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Progress and Development in Treatment of Covid – 19, and Vaccine development: A Review

Vijay P. Sonar^{*}, Priyanka V Dalvi, Shailesh S. Chalikwar

Department of Pharmaceutical Quality Assurance, R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, MS, India.

ABSTRACT

The entire world is facing a worst situation of pandemic ever. It's been more than 18 months after the initial reports on Covid from China, and the pandemic is still going. As per the data available over the WHO website as of 23 June 2021, there have been 178,837,204 confirmed cases of COVID-19, including 3,880,450 deaths, reported to WHO. As of 21 June 2021, a total of 2,414,347,324 vaccine doses have been administered. Despite of having more than 15 vaccines for Covid-19; the challenge to treat a patient with a define line of treatment remains the same. In the present review we have made an attempt to summarize the various medicines which are being used by medical practitioner in India and overseas. Use of different drug molecules like Remdesivir, Tocilizumab, Hydroxychloroquine, Azithromycine, Ivermectin, Steroids, Doxycycline, Ecosprine, Low molecular weight Heparin, Lopinavir and Ritonavir, Nitazoxanide, Baricitinib etc. were highlighted; although the list is long. A focus is made on the different types of vaccines available till date and their status in various countries.

Keywords: Covid-19, Vaccine, Antiviral, Pandemic, Antibiotics.

*Corresponding Author Email: vsonar34@yahoo.com

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INTRODUCTION

The novel coronavirus (severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that erupted from China is a deadly respiratory pathogen that belongs to the same family as the coronavirus for the 2002–2003 severe acute respiratory syndrome (SARS) outbreaks (1). Coronaviruses are members of the Coronaviridae family, a assorted family of RNA viruses that cause respiratory tract infections in human being (2). Coronavirus disease-19 (COVID-19) caused by SARS-CoV, MERS-CoV and SARS-CoV-2, respectively. All three coronaviruses are mentioned in the WHO Blueprint list for priority pathogens (3). Meanwhile the first cluster of cause was identified in Wuhan city, Hubei province, China in December 2019, the Novel coronavirus disease 2019 continues its ruthless march around world as May 12,2020 (1,4). Public misrepresentation regarding treatment has run, especially through traditional and social media. WHO has specifically targeted these questionable proclamations, but prevent these proclamations can be hard to combat in an era of worldwide connectivity (5). In a case study of it was found that, overall case fatality rate (CFR) was 2.3%, in which CFR of the elderly and patients with pre-existing comorbid conditions was higher. Growth period of COVID-19 was 1-14 days with mostly 3-7 days, and maximum growth period could reach 24 days. Wei M, et al. reported that procalcitonin advancement was common in pediatric patients which is different from adults. Senior people with primary diseases including hypertension, cardiovascular disease and diabetes are more prone to COVID-19. It may be due to changes in the elderly's lung anatomy and muscle atrophy leading to changes in respiratory system function. Because older people with COVID-19 are prone to multi-system organ dysfunction. A study carried out by Liu k, et al. illustrated that lymphopenia in older people COVID-19 confirmed patients was remarkably higher than that in adult- aged groups. In addition CRP was remarkably higher in senior patients compared to other age groups. Expecting women are more liable to COVID-19 and severe pneumonia, because they are at physiological commutable changes and immuno suppressive state during parturiency [16]. The leukocytosis and elevated neutrophil ratio were founded to more common in the COVID-19 infected expecting women in the Liu H,et al.study . In a study of Wang X, et al., lab findings included higher leukocyte count, raised neutrophil ratio, lymphopenia and elevated CRP, D-dimer and LDH. However, aminotransferese levels and creatinine were reported in the normal range (6). MERS-CoV was indigenously remoted in Vero and LLC-MK2 cells, and systemized techniques using RT-PCR–based examination of respiratory and other clinical specimen have been issued. These procedures can discover as few

as 10 to 15 viral RNA copies. MERS-CoV infection can be recognize in starting of 2 to 3 weeks after the beginning of sickness using serologic technique, enzyme-linked immuno sorbent assay (ELISA) initially, with confirmation by indirect immunofluorescence assays (IFA) and neutralization assays. Virus was determined by RT-PCR in overlying and bottommost respiratory tract and urine specimens. Initially, in the sickness, sample were found positive only in round about one-third of patient. Virus was detected most often during the second week of sickness. Antibody procedure has been established using tissue cultivation–grown virus and ELISA and IFA (2). Drugs are considered as a vital way for stopping and controlling outbreak of diseases. However, drug discovery is a time-taking, enlightened, and expensive process, which can be always distributed into several essential stages, containing preclinical research, clinical trials and additional analysis process. An average of 15 years are necessary for an investigational drug to transfer from the lab to the patients. Since pharmacokinetic properties and toxicity are the core attention that defined the effectiveness of novel drug upgrading, applicants selected from the standing or licensed drugs in the laboratory could probably be translated into clinical use in a faster pace (28,29). This review is planned to provide information on the pathogenesis of SARS-CoV-2 and the allopathic medicine used in treatment and also the information regarding the progress of vaccine development.

Pathogenesis

SARS-CoV-2 is made up of at minimum 11 ORFs (Open Reading Frames) with the full length of 29903 pp. Its genome is parallel to SARS-CoV with a gene order 5'-ORF1ab-S-E-M-N-3'. A large gene programming a replicase (ORF1ab) is tracked by 4 main structural protein-coding genes: S (Spike protein), E (Envelope protein), M (Membrane protein) also N (Nucleocapsid protein). There are at least 6 attachment ORFs. SARS-CoV-2 fit in to the β coronavirus also its order considerably differs from that of SARS-CoV and MERS-CoV, which have caused epidemics earlier. Phylogenetic study suggests that the neighbouring relatives of SARS-CoV-2 are several viruses originated from bats, such as Bat-CoV RaTG3, Bat SARSr CoV-ZC45 and Bat SARSr CoV-ZXC21. Hence, bats are expected to be the original host of SARS-CoV-2. However, there should be a transitional host, who transfers the novel coronavirus to human because the sequence of SARS-CoV-2 and bat virus Bat-CoV RaTG3 has slight alteration. The doubtful intermediate host has been recommended to be the pangolin by Chinese scientists on the basis of genetic analyses, which has not been accepted till now with the declaration of new pangolin coronavirus genome studies (6). Microscopic image of corona virus is shown in figure 1.

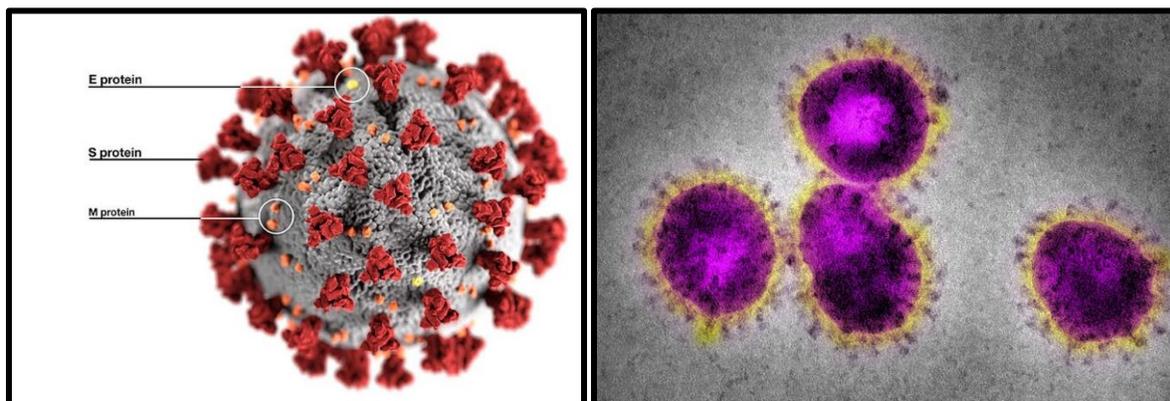


Figure 1: Microscopic image of corona virus

DRUGS/ MEDICINES USED IN MANAGEMENT OF COVID-19

An attempt is made to list and summarize the various molecules which are a part of line of treatment.

Chloroquine and Hydroxychloroquine

It was assumed that chloroquine may have a wide-ranging mechanism of action which may vary depending upon the pathogen studied. It has been progressively studied that the anti-viral and anti-inflammatory activities of chloroquine may have a part in the management of patients with novel COVID-19. Chloroquine rises endosomal pH and interferes with the glycosylation of cellular receptor of SARS-CoV and so it has the capacity to block viral infection. Chloroquine alters the pH of lysosomes and probably inhibits cathepsins, that points to the formation of the autophagosome which destroy SARS-CoV-2 spike protein. Earlier investigational studies have also demonstrated that in vitro study, chloroquine has effective anti-SARS-CoV-1 effects, mainly accountable to a lack in the glycosylation receptors at virus cell surface, so that it can't attached to the angiotensin-converting enzyme 2 (ACE2) articulated in lung, heart, kidney and intestine (7). The outcomes of clinical studies evaluating the influence of hydroxychloroquine do not pillar any efficacy of this drug in patients with COVID-19, due to major significant methodological weaknesses(8). Extension of QT is a constant finding with CQ/HCQ, recommending that patients getting treatment with CQ/HCQ needed the least episodic electrocardiographic assessment or continuous observing (9).

Ecosprin

Acetylsalicylic acid (ASA) has both anti-inflammatory and antithrombotic effects. In addition, a significant ASA-mediated antiviral activity against DNA and RNA viruses, including different human coronaviruses, has been documented (10). Aspirin exerts its antiplatelet effect through inhibition of the platelet cyclooxygenase (COX) pathway and subsequent reduction in

thromboxane A₂ (TxA₂) production. AspirinWorks® is an FDA cleared competitive immunoassay in microplate format that measures levels of 11dhTxB₂ in urine specimens. This test may be used by physicians to monitor aspirin effect and assist in optimizing antiplatelet therapy in individual patients. Platelet aggregation effect are seen in COVID patients so aspirin found very essential in COVID therapy (11). There are some concerns that the delay between SARS-CoV2 test positivity and clinical deterioration is similar to the delay between the last aspirin intake and the end of its clinical effect (12).

Remdesivir

History of remdesivir began in 2016 when it was first established to fight with the Ebola virus disease (EVD) outbreak in Africa, with the improvement code name of GS-5734.1. In short, remdesivir is a nucleoside analog (NA) inhibitor of RNA-dependent RNA polymerase (RdRp). Later the breakdown of remdesivir into its active form (GS-441524), it obstructs with the viral RNA polymerase, limiting viral duplication. It inhibits viral RNA synthesis through deferred chain dissolution. The triphosphate form of remdesivir looks like adenosine triphosphate (ATP) and hence, misguides the viral RdRp as a nucleotide. The *in vitro* and *in vivo* antiviral activity of remdesivir has been inveterate against RNA viruses of the Filoviridae (including Ebola virus) and Paramyxoviridae families (13). While the 3D structure of protease of COVID-19 was forecast using SWISS MODEL server, molecular interaction analysis on protein and ligands were completed using AutoDock software. Pharmacokinetic try-outs in cynomolgus monkeys disclosed that first-pass result of oral remdesivir causes low bioavailability of the drug. Intramuscular injection of 3 mg/kg had a 50% survival rate matched with the control group. In two hours, remdesivir rapidly circulated in peripheral blood mononuclear cells (PBMCs), and quickly afterwards activated to nucleoside triphosphate to reach a peak, with a survival rate of 100%. It has been concealed in the World Health Organization (WHO) Director-General's opening notes at the media briefing on COVID-19 on February 20, 2020 that the two clinical trials on remdesivir of therapeutics ranked by the WHO R&D Blueprint are estimated preliminary outcomes in three weeks (14).

Ivermectin

Ivermectin treatment was associated with lower mortality during treatment of COVID-19, especially in patients with severe pulmonary involvement. Randomized controlled trials are needed to confirm these findings (15). SARS-CoV-2 utilizes the IMPa/b1 heterodimer to enter host cell nuclei after gaining cellular access through the ACE2 receptor. Plasma and lung ivermectin concentrations vs. time profiles in cattle were used to determine the apparent plasma

to lung tissue partition coefficient of ivermectin. This coefficient, together with a simulated geometric mean plasma profile of ivermectin from a published population pharmacokinetic model, was utilized to develop a minimal physiologically-based pharmacokinetic (mPBPK) model. The mPBPK model was also used to simulate human lung exposure to ivermectin after 12, 30, and 120 mg oral doses. The simulated ivermectin lung exposures reached a maximum concentration of 772 ng/mL, far less than the estimated 1750 ng/mL IC₅₀ reported for ivermectin against SARS-CoV-2 in vitro. Further studies of ivermectin either reformulated for inhaled delivery or in combination with other antivirals with differing mechanisms of action are needed to assess its therapeutic potential(16,17) cells infected with SARS-CoV-2 were treated with serial dilutions of ivermectin 2 h post infection and supernatant and cell pellets collected for real-time RT-PCR at 48 h . As above, a > 5000 reduction in viral RNA was observed in both supernatant and cell pellets from samples treated with 5 µM ivermectin at 48 h, equating to a 99.98% reduction in viral RNA in these samples. Again, no toxicity was observed with ivermectin at any of the concentrations tested. Underlining the fact that the assay indeed specifically detected SARS-CoV-2, RT-PCR experiments were repeated using primers (18,19) .

Azithromycin

The strongest evidence of effectiveness for azithromycin concerns its role as an antibacterial drug. Although there is no direct evidence of the effectiveness of azithromycin in COVID-19, some scientific bodies have suggested that the antibacterial properties of azithromycin remain clinically useful in the empirical treatment of community-acquired pneumonia occurring in COVID-19 patients (20). Azithromycin appears to decrease the virus entry into cells. Azithromycin up-regulates the production of type I and III interferons. These mechanisms are universally involved in the innate response against infectious agents, and potentially against SARS-CoV-2 (21). According to study report it is found that combination of azithromycin and hydroxychloroquine are found effective in some patients (22).

Doxycycline

Doxycycline (a semisynthetic derivative of tetracycline) would seem to be a valid alternative to azithromycin. In fact, in addition to its well-defined antibiotic effects (bacteriostatic action by inhibition of bacterial protein synthesis), in vitro studies have shown doxycycline to exert anti-inflammatory effects at low (20-40 mg/day) and high (100 or 200 mg/day) doses with inhibitory action on metalloproteases and modulating effects of pro-inflammatory cytokines IL-6, IL-8, and tumor necrosis factor-alpha (23).

Low Molecular Weight Heparin

Heparin is a member of a family of glycosaminoglycan molecules that include heparan sulphate, chondroitin sulphate, keratan sulphate and hyaluronic acid. These molecules are expressed throughout the body, with diverse biological roles. Administration of anticoagulants or therapeutic doses of low molecular weight heparin in hospitalized COVID-19 patients, instead of prophylactic doses, is the current practice in their practicing institution. Heparin also has other pharmacological actions of potential benefit including inhibition of inflammatory cytokines implicated in COVID-19 and the inhibition of inflammatory cell recruitment into tissues via blocking many of the key adhesion molecules expressed on vascular endothelium, improvement in lung function and increased nitric oxide release (24,25)

Lopinavir and Ritonavir

Lopinavir is a human immunodeficiency virus (HIV) type 1 protease inhibitor with in vitro inhibition of SARS-CoV-1.37 Ritonavir is often combined with lopinavir to rised its plasma half-life. Grouping of lopinavir/ritonavir (LPV/r) was recommended to lead to declined adverse outcomes in the 2004 SARS outbreak (37,38). The arrangements and structures of the LPV/r binding site to SARS-CoV-1 and SARS-CoV-2 proteases are 96% preserved, and it was initially thought that LPV/r could be an active treatment for COVID-19 by inhibiting the virus' main protease (Mpro) (5). Involvements using lpv/r to treat coronavirus have been stated in various study Cao and co-workers presented 199 adult patients with severe COVID-19, no advantage was detected with lopinavir - ritonavir treatment beyond standard care, and mortality at 28 days was similar in LP/r groups and standard care group. Chu and co-workers assessed the effects of LP/r compared to historic controls treated with ribavirin only (26,27).

Nitazoxanide

Nitazoxanide is a wide-ranging-spectrum antiviral agent going through clinical improvement for management of influenza and other additional viral respiratory infections. It shows in vitro activity against Middle East Respiratory syndrome coronavirus (MARS-Cov) and further coronavirus, constraining expression of viral N protein. Nitazoxanide also conquer production of pro-inflammatory cytokines in peripheral blood mononuclear cells and destroys interleukin 6 production in mice. Having been used broadly in clinical trials and in post-marketing experiences, nitazoxanide is an smart drug applicant intended for management of Middle East Respiratory Syndrome (28).

Corticosteroids

Corticosteroids are a class of anti-inflammatory mediators used widely in the initial stages of the COVID19 epidemic. Corticosteroids perform via down regulation of significant pro-

inflammatory fragments and are assumed to be supportive in blunting the cytokine storm seen with the virus. Corticosteroid administered in prior coronavirus outbreaks was fail to deliver a survival advantage and was likely injurious in cases of SARS-CoV-1 and MERS-CoV due to late viral clearance. These studies mainly contain up-to-date WHO recommendation against corticosteroid use initial in epidemic of COVID-19. The WHO recommendations make allowance for cases of refractory septic shock, Commensurate with the Surviving Sepsis Campaign guidelines in 2016. Disagreement with this reference comes when COVID-19 patients develop ARDS. The DEXA-ARDS trial, a recent multi-center Spanish study calculating dexamethasone use in ARDS, indicated a important use in decrease of both machine-driven ventilation and death. The data precise to COVID-19 are inadequate (5,29).

Baricitinib

The part of baricitinib (a selective JAK1 and JAK2 inhibitor) in the management of COVID-19 has been recommended due to its mechanism of action affecting viral endocytosis, even though its real safety profile still remains to be definitively clarified. Baricitinib is permitted for the handling of moderate to severe cases of rheumatoid arthritis, at a prescription amount of 4 mg/day, which have not reported to one or more disorders modifying anti rheumatic drugs. Meanwhile, numerous worries have been raised concerning about security of baricitinib and on accurate timing of administration of baricitinib according to the phases of COVID-19. It seems crucial to recognize which patients might assistance from treatment with JAK (janus kinase) inhibitors. Some authors have raised concerns about a possible facilitating effect of baricitinib on SARS-CoV-2 infection evolution and an increased risk of concomitant infections such as herpes zoster and herpes simplex, due to an impairment of interferon-mediated antiviral response. Data on clinical use of baricitinib in the treatment of COVID-19 patients are very scarce (30) .

Ace Inhibitor

The structure of the receptor-binding gene region is very similar to that of the SARS coronavirus in which both employ the angiotensin-converting enzyme 2 (ACE2) for cell entry, so it uses in covid. ACE2, a negative regulator of the renin-angiotensin system (RAS), is a homolog of ACE, where its expression can be identified principally in the heart, kidney, and airway epithelial cells. It functions as a carboxypeptidase by converting angiotensin II to angiotensin-(1-7), thereby opposing the vasoconstrictive effect of angiotensin II. Coronaviruses' (SARS-CoV, SARS-CoV-2) Spike (S) protein, binds with high affinity to human ACE2 . Before SARS-CoV-2 and SARS-CoV cell entry, their S protein is subjected to a priming process via serine protease TMPRSS2 in order permit the attachment of viral particles to ACE2 and thus on cell surface. This entry

mechanism is confirmed by the fact that TMPRSS2 inhibition or TMPRSS2-KO mice show both decreased, though not abolished, S protein priming, and reduced viral entry, spread, and inflammatory chemokine and cytokine release (3).

Tocilizumab

Tocilizumab (TCZ), a monoclonal antibody against interleukin-6 (IL-6), emerged as an alternative treatment for COVID-19 patients with a risk of cytokine storms recently. Corticosteroids such as MP are the conventional agents used to fight cytokine storms. In an attempt to provide a corticosteroid-sparing effect, TCZ was recommended in COVID-19 patients to prevent or treat cytokine storms. The rationale for the use of the anti-IL-6 receptor antibody TCZ in COVID-19 patients is based on our understanding of the role of IL-6 in this disease and the experience with this drug in the treatment of cytokine release syndrome caused by chimeric antigen receptors redirect T cells. , repeated doses (even repeated with a lower dose) of TCZ might improve the condition of critically ill patients. Therefore, in addition to the safety advantage, a repeated dose of TCZ is more likely to be effective than glucocorticoid in the treatment of COVID-19. Moreover, single dose of TCZ might be expected to benefit these seriously ill patients with about 10 times elevated IL-6. And the moderately ill patient with an extremely higher level of IL-6, almost 90 times of normal, could also benefit from repetitive TCZ therapy. Nevertheless, it seems that repeat the dose at a frequency of daily, every other day, or every 3 days with a totally two to three doses would be sensible in these critically ill patients or patients with an extremely higher level of IL-6. Considering the long half-life time of TCZ and the saturate properties of receptor binding, the dose of TCZ could be reduced when repeated use. Dynamic observation of IL-6 levels is also helpful in understanding the progression of COVID-19 and the response to treatment. Binding of TCZ to IL-6R inhibits receptor-mediated clearance of IL-6, leading to its accumulation in serum (31).

VACCINE DEVELOPMENT

Vaccines are the most effective strategy for preventing infectious disease since they are more cost-effective than treatment, and reduce morbidity and mortality without long-lasting effects. A vaccine against SARS-CoV-2 could be used to prevent infection, disease and death in the global population. The following describes the current status of vaccine development against COVID-19 through various approaches. Details of vaccines developed and their current statuses in different countries is listed in table no.1

Recombinant Subunit Vaccine

Subunit-based vaccine development studies have reported enhancement of T cell immune responses and generation of high titer neutralizing antibodies *in vivo*. Clover Biopharmaceuticals is pre-clinical testing a recombinant subunit vaccine based on the trimeric S protein (S-Trimer) of the SARS-CoV-2. The S protein contains three S1 heads and a trimeric S2 stalk. Clover Biopharmaceuticals confirmed the generation of a natively-like trimeric viral spike in mammalian cell culture-based expression system and the detection of antigen-specific neutralizing antibodies in the sera of fully-recovered COVID-19 patients. Recently, Clover Biopharmaceuticals and GSK announced a partnership to improve immune response by introducing GSK's adjuvant system to S Trimer the University of Queensland is developing subunit vaccines using the "molecular clamp," a transformative technology (32).

DNA Vaccines

DNA vaccines represent an innovative approach by direct injection of plasmids encoding the antigens, accompanied with a wide range of immune responses. These advantages are applied with prophylactic vaccines and therapeutic vaccines. Recently, various DNA vaccine platforms have been developed to improve the efficacy of vaccines by using electroporation to deliver plasmids and adding adjuvant to enhance the immune responses. INO-4800 induces activation of T cells by delivering DNA plasmids that express the SARS-CoV-2 spike. This vaccine platform has advantages that can produce therapeutic antibodies and activate immune cells by delivering the vaccines intradermal into the patient. Inovio Pharmaceuticals is preparing for phase I trials in the U.S.A. and China with support from the Coalition for Epidemic Preparedness Innovations (CEPI) (32) .

mRNA vaccines

mRNA vaccines are rapidly developing technologies to treat infectious diseases and cancers. mRNA-based vaccines contain mRNAs encoding the antigens, which are translated at the host cellular machinery by vaccination. mRNA vaccines have advantages over conventional vaccines, by the absence of genome integration, the improved immune responses, the rapid development, and the production of multimeric antigens. (NIAID) (32).

Protein Subunit Vaccine

Subunit vaccines are based on only a limited number of viral proteins, often the major protein in the capsid or the envelope needed to confer protective immunity. Examples of these include the SP or RBD of SARS-CoV-2. Therefore, subunit vaccines are considered safer than full pathogen-based vaccines. However, single proteins, when expressed and purified in the absence of other viral components, are much less immunogenic. Besides lack of immune-stimulatory

viral compounds, also a partial misfolded conformation of the protein, relative to the native protein, could be responsible for this reduced immunogenicity. Therefore, subunit vaccines often require higher dosing, booster administrations and co-administration of adjuvants to enhance antigen-specific immunity. Virus-like particles (VLPs) are a highly effective type of subunit vaccines that mimic the overall structure of a virus. Sanofi Pasteur is leveraging their previous work on the development a SARS-CoV-1 vaccine to unlock a fast path for developing a COVID-19 vaccine. Sanofi Pasteur uses its recombinant DNA in vitro platform that produces an exact genetic match to SP (33) .

Viral Vector

Viral vector-based vaccines rely on the delivery of one or more antigens encoded in the context of an unrelated, modified virus. This strategy either employs live (replicating but often attenuated) or non-replicating vectors, among which adenovirus (Ad) vectors, measles virus, vesicular stomatitis virus (VSV) and modified vaccinia Ankara (MVA) are the most commonly used. Adenoviruses allow insertion of up to 7-8 kb, supporting the expression of most target antigens as a multivalent vaccine. Ad type-5 (Ad5) has been extensively used and shows superior ability to induce exceptionally potent CD4+ and CD8+(33). The vaccine was tolerated, with reactogenicity increased at the highest dose. Antibodies, neutralizing antibodies in a proportion of vaccines, and cellular responses were induced. A further clinical trial, which was done in the USA, has been reported on medRxiv. The vaccine was a lipid nanoparticle-formulated, nucleoside-modified, mRNA vaccine that encodes trimerised SARS-CoV-2 spike glycoprotein receptor binding domain administered at one or two doses of three dose levels. The vaccine was tolerated, with reactogenicity increased at the highest. Reactogenicity was reduced after a second dose. India is eyeing the Oxford –AstraZeneca vaccine as the likely first shot against COVID-19 to be available for Indians by end of 2020 (34).

Table 1: Status of Covid-19 Vaccine in different countries

Sr. No	Manufacturer	Name of Vaccine	NRA of Record	Platform	Status of assessment
1	Pfizer-BIONTECH	BNT162b2/COMIRNATY Tozinameran (INN)	EMA	Nucleoside modified mNRA	Finalized
2	AstraZeneca-Oxford	AZD1222	Core – EMA Non- COVAX	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	Awaited
3	SK Bio-AstraZeneca-Oxford	AZD1222	MFDS KOREA	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	Finalized
4	Serum Institute of India	Covishield (ChAdOx1_nCoV-19)	DCGI	Recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2.	Finalized
5	Sinopharm/BIBP	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV)	NMPA	Inactivated, produced in Vero cells	In progress
6	Sinovac	SARS-CoV-2 Vaccine (Vero Cell), Inactivated	NMPA	Inactivated, produced in Vero cells	Finalized
7	Moderna	mRNA-1273	EMA	mNRA-based vaccine encapsulated in lipid nanoparticle (LNP)	Finalized
8	Janseen- Johnson & Johnson	Ad26.COV2.S	EMA	Recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored vaccine encoding the (SARS-CoV-2) Spike (S) protein	Not yet started. Use abridged procedure relying on EMA
9	The Gamaleya National Centre of Epidemiology and Microbiology	Sputnik V	Russian NRA	Human Adenovirus Vector-based Covid-19 vaccine	Finalized
10	CanSinBio	Ad5-nCoV	NMPA	Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector)	-
11	Vector State	EpiVacCorona	Russian		-

	Research Centre of Virology and Biotechnology		NRA	Peptide antigen	
12	Zhifei Longcom, China	Recombinant Novel Coronavirus Vaccine (CHO Cell)	NMPA	Recombinant protein subunit	-
13	IMBCAMS, China	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)	NMPA	Inactivated	
14	Sinopharm/WIBP	Inactivated SARS-CoV-2 Vaccine (Vero Cell)	NMPA	Inactivated	-
14	Bharat Biotech	Covaxin	DCGI	Whole-Virion Inactivated Vero Cell	Finalized
15	Novavax	-	EMA	Awaiting decision on submission	

*The Above data is referred from WHO website; Vaccine status may change in near future.

SUMMARY

As on today, 29 June (2021), world is fighting with Covid-19 with available ammunitions like vaccines, antivirals, antibiotics, plasma therapy, steroids etc. Some countries of the world are in the third wave of covid-19 pandemic. In India second wave is just showing declined graph, but arousal of third wave is predicted pretty sure and soon. Use of Remdesivir and Steroid is in dispute. Use of antibiotics is limited to symptomatic relief. The Union Health Ministry and Family Welfare's directorate general of health services (DGHS) has issued revised guidelines to stop the use of Ivermectin and Doxycycline in Covid-19 treatment. The new guidelines have dropped all medicines, except antipyretic and antitussive, for asymptomatic and mild cases.

Meanwhile, about Remdesivir, the DGHS guidelines said, "Remdesivir is a reserved drug approved by DCGI under Emergency Use Authorization only based on limited scientific evidence globally. It is to be used only in select moderate/ severe hospitalized Covid-19 patients on supplemental oxygen within 10 days of onset of disease. "Role of plasma therapy is also questionable. Tocilizumab injection failed in Phase 3 trial for COVID conducted by their inventor Roche in both primary as well as secondary endpoints, no improvement in clinical status & not any single mortality benefits have been seen in CT after taking this injection. 2 – DG (2-Deoxy-D-Glucose), an anticovid drug developed by INMAS, a DRDO lab in collaboration with Dr. Reddy's Laboratory (DRL). 2-DG is used as an adjuvant therapy along with primary treatment. Clinical trials on 2-DG have shown that the drug helps in fast recovery of the hospitalized patients and also reduces the need of oxygen.

On a positive note, vaccination drive seems to be a game changer. Positivity rate has been drastically reduced in countries where effective vaccination program is running. Israel became the first country to declared themselves as Covid free, vaccination is the key factor behind it. Same is the scenario with USA, UK, New-Zealand and EU. India is heading ahead on the same track, being the largest manufacturer of vaccines we are trying to reach out to the maximum population. There are some challenges with the vaccination drive as we are a nation of 1.3 billion. Successful Vaccination drive and Precautions (Mask, Sanitizer, and Social distance) are the ways to save ourselves from Covid-19. Until complete irradiation of the virus, ups and downs will be there in transmission, and it is inevitable. Apart from vaccine, human kingdom still in need of a wonder molecule which would directly work against virus and reduces viral load significantly.

CONFLICT OF INTEREST

Authors declares no conflict interest in relation with the facts and data mentioned in above article.

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