DOI: 10.18605/2175-7275/cereus.v12n3p228-243

ARTIGO DE REVISÃO

<<Recebido em:28/09/2020 Aceito em: 04/10/2020. >>

REVISTA CEREUS ISSN: 2175-7275

Coronavirus disease 2019 (COVID-19): updated evidence of comparative overview, diagnosis and treatments

Doença do coronavírus 2019 (COVID-19): evidência atualizada de visão geral comparativa, diagnóstico e tratamentos

Thyago José Arruda Pacheco[1], Franciéle de Matos da Silva[2], Danielle Galdino de Souza[3], Victor Carlos Mello da Silva[4], Raquel Santos Faria[5]

ABSTRACT

The increase in cases admitted under atypical pneumonia in Wuhan surprised local public health in December 2019. The cause of the clinical condition was associated with a new coronavirus. Despite efforts to control the situation of this etiologic agent, the virus spread throughout the world and the pandemic state was declared on March 11, 2020, by the World Health Organization (WHO). This study aims to provide a comprehensive and up-to-date overview of 2019 new coronavirus disease, presented a comparative overview of the new coronavirus with other viruses of the same family, diagnosis, and possible treatments and vaccines, as well as future expectations for controlling the spread of the virus. Elderly patients with comorbidities are the most affected by the disease. Rapid diagnosis, treatments, and adequate vaccines are needed to control the spread of the virus. Due to the lack of effective treatment or vaccines to date, WHO recommendations are the only way to address this global crisis.

Keywords: Coronavirus. Pneumonia. Pandemic.

RESUMO

O aumento de casos admitidos com pneumonia atípica em Wuhan surpreendeu a saúde pública local em dezembro de 2019. A causa do quadro clínico estava associada a um novo coronavírus. Apesar dos esforços para controlar a situação desse agente etiológico, o vírus se espalhou pelo mundo e o estado de pandemia foi declarado em 11 de março de 2020, pela Organização Mundial da Saúde (OMS). Este estudo tem como objetivo fornecer uma visão geral abrangente e atualizada da nova doença coronavírus 2019, apresentado uma visão comparativa do novo coronavírus com outros vírus da mesma família, diagnóstico e possíveis tratamentos e vacinas, bem como as expectativas futuras para o controle da propagação do vírus. Pacientes idosos com comorbidades são os mais afetados pela doença. Diagnóstico rápido, tratamentos e vacinas adequadas são necessários para controlar a disseminação do vírus. Devido à falta de tratamento ou vacinas eficazes até o momento, as recomendações da OMS são a única maneira de lidar com esta crise global.

Palavras-chave: Coronavírus. Pneumonia. Pandemia.

[1] Post-Graduation Program in Animal Biology, Institute of Biological Sciences, University of Brasília, 70910-900, Brasília, DF, Brazil.

E-mail: thyagojap@gmail.com

[2] Post-Graduation Program in Molecular Biology, Institute of Biological Sciences, University of Brasília, 70910-900, Brasília, DF, Brazil.

E-mail: francielematos75@gmail.com

[3] Post-Graduation Program in Nanoscience and Nanobiotechnology, Institute of Biological Sciences, University of Brasília, 70910-900, Brasília, DF, Brazil.

E-mail:

danielle.galdino@hotmail.com

[4] Post-Graduation Program in Animal Biology, Institute of Biological Sciences, University of Brasília, 70910-900, Brasília, DF, Brazil.

E-mail: victooormellooo@gmail.com

[5] Department of Genetics and Morphology, Institute of Biological Sciences, University of Brasília, 70910-900, Brasília, DF, Brazil.

E-mail: raquelfariarsf@gmail.com

1. INTRODUCTION

The first symptomatic report of the new coronavirus was diagnosed as a “new pneumonia” in Wuhan, Hubei province, China, early in December 2019 (LIAN et al., 2020). Wuhan is a city with a total population of 11 million people, and so the growing increase in severe respiratory infections has left the local hospital on alert (ZHENG, 2020). Almost a month later, after the first reported case, the World Health Organization (WHO) declared 27 cases related to this new Wuhan pneumonia. Until then, this disease had an unknown etiology, and most of them maintained a link with the Huanan Wholesale Seafood Market (SOHRABI et al., 2020).

On January 3, 2020, the virus strains were identified by samples of bronchoalveolar lavage, obtaining the first complete edition of the beta genome of the new coronavirus, initially named 2019-nCoV (TAN et al., 2020). On January 6, China sent a level 2 emergency response to the local Disease Control and Prevention Center (CDC), with the confirmation from the etiologic agent on January 7. Subsequently named coronavirus of severe acute respiratory syndrome 2 (SARS-CoV-2), it was only on January 10, 2020, that the genome was shared with the world (ZHENG, 2020).

The increase in confirmed cases and the first deaths in China were reported by 25 provinces, with 571 infected and 17 deaths on January 22, 2020, with records, three days later, of 1.975 cases and 56 deaths (ROTHAN; BYRAREDDY, 2020). The rulers were optimistic about being able to control the spread of the virus, however, the mass movement of people, due to the New Year holidays and vacation period, contributed to the spread of SARS-CoV-2 in the world (PARRY, 2020).

On January 30, 2020, WHO declared the spread of SARS-CoV-2 as a public health emergency of international interest (LEE, 2020). SARS-CoV-2 is the seventh coronavirus identified as causing human infection (LIAN et al., 2020). The disease triggered by SARS-CoV-2 was named, on February 11, 2020, Coronavirus Disease 2019 (COVID-19) by WHO (LAI et al., 2020). We know that COVID-19 has higher mortality among the elderly, especially those with comorbidities such as hypertension, diabetes, and renal failure (LIAN et al., 2020).

On March 11, 2020, WHO declared the new outbreak to be a global pandemic. At the press conference, the Director-General, Dr. Tedros Adhanom Ghebreyesus, expressed his concern, with a vision in line with the panorama of the last two weeks, in which there was a threefold increase in the number of cases, both in China and in other countries highlighting

the importance of stricter measures to control dissemination across countries (CUCINOTTA; VANELLI, 2020). Since then, many proposals for treatment and attempts to develop vaccines have been made. So, we provide here a comprehensive and a comparative overview of coronavirus, possible diagnostics, treatments and vaccines, as well as future expectations for controlling the spread of the virus.

2. METHODS

A literature review was carried out in studies published from February to September 2020 in PubMed, Scielo, and Google Scholar databases. According to the indexes of the various databases, search terms were used: “new coronavirus 2019”, “COVID-19”, “severe acute respiratory syndrome” without any language restrictions. Those who described a comparative overview of coronavirus, diagnosis, and treatments of COVID-19 were eligible.

3. RESULTS AND DISCUSSION

Comparative overview of coronavirus

In 2002-2003 there was an outbreak of SARS-CoV-1 coronavirus, killing 919 people. Ten years later (2012-currently), another coronavirus outbreak occurred, causing Middle East Respiratory Syndrome (MERS-CoV) with 858 victims. In September of 2020, there were more than a million deaths from SARS-CoV-2 infection. Therefore, in less than 20 years, it is the third outbreak of diseases caused by a coronavirus (https://coronavirus.jhu.edu/map.html) (YANG et al., 2020). Besides, coronaviruses have been regularly identified in mammals such as bats, camels, rats, dogs, and cats, with reports that in 2018, there was a fatal syndrome of acute diarrhea in pigs, caused by a coronavirus, named HKU1, having the bat origin (LU et al., 2020).

The virus of the Coronaviridae family is enveloped by a positive-chain ribonucleic acid (RNA) genome, containing four proteins: the spike (S) protein, envelope (E) protein, membrane (M) protein and nucleocapsid (N) protein (Figure 1) (MARTÍNEZ, 2020).

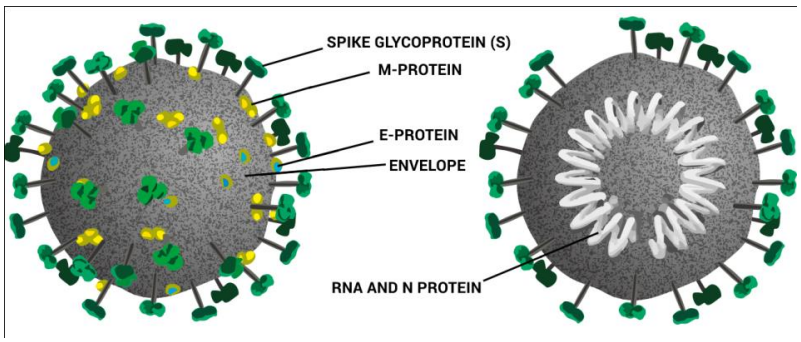

Figure 1. Schematic representation of the viral surface proteins. Spike (S), envelope (E), membrane (M) and Nucleocapsid (N) proteins.

The genomes of coronaviruses consist of single-stranded ribonucleic acid (RNA), ranging from 26 to 32 kilobases in length (ZHENG, 2020). They belong to the Coronaviridae family and form the subfamily Orthocoronavirinae, classified into four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus, in which alpha and beta infect only mammals, while gamma, and delta infect birds and rarely mammals (TAN et al., 2020).

Currently, there are seven species of coronavirus that cause disease in humans, with viruses 229E, OC43, NL63 and HKU1 causing mild cold symptoms (ZHENG, 2020). While the coronavirus SARS-CoV-1, MERS-CoV, SARS-CoV-2 are responsible for outbreaks of epidemic and pandemic, even though beta-coronavirus (HAMED, 2020), cause severe clinical conditions with pneumonia and lower respiratory symptoms such as cough and dyspnea, in addition to the feverish state (GUARNER, 2020). The current pandemic virus, SARS-CoV-2, is a member of the subgenus Sarbecovirus and has a 50% similarity with the structure of genes (genomic homology) of MERS-CoV, a member of the subgenus Merbecovirus, and a 79,6% similarity with SARS-CoV-1 (LAI et al., 2020; XU et al., 2020b; ZHOU et al., 2020). Also, recent studies have shown a genetic similarity of up to 96.2%, 93% and 92.4% between SARS-CoV-2 and coronaviruses found in bats in China (RaTG13), Malaysia (RmYN02) and pangolins (Guangdong pangolin CoV), respectively (LAM et al., 2020; PARASKEVIS et al., 2020).

Although SARS-Cov-2 shows similarities to SARS-CoV-1 that caused the coronavirus epidemic in 2002-2003, SARS-CoV-2 has a faster spread than the previous ones (ZHOU et al., 2020), and with a strong affinity for human respiratory receptors (XU et al., 2020b). Also, both SARS-CoV-1 and SARS-CoV-2 through their protein S, use the same angiotensin-converting enzyme 2 (ACE-2) receptor (PARASKEVIS et al. 2020). The study by Tang et al. (2020) showed that a single nucleotide polymorphism (SNP) in the coding region of the spike protein (S), which modified a serine by lysine, is responsible for making protein S bind more strongly to the ACE-2 receptor (ZHOU et al., 2020).

Close contact with infected people contributes to the spread of the virus from human to human, occurring transmission through coughing, sneezing, that is, respiratory droplets or aerosols, which reach the upper and lower airways (SHEREEN et al., 2020). It spreads at an accelerated rate, as the viral load in those affected remains infectious for two weeks after the cessation of symptoms and with a basic reproduction number of (R0) of 1.4–5.7,

indicating that each contaminated, 1-5 people are also infected by the virus (SINGAL et al., 2020). Although the mortality rate for SARS-COV-1, MERS-COV, and COVID-19 is around 10%, 40%, and 3%, respectively, SARS-CoV-2 has a transmission rate of 1.54 times higher than SARS-CoV-1 and 6.1 times higher than MERS-CoV (CHEN et al., 2020c; SINGAL et al., 2020).

Diagnosis

Approximately 80% of COVID-19 cases have mild symptoms, but the symptoms worsen in elderly people and with comorbidities, which manifest in chest pain, shortness of breath and loss of speech or movement, leading to a mortality rate increased by up to 14.8% in these patients (WU et al., 2020). The quick and accurate diagnosis of COVID-19 is extremely important, so that the patient has the proper care, thus facilitating the identification of people infected with SARS-CoV-2, and detecting symptomatic and asymptomatic carriers that need to be isolated to avoid contamination of more people by limiting the spread of the virus (PADOAN et al., 2020).

The two main types of tests used for infectious diseases are: molecular and serological. Serological tests (antibody detection) for the SARS-CoV-2 virus confirm whether people have been exposed to a specific pathogen by analyzing the body's immune response to a pathogen, other than the polymerase chain reaction (RT-PCR) and other rapid diagnostic tests that identify the presence of viral material, only in people who are currently infected (AMANAT, et al., 2020).

Laboratory tests are of great importance to measure the antibody response and determine seroconversion. Although serological tests are not suitable for detecting acute infections, they have several highly relevant applications. It allows the study of the immune response to SARS-CoV-2 qualitatively and quantitatively, thus being a complementary test in the diagnosis, allowing the identification of seroconversion, characterized by the COVID-19 course, thus being essential for epidemiological studies and vaccine trials (PADOAN et al., 2020; AMANAT, et al., 2020).

Molecular tests are used to diagnose and/or confirm, this is also used for surveillance purposes, and the purpose of this test is to detect the pathogen while circulating in the body. Therefore, the molecular test can detect even fragments of the virus, even if it is no longer able to replicate or cause disease (PADOAN et al., 2020). The technique known as polymerase reverse transcriptase chain reaction (RT-PCR) used to detect the presence of the SARS-CoV-2 virus, providing positive or negative results (qualitative results) and

information on the amount of virus circulating in the sample from a patient (quantitative results). However, there are characteristic limitations of RT-PCR diagnosis, these tests only detect the presence of the infectious agent, previously infected and recovered people are not diagnosed (CEVIK; BAMFORD; HO, 2020). Detection of the SARS-CoV-2 RNA genome through molecular testing is widely used to diagnose COVID-19 disease, as well as asymptomatic infections and transmission chains. Genome sequencing is important for researchers to design primers and probes for RT-PCR, and other nucleic acid tests (CEVIK; BAMFORD; HO, 2020).

Real-time PCR (RT-PCR) is considered the best tool for the diagnosis of COVID-19, as it is fast and accurate. Also, it was found that respiratory samples in the early stage of the disease were positive for the virus in RT-PCR, but negative in the serological test (CHU et al., 2020; PANG et al., 2020). Testing should be quick, and guided by a laboratory specialist, as the type and period of sample collected can play an important factor in the diagnosis (LI et al., 2020). There are seven rapid RT-PCR tests, however, only one is approved for clinical diagnosis, while the other six are only available for research (PANG et al., 2020). Other alternatives for diagnosis are antibody-based techniques, computed tomography of the chest, magnetic resonance imaging, or even a patient history related to symptoms characteristic of COVID-19 (TANG et at., 2020).

Treatments

Currently, there is no treatment for COVID-19. Some clinically approved drugs or other types of therapies are being tested to verify their effectiveness against SARS-CoV-2 (WANG et al., 2020c). chloroquine (CQ) and its less toxic derivative, hydroxychloroquine (HCQ), are considered prophylactic drugs against malaria , and treatments for autoimmune diseases (HU et al., 2020; SCHREZENMEIER et al., 2020). Previous studies have revealed that CQ has therapeutic activity against viruses, including the coronavirus SARS-COV-1 in vitro and in vivo (SAVARINO et al., 2003; KEYAERTS et al., 2009). CQ and its analog HCQ are weak bases, and therefore increase the intracellular pH of endosomes , and lysosomes, which can be crucial to block the entry , and replication of the virus (AL-BARI et al., 2017).

As of April 30, there were 687 clinical tests in the process to treat COVID-19 with several drugs, 21.3% of which were tested with HCQ or CQ (PACHECO et al., 2020). Five months later, on September 30, these drugs still accounted for 14.6% of all 2342 clinical trials in progress (https://www.covid-trials.org/). Some studies with HCQ, and CQ have

shown effectiveness in the treatment of COVID-19, however, others have shown no benefit or have even been harmful (GAUTRET et al., 2020; GELERIS et al., 2020; ROSENBERG et al., 2020). Due to the lack of a greater benefit, some studies have already canceled ongoing clinical trials, including the WHO, and the United States National Institute of Health (NIH) (NIH, 2020; WHO-Solidarity, 2020).

Azithromycin (AZM) represents less than 4% of all clinical trials in progress, however, it has proved effective in some studies, including in association with HCQ (GAUTRET et al., 2020, PANI et al., 2020). However, it is important to note that some studies have found no benefit in using AZM together or alone to treat COVID-19 , and an increase in the QT interval has even been observed (MERCURO et al., 2020; ROSENBERG et al., 2020).

Ivermectin is a broad-spectrum antiparasitic drug but also known to have in vitro antiviral activity against the yellow fever virus, Zika virus, and even SARS-CoV-2 (HEIDARY; GHAREBAGHI, 2020). It inhibits the nuclear import of viral proteins due to the inhibition of importins. According to Heidary; Gharebaghi (2020) the dose of SARS-CoV-2 activity in cell culture is in a range more than ten times greater than the tolerated therapeutic blood level of ivermectin in humans (20 to 80 ng/ml). Therefore, although it has been highly effective in vitro against SARS-CoV-2, there is still no randomized clinical study proving its therapeutic efficiency in COVID-19. (CHOUDHARY; SHARMA, 2020; SHARUN et al., 2020).

Favipiravir is a targeted antiviral approved in Japan to act against the influenza virus. Arbidol (Umifenovir) is approved and used to treat influenza-associated pneumonia in Russia and China (PSHENICHNAYA et al., 2020). Because of their effects against an RNA (influenza) virus, both were considered as potential drugs to treat COVID-19. When patients with COVID-19 were treated using favipiravir or arbidol, 51.67% improved clinically versus 61.21%, respectively. However, the rate of clinical recovery did not differ significantly between groups, so it is not possible to say which would be better for treating COVID-19. However, it is important to note that favipiravir improved the symptoms of fever and cough more quickly, and its most frequently observed adverse effect was increased serum uric acid (CHEN et al., 2020a).

There have already been reports of the use of ribavirin in patients infected with SARS-CoV-1 and MERS-CoV and the addition of lopinavir/ritonavir to the ribavirin regimen has been associated with better clinical outcomes, reducing the mortality rate compared to

the isolated ribavirin regime. Besides, recent studies have shown symptom improvement in more than 70% of patients with COVID-19 (KHALILI et al., 2020).

Remdesivir is a drug that inhibits viral RNA polymerase and has been shown to have broad-spectrum activity, *in vitro*, against members of several virus families, including filovirus (Ebola) and coronavirus (SARS-CoV, MERS-CoV, SARS-CoV-2) (BEIGEL et al., 2020; MULANGU et al., 2020). Therefore, remdesivir had been identified as a promising therapeutic candidate for COVID-19 due to its ability to inhibit SARS-CoV-2 *in vitro* (WANG et al., 2020a). However, in a randomized double-blind clinical study, although remdesivir proved to be superior to placebo in reducing recovery time in adults hospitalized with COVID-19, the difference was not statistically significant (BEIGEL et al., 2020).

The combination of lopinavir-ritonavir is used in the treatment and prevention of HIV and has been shown to have activity in vitro and an animal model, against MERS-CoV. However, in a randomized clinical trial, treatment with lopinavir-ritonavir, despite showing a shorter clinical improvement in 1 day than that observed in the control group (without treatment with lopinavir-ritonavir) was not associated with significant improvement (CAO et al., 2020). Given that, the trials using lopinavir-ritonavir compared to standard care showed little or no reduction in the mortality of COVID-19 patients, and the clinical trials were discontinued by WHO.

For more than a century, convalescent plasma therapy has been applied to the prevention and treatment of many infectious diseases. This adaptive immunotherapy has already been used with satisfactory efficacy and safety, in infections with other coronaviruses such as SARS-CoV-1 or MERS-CoV and even with the virus of the latest pandemic, influenza H1N1 (HUNG et al., 2011; KO et al., 2018). A pilot study on convalescent plasma therapy showed a potential therapeutic effect and low risk in the treatment of COVID-19 in critically ill patients. Therefore, a dose of plasma with a high concentration of neutralizing antibodies can quickly reduce viral load and tend to improve clinical outcomes. It is still necessary to select the ideal dose and time point to confirm the clinical benefits of plasma therapy, so studies should be done with more patients (DUAN et al., 2020).

It is an immunosuppressive humanized recombinant monoclonal antibody with the capacity and high affinity to bind to the interleukin-6 receptor (IL-6), which is a multi-effective cytokine present in many important immune responses with anti-inflammatory

and pro-inflammatory effects. It is mainly used as a biological agent for the treatment of refractory rheumatoid arthritis. The principle of action in SARS-CoV-2 infection would be not to allow the binding of the IL-6 produced to its receptor and, thus, to prevent the cascade of pro-inflammatory cytokines associated with severe COVID-19 (ZHANG et al., 2020).

A clinical trial in China with a sample of 21 patients with COVID-19 in serious or critical condition, showed good results with the use of tocilizumab. It was confirmed that after a few days of treatment, the body temperature of patients with fever returned to normal and all other symptoms presented were significantly improved. The small sample clinical trial concludes that tocilizumab has good efficacy from a pharmacoeconomic point of view, suggesting its use in critically ill patients with COVID-19 with significantly elevated IL-6 (XU et al., 2020a; ZHANG et al., 2020).

There are several strategies and references for the prevention and treatment of COVID-19 with Traditional Chinese Medicine (TCM). There are dozens of clinical treatments for COVID-19 using TCM, however, it still needs to be adjusted and improved with the accumulation of clinical results. The combination of this type of treatment with the employee by the West can complement the advantages of the treatments (WANG et al., 2020b).

A Lancet study earlier this year had already assessed that the use of the corticosteroid dexamethasone was able to alter pulmonary and systemic inflammation and result in a decrease in the duration of mechanical ventilation and mortality in patients with the SARS (VILLAR et al., 2020). Subsequently, it was demonstrated that dexamethasone was also able to reduce the mortality of critically ill patients with COVID-19, becoming the first drug proven to be effective in decreasing deaths from complications of the new coronavirus. The Recovery Trial study involved 2.104 patients who received dexamethasone and at drug was able to reduce death by up to a third in hospitalized patients with severe respiratory complications from COVID-19. However, there was no benefit among patients who did not need oxygen (HORBY et al., 2020).

Vaccine

Several structural proteins are produced by the coronavirus, including envelope, membrane, nucleocapsid, and protein S. Each of these proteins can serve as an antigen to induce protective responses with neutralizing antibodies. In particular, coronavirus entry

into the host cell depends on protein S and host cell protease activation and is, therefore, an important target for immunization (DU et al., 2009; HOFFMANN et al., 2020).

There was little interest in producing the vaccine against the similar coronavirus that caused the 2002 epidemic; a strategy that could have been important against other emerging infections (DU et al., 2009). However, the same is not observed concerning COVID-19, as according to a WHO balance sheet of September 25, 189 vaccines are being developed, 149 in the preclinical stage, and 40 in the clinical stage. The 9 vaccines in the final stage are listed in Table 1 (WHO landscape, 2020).

The vaccine that arrived most quickly in the last evaluation phase was that of Oxford/AstraZeneca. Although Russia was the first to approve a vaccine against COVID-19, it has not yet completed results from phase 3 trial (BURKI, 2020).

Vaccine	Organization/Country	Technology	Phase/Register – Clinical Trial
AZD1222 (ChAdOx1 nCoV-19)	University of Oxford-AstraZeneca/ England and Sweden	Non-Replicating Viral Vector	**Phase I/II** PACTR202006922165132 2020-001072-15 **Phase II** 2020-001228-32 **Phase III** ISRCTN89951424 NCT04516746 NCT04540393
mRNA-1273	ModernaTX, Inc./ United States	RNA-based vaccine, lipid nanoparticles.	**Phase I** NCT04283461 **Phase II** NCT04405076 **Phase III** NCT04470427
CoronaVac	Sinovac Biotech Co., Butantan Institute/ China and Brazil	SARS-CoV-2 Inactivated Vaccine.	**Phase I/II** NCT04383574 NCT04352608 **Phase III** NCT04456595 669/UN6.KEP/EC/2020
Unnamed	Wuhan Institute of Biological Products/Sinopharm/ China	SARS-CoV-2 Inactivated Vaccine.	**Phase I/II** ChiCTR2000031809 **Phase III** ChiCTR2000034780
BBIBP-CorV	Beijing Institute of Biological Products/Sinopharm/ China	SARS-CoV-2 Inactivated Vaccine.	**Phase I/II** ChiCTR2000032459 **Phase III** ChiCTR2000034780 NCT04560881
BNT162 (a1, b1, b2, c2)	BioNTech/Fosun Pharma/Pfizer/ United States and Germany	RNA-based vaccine 3 LNP-mRNAs	**Phase I/II** 2020-001038-36 ChiCTR2000034825 NCT04537949 **Phase III** NCT04368728

Ad26COVS1	Janssen Pharmaceutical Companies/ United States and Belgium	Adenovirus serotype 26 vector-based vaccines	**Phase I/II** NCT04436276 **Phase III** NCT04505722
Ad5-nCoV	CanSino Biological Inc./Beijing Institute of Biotechnology/ China and Canada	Non-Replicating Viral Vector Adenovirus Type 5 Vector	**Phase I** ChiCTR2000030906 **Phase II** ChiCTR2000031781 **Phase III** NCT04526990 NCT04540419
Sputnik V	Gamaleya Research Institute/ Russia	Non-Replicating Viral Vector Adeno-based (rAd26-S+rAd5-S)	**Phase I** NCT04436471 NCT04437875 **Phase III** NCT04530396 NCT04564716

Table 1. Candidate vaccines phase 3. Intramuscular administration (On September 25, 2020).

Challenges and perspective

SARS-CoV-2, similar to SARS-CoV-1, can remain on surfaces such as steel, cardboard, paper, dust and can further spread the disease (VAN DOREMALEN et al., 2020). New mutations in the coronavirus spike protein can also be a hindrance to curb the disease (KORBER et al., 2020). There is still no effective and available treatment for COVID-19, and more than 30 million people have already been infected globally, with over a million dead (Figure 2).

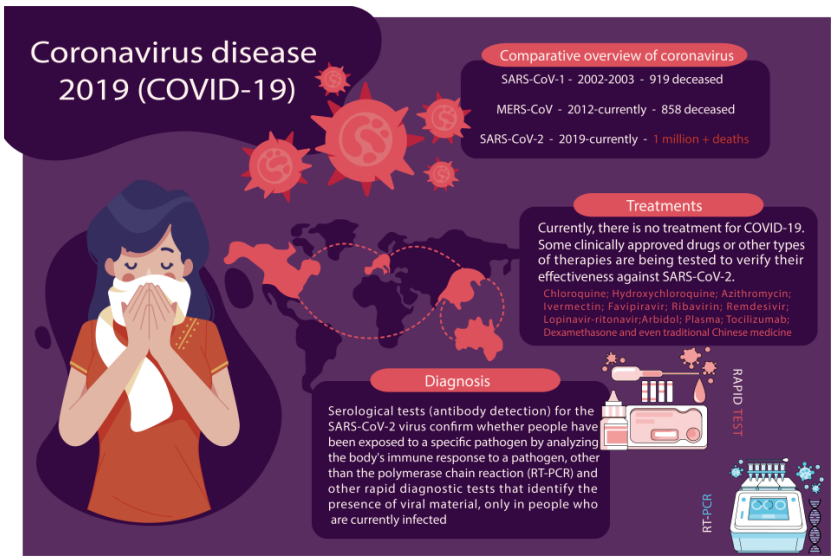

Figure 2. Infographic abstract.

An alternative is urgently needed to stop SARS-CoV-2. Although there are several therapeutic strategies, none can cure COVID-19. Although there are still no alternatives to stop permanently the virus, many discoveries have been made since the discovery of SARS-CoV-2. Recent studies even show that genetic factors may be related to a more

severe form of the disease, asymptomatic people may have their lungs affected, and people who have already been infected have their neutralizing antibodies lowered in about three months (ELLINGHAUS et al., 2020; LONG et al., 2020).

While there is still the search for a vaccine or efficient treatment, precautionary measures are necessary, such as testing the population and isolating infected or suspected individuals, since observing collective infection control measures can reduce the frequency of infection in the population (RAOULT et al., 2020).

4. CONCLUSION

The COVID-19 pandemic has already killed more than a million people and there is still no vaccine or efficient treatment. It is urgent to better understand the virus and propose alternative therapies in the face of this pandemic. So far, of all the drugs tested, the only dexamethasone was statistically significant in decreasing deaths in a large randomized clinical trial. There are several vaccines under development, the most advanced is from the University of Oxford/AstraZeneca and the results of phase 3 of the study will be released soon.

REFERÊNCIAS

AL-BARI, M.A.A. Targeting endosomal acidification by chloroquine analogs as a promising strategy for the treatment of emerging viral diseases. **Pharmacology Research and Perspectives**, v. 5, n. 1, p. 1–13, 2017.

AMANAT, F. et al. A serological assay to detect SARS-CoV-2 seroconversion in humans. **Nature Medicine**, v. 26, n. 7, p. 1033–1036, 2020.

BEIGEL, J. H. et al. Remdesivir for the Treatment of Covid-19 — Preliminary Report. **New England Journal of Medicine**, p. 1–12, 2020.

BURKI, T. K. The Russian vaccine for COVID-19. The Lancet Respiratory Medicine, v. 6736, n. 20, p. 19–20, 2020.

CAO, B. et al. A trial of lopinavir-ritonavir in adults hospitalized with severe covid-19. **New England Journal of Medicine**, v. 382, n. 19, p. 1787–1799, 2020.

CEVIK, M.; BAMFORD, C. G. G.; HO, A. COVID-19 pandemic - a focused review for clinicians. **Clinical Microbiology and Infectious**, v. 26, n. 1198– 743X, p. 842–847, 2020.

CUCINOTTA, D.; VANELLI, M. WHO declares COVID-19 a pandemic. **Acta Biomedica**, v. 91, n. 1, p. 157–160, 2020.

CHEN, C. et al. Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial. 2020a.

CHEN, Z. et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. v. 7, 2020b.

CHEN, J. **Pathogenicity and transmissibility of 2019-nCoV—A quick overview and comparison with other emerging virusesMicrobes and Infection**, 2020c.

CHOUDHARY, R.; SHARMA, A. K. Potential use of hydroxychloroquine, ivermectin and azithromycin drugs in fighting COVID-19: trends, scope and relevance. **New Microbes and New Infections**, v. 35, p. 100684, 2020. Disponível em: <https://doi.org/10.1016/j.nmni.2020.100684>.

CHU, D. K. W. et al. Molecular Diagnosis of a Novel Coronavirus (2019-nCoV) Causing an Outbreak of Pneumonia. **Clinical chemistry**, v. 7, p. 1–7, 2020.

DASHRAATH, P. et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. **American Journal of Obstetrics and Gynecology**, v. 222, n. 6, p. 521–531, 2020.

DU, L. et al. The spike protein of SARS-CoV - A target for vaccine and therapeutic development. **Nature Reviews Microbiology**, v. 7, n. 3, p. 226–236, 2009.

DUAN, K. et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. **Proceedings of the National Academy of Sciences of the United States of America**, v. 117, n. 17, p. 9490–9496, 2020.

ELLINGHAUS, D. et al. Genomewide Association Study of Severe Covid-19 with Respiratory Failure. **The New England journal of medicine**, 2020.

GAUTRET, P. et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. **International Journal of Antimicrobial Agents**, v. 56, n. 1, 2020, 105949.

GELERIS, J. et al. Observational study of hydroxychloroquine in hospitalized patients with COVID-19. **New England Journal of Medicine**, v. 382, n. 25, p. 2411–2418, 2020.

GUARNER, J. Three Emerging Coronaviruses in Two Decades: The Story of SARS, MERS, and Now COVID-19. **American Journal of Clinical Pathology**, v. 153, n. 4, p. 420–421, 2020.

HAMED, M. A. An overview on COVID-19: reality and expectation. **Bulletin of the National Research Centre**, v. 44, n. 1, 2020.

HEIDARY, F.; GHAREBAGHI, R. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. **Journal of Antibiotics**, v. 73, n. 9, p. 593–602, 2020.

HOFFMANN, M. et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. **Cell**, v. 181, n. 2, p. 271- 280.e8, 2020.

HORBY. Dexamethasone in Hospitalized Patients with Covid-19-Preliminary Report. **New England Journal of Medicine**, 2020.

HU, T.Y.; FRIEMAN, M.; WOLFRAM, J. Insights from nanomedicine into chloroquine efficacy against COVID-19. **Nature Nanotechnology**, v. 15, n. 4, p. 247–249, 2020.

HUNG, I.F.N. et al. Convalescent plasma treatment reduced mortality in patients with severe pandemic influenza A (H1N1) 2009 virus infection. **Clinical Infectious Diseases**, v. 52, n. 4, p. 447–456, 2011.

KEYAERTS, E. et al. Antiviral activity of chloroquine against human coronavirus OC43 infection in newborn mice. **Antimicrobial Agents and Chemotherapy**, v. 53, n. 8, p. 3416–3421, 2009.

KORBER, B. et al. Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus. **Cell**, v. 182, n. 4, p. 812- 827.e19, 2020.

KO, J.H. et al. Challenges of convalescent plasma infusion therapy in Middle East respiratory coronavirus infection: A single centre experience. **Antiviral Therapy**, v. 23, n. 7, p. 617–622, 2018.

KHALILI, J.S. et al. Novel coronavirus treatment with ribavirin: Groundwork for an evaluation concerning COVID-19. **Journal of Medical Virology**, v. 92, n. 7, p. 740–746, 2020.

LAI, C. et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. **International Journal of Antimicrobial Agents journal**, v. 55, n. 105924, 2020.

LAM, T.T.-Y. et al. Identification of 2019-nCoV related coronaviruses in Malayan pangolins in southern China. **bioRxiv**, p. 2020.02.13.945485, 2020.

LEE, A. Wuhan novel coronavirus (COVID-19): why global control is challenging? **Public Health**, v. 179, p. A1–A2, 2020.

LI, Q. et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. **New England Journal of Medicine**, v. 382, n. 13, p. 1199–1207, 2020.

LIM, L.M. et al. Special Report and pregnancy. The American Journal of Obstetrics & Gynecology, v. 222, n. 6, p. 521–531, 2020.

LIAN, J. et al. Analysis of Epidemiological and Clinical Features in Older Patients With Coronavirus Disease 2019 (COVID-19) Outside Wuhan. **Clinical infectious diseases : an official publication of the Infectious Diseases Society of America**, v. 71, n. 15, p. 740–747, 2020.

LONG, Q. X. et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. **Nature Medicine,** v. 26, n. 8, p. 1200–1204, 2020.

LU, R. et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. **The Lancet**, v. 395, n. 10224, p. 565–574, 2020.

MARTÍNEZ, A. Cloroquine and Hydroxychloroquine: the Yin-yang of these Drugs from a Theoretical Study. **Journal of the Mexican Chemical Society,** v. 64, n. 3, p. 230–237, 2020.

MERCURO, N. J. et al. Risk of QT Interval Prolongation Associated with Use of Hydroxychloroquine with or without Concomitant Azithromycin among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19). **JAMA Cardiology**, 2020.

MULANGU, S. et al. A randomized, controlled trial of Ebola virus disease therapeutics. **New England Journal of Medicine**, v. 381, n. 24, p. 2293–2303, 2019.

NIH halts clinical trial of hydroxychloroquine | National Institutes of Health (NIH). Disponível em: <https://www.nih.gov/news-events/news-releases/nih-halts-clinical-trial-hydroxychloroquine>. Acesso em: 21 jun. 2020.

PACHECO, T. J. A. et al. Panorama mundial de estudos com a hidroxicloroquina para o tratamento da Global perspective of studies with hydroxychloroquine for the treatment of. **Journal of Health & Biological Sciences**, v. 8, n. 1, p. 1–4, 2020.

PADOAN, A. et al. IgA-Ab response to spike glycoprotein of SARS-CoV-2 in patients with COVID-19: A longitudinal study. **Clinica Chimica Acta journal**, v. 507, n. 164–166, 2020.

PANG, J. et al. Potential Rapid Diagnostics, Vaccine and Therapeutics for 2019 Novel Coronavirus (2019-nCoV): A Systematic Review. **Journal of Clinical Medicine**, v. 9, n. 3, p. 623, 2020.

PANI, A. et al. Macrolides and viral infections: focus on azithromycin in COVID-19 pathology. **International Journal of Antimicrobial Agents**, v. 56, n. 2, p. 106053, 2020. Disponível em: <https://doi.org/10.1016/j.ijantimicag.2020.106053>.

PARASKEVIS, D. et al. Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. **Elsevier**, v. 79, n. 104212, 2020.

PARRY, J. China coronavirus: cases surge as official admits human to human transmission. **BMJ (Clinical research ed.)**, v. 368, n. January, p. m236, 2020.

PSHENICHNAYA, N. Y. et al. Clinical efficacy of umifenovir in influenza and ARVI (study ARBITR). **Therapeutic archive**, v. 91, n. 3, p. 56–63, 2019.

RAOULT, D. et al. Coronavirus infections: Epidemiological, clinical and immunological features and hypotheses. **Cell Stress**, v. 4, n. 4, p. 66–75, 2020.

ROSENBERG, E. S. et al. Association of Treatment with Hydroxychloroquine or Azithromycin with In-Hospital Mortality in Patients with COVID-19 in New York State. **JAMA - Journal of the American Medical Association**, v. 323, n. 24, p. 2493–2502, 2020.

ROTHAN, H. A.; BYRAREDDY, S. N. The epidemeology and pathogensis of coronavirus (Covid-19) outbreak. **Journal of Autoimmunity**, v. 109, n. January, p. 1–4, 2020.

SAVARINO, A. et al. Effects of chloroquine on viral infections: An old drug against today's diseases? **Lancet Infectious Diseases**, v. 3, n. 11, p. 722–727, 2003.

SCHREZENMEIER, E.; DÖRNER, T. **Mechanisms of action of hydroxychloroquine and chloroquine: implications for rheumatologyNature Reviews Rheumatology**, 2020.

SHARUN, K. et al. Ivermectin, a new candidate therapeutic against SARS-CoV-2/COVID-19. **Annals of Clinical Microbiology and Antimicrobials**, v. 19, n. 1, p. 1–5, 2020.

SHEREEN, M. A. et al. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. **Journal of Advanced Research**, v. 24, p. 91–98, 2020.

SINGAL, C. M. S.; JAISWAL, P.; SETH, P. SARS-CoV-2, More than a Respiratory Virus: Its Potential Role in Neuropathogenesis. **ACS Chemical Neuroscience**, v. 11, n. 13, p. 1887–1899, 2020.

SOHRABI, C. et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). **International Journal of Surgery**, v. 76, n. February, p. 71–76, 2020.

TAN, W. et al. **A Novel Coronavirus Genome Identified in a Cluster of Pneumonia Cases — Wuhan, China 2019−2020China CDC Weekly, 2020.**

TANG, X. et al. On the origin and continuing evolution of SARS-CoV-2. **National Science Review**, p. 1–24, 2020.

VAN DOREMALEN, Neeltje et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. **New England Journal of Medicine**, 2020.

VILLAR, J. et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. **The Lancet Respiratory Medicine**, v. 8, n. 3, p. 267–276, 2020.

WANG, M. et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. **Cell Research**, v. 30, n. 3, p. 269–271, 2020a.

WANG, S. et al. Diagnosis and treatment of novel coronavirus pneumonia based on the theory of traditional Chinese medicine. **Journal of Integrative Medicine**, v. 18, n. 4, p. 275–283, 2020b.

WANG, Y. et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. **The Lancet**, v. 395, n. 10236, p. 1569–1578, 2020c.

WU, Z.; MCGOOGAN, J.M. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases from the Chinese Center for Disease Control and Prevention. **JAMA**, v. 323, n. 13, p. 1239–1242, 2020.

WHO. Draft of the landscape of COVID-19 candidate vaccines. **World Health Organization**, n. April, p. 4, 2020. Disponível em: <https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf?ua=1>.

WHO. **Solidarity clinical trial for COVID-19 treatments**. Disponível em: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments>. Acesso em: 21 jun. 2020.

XU, X. et al. Effective treatment of severe COVID-19 patients with tocilizumab. **Proceedings of the National Academy of Sciences of the United States of America**, v. 117, n. 20, p. 10970–10975, 2020a.

XU, X.W. et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: Retrospective case series. **The BMJ**, v. 368, n. January, p. 1–7, 2020b.

YANG, Y. et al. The Deadly Coronaviruses: The 2003 SARS Pandemic and The 2020 Novel Coronavirus Epidemic in China, The Company's Public News and Information. **Journal of Autoimmunity**, v. 109, n. January.

ZHANG, Y. et al. Current targeted therapeutics against COVID-19: Based on first-line experience in China. **Pharmacological Research**, v. 157, 2020.

ZHENG, J. SARS-coV-2: An emerging coronavirus that causes a global threat. **International Journal of Biological Sciences**, v. 16, n. 10, p. 1678–1685, 2020.

ZHOU, H. et al. A Novel Bat Coronavirus Closely Related to SARS-CoV-2 Contains Natural Insertions at the S1/S2 Cleavage Site of the Spike Protein. **Current Biology**, v. 30, n. 11, p. 2196- 2203.e3, 2020.