoV infection in the post-infection phase. HCQS has the same mechanism of action but a better safety profile than chloroquine, making it a preferred medication. Each of these drugs has also demonstrated immunomodulatory effects and can inhibit the increased immune factors. Chinese investigators had performed the first-ever human chloroquine trial against COVID-19 (Browning 2014). Long term use of these drugs may lead to development of resistant strains of virus (Ashwin and Muralidharan 2015) . The patients with COVID-19 should be protected from nosocomial infection in hospitals (Priyadharsini et al. 2018a), (Priyadharsini et al. 2018b), (Marickar, Geetha, and Neelakantan 2014). Co-infections with drug resistant bacterial pathogens are also common, thus proper antibacterial interventions can also be considered (Smiline, Vijayashree, and Paramasivam 2018). Anti inflammatory drugs can be used to prevent multiple organ failure due to systemic inflammation and natural medications can also be administered (M, Geetha, and Thangavelu 2019). The study conducted in over 100 patients found that chloroquine was superior in minimizing symptom length, exacerbating pneumonia, improving radiology, and contributing to virus-negative seroconversion (Rowland Yeo et al. 2020). Both of these medications have also demonstrated immunomodulatory effects and can inhibit the enhanced immune factors. This may play a role in reducing coronavirus disease severity Chinese investigators had performed the first-ever human chloroquine trial against COVID-19 (Costanzo, De Giglio, and Roviello 2020). Hydroxychloroquine was studied by the French group of investigators along with azithromycin. It was a non-randomized control trial which was open-label (Fu et al. 2020). They included 36 patients in the trial and 20 patients received a dosage of 600 mg of hydroxychloroquine daily along with azithromycin(Fredj and Chérif 2020). The authors observed a substantial reduction in viral load on day 6 of the treatment and a significantly lower average period of the virus relative to the control group. The effect of both prophylaxis and treatment is currently being investigated in various studies (Hedya, Safar, and Bahgat 2019).

Remdesvir and its action:

Remdesivir is a monophosphate prodrug which undergoes metabolism to an active C-adenosine nucleoside triphosphate analogue (Dutta, Mazumdar, and Gordy 2020). Remdesivir is a promising potential therapy for COVID-19. Due to its broad spectrum, potent viral activity against several nCoVs including SARS-COV-2 have been documented. There are the drugs that are most commonly used world wide for the treatment of novel coronavirus (Rubin 2020). Since the complete pathogenesis of the virus is still under study it is wise to take treatment with minimal side effects without any systemic toxicity and to decrease the viral load, remdesvir is recommended for the same. Remdesvir is also known for its action to suppress the viral replication and to target the potent viral structures of CoV (Kumar n.d.). Latest literature, previous articles and the latest update from the WHO showed remdesvir has antiviral effect against covid. However, drug resistant microbial pathogens prevail (Priyadarshini et al. 2020), administration of remdesvir has to be considered with care and requires further clinical experimental validation to prove its exact action against CoV.

Vaccine strategies:

Many vaccine strategies against covid are under trial world-wide but require more time-period to administer the same in patients. Preclinical experience with SARS and the Middle East respiratory

syndrome (MERS) vaccine candidates has raised concerns about exacerbating lung disease, either directly or as a result of antibody-dependent enhancements (Masic, Naser, and Zildzic 2020). A Type 2 helper T-cell (Th2) response may be associated with such an adverse effect. Therefore research in an acceptable animal model and thorough monitoring of the safety in clinical trials would be important (Fischer et al. 2020). Defining successful animal models is still too early; rhesus macaques seem very promising, as do hamsters and ferrets. When adjuvants are needed to produce an appropriate immune response or to spare the dose, those that cause a Th1 response and show a strong neutralizing-antibody response are theoretically more likely to be protective and avoid the risk of immunopathology (Baghizadeh Fini 2020). A recent study had documented the success rate of securing Phase I approval to successful Phase III trials was 16.2 percent for vaccines, and CEPI suggests a possible success rate of just 10 percent for candidates for vaccines in production in 2020 (Tung and Lim Tung n.d.).

Immunotherapy:

The intervention of plasma therapy and immunoglobulin on patients infected with 2019-nCoV could improve clinical outcomes. The immunoadhesin vaccines and the ACE2 have not yet been tested (Agur et al. 2020). The monoclonal antibody has only been performed for SARS, as the preferred immunotherapy method; however, this approach has not yet been tested. Most publications in this area are review papers suggesting 2019-nCoV immunotherapy for 2019-Nov with reasons and evidence of previous studies on two other coronaviruses SARS-CoV and MERS-CoV (Dörries et al. 1987). In the region, there is only one clinical trial study that addresses any of these approaches in 2019-Nov (Al-Hazmi 2016). The promising findings in monoclonal antibodies targeting spike protein in SARS-CoV and MERS-CoV allow researchers to use them in combating 2019-Nov. The monoclonal cocktail antibody or a mixture of multiple monoclonal antibodies that identify specific epitopes on the viral surface may increase the effectiveness of virus-neutralizing (Narain et al. 2020). Many targets that seem important in COVID-19 immunotherapy are cytokines.

The specificity of IL-6 in COVID-19 among cytokines comes from the fact that Elevated IL-6 is associated with the intensity of the inflammatory cytokine storms (Eldin n.d.). Therefore targeting Siltuximab and tocilizumab monoclonal antibodies (mAb) to IL-6 and its receptor (IL6R) May alleviate cytokine-related symptoms in extreme COVID-19 patients (Prutton, Barnum, and Pusterla 2019). Despite substantial progress in the production of inactive, monoclonal antibody-based immunotherapy for coronavirus infection, there is no monoclonal antibody on the market (Jha 2020). What hinders the use of antibodies is that large-scale processing of monoclonal antibodies is laborious, costly, and time-consuming for clinical application. Thus it is urgent to design and build advanced protein production platforms and expression systems to provide effective monoclonal antibodies in a short time at an affordable cost(Steinmann et al. 2015). While no study has been conducted and no vaccines or antiviral therapeutic agents have been approved to treat COVID-19 until now, the vaccines could be effective due to the unique structure of the virus (Ambekar n.d.). Besides, current data on SARS-CoV and MERS-CoV immunotherapy hold the potential for use in the 2019-nCoV system. Many natural oils have antiviral and antibacterial activity that can be used for prophylaxis of COVID-19 and also known to boost immunity against viruses (Vaishali and Geetha 2018).

Limitation:

The rapid development and urgency of developing a COVID19 pandemic vaccine will increase the risk and failure rate of providing a safe, effective vaccine. While the quality and quantity of a potential vaccine's antibody output are intended to neutralize the COVID-19 infection (Struben n.d.), antibody-dependent disease (ADE) associated with proinflammatory cytokine secretion upregulation and increased lung pathology need to be considered. While the nation and the world rightly focus on the COVID-19

pandemic, it is not the first time national emergencies have threatened access to medication, nor will it be the last (Chen et al. n.d.). Lack of research funds and ethical issues were also few limitations to add.

CONCLUSION:

The COVID-19 pandemic reflects this generation's largest, and global public health issue. The volume of clinical trials undertaken to evaluate possible COVID-19 therapies underscore both the need and capacity to deliver high-quality therapeutic strategies. To date, no effective treatments have been identified against covid. This review thus, summarizes the medications available currently to treat the covid patients as a supportive therapeutic measure in the preliminary stages with their own limitations. The review also urges the need for the discovery of novel drugs and vaccines against covid disease in a less possible time period with much efficacy.

AUTHOR CONTRIBUTION :

J.Dhayanithi contributed more in execution of the work,data collection and drafting of manuscript .A.S Smiline girija helped in study design ,validation of the data collection ,revision and proofreading of the review.M.P Brundha helped in validation of the data collection ,revision and proof - reading of the review

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CONFLICT OF INTEREST :

None to declare

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