EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 10
339-343
Year: 2020

FEATURES, PATHOPHYSIOLOGY AND TREATMENT OF *COVID-19*

Neelam Yadav*[1] and Sahil Hussain[2]

[1]Assistant Professor, Era College of Pharmacy, Era University Sarfarzganj, Lucknow - 226003, India.
[2]B-Pharma 3rd Year Student, Era College of Pharmacy, Era University, Lucknow.

***Corresponding Author: Neelam Yadav**
Assistant Professor, Era College of Pharmacy, Era University Sarfarzganj, Lucknow - 226003, India.
Email ID: yadava.neelam@gmail.com,

Article Received on 11/08/2020 **Article Revised on 01/09/2020** **Article Accepted on 21/09/2020**

ABSTRACT
COVID – 19 is declared as pandemic in early 2020, the main target of novel coronavirus is the respiratory system both upper respiratory system and lower respiratory system. Cardinal symptoms are shown such as fever, sore throat, malaise, shortness of breath. As far now, no vaccine or any kind of cure is present for this novel coronavirus although symptomatic treatment is given as per the protocol. Antimalarial drug Hydroxychloroquine is being used in high risk patients who have other morbidities such as diabetes mellitus, hypertension, end stage renal disease or any immunosuppressive disorder etc.

KEYWORDS: COVID – 19, Pandemic, Hydroxychloroquine, Remdesivir, ChAdOx1 nCoV-19, Vaccine, Breathlessness.

INTRODUCTION

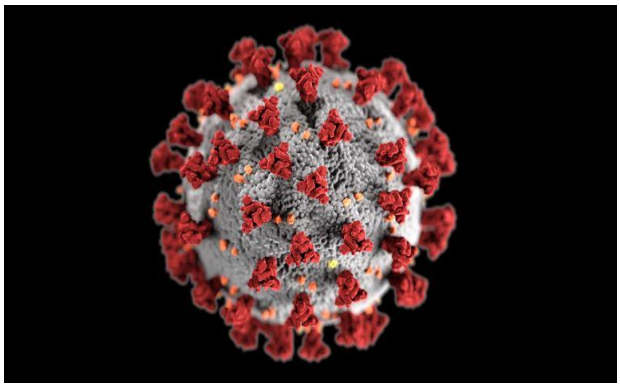


Fig. 1:

Severe Acute Reparatory Syndrome Coronavirus 2 – SARS CoV2 caused by novel coronavirus. Recent research shows it can also spread by fecal-oral transmission. Significant symptoms before an onset of respiratory symptoms are diarrhea, nausea, vomiting and abdominal discomfort. Respiratory droplet can infect a person within a radius of 2 – 6ft. New researches say it can be potentially present in air for 3 hours. If someone walks through the area where someone coughs or sneeze, he/she can be contaminated. Most recently, a novel coronavirus (SARS-CoV-2, also known as COVID-19).

COVID-19: (Origin and Transmission)
The first cases of coronaviruses found in 1965 in human, by Tyrrell and Bynoe. They observed that they could passage a virus named B814. The first cases were seen in Wuhan City of China in December 2019, and have been linked to the Seafood Market and the infection has spread to several countries around the world wide. The novel coronavirus originated from the Hunan seafood market at Wuhan, where raccoon dogs, bats, snakes, palm civets, and other animals are sold, and rapidly spread up to 109 countries of world. The recombination of DNA was found to be involved at spike glycoprotein which assorted SARS-CoV (CoVZXC21 or CoVZC45) with the RBD of another Beta CoV, thus could be the reason for cross-species transmission and rapid infection.

Limited research is available on how HCoV spreads from one person to another one. However, researchers believe that these viruses can transmited via fluids in the respiratory system, such as mucus.

Coronaviruses make a large family of viruses that can infect birds and mammals, including humans, according to world health organisation (WHO). These viruses have been responsible for several outbreaks around all over the world, including the severe acute respiratory syndrome (SARS) pandemic of 2002-2003 and the Middle East respiratory syndrome (MERS) outbreak in South Korea in 2015. Most recently, a novel coronavirus (SARS-CoV-2, also known as COVID-19) triggered an outbreak in China in December 2019, sparking international concern. While some coronaviruses have caused devastating epidemics, others cause mild to moderate respiratory infections.

Pathogenesis

Target – respiratory system, alveoli to be specific. Alveoli have type -I and type – II pneumocytes. Type – I pneumocytes helps in gas exchange. Type – II produces surfactant, reduce surface tension and avoid alveolar collapse. nCov-2 basically attacks type – II pneumocytes. nCoV-2 has different types of spike proteins on them Single Stranded RNA proteins. Amongst this s – spike proteins are nost important. It attaches to the receptor on type – II pneumocytes. Receptors are ACE – II (Angiotensin Converting Enzyme – II) receptors. Virus gets into the cell and hijacks the ribosome and start synthesis of protein molecule. It is the different structural protein of virus itself that is produced by ribosome after invasion. It also uses important enzyme RNA dependent RNA polymerase. It can synthesize more RNA from this, it synthesizes SS-RNA combination of all of these give rise to new virus.

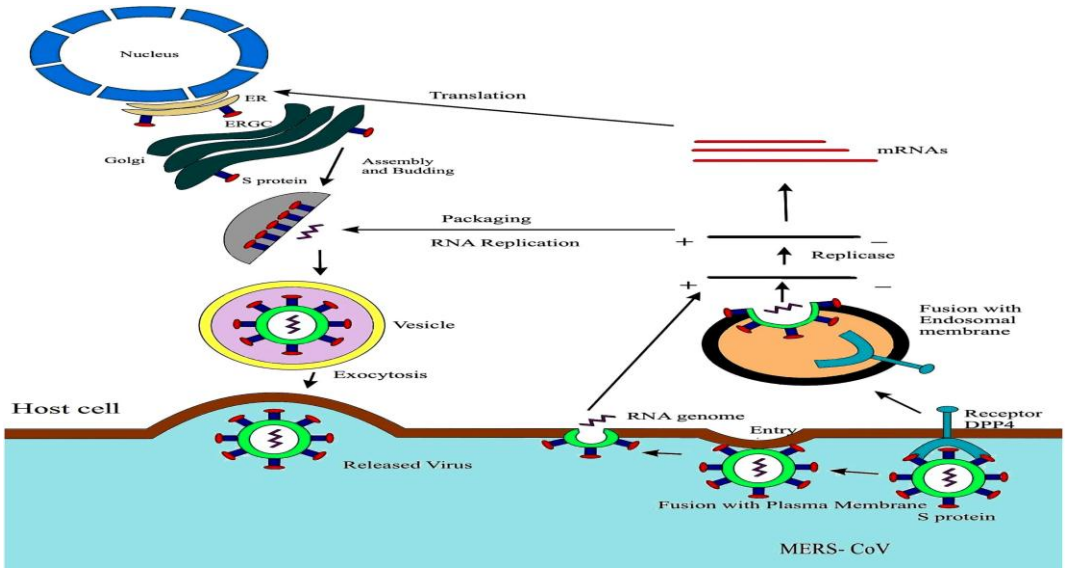


Fig. 2:

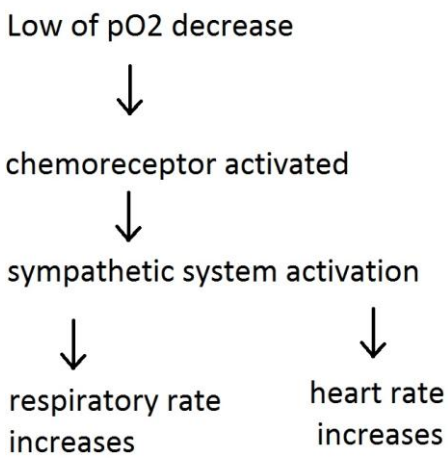
After damaging type – II pneumocytes, it starts releasing inflammatory products into the alveoli. Due to release of alveolar inflammatory products it activates alveolar macrophages. Macrophages now releases interleukins – 1, interleukins – 6 and tumor necrosis factor. They aggregate into the capillary surrounding the cell contraction; it leads to vasodilation and increase capillary permeability.alveoli and cause capillary smooth muscle relaxation. They are also responsible for endothelial cell.

Increased Capillary Permiability
↓
Accumulation of fluid in alveolar spaces
↓
Type - II pneumocytes damage
↓
Increase in surface tension
↓
Alveolar collapse
↓
Hypoxemia and Breathlessness

Now, due to increased inflammatory cytokinin neutrophils get activated. It releases Reactive Oxygen Spaces (ROS) and proteases to kill virus and virus infected cell.

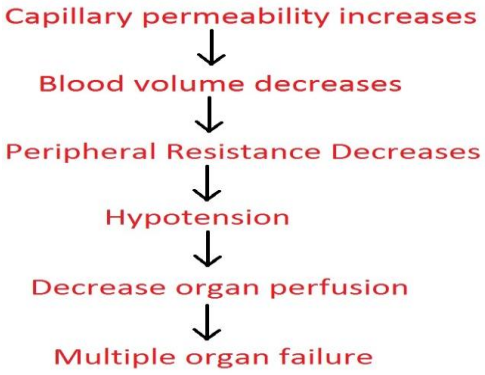
ROS and Proteases
↓
Damage Type - I and type - II pneumocytes
↓
Difficulty in gas exchange

In alveoli there will be accumulation of cellular debris and proteinaceous material and fluid. Due to this there is consolidation of alveoli which causes decrease in gas exchange and stimulate cough reflex. Now interleukins – 1 and interleukins – 6 signals the hypothalamus to release prostaglandins which is responsible for increasing body temperature hence, fever! Now due to low pO2 can stimulate the chemoreceptors and it will stimulate the sympathetic system.



In Severe Condition

It can cause Systemic Inflammatory Response Syndrome (SIRS). Is an inflammatory state affecting the whole body. It is the body's response to an infectious or noninfectious insult. Although the definition of SIRS refers to it as an "inflammatory" response, it actually has pro- and anti-inflammatory components. SIRS is a serious condition related to systemic inflammation, organ dysfunction, and organ failure. It is a subset of cytokine storm, in which there is abnormal regulation of various cytokines. SIRS is also closely related to sepsis, in which patients satisfy criteria for SIRS and have a suspected or proven infection.



Hypoxia, ground glass infiltrates, and progression to ARDS

About 20% of the infected patients will progress to stage 3 disease and will develop pulmonary infections and some of them developed very severe disease. Initial estimated fatality rate are around 2%, but this varies markedly with age. The fatality and morbidity rates may be revised once the prevalence of mild and asymptomatic cases is better defined as well. The virus now reaches to the gas exchange units of the lung and infects alveolar type II cells. Both SARS-CoV and influenza preferentially infect type II cells compared to type I cells.

Treatment

There is no specific treatment recommended for SARS-CoV- 2. Although vaccine has been made by several countries amongst them **ChAdOx1 nCoV-19** developed by oxford university show the promising result but wide scale trials are still left.

Fig. 3:

Symptomatic treatment is given to patients and oxygen therapy is the first step for respiratory impairment. In the case of respiratory failure both non – invasive and invasive mechanical ventilation is given.

Other medical treatments

Corticosteroids: In severe conditions these drugs are usually used such as methylprednisolone 1mg/kg/day.
Clinical research shows that dexamethasone reduces deaths by one third among severely ill COVID -19 patients.

Antiviral drugs

No antiviral treatments have been approved yet. However, several approaches have been made such as lopinavir/ritonavir (400/100mg orally every 12 hours). It demonstrated benefit over standard treatment.

Remdesivir an inhibitor of RNA polymerase was used during Ebola virus outbreak and could be effective for both prophylaxis and treatment of COVID – 19.

Plasmatherapy

Healed patients' antibodies are taken and represent a therapeutic option currently under study.

REFERENCES

1. WHO. Coronavirus disease (COVID-19) situation report—181.Geneva: World Health Organization, 2020.
2. WHO. Draft Landscape of COVID-19 candidate vaccines. July 14. https://www.who.int/publications /m/item /draftlandscape-of-covid-19-candidate-vaccines.(accessed July 14, 2020), 2020.
3. Fidler, S.; Stohr, W.; Pace, M. Antiretroviral Therapy Alone Versus Antiretroviral Therapy With a Kick and Kill Approach, On Measures of the HIV Reservoir in Participants with Recent HIV Infection (The RIVER Trial): A Phase 2, Randomised Trial. *Lancet*, 2020; 888–98.
4. Hanke, T. Aiming for Protective T-cell Responses: A Focus on the First Generation Conserved-Region HIV Consv Vaccines in Preventive and Therapeutic Clinical Trials. *Expert Rev Vaccines*, 2019; 18(10): 1029–1041.
5. Mothe, B.; Manzardo, C.; Sanchez B. A. Therapeutic Vaccination Refocuses T-cell Responses Towards Conserved Regions of HIV-1 in Early Treated Individuals (BCN 01 study). *E Clinical Medicine*, 2019; 11: 65–80.
6. Coughlan, L.; Sridhar, S.; Payne, R. Heterologous Two-Dose Vaccination with Simian Adenovirus and Poxvirus Vectors Elicits Long-Lasting Cellular Immunity to Influenza Virus A in Healthy Adults. *E Bio Medicine*, 2018; 29: 146–54.
7. Van, D. N.; Haddock, E.; Feldmann, F. A Single Dose of ChAdOx1 MERS Provides Protective Immunity in Rhesus Macaques. *Sci Adv*, 2020; 6(24): 1-10.
8. Folegatti, P.M.; Bittaye, M.; Flaxman, A. Safety and Immunogenicity of a Candidate Middle East Respiratory Syndrome Coronavirus Viralvectored Vaccine: a Dose-Escalation, Open-Label, Non-Randomised, Uncontrolled, Phase 1 Trial. *Lancet Infect Dis*, 2020; 20: 816–826.
9. Van, D. N. ChAdOx1 nCoV-19 Vaccination Prevents SARS-CoV-2 Pneumonia in Rhesus Macaques. *Bio Rxiv*, 2020.
10. Dicks, M.D.; Spencer, A.J.; Edwards, N.J. A Novel Chimpanzee Adenovirus Vector with Low Human Seroprevalence: Improved Systems for Vector Derivation and Comparative Immunogenicity. *PLoS One*, 2012; 7: 40385.
11. Morris, S.J.; Turner, A.V.; Green, N.; Warimwe, G.M. Laboratory-Scale Production of Replication-Deficient Adenovirus Vectored Vaccines. *Methods Mol Biol*, 2016; 13(49): 121–135.
12. Bliss, C.M.; Bowyer, G.; Anagnostou, N.A. Assessment of Novel Vaccination Regimens Using Viral Vectored Liver Stage Malaria Vaccines Encoding ME-TRAP. *Sci Rep*, 2018; 8: 3390.
13. Folegatti, P.M.; Bellamy, D.; Roberts, R. Safety and Immunogenicity of a Novel Recombinant Simian Adenovirus ChAdOx2 as a Vectored Vaccine. *Vaccines (Basel)*, 2019; 7(2): 40.
14. Murphy A, and Bell D.J, et al. COVID-19, Radiopedia. https:// radiopaedia.org/articles/covid-19-2?lang=us.
15. Shereen M.A, Khan S, COVID-19 infection: origin, transmission, and characteristics of human coronavirusesJournal of Advanced Research, 16 March. httSee discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/340362876 A REVIEW ON CORONA VIRUS (COVID-19), 2020.
16. Unhale, H.S.; Ansar, Q.B.; Sanap, S.; Thakhre, S.; Wadatkar, S.; Bajragi, R.' Sagrule, S.; Biyani, K.R. A REVIEW ON CORONA VIRUS (COVID-19),*Int. J. of Pharm and Life Sci.*, 2020; 6(4): 109-115.
17. Wu Z, McGoogan J.M. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020*; in press [*https://doi.org/10.1001/jama.2020.2648*]*.
18. Mossel EC, Wang J, Jeffers S, et al. SARS-CoV replicates in primary human alveolar type II cell cultures but not in type I-like cells. Virology, 2008; 372: 127–135.
19. Weinheimer VK, Becher A, Tonnies M, et al. Influenza A viruses target type II pneumocytes in the human lung. J Infect Dis, 2012; 206: 1685–1694.

20. Mason, R.J. Pathogenesis of COVID-19 from A Cell Biology Perspectivve, *Eur Respir J.*, 2020; 55: 20000607.
21. Yadav.V.K, Yadav.V.K, Kumar.P 3, Singh.A,Kumar.M And Devi.U, Corona Virus Disease-2019 (Covid-19) Pandemic: A Review Of The Current Evidence, European Journal Of Biomedical And Pharmaceutical Sciences, 2020.