
Corona Virus: A Review on Types of Vaccines, Plasma Therapy and Role of Hydroxychloroquine

Anupam Dubey*, & Rehan Uddin**

**B.Pharm, Sir Madanlal Institute of Pharmacy, Etawah(U.P.)*

*** Assistant Professor, Department of Pharmaceutics, Sir Madanlal Institute of Pharmacy, Etawah(U.P.)*

ABSTRACT:

As not only India, but also the whole World is suffering from the pandemic corona virus. It is named as COVID-19 and its full form is Corona Virus Disease 2019. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. A number of novel corona virus infections rises daily across the globe, strategies for developing a safe and effective vaccine are rapidly moving forward. In this review we will see all about COVID-19 and kinds of therapies that may be beneficial in the future.

KEYWORDS: Corona virus disease (COVID-19)

INTRODUCTION:

Corona virus disease (COVID-19) is a disease that is highly infectious, generated by a newly discovered corona virus. Most people infected with the COVID-19 virus are experiencing mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer can be easily infected with this virus and it may result in severe condition. The best way to be safe and slow down transmission is being well informed about the COVID-19 virus, the disease it causes and how it spreads. Protection of yourself and others from infection can be done by washing your hands or using an alcohol based rub frequently and not touching your face. The spreading of COVID-19 virus is identified primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it becomes important that you also perform respiratory etiquette (for example, by coughing into a flexed elbow). At this time, there are no vaccines or treatments available for COVID-19. However, there are many clinical trials being conducted for evaluating potential treatments. WHO is continuously providing updated information as soon as clinical findings become available.^[1]

SYMPTOMS:

COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization. Most common symptoms are fever, dry cough and tiredness. Less common symptoms are aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, rashes on skin, or discolouration of fingers or toes. Serious symptoms are difficulty breathing or shortness of breath, chest pain or pressure, loss of speech or movement. People with mild symptoms who are otherwise healthy should

manage their symptoms at home. It takes 5–6 days average from when someone is infected with the virus for symptoms to show, however it can take up to 14 days.^[2]

PATHOPHYSIOLOGY

Pathogenesis of lung injury:

The RBD of the S protein of SARS-CoV-2 specifically identifies the host angiotensin-converting enzyme 2 (ACE2) receptor. It is optimized for binding to the human receptor ACE2. Similarly to SARS-CoV-2, SARS-CoV also binds with the ACE2 receptor to gain entry into human cells. Upon binding, host serine protease TMPRSS2 cleaves the S protein and results in the fusion of the viral and cellular membranes. The S protein of SARS-CoV-2 and SARS-CoV have almost identical three-dimensional structures, and, given this, researchers hypothesize that SARS-CoV-2 likely uses a similar mechanism. The ACE2 receptor is expressed in type 2 alveolar epithelial cells in the lungs, heart, kidney, and gastrointestinal tract. However, the lungs seem to be particularly vulnerable to SARS-CoV-2 because of their large surface area and because alveolar epithelial type 2 cells seemingly act as a reservoir for virus replication. Direct injury to the lung tissue from a viral infection-mediated local inflammatory response is one of the proposed mechanisms behind the pulmonary manifestations of COVID-19.^[3]

CYTOKINE STORM AND THE SYSTEMIC INFLAMMATORY RESPONSE:

Cytokine storm syndrome (CSS) is an accentuated immune response to triggers such as viral infections. Macrophage activation syndrome (MAS) and secondary hemophagocytic lymphohistiocytosis (sHLH) are known to be two clinically similar CSSs. MAS is a CSS that is usually seen in the context of rheumatological diseases. HLH can be seen in patients with severe infection. It results from an excess of proinflammatory and inadequate anti-inflammatory stimuli. Some of the proinflammatory stimuli include foreign antigens, cytokines such as interleukin (IL)-1 β , IL-2, IL-6, IL-7, IL-12, IL-18, tumor necrosis factor (TNF)- α , interferon (IFN)- γ , and granulocyte colony-stimulating factor (GCSF). Some of the anti-inflammatory stimuli include regulatory T cells, cytokines such as IL-10, transforming growth factor (TGF)- β , and IL-1ra.^[4] Increased production of IFN γ by hematopoietic stem cells in response to viral infections is thought to trigger CSS. CSS is characterized by unremitting fever and multiorgan involvement, including acute respiratory distress syndrome (ARDS) and acute cardiac and renal injury. Laboratory abnormalities include cytopenias, increased ferritin, D-dimer, and increased serum levels of proinflammatory cytokines.^[5]

DEVELOPMENT OF VACCINE:

A number of novel coronavirus infections are increasing daily across the globe, strategies for developing a safe and effective vaccine are rapidly moving forward. In response to this public health crisis, researchers in the Precision Vaccines Program (PVP) at Boston Children's Hospital remain on the front lines of developing a vaccine specially targeted toward older populations — those who are at greatest risk of developing coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome-2 coronavirus (SARS-CoV-2).

Focusing on adjuvants:

The current antigen used for vaccine development is known to be the corona virus spike protein, so named such because it sits at top of the spike of a corona virus particle. This is the part of the virus that the immune system remembers.

Age specific:

The PVP plans on testing a variety of adjuvants and adjuvant combinations in human white blood cells sourced from older people. Researchers will then study the adjuvant-induced immune responses. “Our screen, comparing individual and combination adjuvants with and without the coronavirus antigen, will identify an adjuvant combination that most effectively induces an optimal immune response in the elderly,” Levy said. These screens will start immediately and continue over the next six to eight weeks.

Testing in mice:

The group is also studying coronavirus immune responses in a living animal model. The first mice have already been inoculated with a similar coronavirus spike protein derived from the SARS-2003 coronavirus with or without a lead adjuvant combination to get an early read on measuring an antibody response.

Three COVID-19 vaccine concepts:

Levy and Dowling estimated that more than 24 COVID-19 vaccine candidates are in development globally. These vaccines fall into three general types:

RNA-based vaccines:

The first COVID-19 vaccines in development have utilized SARS-CoV-2 RNA. “This approach is innovative and attractive, but even if proven effective it may be difficult to create hundreds of millions of doses, and each dose may be relatively expensive as it may require a fair amount of RNA,” said Dowling. “While there is less experience with human testing for this approach, it is possible that adjuvants may help enhance the immune response when such vaccines are administered to older populations and may reduce the amount of RNA needed in each vaccine.”

DNA-based technology:

Like RNA-based vaccines, this promising approach uses the genetic material of the virus to produce a vaccine. “You can make more vaccine doses with DNA than with RNA, but it is unclear whether the production could be rapidly scaled to meet the massive international demand,” said Dowling. “And, to our knowledge, these nucleic acid vaccines have not yet been tested in elderly patients either.”

Building on earlier coronavirus vaccines:

This is the approach PVP is taking that is learning from earlier vaccines from prior coronavirus outbreaks and making them more effective. “If you add an adjuvant chosen specifically for optimal activity in an older population, not only does it work better in that group, but it may dramatically reduce the cost per vaccine dose by reducing the amount of antigen required,” said Dowling.^[6]

Plasma Therapy – A New Hope:

When a person has Covid-19, their immune system responds by creating antibodies, which attack the virus. Over time these are built up and can be found in the plasma, the liquid portion of the blood. NHSBT now approaches patients who have recovered from Covid-19 to see if plasma from them can be given to people who are currently ill with the virus. A statement from the organisation said: "We envisage that this will be initially utilized in trials as a possible treatment for Covid-19." If fully approved, the trials will investigate whether convalescent plasma transfusions could improve a Covid-19 patient's speed of recovery and chances of survival. "All clinical trials have to follow a rigorous approval process to protect patients and to ensure robust results are generated. We are working closely with the government and all relevant bodies to move through the approvals process as quickly as possible."^[7]

Role of Hydroxychloroquine:

The Indian Council of Medical Research, under the Ministry of Health and Family Welfare, has recommended chemoprophylaxis with hydroxychloroquine (400 mg twice on day 1, then 400 mg once a week thereafter) for asymptomatic health-care workers treating patients with suspected or confirmed COVID-19, and for asymptomatic household contacts of confirmed cases.^[8] The document states "its use in prophylaxis is obtained from available evidence of benefit as treatment and supported by preclinical data". Although some in-vitro evidence supports the antiviral activity of hydroxychloroquine and its precursor chloroquine, there is no peer-reviewed publication that evaluates either drug for exposure prophylaxis of SARS-CoV-2 infection. Even for treatment of diagnosed cases, only one small study reported faster nasopharyngeal viral clearance, with no data for clinical improvement.^[9] This evidence, or the lack thereof, hardly justifies state-endorsed, widespread use of hydroxychloroquine for prophylaxis.^[10]

REFERENCES

- i. https://www.who.int/health-topics/coronavirus#tab=tab_1
- ii. https://www.who.int/health-topics/coronavirus#tab=tab_3
- iii. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J Virol*. 2020 Mar 17. 94 (7):[Medline].
- iv. Canna SW, Behrens EM. Making sense of the cytokine storm: a conceptual framework for understanding, diagnosing, and treating hemophagocytic syndromes. *Pediatr Clin North Am*. 2012 Apr. 59 (2):329-44. [Medline]
- v. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020 Mar 28. 395 (10229):1033-1034. [Medline].
- vi. <https://news.harvard.edu/gazette/story/2020/03/in-creating-a-coronavirus-vaccine-researchers-prepare-for-future/>

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- vii. <https://www.bbc.com/news/health-52348368>
 - viii. National Taskforce for COVID-19 Advisory on the use of hydroxy-chloroquine as prophylaxis for SARS-CoV-2 infection.
 - ix. <https://www.mohfw.gov.in/pdf/AdvisoryontheuseofHydroxychloroquinasprophylaxisforSARSCoV2infection.pdf>
 - x. Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020; 2020 (published online March 20.) DOI:10.1016/j.ijantimicag.2020.105949
 - xi. Marchione M “Game changer”? Trump-touted malaria drugs spur hope, shortages. <https://www.washingtontimes.com/news/2020/mar/23/chloroquine-and-hydroxychloroquine-donald-trump-to>