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DERLEME MAKALE (Review)

A REVIEW: SEVERE TREATMENTS, DRUG AND VACCINE STUDIES FOR CORONAVIRUS DISEASE (COVID-19)

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ABSTRACT

In 2019, a new type of coronavirus, Severe Acute Respiratory Syndrome Coronavirus (SARS CoV 2) (COVID-19), emerged in Wuhan, China, and this virus spread all over the world and seriously threatened human life. In this review article, the drug and vaccine treatment methods applied against the COVID-19 virus, which seriously threatens the whole world and takes human health to fatal cases, are examined in detail. In some of the applied drug and vaccine treatments and negative effects can be seen as well as positive effects. Due to this reason, the application of some treatment methods has been stopped. Drug and vaccine studies vary from country to country. For this reason, this study aimed to discuss the examples of treatment practices of countries and explain the treatment process.

Keywords: *COVID-19, Coronavirus, Drug Treatment, Vaccine Treatment.*

1. INTRODUCTION

The novel respiratory disease that name is COVID-19 in the coronavirus family has caused by severe acute respiratory syndrome coronavirus SARS-CoV-2, which appeared in December 2019, in Wuhan city, China [1, 2], and spread worldwide [3]. As of November 12, 2020, there have reports, resulting in more than 33 million confirmed deaths, and COVID-19 has caused more than 1 million deaths in the first 6 months [4]. According to the World Health Organization (WHO) report from 30 December through 11 October, the number of infections has been over 37 million, and the number of deaths via COVID-19 has been one million [5]. In 2022, the number of people who died from COVID-19 worldwide will be around 1 million per year [6]. Tyrell and Bynoe made the first definition of coronavirus in 1966 [7]. Coronaviruses are zones of infectious diseases, and coronaviruses can be transmitted from a range of animals, as found in humans, pigs, chickens, bats, and dogs [8]. The ways of transmission of COVID-19 to humans are divided into two indirect and direct via contacting the infected surfaces, and mouth, nose, and eyes [9]. Another way of transmission is from person to person by inhalation of droplets [10]. Coronaviruses cause severe diseases in the respiration system and pathology, gastrology, and neurology fields. The first coronavirus (SARS-CoV) caused severe respiration disease which was thought to originate in Foshan, China in 2002-2003[11], [12]. The second coronavirus MERS-CoV originated from Arabian Peninsula in 2012 [13]. The third coronavirus COVID-19 has caused severe diseases in humans to spread globally in the past 2 decades

[14]. These CoV viruses of them are zoonotic, and they cause infection in humans [15]. CoV viruses (SARS-CoV, MERS-CoV, and COVID-19) are enveloped single-stranded RNA beta coronaviruses, positive-polarity, and they have non-structural proteins [16–18]. Ongoing vaccine trials are testing with several immune antiviral modulators.

A wide variety of COVID-19 treatment methods have been applied to date. While some of the treatment methods are the methods of application on drugs, some of them are studies on vaccines for the prevention of the disease. It is in the form of favipiravir, chloroquine and its derivatives, Lopinavir, Ritonavir, and various supportive drugs, etc., for patients who have the disease. Various vaccine studies have been carried out to prevent and minimize the transmission of the disease from the beginning, and some of these vaccine studies are being applied today. Vaccine studies are in the form of DNA and RNA-based studies. The most common vaccine treatment method applied today is Biotech and Sinovach vaccines. Apart from these, there are various vaccine studies such as Moderna, Sputnik, recombinant vaccines, and Live Attenuated vaccines. In this review, detailed information about the drug and vaccine studies applied in the treatment of COVID-19 is explained in the relevant places.

2. PATHOLOGICAL PROCESS OF COVID-19

When the COVID-19 species enter the human body, it poses a great danger to humans because it affects cellular and humoral immunity of the human. However, this situation is difficult because the COVID-19 virus uses (Angiotensin Converting Enzyme) ACE 2 and hides inside the cell [19]. Because the COVID-19 virus uses cell membranes, the cell surface serine protease TMPRSS2 and CD147 proteins37,38,39 and thus it is very difficult to hold and die in the cell [19–22]. The mortality rate of COVID-19, which is an acute disease, is generally around 2% according to the reports in the literature. The onset of severe discomfort due to massive alveoli can cause respiratory failure [12, 23, 24]. Xu et al. reported the pathological findings of COVID-19 and the findings of clinical tests [23]. According to this report, a 50-year-old man presented with symptoms such as fever, chills, and dry cough when he was admitted to the fever clinic. It was stated that this patient had a dry cough with mild tremors on the first day of his illness but did not go to the doctor and continued his work until the 9^{th} day of his illness. On the 9^{th} day, it was stated that he caught COVID-19 with inverse time PCR performed by the doctors. Oxygen therapy has been initiated. Subsequently, a moxifloxacin (0-4 g once a day, intravenously) supplement was initiated to prevent secondary infection with 5 million units of interferon alfa-2b twice a day and 500 mg lopinavir plus ritonavir twice daily. 80 mg methylprednisolone was administered twice to reduce respiratory distress. However, the cough and weakness did not decrease. On the 12^{th} day of the disease, progressive infiltration and widespread grid shadow occurred in both lungs. Although the oxygen saturation was 95% on the 13th day, other symptoms did not improve. On the 14th day, the oxygen saturation dropped to 60 percent and the patient died due to a heart attack. According to these results, desquamation and hyaline membrane formation were observed in the right lung tissue of the patient. This was observed to cause shortness of breath in the patient. It was stated that pulmonary edema and hyaline membrane formation in the left lung wall membrane suggested early stage acute (Respiratory Distress Syndrome) ARDS. In liver biopsy test results, microvascular steatosis and mild lobular and portal activity were observed. These were caused by the drugs given. There were no significant signs of damage to the heart tissue[23]. The death rate of COVID-19 due to diseases is as in Figure 1.

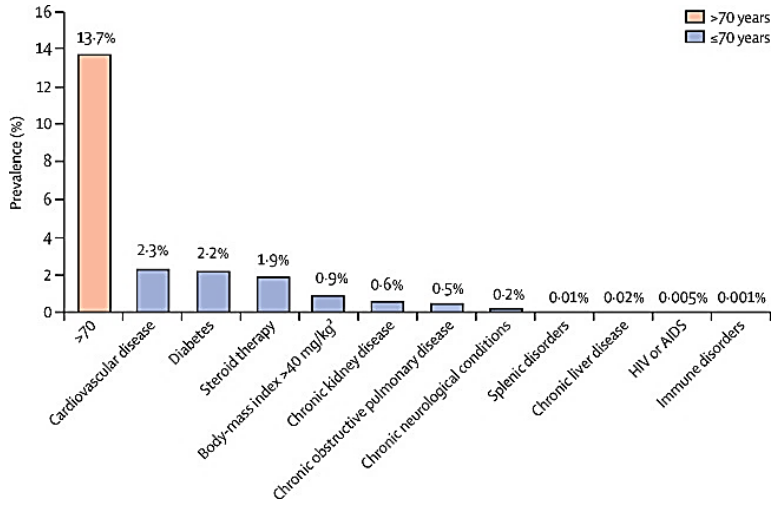

Figure 1. COVID-19-related death rate of diseases [25].

"Reprinted from [25]-Draft landscape and tracker of COVID-19 candidate vaccines- Estimating excess 1-year mortality associated with the COVID-19 pandemic according to underlying conditions and age: a population-based cohort study-2022).

3. DRUG THERAPY AGAINST COVID-19

It can be evaluated under two headings as antimicrobial drugs and supportive drugs.

3.1. Antimicrobial Drugs against COVID-19

Drugs showing antimicrobial effects against COVID-19 virus are Remdesivir, Favipiravir, Chloroquine, Hydroxychloroquine, and Lopinavir / Ritonavir. Remdesivir treatment is an antiviral for research purposes and clinical studies are still ongoing. Similarly, Favirapir continues for research purposes. Chloroquine and hydroxychloroquine have a limited number of uses[26].

3.1.1. Remdesivir (GS-5734)

This drug application is in the investigational nucleoside analog classification [26]. It is from the antimicrobial class with Remdesivir activity and has been used against COVID-19 as an antiviral in a wide-broad range [26–28]. Remdesivir (Gilead Sciences Inc., Foster City, CA, USA) is administered to the patient during the 10-day, 200 mg on the first day and 100 mg on the other days as a supplement [29]. This drug can bind to the RNA enzyme RNA polymerase (RNARp) in the form of a substrate, thus integrating as part of the virus RNA loops [29, 30]. When the cases in the past are examined, this drug has been used for SARS-CoV, MERS-CoV, and Ebola virus for patients [27, 29]. In the studies performed in mice, it was observed that viral load decreased after virus exposure, and early Remdesivir drug use (i.e.,> 2 orders of magnitude on day 2–5 post-infection). Thus, it has been observed that Remdesivir clearly improves the respiratory distress observed because of the disease caused by the virus, significantly reduces the disease caused by the virus, and stops its progression [31, 32]. According to data obtained from various countries, patients exposed to COVID-19 virus were treated with the Remdesivir drug, and the recovery rate was statistically 68% with this drug. 53

out of a total of 58 patients improved with this drug supplement [29, 33]. However, it is a drug used in antiviral treatment methods, and it is an antiviral drug used in the treatment of COVID-19 (SARS-CoV 2) [29, 31].

3.1.2. Favipiravir

Another RNA polymerase inhibitor drug, like Remdesivir, is Favipiravir. Favipiravir (Fujifilm Toyama Chemical Co. Ltd, Tokyo, Japan) is used in the treatment of COVID-19 [31, 34]. This drug is known for its effectiveness against oseltamivir-resistant influenza A, B, and C viruses in vitro. This drug is known for its effectiveness against oseltamivir-resistant influenza A, B, and C viruses in vitro. It is a wide range of broad spectral antiviral spectrum against COVID-19 and coronavirus family[28, 35]. In COVID-19 patients, favipiravir (n = 35) treatment was supplemented in combination with inhaled interferon alfa compared to ritonavir (n = 45) [35]. In the favipiravir application, it is given to the patient in two ways. For this, after 1600 mg is given on the first day, it is given at intervals of 600 mg for 2-5 days. In the second application, 1800 mg is given on the first day. 800 mg administered at intervals of 2-5 days. Tocilizumab 22 and Chloroquine 23 can be used together as supplements[36]. Favirapy-induced maximum plasma protein binding is two hours after dosing and 54% for humans [35].

3.1.3. Chloroquine

This drug is antimalarial classification [26]. Chloroquine is one of the drugs used against the SARS-CoV 2 virus with its immunomodulating property [26, 28, 37, 38]. The mechanism of this drug is likely to involve viral DNA or RNA assembly, and viral protein glycosylation. ACE2 inhibition and the emergence of the immunomodulating property of the released cytokine are other mechanisms [26, 39–41]. In in vitro tests, this drug has been observed to inhibit the development of the COVID-19 virus. This situation has also been supported by clinical tests. According to these clinical tests, the virus-inhibiting properties of chlorogenic were also supported in approximately 100 patients with COVID-19 disease [28, 38]. The long-term use of chloroquine seriously affects human life negatively, so long use is not recommended [42].This drug has been used previously in MERS-CoV and SARS-CoV 1, which are members of the coronavirus family, and its effectiveness in inhibiting viruses is reported. It has been proven to inhibit the COVID-19 virus (SARS-CoV 2) in Vero E6 cells with a value of 1.13 µM in 48 hours. For 39 cases diagnosed with COVID-19, 2 X 300 mg of hydroxychloroquine was administered for 10 periods [42, 43]. On day 6, a significantly higher loss of viral RNA was observed in nasopharyngeal sampling [42, 43]. Using azithromycin and hydroxychloroquine in six patients, viral clearance was 100% on day 6. For the monthly study, 78 of 80 COVID-19 cases were achieved by clinical regression, and the rate of obtaining negative data in PCR results after one week was 83%. On the 8th day, this rate increased to 93% [42, 44]. This drug has the status of a drug that prevents the virus from entering the cell.

3.1.4. Hydroxychloroquine

This drug is a derivative of chloroquine and this drug is in the antimalarial class [25]. Like chloroquine, it has immunomodulating properties of the COVID-19 virus[26, 28]. Chloroquine and hydroxychloroquine are used for antiviral prophylaxis due to their ability to prevent the COVID-19 virus from entering cells [26, 42]. However, enough clinical studies and statistical data have not been reported for this treatment use[45]. Steps such as inhibition of viral enzymes, transport of DNA or RNA polymerase, transport of new virus particles, and virus release can be observed in the process of mechanism. In addition, processes such as ACE 2 cell receptor inhibition, and cytokine release immunomodulation can be observed [28, 38–40, 46, 47].

3.1.5. Lopinavir / Ritonavir

Similarly, another drug is Lopinavir. Lopinavir is a protease inhibitor. It is produced from ritonavir and is usually co-administered with lopinavir. It has been shown that when co-formulated drugs are administered, the viral load is significantly suppressed in adults and children [48]. These two drugs are in the HIV protease inhibitor classification [49–51]. While International Chest Diseases experts recommend the administration of these two drugs to COVID-19 patients with moderate levels [52], it is given to patients with moderate and severe COVID-19 disease in Europe. Of the 199 patients who had COVID-19 disease and were laboratory-confirmed, 99 received lopinavir/ritonavir therapy. Gastrointestinal adverse side effects were not commonly observed in the standard group in this observation. While the percentages of patients with different time intervals with viral RNA showed a similar effect, clinical improvement was reported 1 day earlier in lopinavir/ritonavir therapy than in standard care [48].

3.2. Supportive Drugs

Drugs in this group support other treatment applications used against the COVID-19 virus. It is recommended to use heparin together with venous thromboembolism prophylaxis. Since the molecular weight of heparin (LMWH) is not very high, it is recommended to use this pair. Azithromycin is used in adjunctive therapy according to theoretical knowledge. It is a metered dose inhalation application of bronchodilators against the risk of viral COVID-19 transmissions [53, 54].

3.2.1. Anticoagulation

In cases caused by COVID-19 infection, thrombosis is a very common condition. This is thought to be due to infection, advanced age, and comorbidities. Venous thromboembolism (VTE) prophylaxis is stopped for a fibrinogen count less than 0.5 g / L [26, 53, 55, 56]. Anticoagulation is not recommended for patients diagnosed with COVID-19 in the absence of venous thromboembolism [26, 57]. It has been reported in the literature that vasculitis and increased occlusion of small pulmonary vessels in patients infected with postmortem lung infection materials [58], [59].

3.2.2. Azithromycin

Azithromycin is a drug in macrolide antibacterial in classification [60]and, is used against COVID-19 virus for supportive and adjunctive drugs. The macrolide class in which this drug is present shows its role as an immunomodulator in pulmonary inflammatory conditions. This means that reactive oxygen type radicals that accumulate in the lungs and damage cells are reduced, inhibited, and their negative effects are eliminated [42, 61–64]. Drugs such as Clarithromycin, erythromycin, bafilomycin A1 and telithromycin are the counterparts of azithromycin and have immunomodulating activity [65]. Therefore, they are used in COVID-19 viral therapy [65, 66]. It is given to the patient with other drugs and is an additional drug. In a clinical trial on 20 patients in France, patients were administered hydroxychloroquine and compared 16 times with controls. These controlled patients refused the combination of contraindication and hydroxychloroquine. He was treated with a combination of six 200 mg hydroxychloroquine 3 times a day for 10 roses of the process. For the 4-day process, 500 mg azithromycin was administered on the first day and 250 mg azithromycin was administered on the other days. According to the results, 100% of the patients treated with the combination in the 6 days showed that using only hydroxychloroquine, the azithromycin combination, or the control groups, 100% of the patients were cured. In treatment with hydroxychloroquine, 57.1% of patients are cured and 12.5% are under control [65].

3.2.3. Interleukin-1 (IL-1) antagonists

Franzetti et al reported the first treatment of interleukin-1 (IL-1) antagonists anakinra with available therapy for COVID-19 disease [67]. According to this report, it was observed that he got COVID-19 disease when he applied at the hospital with symptoms such as 39 C fever, cough, and sore throat on March 10, 2020. This patient did not have any health problems except that he was a smoker and his body mass index was 30.8 kg / m^2. Various drug treatments were started for this patient, whose oxygen saturation was 92%. Although the treatment process was initiated with certain doses of drugs such as lopinavir/ritonavir, hydroxychloroquine, azithromycin, and remdesivir, this patient's condition became very critical. On the 7^{th} day, the ratio of arterial oxygen partial pressure to fractional inspired oxygen (P / F) was 50%. Fever, asthenia, and anorexia also got worse. This patient was immediately started on anakinra treatment with a dose of 100 mg every 6 hours for 7 days. The patient's test turned negative, but permanent critical respiratory functions occurred during the normalization process. On the 32^{nd} day, the oxygen saturation of this patient was 93% [67].

4. VACCINE STUDIES

One of the most steps in the fight against Covid -19 is vaccination studies. Vaccine studies are generally of two types. These are passive and active immunity. Vaccines constitute one of the biggest success stories in the healthcare industry [68].

The vaccination trial should also have a high benefit for each population. According to WHO, "The vaccine should provide a reasonably positive benefit-risk distribution; it should show high efficacy, show only moderate or transient side effects, and not cause extreme pain." The vaccine should be safe enough to be prescribed to women of all ages, including pregnant and lactating women, and should include an accelerated onset of protection with a single dose and at least one year of protection [69].

4.1. Traditional Viral Vaccines

Inactivated or attenuated viruses are used in conventional viral vaccines. Thanks to advances in molecular virology consistent with viral immunology, it is now possible to genetically engineer vectors expressing only viral antigens that cause immune correlates of defense [70].

However, there are significant trust issues in terms of vaccine trials. Public issues regarding vaccination should include vaccine safety, vaccine costs, and the latest scientific results, in addition to vaccination policy and guidelines. Public vaccine admission decisions are based on a combination of scientific, psychological, sociocultural, and political considerations, all of which need to be better understood. These problems are very difficult to overcome. Conditions such as lot size required for production, release controls to market, shelf life required for the drug, filling into single or multiple dose vials or syringes, and the production of freeze-dried or stabilized liquid formulations cause global uncertainty in vaccine supply. The transport of vaccines can also pose a problem. It must follow various specifications, including cold chain standards as well as packaging and labeling in various languages for various markets [71, 72].

Different cell lines can be used in animal cell culture. Each cell line, virus type, and vaccine definition require a separate production and purification method. Each cell line also feels different environmental conditions and stabilization requirements [73, 74].

4.2. Live Attenuated Vaccines

Pathogens in live attenuated vaccines have been selected to be less virulent. They cannot reproduce the true disease or soberly mimic the disease in its altered state [75]. The pathogens in live attenuated vaccines are attenuated, so they mimic the normal infection cycle. By continuously moving the pathogen to tissue cultures, damaged types of microorganisms may be collected. In either one or two doses, live attenuated vaccines will offer lifetime protection in the body against the disease-causing microorganisms. Measles, smallpox, and yellow fever virus vaccines, as well as the tuberculosis vaccine as a bacterial vaccine, are examples of these vaccines [76]. Pathogenic or genetically engineered microorganisms capable of expressing one or more defensive genes from another microorganism make up live recombinant vector vaccines. These vectors cannot grow into the original virulent virus, and they are not pathogenic in hypersensitive species [77].

4.3. Recombinant Vaccines

Recombinant protein vaccines are a central component of second-generation vaccines, and they've been thoroughly investigated since the 1990s. Such research relies on live recombinant bacteria, fungi, or viruses that can express antigens from Leishmania parasites. In these systems, bacteria, parasites, or viruses serve as antigen carriers and adjuvants [76]. The artificial realization of genetic recombination events is the basis of rDNA science. The technology entails using an appropriate vector to move DNA fragments of a target gene sequence from several sources to another host (expression systems). This technology, which has a wide range of uses, could address critical life problems such as improving health, rising food supplies, and reducing the harmful impacts of various environmental factors. Aside from the safe use of recombinant pharmaceuticals, this technology is used in biotherapy and intervention in major diseases, as well as gene therapy and genetic engineering [78].

The following coronavirus vaccine experiments have begun phase III trials and have been published in the literature. Only the most commonly available vaccines are discussed in this publication. Figure 2 shows the achievements of some countries in vaccination studies [79].

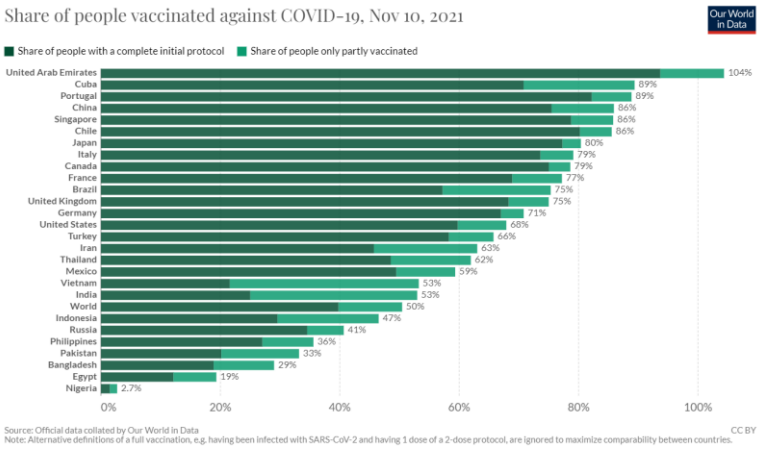

Figure 2. Share of people vaccinated against COVID-19 (Nov.2021) ("Coronavirus (COVID-19) Vaccinations - Our World in Data," 2021) **"**Reprinted (adapted) from [80] Official data collated by Our World in Data (2021).

4.4. Sinovac/Coronavac

In collaboration with the Bhutan Institute, Sinovac has started a Phase III vaccine trial to evaluate the efficacy and safety of 9,000 volunteer healthcare professionals in six Brazilian states [81].
It is a company managed by Helen Yang headquarters based in China. SinoVac Biotech Ltd. has prepared a vaccine called "CoronaVac". Volunteers in Indonesia and Brazil carried out the first phase of the studies. CanSino Biologics Inc. announced that it achieved a satisfactory immune response against the COVID-19 virus in a phase 2 trial on 508 volunteers [82]. The vaccine is manufactured by Sinovac Life Sciences (Beijing, China) and contains 3 μg / 0.5 mL inactivated SARS-CoV-2 virus and aluminum hydroxide as an adjuvant [83].

Sinovac is currently the main covid-19 vaccine in many low- and middle-income countries. The first trials of Sinovac in China have only been reported in Indonesia on adults under 60 years of age [84]. [82]. Sinovac/CoronaVac has fully inactivated virus vaccines as an adjuvant. [85].
Conducted Phase III, randomized, multicenter, endpoint-guided, double-blind, placebo-controlled clinical trials to evaluate the efficacy and safety of the adsorbed COVID-19 vaccine (inactivated) produced by Sinovac [83].

They published a publication for business officials for Phase III research. Sinovac: "This is a phase III clinical trial involving healthcare professionals to evaluate the efficacy and safety of Sinovac's Adsorbed COVID-19 (inactivated) vaccine. It will be a placebo-controlled, double-blind study in which participants will be randomly assigned to either arm (placebo or vaccine). In the vaccination method, two doses of intramuscular doses (deltoid) are used at 14-day intervals. After the second week after vaccination, the study will evaluate cases of COVID-19 reported as symptomatic SARS-CoV-2 infections. Adults (18-59 years old) and Elderly (18-59 years old) are divided into two age classes for protection and immunogenicity (60 years and over). The safety database aims to identify adverse reactions with a frequency of 1: 1000 or more in adults and 1: 500 in the elderly. Two groups were evaluated for 12 months. (Clinical experience background: NCT04456595 Change History for the Study), Actual Register ICMJE (Submitted on February 10, 2021)"[83].

4.5. Pfizer/Biontech

Pfizer and BioNTech announced on November 9 that Covid-19 vaccine candidates are closer to being accepted. After seven days of testing on 43,500 people in phase III phase clinical trials, it was found to be met with a 90 percent efficacy rate. It has been reported that the vaccine is free from safety concerns [86]. Pfizer-BioNTech COVID-19 vaccine contains the following components: *"mRNA, lipids ((4-hydroxybutyl) azanediyl) bis (hexane-6,1-diyl) bis (2-hexyldecanoate), 2 [(polyethylene glycol) -2000] -N N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine and cholesterol), potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate and sucrose"* [87, 88]. During the delivery, packaging, and storage of the vaccine, the cold chain should be noted. Pfizer vaccine must be stored at 70 °C [89]. On December 10, an independent advisory panel of the US Food and Drug Administration (FDA) recommended the Pfizer BioNTech covid-19 vaccine for emergency use. Following this consent, work on implementation will continue in all 50 states. It is expected that full FDA approval will be issued in a limited period [90]. This permission: On December 11, 2020, the FDA will take place by the use of the Pfizer-BioNTech COVID Pathogens in live attenuated vaccines have been selected to be less virulent. They cannot reproduce the true disease or soberly mimic the disease in its altered state. -19 vaccine to prevent COVID-19, administered in 2 doses 21 days apart. Likewise, the European Medicines Agency (EUA) has issued an emergency use permit. The first dose of Pfizer-BioNTech

COVID-19 vaccine was administered, which was reported on December 12, 2020, in the United States. In the United States of America; 4.393 (0.2%) adverse events were reported after the Pfizer BioNTech COVID-19 vaccine was received (Usually anaphylaxis and severe allergic reactions - to the Vaccine Adverse Event Reporting System (VAERS)) (as of January 3, 2021) [91].

Based on the Pfizer-BioNTech COVID-19 vaccine clinical trials (Phase II/III); A large randomized, double-blind, placebo-controlled trial was conducted involving more than 43,000 people (median age = 52, range = 16). The vaccine was stated to be 95.0% effective in preventing the disease [87].

In the sample, there were reportedly 170 confirmed cases of covid-19, of which 162 were in the placebo category. Phase III trial commencement started on 27 July with the participation of 43,661 people. In the United States, 45 percent of the participants were between the ages of 56 and 85. Pfizer claims the potential is the same regardless of age or gender. In people over 65 years of age, racial, racial, and ethnic demographic characteristics are 94 percent effective [92].

4.6. Moderna/ MRNA-1273

Messenger RNA (mRNA) is a very unstable molecule that cells employ to make proteins. In a laboratory, mRNA may be generated, and when injected into cells, it can induce protein fragments to be produced. When these little protein fragments (peptides) exit the cell, the body might mount an immunological response against them. Using this approach to vaccinate people against COVID-19 infection in Moderna, USA [93]. The MRNA-1273 vaccine is based on mRNA encapsulated in lipid nanoparticles encoding the prefusion-stabilized full-length spike protein of SARS-CoV-2, the virus that causes Covid-19. It has been stated that there are no known safety risks other than intermittent local and systemic reactions [94] The European Emergency Use Authorization (EUA) for a lipid nanoparticle encapsulated Moderna COVID-19 (mRNA-1273) vaccine was released by the Food and Drug Administration (FDA) on December 18, 2020. (ModernaTX, Inc; Cambridge, Massachusetts) [95]Moderna COVID-19 vaccine, efficacy: 94.1%; 95% CI: 89.3%, 96.8% reported. Vaccine composition; Based on the SARS-CoV-2 spike glycoprotein (S) antigen encoded by RNA; Formulated in lipid nanoparticles (LNP). According to the company's statement; *"Dosing regimen Intramuscular 2 series of doses 28 days apart; It has been explained that individuals aged 18 years and older should be given 100 µg each caused by SARS-CoV-2"* [96]. Moderna needs to be kept at −20 ° C [89]. On December 8, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Permit (EUA) for the Moderna COVID-19 vaccine, administered in 2 doses 1 month apart to prevent COVID-19. The Vaccination Practices Advisory Committee (ACIP) issued another provisional recommendation for the use of the Moderna COVID-19 vaccine on December 19, 2020 [97].

4.7. AstraZenica/ ChAdOx1 nCoV-19/ University of Oxford

This vaccine has been obtained in collaboration with UK research centers and AstraZeneca. Older individuals seem to tolerate the disease better than younger individuals. It has also been reported to have similar immunogenicity in all age groups [98].

4.8. Sputnik V/ Gam-COVID-Vac

Gamaleya National Center for Epidemiology and Microbiology in Moscow, Russia reported from the beginning of the pandemic that it was working on a prototype of Sputnik V funded directly by the country's sovereign wealth fund (RDIF) [99]. The Sputnik V vaccine of Russia was developed and registered by the Gamaleya National Center for Epidemiology and Microbiology. The vaccine is

currently not widely used, although phase III clinical trials have not been completed. Latin America (Mexico and Brazil), Russia, and several Gulf countries (Saudi Arabia and UAE) hosted phase III trials with 2,000 volunteers [86]. Sixty-two (1-3%) of the 4902 participants in the placebo group and 16 (01%) of the 14,964 participants in the vaccination group chose to accept the second dose of vaccine 21 days after the first dose. According to the graph of the event rate in the two groups that resolved over time, the immunity required to avoid disease was achieved within 18 days after the first injection. This security applies to individuals of all ages, including those over the age of 60. Those affected but vaccinated show that the severity of the disease decreases as immunity improves. Three deaths in the vaccination community resulted in patients with common comorbidities and were considered unrelated to the vaccine. A negative result was not found regarding the side effect of the vaccine. Based on the number of confirmed COVID-19 cases, it was confirmed that the vaccine efficacy was 91 percent 21 days after the first injection, with a predicted reduction in disease incidence. It has been stated that the vaccination after one dose is very useful in terms of maintenance [100, 101].

4.9. Vaccine Treatment Results

The results of different vaccine studies conducted in 2021 as a result of clinical examinations are as in Table 1. According to the findings, some vaccines give a cure result of about 100%, while the lowest rate is 83%.

Table 1. Recovery vaccine results against COVID-19 in 2021 [102].

Vaccine name	Doses	Who get vaccine	Protection from COVID-19 (at home)
Moderna	2	~15000	97%
Pfizer / Biontech	2	~18600	100%
Sinovac/ Coronavac	2	~12500	83%
Astrazenaca	2	~8588	100%
Johnson&Johnson	1	~22000	85.4%
Sputnic V	2	~14964	100%
Novavax	2	~8833	100%

5. CONCLUSION

In this review article, detailed information about the drugs and vaccine applications used in the treatment process from the onset of COVID-19 disease is given. Clinical reports from treatment methods are discussed. Drug treatments are generally applications in the form of antimicrobial drugs and supportive drugs. Drugs used in drug treatments are generally as follows: Emdesivir, Favipiravir, Chloroquine, Hydroxychloroquine, Lopinavir / Ritonavir, Chloroquine / Hydroxychloroquine, and supporting agents. Some of these drugs are in clinical practice. DNA and RNA-based vaccines have been developed for patients with COVID-19 disease. The main ones of these vaccines are Sinovac, Biotech, Moderna, AstraZeneca, Sputnik V, etc. Although there are many vaccines, they include the most effective and those that have been authorized and implemented by the FDA and EUA. Vaccine studies continue in developed and developing countries. In this way, it is aimed to get away from the economic pressure on countries and psychological factors on people. COVID-19 drug and vaccine studies are also applied to the structure of the coronavirus family. Therefore, these treatment methods

will be applied against new coronavirus mutations in the future and will guide new drug and vaccine studies.

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