A review on COVID-19: Pathogenesis, control and medicine.

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Abstract

COVID-19 pandemic is now a day known to everyone. It affects socio-economic life of human being. Very few drugs are available and they are effective to some extent. Only safeguard method is applied in this condition till date. However, we present some important drugs and their mechanism for some possible references. Primary precaution is very effective in this condition. Here we also describe primary precaution and sanitization to some extent.

Introduction

Coronavirus is a group of RNA viruses capable of causing common flu-like symptoms to severe conditions such as common cold to Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) and COVID-19. WHO (World Health Organization) pronounced an obscure progressive type of pneumonia and termed the disease as COVID-19. Earlier it was termed as Wuhan coronavirus or 2019 nCov. International committee on taxonomy of virus named the coronavirus, causing the disease as SARS-CoV2. Recent studies of SARSCoV-2 states as it is a β Coronavirus of sub-genus *Botulinum* belongs to *Coronaviridae* group, and known as zoonotic coronavirus. Coronaviruses constitute the subfamily *Orthocoronavirinae*, in the family *Coronaviridae,* order *Nidovirales*, and realm *Riboviria*. They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. They have characteristic club-shaped spikes that project from their surface, which in electron micrographs create an image reminiscent of the solar corona, from which their name derives. However, subterranean insect-eating pangolin was identified as the primary source of this virus, based on the investigation that some pangolin corona viruses showed 99% of similarity in restriction binding domain with the COVID-19 virus-infecting human [1-5].

COVID-19 offers over 88% homology with two bat-inferred extreme intense respiratory disorder (SARS) related coronaviruses, which are: Bat-SL-CoVZC45, and bat- SLCoVZC21, and that bats might be the most probable common hosts of these viruses. Generally speaking, whether the SARS-CoV-2 transmits straightforwardly from bats or Pangolin or through a host is still yet questionable [6].

Literature Review

The first cases were reported in December 2019 then various possibilities of virus was identified. One of the identification related to various animals such as mice, pigs, chicken ducks, bats, snakes, pangolins etc. various animals were found infected with this virus. But real pandemic was concern as large population of human affected by it. This COVID-19 not only effect on health but also on socio-economical life of human being. Extensive measures to reduce person-to-person transmission of COVID-19 are required to control the current outbreak. Main attention should be given to including children and elderly people. The early death cases of occurred primarily in elderly people, possibly due to a weak immune system that permits faster progression of viral infection. Treatment is basically based on symptoms presented by the COVID-19 patients; however, primary treatment of immunizations and antiviral drugs are in progress. Currently, antibodies or direct antiviral medications for COVID-19 are not present at this moment. Researchers are testing a variety of possible treatments. More than 60% of the people using drugs and medicine in any medical problem or we can say that for every disease and illness we often take a medicine or multiple medicines. In this condition various medicine such as Hydroxychloroquine, Remdesivir, Favipiravir, Methylprednisol- one and Cipremi used. The US food and drug administration allows Remdesvir to treat severe COVID-19 pandemic. But it is effective to some extent.

Primary precaution is very important in this situations such as frequently washing hand, use sanitizers, cleaning, wearing mask, keep social distance and aware of this disease. Some supportive cares are also important such as take pain relievers (ibuprofen or acetaminophen), cough syrup, homemade syrup, rest, fluid intake etc. In mild symptoms, recovery will occur at home and in this condition home quarantine is necessary. Overall a safe and effective vaccine is required to end such pandemic. During this period, numerous companies and laboratory involve in plasma therapy test, vaccine

development etc and they are progressing on their way. We have to concern about this pandemic and should try to fight against it with proper care. There are numerous drugs available in this condition but effectiveness will be occurring only at will power. So don't fear about it and keep fighting with care. By this review we are trying to present the drug scenario and their mechanism which may help in this pandemic.

Pathogenesis

It was demonstrated that the virus might infect human *via* the mucous membranes, particularly the nasal and throat mucosa, then ingress into the lungs *via* the respiratory tract. The alveolar epithelial cells in the lungs are found to be the fundamental cell affected by the SARS-CoV-2 virus. The S protein has been revealed as a remarkable impetus of the virus entry into host cells [7].

The envelope spike glycoprotein ties up to its biological receptor ACE2, adjacent to alveolar epithelial cells in the lungs. After that, the SARS-CoV-2 spikes bind ACE2 with around 10 time higher affinity than SARS-CoV and promotes the inclusion of its genetic material mechanism is poorly understood. There is local propagation of the virus but a limited innate immune response. At this stage the virus can be detected by nasal swabs. Although the viral burden may be low, these individuals are infectious. In next few days the virus propagates and migrates down the respiratory tract along the conducting airways, and in severe condition immune response is triggered. Viral infected epithelial cells are a major source of beta and lambda interferons [8-14]. CXCL10 is an interferon responsive gene that signal to alveolar type II cell response to both SARS-CoV and influenza and as disease marker in SARS. Upper and conducting airways is only infected in mostly 80% infected patients. About 20% of infected patients undergo stage 3 which identified by pulmonary infection and only 2% found severe condition as fatal depending on age and health. The virus may reaches from pulmonary to the lung and infects alveolar type II cells. From lungs, virus propagates within type II cells and large number of viral particles is released resulted into cells apoptosis and death [14-19].

The released viral particles infect type II cells and type I as type II cells are the precursor cells for type I cells. Both SARS and COVID-19 damage alveoli and fibers. Aged persons are at risk because of their reduced immune response and ability to repair the damaged epithelium. The apical cilia on airway cells and microvilli on type II cells may be important for facilitating viral entry. However detail study is still going on [20-22].

The latest reports showed the enormous decline of the CD4^{+} and CD8^{+} T cells in the peripheral blood of the COVID-19 patients. During this infection provocative cytokines and chemokines become uncontrolled. The uncontrolled provocative cytokine triggered by the immune system resulted into obstructions in the respiratory system cause Acute Respiratory Distress Syndrome (ARDS), and finally causing death. However, more immune-associated investigations are required to assist the pathogenesis of the disease [23,24].

Symptoms

The symptoms of COVID-19 include fever, cough, fatigue, shortness of breath. All symptoms usually are mild at the initial stage; however, they gradually become severe in the next seven days, following respiratory symptoms including runny nose and sore throat (Centers for Diseases Control and Prevention). Cerebral pain or hemoptysis generally is asymptomatic in the modest number of patients.

In old patients, serious alveolar harm leads to have respiratory disappointment. In beginning of COVID-19 conditions patients show stun, intense cardiovascular injury, intense respiratory pain disorder (ARDS), and intense kidney injury. Patients may show ordinary or lower white platelet checks, lymphopenia or thrombocytopenia, with broadened initiation thromboplastin time and expanded C-responsive protein level in the plasma or serum. Thus, a patient having fever and upper respiratory tract manifestations with lymphopenia or leukopenia ought to be of suspected infection [25].

Control and Prevention

There are several problems in controlling contamination with the COVID-19 at the hospitals. It is suggested by the CDC that the medical service providers, doctors, nurses, wardboys etc. should use the Personal Protective Equipment (PPE), apply sanitizers, contact, wear protective outfits, gloves and airborne safety measures. Natural cleaning and sanitization methods are perfect to avoid this contaminations which can be obtained as control like a physical distance between patients in shared regions, cleaning air with filtration and sanitization which could diminish the general size of an outbreak.

Regular washing of hands with cleanser and water for 20 sec, and utilization of liquor based hand rub with at least 60% liquor, avoid contacting eyes, nose, mouth with unwashed hands, and keep away from close contact with individuals who are positive or negative.

Drugs related to COVID-19

COVID-19 is a new disease and there is no drug or vaccine for it as of now medicines that were used for treating other viral infections is given to the patients. At least five medicines have either been given to treat coronavirus infected patients in India. There is list of drugs as follows.

Hydroxychloroquine treats rheumatic disorders such as systemic lupus erythematosus, rheumatoid arthritis, and porphyria cutanea tarda, and certain infections such as Q fever and certain types of malaria. It is taken orally. Hydroxychloroquine inhibits stimulation of the Toll-Like Receptor (TLR) 9 family receptors. TLRs are cellular receptors for microbial products that induce inflammatory responses through activation of the innate immune system. By another report hydrochloroquinine and involves the inhibition of hemozoin biocrystallization, which facilitates the aggregation of cytotoxic heme which accumulates in the parasites, causing death. These reports indicate the mechanism of action of Hydroxychloroquine in malarial parasites. However for Coronavirus Hydroxychloroquine increases lysosomal pH in

antigen-presenting cells. In inflammatory conditions, it blocks toll-like receptors on Plasmacytoid Dendritic Cells (PDCs). Hydroxychloroquine, reduces the activation of dendritic cells and the inflammatory process. The common side effect of this drug is nausea, headache [26-29].

The drug Covifor is brand name of Remdesivir in India. It also sold as Veklury. It is taken as injection in vein. The active metabolite of Remdesivir interferes with the action of viral RNA-dependent RNA polymerase and causing a decrease in viral RNA production. In some viruses such as the respiratory syncytial virus it causes the RNA-dependent RNA polymerases to pause, and to induce an irreversible chain termination. Remdesivir is classified as a direct-acting antiviral agent that works as a delayed chain terminator. The most common side effect in is raised blood levels of liver enzymes, nausea [30-33].

Antiviral drug favipiravir, under the brand name FabiFlu, for the treatment of mild to moderate COVID patients. Favipiravir, sold under the brand name Avigan among others is an antiviral medication taken orally used to treat influenza. It inhibits RNA-dependent RNA polymerase of virus. In other research report suggested that favipiravir induces lethal RNA transversion mutations, producing a nonviable viral phenotype. Favipiravir does not inhibit RNA or DNA synthesis in mammalian cells and is not toxic to them. However, favipiravir has not been shown to be effective in primary human airway cells, casting doubt on its efficacy in influenza treatment. It has side effect on pregnant women and baby [34-39].

Conclusion

Methylprednisolone, is a corticosteroid medication used to suppress the immune system and decrease inflammation. It is given by mouth, by injection into a vein, muscle, or joint, or applied to the skin. Corticosteroids are widely used in pediatric open-heart surgery to reduce systemic inflammatory response and to mediate possible cardioprotective effects. Serious side effects may include increased risk of infection, osteoporosis, cataracts, weakness, easy bruising etc. Cipla, an Indian multinational pharmaceutical and biotechnology company, has launched its own antiviral drug named cipremi for treating COVID-19 patients. The medicine is in the form of lyophilized powder (freeze dry) for injection 100 mg, company shared the information. The drug is available as injection. The mechanism of action and may side effect will be same as Remdesivir.

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