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Efficacy of Different Vaccines in Preventing Covid-19: Retrospective Cross-Sectional Study

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Abstract

With the serious advent of the COVID-19 pandemic and the lack of an effective antiviral therapy, the development of vaccines has become the arsenal of first choice, however the urgency of developing these on an emergency basis has raised questions about their effectiveness. The present study aimed to evaluate the possibility of the occurrence of positive serological tests for IgG against S and N proteins, in individuals who have completed at least one month after the third dose of the vaccination schedule available in Brazil, involving four different brands of vaccines, and as well as to verify the real protection capacity against COVID-19 infection. It was possible to observe an absence of patients who tested positive after undergoing immunization with the vaccine regimens involving at least one of the three doses with Janssen vaccine, allowing inferring that this immunogen possibly induces an highly efficient immune response. Through the results obtained, it was also possible to observe that all vaccine protocols that were applied to the research participants proved to be efficient and satisfactory, because, although some patients were infected, there was production of anti-IgG-S antibodies by all of them and all vaccine protocols were 100% effective in protecting research participants from hospitalizations and deaths.

Keywords: COVID-19; Vaccination; Efficacy; Humoral Immunity; IgG Antibodies

Introduction

Since the beginning of the COVID-19 pandemic, many efforts and strategies have been used to stop the advance of this disorder to global public health. The high severity of this process has impacted not only on high mortality and morbidity, but also with an extrapolation of the capacity of world health systems to accommodate thousands of infected people and provide assistance to extreme cases that require treatment in the Intensive Care Unit (ICU) [1,2]. It is known that there is no exclusivity of predisposition to acquire such a viral infection, although several studies indicate that patients with higher risk are those affected by some comorbidities and co-infections, which can increase the possibility of worsening the disease in people infected with this virus [3,4]. On the other hand, immunization through the vaccines available today can prevent the patient from progressing to severe symptoms, hospitalization and even death after being infected [5].

In this sense, statistical data prove after observational studies carried out with data from 90 countries that, by increasing the population's vaccination coverage by 10%, mortality reduces 7.6%. In addition, it is possible to observe that the hospitalized rate is higher in unvaccinated people [6,7]. Although developed and produced in record time, we currently have four manufacturers of the immunizer against the coronavirus authorized in Brazil - Pfizer, AstraZeneca in partnership with Oxford University, Johnson & Johnson, Sinovac together with the Butantan Institute, which make vaccines available to known populations such as: BNT162b2 (Pfizer), ChAdOx1-S [recombinant] COVID-19 (AstraZeneca), Ad26.COV2.S (Janssen), inactivated SARS-CoV-2 virus (Coronavac). Much is questioned about the possible side

effects arising from this rapid process of vaccine production, however, bodies of great importance such as the World Health Organization (WHO) attest to the reliability and safety of immunizers, in addition to the release of competent bodies such as the National Surveillance Agency Health (ANVISA) [8,9].

The technology used to stimulate the production of antibodies by the immune system differ among manufacturers. Coronavac uses the most traditional technology, which consists of inoculating the inactivated virus (SARS-CoV-2 strains) into the body in order to induce the immune response, among them the production of IgG antibodies. AstraZeneca and Janssen vaccines opted for viral vector technology, where a common virus is genetically modified, infecting the cells of the human body, but failing to replicate. Thus, the genetic content of the simian virus is removed and replaced by the genetic material of the coronavirus. This vaccine induces a robust immune response, including a cellular response after the application of two doses [1]. The immunizer from pharmaceutical Pfizer in partnership with the BioNTech laboratory is based on messenger RNA technology, or mRNA. The synthetic messenger RNA molecule gives the organism instructions for the production of virus surface proteins [10].

The main viral glycoprotein used by some of these vaccines, in order to induce the organism to produce an immune response, is known as Spike glycoprotein (S), which, under normal conditions of infection by the pathogenic agent, makes it possible for the virus to enter the host cell effectively. However, there are also those that focused on the Nucleocapsid (N) protein from the viral capsule to stimulate the production of antibodies in the body [11]. Once the viral protein is identified by the human immune system, the humoral response (among others) is activated and proteins of the IgG class are produced, thus promoting the neutralization of the pathological agent or making the organism capable of activating other defenses against the virus, thus preventing the infected individual from manifesting the disease or progressing from mild symptoms to severe symptoms [12]. Currently, the application of more than one dose of the immunizing agent is necessary to confer the possibility of immunity against the coronavirus through the stimulation of the cellular response and humoral response of the organism. Thus, a large part of the scientific community believes that a solution to control this pandemic is to encourage the immunization of the population through vaccines against COVID-19 [13].

Given the importance of developing immunity against the coronavirus and the role of Immunoglobulin G against viral protein S and N protein, it is essential to understand whether the immunity conferred by the vaccine that is now available to the population is lasting or transient, in a way that to contribute with preventive actions and protocols and thus avoid further contagion and spread of the disease, especially among the population at risk (people with different comorbidities). Therefore, it is important to carry out a serological test to investigate the positivity of the IgG antibody, in order to establish the effectiveness of vaccines in immunized individuals and thus contribute to the elaboration of preventive protocols that help to combat the spread and development of the virus.

Based on the above, the objective of this research was to verify the possibility of the occurrence of positive serological tests for IgG against S and N proteins, in individuals who have completed at least one month after the third dose of the vaccination schedule, involving four types of vaccine, named: Janssen, Coronavac, AstraZeneca and Pfizer vaccines, as established as a protocol by the Ministry of Health in Brazil and as well as to verify the real protection capacity against COVID-19 infection.

Methodology

The present research was carried out in a private clinical analysis laboratory in the municipality of Pindamonhangaba-SP, Brazil. This is a retrospective study, in which information from the results of serological tests of vaccinated individuals regarding the levels of IgG antibodies produced after immunization were used, tests that were performed using an immunochromatographic technique (rapid test). The individuals whose test results composed the present study enjoyed an adequate health status, without manifestation of signs or symptoms of COVID-19 during the course of the research, since it is a retrospective study whose main focus was to evaluate the acquired immunity after receiving the third dose of vaccines against COVID-19, which could only have occurred if they had not been infected with the virus or showing signs of illness resulting from this process. They were aged between 18 and 77 years old, with an average of 46.1 years. All reports from 150 patients who received three doses of the different vaccines analyzed for COVID-19 and whose levels of IgG antibodies were identified using the aforementioned rapid test were included.

The study used the results of exams carried out from February to April 2022. The data were analyzed in epidemiological terms, correlating the data regarding the number of participants with the post-vaccination results. The effectiveness of the vaccines evaluated, translated by the ability or not to protect against a future infection by COVID-19, was statistically evaluated using the chi-square test, at a significance level of 5%, and the Bioestat 5.0 software as a supporting tool. The present research was submitted to the ethics committee in research with human beings of the FUNVIC University Centre, via the Brazil platform, and was

approved for execution, under protocol number 5,376,827.

Results and Discussion

In the present work, we sought to consider the effectiveness of the immunization processes analyzed both through two considerations:

- Observation of the occurrence or not of viral infection after starting the different vaccine protocols;
- Analysis of the profile of antibodies produced after this same period.

Assessment of the Occurrence of Viral Infection after Vaccination

Regarding the possibility of occurrence or not of viral infection after the first dose of the different vaccine protocols, it was possible to classify the participants into 4 initial groups, corresponding to the scheme shown in Table 1.

1st Dose Vaccine Type	Total of Participants	Covid-19 After Vaccination
PFIZER	21	2 (9,52%)
ASTRA-ZENECA	66	0 (0%)
CORONAVAC	55	0 (0%)
JANSSEN	8	0 (0%)

Table 1: Distribution of research participants regarding the type of immunogen received in the first dose of the vaccine schedule and the occurrence of COVID-19 after this process.

Then, to verify the possibility of occurrence or not of viral infection after the second dose of the vaccination schedule, the 150 research participants were reclassified and analyzed for the occurrence or not of COVID-19 after this process. For this stage, all participants who received the same immunogen in both doses were selected, and these results are shown in Table 2.

1st Dose Vaccine Type	2nd Dose Vaccine Type	Total of Participants	Covid-19 After Vaccination*
PFIZER	PFIZER	20	2 (10%)
ASTRAZENECA	ASTRAZENECA	56	5 (8,93%)
CORONAVAC	CORONAVAC	52	3 (5,77%)
JANSSEN	JANSSEN	5	0 (0%)

* With no significant difference in the percentage of infected, in the different vaccine protocols.

Table 2: Distribution of research participants regarding the type of immunogen received, with no change of type in the first two doses of the vaccine schedule and the occurrence of COVID-19 after this process.

Finally, an evaluation was prepared based on the third dose received, seeking to show what was the vaccination pattern of the 7 remaining patients who, even after receiving the third dose, acquired COVID-19, allowing to observe that of these, 5 (71.43%), regardless of the vaccination schedule of the first 2 doses, received the third dose of the Pfizer vaccine, while 1 (14.28%) had received Coronavac as the third dose and the same amount (14.28%) had received AstraZeneca.

By carrying out a careful analysis of the results presented in tables 1, 2 and in the paragraph above, a ranking of "failure" in inducing protection of vaccines against COVID-19 was created, by compiling the patients who became infected, based on the last dose that was applied to the participants, before they were infected, allowing to expose a lower overall protective efficacy of the Pfizer vaccine, as shown in Table 3.

Vaccine Received	COVID-19 + After 1st Dose	COVID-19 + After 2nd Dose	COVID-19 + After 3rd Dose*
PFIZER	9,52%	10%	71,43%
CORONAVAC	0%	5,77%	14,28%
ASTRAZENECA	0%	8,93%	14,28%
JANSSEN	0%	0%	0%

*With no significant difference in the percentage of infected, in the different vaccine protocols.

Table 3: Sum of patients who tested positive for COVID-19 based on the last dose of vaccine received.

The trend of lower efficacy of the AstraZeneca and Pfizer vaccines may be related to the fact that, although the use of a viral vector or messenger RNA allows for the induction of high antibody titers, these are directed exclusively to the S protein, which has been target of most studies with vaccines that use these technologies, given their important role in the invasion process, but flaws or gaps in this process can culminate in possible oscillations of immunogenicity over time. The trend of lower effectiveness of the Pfizer vaccine proposed here corroborates the results of previous studies, including those from a prospective longitudinal study developed by Levin EG, et al. [14]. These authors followed 4686 participants who were immunized exclusively with the aforementioned immunotherapy and showed a large production of antibodies at the beginning of the post-vaccination period, but a substantial drop in the humoral response to protein S over the course of a few months, probably being a base factor for explain that, although vaccination coverage has increased in the country where the research was carried out, there was an increase in the number of incident cases, without, however, negatively influencing protection against hospitalization and death.

Another factor that may explain the possible lower efficacy of the Pfizer vaccine concerns the nature of its composition, which, as already mentioned, is messenger RNA. Such a molecule is capable of inducing host cells to produce the antigen of interest in large quantities, but it is liable to suffer instabilities that can lead to both a decrease in immunogenicity and unpredictable adverse reactions, thus implying the demand for technological investments aimed at to improve the stability and delivery of viral mRNA and thus ensure greater effectiveness of this vaccination method. With regard to AstraZeneca, a complementary factor that may explain the partial loss of efficacy concerns the possibility that some individuals may already have a previous memory immune response against the viral vectors used. According to Li M, et al. [15], although adenoviruses are not easily neutralized by pre-existing immunity, high titers of neutralizing antibodies have already been evidenced in significant portions of populations in Asia, reaching 80% in Kenya and these pre-existing antibodies Existing adenoviruses may reduce the immunogenicity of such vaccines.

However, it should be noted that, if only the borderline dose between immunization and infection is taken into account, the evidence presented in table 4 allows us to hypothesize that the vaccine from the Janssen laboratory, which also uses a viral vector that encodes the production of protein S, was the only one that induced greater protection for participants, since all patients who were at some point immunized with such an immunogen did not test positive for COVID-19. Such evidence may possibly be related to the type of viral vector used to compose this vaccine or to other genetic engineering tools that may have better targeted the delivery of viral genetic material to the host cell. As already mentioned, depending on the adenovirus used to carry the genetic information, some disadvantages may or may not occur, among which the possibility of pre-existing immunity to the vector, which can reduce vaccine efficacy, and, in another way, through tools of genetic engineering, viral vectors can be pseudotyped and genetically modified to maximize and direct the delivery of genetic material preferentially to specific cells, such as antigen-presenting cells, which would provide greater effectiveness in generating a more efficient immune response and lasting [16].

Another important factor that may explain the results presented in the present work is related to several scientific evidence, according to which SARS-Cov-2 does not only use protein S as a way of interacting with the host's cells to achieve the infection, and such vaccines may not prevent the virus from using other strategies to circumvent the initial blockade of the S protein [15,17]. In fact, protein S is one of the structural proteins of the virus and is of great importance in protecting the inner RNA and forming the outer particles of SARS-Cov-2, being a transmembrane glycoprotein that literally forms "nails" on the surface of the virus. , some of which extend to and bind to angiotensin-converting enzyme 2 (ACE-2), allowing invasion of the host cell.

However, there are other viral proteins that exert important interactions that are fundamental for the success of viral invasion, such as the N protein and the M protein. According to Peng XL, et al. [18], the N protein is the only protein that forms the nucleocapsid, which has as its main function to maintain the stability of the RNA within the viral particle, being very immunogenic and also considered essential for the invasion of SARS-Cov-2. Otherwise, Zambalde EP, et al. [17], demonstrated that the M protein, which is the most abundant structural protein of SARS-Cov-2, can interact with the N and S proteins, in order to maximize their functions during the invasion process, and interacts with the nuclear antigen. Proliferation in human cells, resulting in a manipulation of cellular metabolism that favors viral replication.

Therefore, the considerable effectiveness of Coronavac, which within the sample spectrum of the present study, behaved more promisingly than two of the other three vaccines evaluated (AstraZeneca and Pfizer) may be related to the fact that of the 4 vaccines, only this one has in its composition the whole and inactivated virus, and, thus, its effectiveness can be visualized, in immunological terms, through the induction of antibodies potentially capable of recognizing and inactivating other antigenic targets, in addition to the S protein, such as the N proteins, E and M [15,17].

Analysis of the Profile of Antibodies Produced After Starting the Different Vaccination Protocols

In order to comparatively evaluate the effectiveness of antibody production of Coronavac (inactivated virus) and other vaccines (viral vector and mRNA), the results were computed only for patients who received the three doses of Coronavac (Coronavac group), which totaled 14 participants (9.33% of a total of 150 participants) of which 13 (92.85%) produced anti-S IgG and 11 (78.57%) produced anti-S IgG and anti-N IgG, attesting that , among this group, Coronavac was significantly efficient in achieving the objective that the vaccine was originally proposed for, since by using the inactivated virus there would be an induction of production of antibodies capable of neutralizing two or more antigenic targets of the virus, which would maximize the possibility of protection of the immunized, it is worth noting, however, that the antibody detection method used in the present work is a rapid immunochromatographic test that does not allow measuring the amount of antibodies produced.

Still in relation to the Coronavac group, regarding the production of anti-S IgG, 10 of the participants (71.42%) who produced such an antibody were not affected by COVID-19, and two possibilities can be inferred: a) Coronavac induced production of sufficient anti-S IgG to provide protection against future infection and b) Coronavac induced moderate or low production of anti-S IgG and the patient had no future contact with the virus. Another important data obtained in the present study concerns the fact that 3 (23.07%) of the 13 participants who took only Coronavac mentioned that before receiving the first dose they had been infected with the virus, and thus had COVID-19 before to be vaccinated, raising the possibility that the production of IgG anti-S and IgG anti-N may have been a consequence of either the previous infection or the immunization after the initial infection.

Still in relation to the Coronavac group, one of the patients showed a totally atypical behavior, since, even having been affected by COVID-19 and receiving 3 doses of the aforementioned vaccine, he was not able to produce either anti-S IgG or anti-N IgG. . It should be noted that this is a patient over 75 years of age who, due to his advanced age, already suffers from a tendency to immunological "lapse", which characterizes immunosenescence. According to Leal AS, et al. [19] when considering general immunological aspects, senescence has been summarized as the progressive loss of homeostasis, translated by the progressive decrease in the ability of senile individuals to build immune responses in infectious processes. According to Barbosa EL, et al. [20], it can be understood that senescence in the face of COVID-19 leads to a state of greater vulnerability of the immune system, thus weakening the aged organism even more. With the involvement of several immunological factors in the aged organism, when there is contact with the SARS-CoV-2 virus, due to the immunological fragility resulting from aging, it is possible to potentiate the reduction of the epidemiological heterogeneity for COVID-19, causing low antibody production.

Also by analyzing the results obtained, it was possible to classify a second group of participants (Coronavac Mix), who did not have COVID-19 before the first dose or during treatment, and who, for these, were recommended a vaccination schedule with two doses of Coronavac and a third booster dose composed of vaccines of another composition, regardless of the technology used, as long as it was not similar to the one that uses the exclusively attenuated virus. In this group it was observed that all patients (100%) were able to produce anti-S IgG, a portion that was practically similar to that which was able to produce this antibody in the group that received only Coronavac in the 3 doses (Coronavac group). It is important to highlight that in the present study, a qualitative assessment of the production of antibodies was carried out, not allowing to infer discussions about the magnitude of the humoral response, but based on scientific evidence published by other researchers, among which Vargas L, et al. [21], the importance of administering a third dose of vaccine when using Coronavac exclusively is justified, since, according to these authors, after only two doses of this immunogen, the induced immune response would not be quantitatively significant, resulting in a possible fruitless immunization, despite its ability to induce an immune response capable of neutralizing two or more antigenic targets of the virus.

This Coronavac vaccine bottleneck was confirmed by the aforementioned researchers, since, in their research carried out in Chile, they showed that the third dose of this vaccine induced a 6-fold increase in anti-S IgG titers, this value being significantly lower than that observed when the vaccine was administered. Application of the third booster dose using other immunobiologicals, which, according to these authors, induced about twice the increase in anti-S IgG titers in relation to the titer observed after boosting with Coronavac. Such evidence is explained by Li M, et al. [15] according to which vaccines that use the whole inactivated virus as an immunogen, despite being able to induce a greater range of antibodies against more antigens, may possibly imply a more quantitatively limited spectrum of immunity induction, due to the fact that the virus is killed. , and consequently unable to replicate and proliferate, thus not inducing a memory immune response quantitatively sufficient to quell a future infection.

An explanation for this discrepancy concerns the fact that the other vaccines evaluated in the present work use

recombinant material or viral vector technology, which implies that their effectiveness is evaluated only through the production of IgG antibody against protein S, However, with some important advantages, mainly because they are capable of inducing the host cell to produce the antigen of interest (the S protein itself), triggering a specific and amplified response to the target antigen, this amplitude being greater than that induced by the virus. Inactivated, since in this type of vaccine the amount of antigen is limited to that which was inoculated, with no production of greater antigenic load in the organism, which at first could culminate in a greater possibility of risk of successful infection in immunized individuals exclusively with Coronavac. Finally, this is an observational study rather than a clinical trial, and, therefore, the effectiveness of the four types of vaccines cannot be directly compared, being necessary the design of future clinical studies that allows a more precise comparison of the effectiveness of the referred immunogens.

Conclusion

Based on the results obtained, the following conclusions can reach:

- Vaccination regimens involving at least one of the three doses with Janssen vaccine were potentially more effective in inducing a protective immune response, as they allowed for the absence of participants who tested positive for COVID-19 when subjected to these processes;
- Vaccination of participants exclusively with Coronavac proved to be effective in protecting against infection, but not fully, since some patients who received this vaccine schedule were positive for COVID-19;
- The AstraZeneca vaccine proved to be comparatively as partially effective as the Coronavac in protecting against infection, since some patients who received such an immunogen as the last dose, regardless of the stage and vaccine schedule, tested positive for COVID-19;
- The Pfizer vaccine was the least efficient, as it allowed for a greater occurrence of infected patients, after receiving this immunogen as the last dose, regardless of the stage and the vaccination schedule;
- All vaccine protocols that were applied to the research participants proved to be efficient and satisfactory, because, although some patients were infected, there was production of anti-IgG-S antibodies;
- The vaccine protocol composed exclusively of Coronavac induced qualitatively satisfactory production of IgG-N antibodies;
- All vaccine protocols were 100% effective in protecting research participants from hospitalizations and deaths.

Final Considerations

As final considerations, some limitations of the present work can highlight, mainly related to the number of research participants and the lack of implementation of techniques that would allow the quantification of antibody titers produced after the various doses of immunizing agents. Another limitation is the lack of evidence to prove that all research participants had or had not had contact with the COVID-19 virus after starting the vaccination schedules, which could been evidenced by methods of detection of genetic material (RT-PCR), and that could definitely prove the real effectiveness of the evaluated vaccine regimens.

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