Current Treatment Approaches for Pandemic Corona Virus Disease 2019 (Covid 19)

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Abstract

Coronavirus disease 2019 (COVID-19) is a respiratory disease, spread through personal contact or contact of person with the surface containing virus. First patient of COVID-19 was found in Wuhan, China which is now been spreading all over the world.Coronaviruses belongs to the Coronaviridaefamily. Genomic characterization has shown that probably bats and rodents are the gene sources of Coronaviridaefamily. Today, more than 10 drugs are being undergonein clinical trials for the treatment of COVID-19. The present review article includes the causes of COVID-19 spread, symptoms of infections and their complications involved, current treatment strategies which various countries have been applying including plasma therapy, treatment using combination of antiviral drugs. It also comprises of ongoing clinical trials of vaccines on COVID 19 patients. Overall, the present article gives the global current scenario of the COVID 19.

Keywords: *COVID-19, SARS-CoV, CORONA.*

Introduction

Today, more than 18,53,168 people are infected with pandemic COVID 19. Among all 200 countries, United States of America leading at the top position with more than 13 million corona positive cases. COVID-19 is a respiratory infectious illness that can spread from person to person. Corona virus Infected person shows mild to moderate respiratory illness which can be treated without any special strategic treatment. Older person and those who are having already medical complications like cardiovascular disease, diabetes, chronic respiratory disease, kidney problem and cancer are more vulnerable to get serious development of illness. The best way to prevent and stop the transmission of coronavirus infection are to maintain 6 feet distance from infected person wash your hand with soap or 70%(V/V) alcohol based sanitizer and at regular interval of time and avoid touching of your hand to your face, mouth and Eyes. Coronavirus spreads through droplets of saliva or liquid discharge from the nose whenever an infected person cough or sneeze he should cover his mouth with tissue paper or handkerchief or he should cough or sneeze into his flexed elbow[1,2] So far, there is no potential medicine or vaccine for the treatment of corona virus infection or covid-19. However, many clinical trials are going on to evaluate the potential vaccine or strategic treatment[3-5]. The dynamics of SARS-Cov-2 are currently unknown, but there is speculation that it also has an animal origin and that is Bat.Novel Corona virus has potential to become a pandemic infectious disease and a threat to the public health. Worldwide it is seen that many countries are in the stage of human to human transmission and there are lakhs of people are infected and thounds of deaths are reported and observing this situation WHO declared the COVID-19 a pandemic[6].

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Etiology: Coronavirus positive-sense single-stranded RNA genome and a nucleocapsid of helical

symmetry, when it is observed under an electron microscope it shows the cahracteristics of club-shaped spikes which are glycoprotein that project from its outer surface and it look like a crown. (coronam is the Latin term for crown). Coronaviruses constitute the subfamily Orthocoronavirinae belongs to the family Coronaviridae and it classifies into four genera of CoVs: Alphacoronavirus (alpha CoV), Betacoronavirus (beta CoV), Deltacoronavirus (delta CoV) and Gammacoronavirus (gamma CoV). Genomic characterization has shown that probably bats and rodents are the gene sources of alpha CoVs and beta CoVs. On the contrary, avian species seem to represent the gene sources of delta CoVs and gamma CoVs[7,8]. Other human CoVs that is beta CoVs can cause epidemics with variable clinical severity featuring respiratory and extra-respiratory manifestations[9,10,11]. Coronavirus positive-sense single-stranded RNA genome contains 29891 nucleotides, encoding for 9560 amino acids. However from which species it is originated it is not confirmed till now but the study of genome of the novel corona virus comes out with the findings that COVID 19 probably evolved from a strain found in bats but the intermediate species between bats and humans is not known[12-14].

Transmission: Analysis of the data related to COVID-19 shows that Virus gets transmitted from human to human only when the individuals comes in contact with infected person. It is seen that initially the family members, Health Care professionals gets infection only when they comes in contact with the infected person. Studies comes out with the findings that the incubation period of the novel coronavirus is 3 to 14 days. Studies also showed that this novel corona virus swiftly transmitted from human to human and Gets doubled in about one week[15-18].

Treatment: After studying we have identified around 15 drugs which are undergoing clinical trials of different phases. After medical intervention. It was found that COVID 19 or Corona virus could be treat by using drugs like Chloroquine, Hydroxychloroquine, Remdesivir, Ribavirin, Ribavirin plus Interferon, Camostat Mesilate, Lopinavir/Ritonavir, Darunavir/Cobicistat, Favipiravir, Umifenovir, Oseltamivir, Baloxivirmarboxil, Tocilizumab, Sarilumab Eculizumab. Chloroquine drug molecule and hydroxychloroquine drug molecule not only shows antimalarial activity but also have antiviral effect against (HIV) Human Immuno Deficiency Diseases virus by showing mechanism of action against the virus by preventing the virus to enter into the host cells. Hydroxychloroquine drug have shown the positive effect in order to treat Acquired Immuno Deficiency Syndrome (AIDS). In the ongoing clinical trials for the treatment of COVID 19 come out with the results that Hydroxychloroquine drug if given with macrolide anti-biotic azithromycin shows that 100% of Corona positive patients are cured as if only Hydroxychloroquine drug given alone then only 57.1 % Corona positive patients are cured. Now the clinical trails are undergoing to test weather the Hydroxychloroquine drug can use for treatment of COVID 19 positive patient those having Pneumonia[4, 23-26].

There are 2 clinical trails are undergoing using the drug Remdesivir in the mild to severe respiratory viral infection by COVID 19. Remdesivir is a nucleotide analog inhibitor of the EBOV RNA-polymerase RNA-dependent (RdRp). Dyer et al. 2019 depicted the primary outcomes the mortality rate of 33 % in 499 patients treated with Remdesivir drug against the EBOV diseases in initial stages. Also noted that a mortality rate of 75 % in 1900 patients of non treated infected patients during the same epidemic time period. Wang et al. 2020 depicted the alalysis indicating that Remdesivir is giving effective results in the treatment of COVID 19 in Vero E6 cells (EC90 1.76 μM). He also implied the mechanism of remdesivir drug involves the inhibition of viral application[19, 27].

China already approved the Umifenovir in order to treat influenza viral infectious diseases since it has not shown any adverse effects while treating the SARS. Umifenovir involves the mechanism of anti- viral action against the influenza virus A and B by virul fusion inhibition with targeted membrane in order to block the entry of virus into the cell.

Remdesivir: Remdesivir drug is a antiviral drug which has already used in the treatment of Paramyxo virus, Filo virus, Pneumo virus and Corona Virus. In vitro it is observed that Remdesivir shows the potent to control the clinical symptoms in SARS- CoV-1; MERS-CoV and in recent studies it is also shows against COVID 19 and comes out with the result that Remdesivir drug can be act as a SARS- CoV-2 inhibitor which is replicate in nasal and bronchial airway epithelial cells. However, in COVID 19 the clinical symptoms improvement and antiviral efficacy of remdesivir drug remains to be established. Gilead Sciences Inc., developed the Remdesivir on which the Adaptive COVID 19 Treatment Trial or ACTT was conducted by National Institute

of Allergy and Infectious Diseases (NIAID) at NIH in to order to study the infection causes and to design a effective standard procedure to cure COVID -19[4].

Placebo controlled randomised trial of remdesivir in the sever patients of COVID-19 with the method of double –blind trial in order to check the efficacy and adverse effect of remdesivir drug in adults (aged ≥18 years). In this trial only men and non- pregnant women who are positive with SARS-CoV-2 and suffering from Pneumonia and having oxygen saturation of 94% or lower on room air or a ratio of arterial oxygen partial pressure to fractional inspired oxygen of 300 mm Hg or less and were within 12 days of symptom onset were eligible. For this trial patients were given Remdesivir intravenously that is 200 mg on first day and 100 mg followed by second to tenth day in single infusion or infused placebo for same time period. Laboratory parameters were regularly monitored and assessed the adverse effects.

From the time period 6 February 2020 to 12 March 2020 trial was done on 236 eligible patients of whom Remdesiver were given to 158 eligible patients and 78 patients were given placebo. Mostly patients was suffering from common disease like Coronary heart disease, hypertension and diabetes and maximum patients of these disease were in the Remdesivir group as compared to the placebo group. Some patients were given Lopinavir–Ritonavir drug in the trial. It was observed that the patients in placebo group shows the symptoms for 10 days and in case of Remdesivir group the patients had shown the respiratory rate of more than 24 breaths per minutes and those patients administered with Remdesivir drug shows the significant improvement in the clinical symptoms and laboratory parameters within 10 days after the trial starts. In patients with use of remdesivir within 10 days after symptom onset, 28-day mortality was not significantly different between the groups, although numerically higher in the placebo group; by contrast, in the group of patients with late use,

Adverse effects were noted during the trial in both the group and it was observed 102 patients in Remdesivir group and 78 patients in placebo group reported the common adverse effects. In Remdesivir group common adverse effects like constipation, anaemia, hypoalbuminaemia, thrombocytopenia, hypokalaemia and increased total bilirubin were reported. In placebo group common adverse effects like constipation, anaemia, hypoalbuminaemiahypokalaemia increased aspartate aminotransferase, increased blood lipids and increased total bilirubin were reported. All deaths during the observation period were judged by the site investigators to be unrelated to the intervention.

Vaccine: Till date 8 april 2020 the COVID-19 vaccine Reasearch and Development are doing by 115 Vaccine making entities, of which 78 as an active project in which 73 are currently at the stage of exploration and preclinical trial and remaining 37 entities are unconfirmed (development status cannot be determined from publicly available or proprietary information sources). The most progressive entities have recently undergone into development of clinical studies which includes mRNA-1273 from Moderna, Ad5- nCoV from CanSino Biologicals, INO-4800 from Inovio and LV- SMENP-DC and pathogen- specific aAPC from Shenzhen Geno-Immune Medical Institute. Many vaccine developers entities have shown their plans to start the human clinical trials in 2020. This COVID-19 vaccine developers is evaluating the different technologies like nucleic acid (DNA and RNA), virus- like particle, peptide, viral vector (replicating and non- replicating), recombinant protein, live attenuated virus and inactivated virus approaches. Many of these technologies are not the basis for licensed vaccines but the Oncology study experience convinces vaccine developers to explore the novel alternative resources in the new world in order to swift the development of vaccine[29].

Plasma Therapy: Covalescent Plasma Therapy (CP) has been used since 100 years for treating several infectious diseases including viral diseases. CPis an adaptive immunotherapy which helps in improving the patients immunity to fight against the specific infection. CP therapy was reported to be used for the treatment of SARS (write the long form), H1N1 (write the long form) and MERS (write the long form) with no adverse effect. However it was also reported that the CP therapy fails to decrease the mortality rate due to Ebola Virus disease. Because there is no data available for neutralising antibody titration for stratified analysis (It is not connecting to the previous sentence). Virological Studies and clinical studies comes out with findings that MERS, SARS and COVID 19 shows similarity and therefore CP therapy might be useful for the treatment of COVID 19. In the CP therapy, neutralizing antibody titer from COVID 19 recovered patients can be used for the affected individual.

For clinical trail of CP therapy 10 critical patients

were identified with COVID 19 positive. 200 Ml single dose of convalescemt plasma derived from recently recovered healty donors with neutralizing antibody titers above 1:640 and this plasma was transfused to these patients with the combination of antiviral drug Lopinavir and Ritonavir and extra supportive care.

Conclusion

Overall, the present review article summarizes the history of COVID 19, its etiology, transmission and various treatment strategies so far have been tried by various medical experts. Considering the work progress for the treatment or prevention of COVID 19, it is expected that vaccine will soon be available in the market.

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