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REVIEW ARTICLE

MOLECULAR CHARACTERIZATION, CLINICAL MANAGEMENT AND DEVELOPMENT OF THE VACCINES AGAINST THE TARGETED VIRAL COMPONENTS OF COVID-19

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Summary

Spike proteins on the surface of human corona viruses is important to enhance it's competency to get transmit into other healthy population. Because of it's specific spike protein, the virus got its name corona in 1960s. Afterward, it was renamed as Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) in 2002 and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in 2012. It was mortal for old population, new born babies and immune-compromised individuals, who didn't have sufficient immunity or defense system. On February 11, 2020, World Health Organization (WHO) gave the names of COVID-19 and SARS-CoV-2. A characteristic of nCoV-19, which is a cause of COVID-19, was identified as major cause of pneumonia. However, the healthcare professionals worked hard to to stop it's outbreak and transmission all over the world. But, there was no medicines that have been cleared by the FDA to treat COVID-19 successfully. So, the goal of this study is to look at the scientific data that is already available about clinical care and therapy of this disease. Some of the sources that were checked for this study were BioRxiv, medRxiv, Google Scholar, Embase, PsychINFO, WanFang Data, and PubMed. A lot of work went into finding out what medicines could be used to avoid and treat COVID-19 illnesses. Remdesivir, chloroquine, hydroxychloroquine, and immunosuppressant drugs have all been shown to help to fight the virus. Until a treatment for the COVID-19 virus is found, it is best to stay away from other people and follow strict hygiene. Most medicinal treatments still have a lot of unknown effects, and different medicines and vaccines are being trialed and tested succefully to stop prevelance, transmission and develop the symptoms.

Key words: COVID-19; Virology; Vaccine entities; Pharmacotherapy; Nanotechnology

Introduction

The most recent information from DNA sources shows that the human nCOVID-19 comes from animals. The coronavirus types HCoV-OC43, HCoV-229E, HCoV-HKU1, and HCoV-NL63 cause mild signs in the lungs.

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The population with People with poor immune systems got sick from illnesses caused by the COVID-19 and the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2002 and 2012, respectively. COVID-19 was found to be a possible threat in December 2019, and a world pandemic was predicted for 2022. The quick movement of the people around the world, helped the virus to get transmit promplty. The real number of cases is underestimated because there isn't a good database, the illness is quiet, people aren't tested as often as they should be, and most importantly, testing processes and standard methods aren't used. The COVID-19's genetic code was made public so that it could be studied quickly and well. The Alpha (UK) version (also known as B.1.1.7), the Beta (South Africa) version (also known as B.1.351), the Gamma (Brazil) version (also known as P.1), and the Delta (India) version (also known as B.1.617.2) are the four most popular types of COVID-19 seen around the world.

Vaccination and immunotherapy

Over the past 150 years, both natural and learned immunity have made a big difference in life expectancy and changed the way society and the global economy work. Therefore, the vaccines are being developed quickly and made available to a lot of people, which is helping to lessen the terrible effects of many deadly diseases. The surprise drop in treatment costs and the health care budget led to a big benefit for the economy and society. The broad preventative vaccine is a key part of keeping the population safe from viral sicknesses in a way that is both long-lasting and effective. It has led to the end of the disease and a drop in its spread among the population. So, it was decided that these treatments and precautions would be used to fight against COVID-19. Clinicians are told to use monoclonal antibodies, convalescent plasma, and new uses for old drugs. The researchers are working hard to make a wide range of vaccines. They are exploring and using cutting-edge immunological, genetic, and microbiological methods. Over 200 possible vaccines are now being looked into all over the world. But making a COVID-19 vaccine that is safe and gives people a strong immune response is not easy. The failure to create long-lasting immunity and stop the cytokine storm (5); this was because it was hard to test and target the right vaccine platform technologies.

Molecular characterization and virology COVID-19

COVID-19 is an RNA virus with a spike-shaped glycoprotein shell. The genome has four important proteins and is 79.6% the same as the SARS-CoV genome. Nucleocapsid (N) protein helps viruses grow, copy themselves, and make mRNA by sticking to viral RNA and encouraging the formation of nucleocapsids. The spike (S) protein makes it easier for the virus to attach to and enter the target cell. Membrane (M) proteins are important parts of the virus membrane. The envelope (E) protein is thought to help the virus put itself together, spread, and be dangerous, but its structure and how it works are not fully understood. Before transmembrane protease serine (TMPRSS2) can activate the virus and let it enter human cells, the virus's S protein has to bind to the ACE2 receptor. TMPRSS2 splits the S protein into its S1 and S2 parts after the virus's membrane has joined and it has entered the target cell. About the same amount of ACE2 is found in the lung, nose epithelium, kidney, gut, and heart. But new study has found other sensors that make it easier for viruses to get into host cells.

Emerging nanotechnology to develop vaccine

The nanotechnology is being used to make medicines against many specific pathogenic proteins. This advanced technology is mor flexible and can speed up the process of developing the structures of vaccines, that was take lot of the time before (7). However, there was also traditional methods to stop the pandemic of COVID-19, the usual way to make antibodies is to inject the dead, weakened, or inactive parts of viral vectors. This may not work well when there is a pandemic of COVID-19. So, the viral RNA is used to speed up the process, make it more accurate, and protect the population currently at the risk. But people aren't asked to help at first because there are major health risks. The candidates vaccines with more complicated cases are held back on purpose if they can't answer questions about how safe they are in the long run and how much protection they are supposed said to give.

Another high risk of using S-protein vaccines is that the RNA sequence of COVID-19 could change. COVID-19 variants have been found in people all over the world who are carriers. Therefore, the current scientific information on how the immune system responds and how the virus antigen behaves when it causes disease helps to support the treatment options and improve clinical and pharmaceutical patient care. Then, we can make plans for how to make COVID-19 and how to use transportation systems to help fight this historic disease.

Spike (S) protein of COVID-19

Neutralizing the COVID-19 Spike (S) protein was also the main goal of immunizing the sample group. For the best level of safety, possible COVID-19 vaccines go through many rounds of testing and reworking. Antigen, adjuvant(s), and a way to give the vaccine have always been thought to be important parts of a good vaccine against a certain virus illness. That should make sure (8) that it is safe for a wide range of people, is liked by most people, and gives the needed long-term protection.

Pharmacotherapy and treatment options for COVID-19

The similarities between COVID-19 and MERS-CoV and SARS-CoV helped us to learn more about the viral genetic properties, clinical behavior, and pattern of transmission. The major goal was to improve the efficacy as quickly as possible and provide the maximum relieve to the patient in clinical setting. Additionally, we can use the same physiological, pharmacological, and scientific data to make sure safety of patients. Hence, the FDA has given permission or is looking into whether the antiviral medicines can be used to treat other viral illnesses (9).

Repurposed drugs for COVID-19

Drugs	Mechanism of action	Status of clinical use
Anti-viral drugs		
Lopinavir-Ritonavir	Protease enzyme inhibition (antiretroviral drugs)	During clinical tests
Umifenovir	The suppression of viral and cellular membrane fusion	During clinical tests
Azithromycin	Immunosuppressive impacts on the immune system	During clinical tests
Anakinra	Receptors for interleukin-1 and their downstream signaling pathways are blocked	During clinical tests
Remdesivir	Containing the Pandemic	Certified by the FDA
Favipiravir	The suppression of viral-RNA dependent RNA polymerase activity	During clinical tests
Hydroxychloroquine	viral entrance inhibition, endosomal pH elevation, and ACE2 glycosylation interference	The FDA has banned its usage in emergencies because to the risk of serious heart problems
Tocilizumab	Inhibiting IL-6 by preventing its receptors from sending signals	During clinical tests
Camostat (TMPRSS2 inhibitor)	Preventing viruses from developing and entering host cells	During clinical tests
Anti-inflammatory		
Ruxolitinib	Subduing the Immune System by Blocking JAK Signaling	During clinical tests
Baricitinib	Virus entry inhibition, JAK signaling inhibition, immune suppression	During clinical tests
Thalidomide	Inflammatory cell invasion and cytokine storm suppression	During clinical tests
Glucocorticoids	Reduction in the body's inflammatory and immunological responses	Approved Dexamethasone Use for Severely Ill Patients
Monoclonal antibody		
Bamlanivimab	Block the passage of viruses into host cells	Permission for Use in an Emergency
Casirivimab and imdevimab	Block the passage of viruses into host cells	Permission for Use in an Emergency
Plasma therapy		
Convalescent plasma	Virus eradication using antibodies that target just the virus	During clinical tests
Cell-based therapy		
Mesenchymal stem cell	Aid in healing wounds and dampening the immune system	During clinical tests
NK cell	Improve your body's natural defenses	During clinical tests

Modified from Maharjan & Choe (11)

Moreover, we can use these procedures to treat COVID-19 in the pharmaceutical and in therapeutic settings. The FDA has approved veklury (remdesivir) as the first medicine to treat COVID-19. The monoclonal antibodies bamlanivimab and casirimab/ imdevimab were then given EUA, which stands for Emergency Use Authorization. In both clinical treatment and study, the COVID-19 virus is now the main target of antiviral chemotherapy drugs. A few examples are regulating the immune system, making cell-based treatments better, and stopping the spread of viruses. COVID-19 might spread more slowly if convalescent plasma is used or if the inflammatory processes that cause cytokine storms are stopped. The goal of these steps is to make COVID-19 disease less severe by reducing the amount of virus in people who have it.

Entities of the COVID-19 Vaccine

Antibodies against COVID-19 can potentially be examined for learned and understand the all different strains of coronaviruses, such as SARS-CoV and MERS-CoV. Once the target antigen has been Identified, the next step is to find the best way to develop the vaccine, add adjuvants, and finalize the safe and effective quantity of dose and dosage forms. So, the quick sharing of genetic and molecular information has helped to speed up the process of developing the effective vaccine against COVID-19.

COVID-19 vaccines

Vaccine form	Antigen	Production	Advantages	Disadvantages
Viral vector-based vaccine	S protein	Encoded target gene genetic modification	Increased cellular and humoral immune responses, without the risks	Various immunological reactions may be seen
Recombinant protein	S protein	Complete or partial antigenic components	Immune response in both cells and the humoral system, high level of safety, constant output	Consistent dosing and adjuvants are needed, and the expense is high
RNA	S protein	Synthetic RNA used to produce an antigen in a laboratory	Simple in conception, very flexible, and capable of eliciting a robust immunological response	Extremely dangerous instability
DNA	S protein	DNA modified in a laboratory to produce an antigen	High-titer neutralizing antibodies that are simple to create and scale up	Required certain delivery method, Immune suppression; possible harm with prolonged usage
Inactivated virus	Whole virion	Virus particles rendered harmless by exposure to high temperatures, poisons, or x-rays	High-titer neutralizing antibodies that are simple to manufacture and safe to use	Potential triggers for sensitivity
Attenuated live virus	Whole virion	decreased infectiousness while yet maintaining viability	Quick progress, less side effects, and a robust immunological response	Reversion to a previous phenotype or genotype; not appropriate for use in all age groups (safety testing)

Modified from Maharjan & Choe (11)

The advancement in vaccine technology has changed the clinical translation and conventional antigen administration. Nanotechnology has contributed a wide variety of antigenic moieties for vaccine delivery (12). Nano-sized particles of synthetic or natural source are modified to desired size to administer through intended route at targeted immune cells to attain the adaptive and/ or innate immunity. So, the COVID-19 vaccines are developed from the viral proteins components, nucleic acids subunits encoding viral antigen, inactivated or live-attenuated viruses, virus-like particles, replicating and non-replicating viral vectors and cell-based vaccines (13).

Development of COVID-19 vaccines

Developer	Platform	Protocol	Immunogenicity
RNA Vaccines			
Research Consortium on Vaccines; Academy of Military Sciences, People's Liberation Army (PLA); Walvax Biotech	messenger RNA for the S protein	IM, (0, 14 or 0, 28)	There is evidence that non-human primates may be induced to produce neutralizing antibodies
Pfizer, BioNTech, and Fosun Pharma's BNT-162	Three mRNA capsules in LNP shape	IM (0, 21)	Antibody and neutralizing titers, as well as CD4+ and CD8+ T cell responses, at high levels
Moderna/NIAID mRNA-1273	LNP-encapsulated S-protein mRNA was stabilized by prefusion	IM (0, 28)	Neutralizing antibodies and CD4+ and CD8+ T cell responses are elicited after repeated dosing
Imperial College London LNP-nCoVsaRNA	RNA that can copy itself is packed into tiny amounts of fat	IM	The production of neutralizing antibodies and T cell responses has been shown in published preclinical studies
The CVnCOV/Curevac	Encapsulated messenger RNA in lipid nanoparticles	IM (0, 28)	Strong CD4+ T cell and neutralizing antibody responses
Arcturus/Duke-NUS, LUNAR-COV19	A lipid-mediated mRNA amylation mechanism	IM	It seems that following a single injection, a large amount of neutralizing antibodies is induced
DNA Vaccines			
ZyCoV-D/ Zydus Cadila	Plasmid DNA encoding for S protein	ID (0, 28, 56)	Several animal species' immunological responses have been documented
INO-4800, Inovio Pharmaceuticals	Electroporation-mediated DNA plasmid vaccination	ID (0, 28)	Low risk and a robust immunological response
COVID-19 Vaccine/ Takara Bio, Osaka University	Adjuvant + DNA plasmid encoding S protein	IM (0, 14)	N/A

Maharjan & Choe (11)

Conclusion

COVID-19 potentially needs attention and resources because of it's distinctive moledulare features and transmitting pattern. It also has a strange pathophysiology and epidemiology, hat helped scientists to develop the vaccines, that work successufly, effectively and safely. On behalf of the previous scientific information and research data of MERS-CoV and SARS-CoV, the vaccines were developed made available around the world. The teaching institutions, drug companies, and government health agencies work collaboratively to counteract and mitigate the disease. Additionally, the competition in the pharmaceutical business and research scientists, the clinical studies were completed fastly and on a larger scale than ever before. Cell-mediated protection, strong antigenicity, and high antibody titers are major components of these vaccines. Additinally, the nanomaterials help to carry the viral components and qualify the defined standards for COVID-19 vaccines. Thus, the molecular characterization, clinical management and development of vaccines against the targeted viral components of COVID-19 has played primary role the stope the mortalities because of this pandemic disease.

Abbreviations

Antigen-presenting cells (APCs), dendritic cells (DCs), adenoviruses (ADs), adeno-associated viruses (AAVs), lipid nanoparticles (LNPs), acute respiratory distress syndrome (ARDS), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-19), middle eastern respiratory syndrome (MERS-CoV), CDC, and the World Health Organization. WHO, FDA, EUA, and the Food and Drug Administration all have to do with public health. Transmembrane Protease Serine 2 (TMPRSS2); Angiotensin Converting Enzyme 2 (ACE2); RBD Receptor Binding

Domain; NTD N-terminal binding Domain; S-protein Spike-protein; N-protein Nucleocapsid Protein; E-protein Envelope Protein; M-protein Membrane Protein; Type-1 interferons (IFNs), Toll-like receptors (TLRs), pattern recognition receptors (PPRs), natural killer cells (NK cells), respiratory syncytial virus (RSV), mesenchymal stem cells (MSCs), cytotoxic T-lymphocytes (CTLs), antibody-dependent enhancement (ADE), and toll-like receptors (TLRs).

Conflict of Interest

The authors declare that they have no conflicts of interest regarding the publication of this article.

Adherence to Ethical Standards

This article does not contain any studies involving animals performed by any of the authors. This article does not contain any studies involving human participants performed by any of the authors.

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