Asian Journal of Immunology

Volume 6, Issue 1, Page 153-162, 2023; Article no.AJI.103259

Pharmacology of Vaccines against Coronavirus Disease in Clinical Use Globally: A Review

Casimir C. Ofor [a*], Godwin C. Akuodor [b], Eugene O. Ohanme [c] and Chikere Anusiem [d]

[a] Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, College of Health Sciences, Ebonyi State University, Abakaliki, Nigeria.
[b] Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Nigeria.
[c] Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, Alex Ekwueme Federal University, Abakaliki, Ebonyi State, Nigeria.
[d] Department of Pharmacology and Therapeutics, College of Medicine, University of Nigeria, Enugu Campus, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author CCO conceptualized the study, participated in the literature search and manuscript drafting. Authors GCA and EOO also participated in the literature search and drafting of the manuscript. Author CA supervised, reviewed and approved the final manuscript. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/103259

Review Article

Received: 21/05/2023
Accepted: 26/07/2023
Published: 02/08/2023

ABSTRACT

Following the lethal nature of the coronavirus disease and the high transmissibility of the disease, a concerted effort has been made throughout the world to produce viable and affordable vaccines to curb the impact of the disease globally. Various technologies have employed in the process of developing vaccines against the coronavirus disease. Adverse events following immunization is very common in patients receiving immunological and biological products. These events are characterized by some serious clinical manifestations in the patients.

**Corresponding author: E-mail: trendicas@gmail.com;*

Over three thousand, five hundred adverse events reports were made by clients receiving some coronavirus vaccines in the United States of America by the center for disease control in June, 2021. Some of the features manifested by the patients include: convulsions, irregular heart beats, serious abdominal discomfort and signs resembling cerebrovascular accidents.
Well over one thousand case reports of inflammation of the heart muscles and the pericardium were reported to the Vaccine Adverse Events Reporting system following the inoculation with mRNA-based coronavirus vaccine produced by Moderna and Pfizer-BioNtech pharmaceutical companies in the United States of America (USA) according to the CDC reports in April, 2021.

Keywords: Coronavirus vaccine; SARS-Cov2; immunology; disease; adverse events.

1. INTRODUCTION

The overall impact of COVID-19 pandemic on the social determinants of health globally has been far-reaching and grossly debilitating. The world was clearly cut unawares by this scourge which was completely strange to the present world population. As time progressed, the need for the implementation of an extensive vaccination of the world population became inevitable and imperative so as to curb the impact he impact of the coronavirus disease globally [1]. Apart from the immunization of individuals against the disease, it is also important to engage in the extensive protection of some vulnerable and exposed groups in the society who for some reasons may not have access to the immunization package [2].

The vaccines in current use clinically against the coronavirus disease were developed by some of the technological processes listed as follows: (a) vaccines that are mRNA-based (b) viral vector-based vaccines, (c) vaccines with protein subunits, and (d) whole virus or inactivated virus vaccines [3]. In consequence, vaccines that belong to the mRNA-based and the viral vector-based technologies which ultimately produce antibodies specific to spike proteins have been given approval by the European Medicines Agency (EMA) [4].

The vaccine development that is based on mRNA-based technology is to some extent new in the vaccine production pharmaceutical companies. The technology employs the molecular templates of messenger RNA (mRNA) to deliver the genetic information to produce the spike (S) glycoprotein antigen. It does not the specific antigen by itself [5]. The viral vector-based vaccines used against coronavirus disease is usually a non-replicating innocuous type of adenovirus as a medium to deliver the genetic code of the S glycoprotein antigen. This will invariably lead to evoking the immune response that is clinically targeted in the clients [6].

A lot of European countries were affected by the coronavirus disease with consequent mortality. Among the countries seriously affected by the pandemic is Germany. The country has a population of around 84 million. The incidence of the disease was 3,729,682 with mortality of 91,007 as reported by the month of July of the year 2021 [7]. Up until now, a total of four coronavirus vaccines had been given approved in Germany between 2020 and 2021. The new vaccines include, Pfizer-BioNTech (mRNA-based vaccine) approved since 2020, Moderna (mRNA-based vaccine) approvedJanuary 2021, AstraZeneca-Oxford (viral vector-based vaccine) approved January 2021, and Janssen (viral vector-based vaccine) approved 2021 [8]. On 1 July 2021Vaccine doses of 926,463 were inoculated in patients in Germany, leading to 31.487.487 people (37.9% of the total population) being fully vaccinated and 46,249,449 people (55.6%) being exposed to a minimum of a single dose of the vaccine. The German government imported -to date- 57,619,463 doses of Pfizer-BioNTech, 13,869,863 doses of AstraZeneca Oxford, 7,641,280 doses of Moderna, and 2,893,697 doses of Janssen. Health workers were given top priority in the immunization especially in those in the forefront of coronavirus disease treatment in Germany [9].

There has been a global attempt to develop a vaccine against the coronavirus was commenced, in view of the seriousness of the disease, the significant rate of transmission, and the high demand for clinical attention by infected patients. Several technologies are used to produce vaccines against coronavirus disease and at an alarming pace. The vaccine trial has unprecedentedly reached the clinical stage in a period of less than half of the year. Because of the emergency nature of the epidemiology of the

coronavirus disease in Brazil, a makeshift approval was granted for the use of some of the vaccine candidates to help stem the onslaught being inflicted on their population by the pandemic [10].

A pharmacovigilance department to monitor the serious adverse events (serious undesirable and untoward signs and symptoms following the administration of new vaccines and immunologicals) in the population has become very imperative [10,11,12,13].

The decision to commence the production of the coronavirus vaccine was made immediately the genome of the virus was made public in the month of January of 2020 [12,13]. About 186 vaccine candidates for coronavirus disease and 87 of were commenced on human clinical trials [14]. Many different vaccine technology platforms have been used to develop a safe and effective vaccine. Currently, Four types of using different vaccine technologies have been granred approval fpr clinical use. These comprise nucleic acid (mRNA) platforms, viral vector platforms, inactivated virus platforms and subunit vaccine platforms [15,16,17]. The emergence of new variants of SARS-CoV-2 is another problem in vaccine development. Lately, three coronavirus variants, B.1.1.7 (501Y.V1) in United kingdom, B.1.351 (501Y.V2) in South Africa and B.1.1.28.1 (P.1) [15].

2. VACCINE NAMES, TYPES AND MANUFACTURER (DEVELOPER)

By 19th of June, 2021, seventy eight (78) vaccine candidates were in development in 201 different ongoing clinical trials. Among them, 12 vaccines were approved by the US FDA, (WHO) and the EMA [18]. In the wake of the rapid spread of the virus among the population, mutant variants continued to emerge in the world. This development is worrisome as there is no obvious guarantee that the already developed vaccines would be effective in the control of the new variants of the coronavirus. Measures have been put in place to evaluate the efficacy and potency of the vaccines against the new mutant variants of the virus [14].

Currently approved covid-19 vaccines by the World Health Organization (14) are as follows:

1. **mRNA-BNT 162b2-Comirnaty:** This vaccine was developed by Pfizer/BioNTech + Fosun Pharma in Germany and United states of America. The vaccine platform is mRNA-based.
2. **mRNA-1273:** This vaccine was developed by Moderna + National Institute of Allergy and Infectious Diseases (NIAID) in the United states of America (USA). The vaccine platform is mRNA.
3. **ChAdOxI-S-AZD1222:** Developed by Astrazeneca + University of Oxford in the United Kingdom and Sweden. The vaccine platform is non-replicating Viral Vector.
4. **Sputnik V:** Developed by Gamaleya Research Institute + Health Ministry of the Russian Federation in Russia. The vaccine platform is non-replicating Viral Vector.
5. **Ad26 COV2S-JNJ 78436735:** This vaccine was developed by Johnson and Johnson + Janssen pharmaceuticals in Germany and United states of America (USA). The vaccine platform is Recombinant, replication-incompetent human adenovirus type 26 vector.
6. **Convidecia:** Developed by Cansino Biological Inc. + Janssen pharmaceutical in China. The vaccine platform is inactivated vaccine.
7. **BBIBP-CorV:** Developed by Sinopharm + China National Biotec Group company in China. The vaccine platform is inactivated vaccine.
8. **CoronaVac:** This vaccine was developed by Sinovac Research and Development company limited in China. The vaccine platform is inactivated vaccine.
9. **BBV152-Covaxin:** Developed by Bharat Biotech International limited in India. The vaccine platform is inactivated vaccine.
10. **NVX-Cov2373:** Developed by Novavax in United States of America (USA). The vaccine platform is subunit.
11. **EpiVacCorona:** Developed by the Federal Budgetary Research Institution State Research Center of Virology and Biotechnology 'Vector' in Russia. The vaccine platform is peptide vaccine.
12. **Covishield:** Developed by serum institute of India. It is an adenovirus vaccine.

3. COMPOSITION OF COVID-19 VACCINES, ROUTES OF ADMINISTRATION, AND EFFICACY (14)

1. **mRNA-BNT 162b2 – Comirnaty:** The vaccine is composed of mRNA vaccine encoding for the RBD of the SI protein. The vaccine contains single nucleoside incorporations of 1-methylpseudouridine. RBD antigen contains a T4 fibritin-derived

fold-on trimerization domain. Encapsulated within an LNP. Efficacy of the vaccine is 95%.

2. **MRNA-1273:** Composed of mRNA vaccine encoding for the profusion form of the S-antigen that includes a transmembrane anchor and an intact S1-S2 cleavage site in its production form. Encapsulated with an LNP. Efficacy is 94.1%.
3. **ChAdOxl-S-AZDl222:** Composed of adenovirus derived from chimpanzee with EI and E3 deletions, encoding for this full-length S protein with a tissue plasminogen activator signals peptide. Efficacy is 70.4%.
4. **Sputrik V:** This vaccine is composed of adenovirus base combining 2 adenoviruses, Ads and Ad26. Efficacy is 91.6%.
5. **Ad26 Cov2 S-JNJ-78436735:** Composed of recombinant, replication incompetent adenovirus serotype 26 (Ad26) vector encoding a full-length and stabilized SARS-Cov-2 spike (s) protein. The vaccine was derived from the clinical isolate of Wuhan Strain. Efficacy is 72%.
6. **Convidecia:** Vaccine is composed of Ad5 with E1 and E3 deletions encoding for the full-length S protein. Gene was derived from the Wuhan-Hu-1 sequence for SARS-Cov2 and contains a tissue plasminogen activator signal peptide. Efficacy is 65.28%.
7. **BBIBP-Cor V:** Composed of β-propionolactone inactivated vaccine of SARS-COv-2. Efficacy is 79.34%.
8. **Coronavac:** Also composed of β-propionolactone inactivated vaccine of SARS-cov-2. Efficacy is 50.38% - 83.50%.
9. **BBV152 – Covaxin:** Vaccine is composed of a whole virion inactivated SARS- Cov-2 vaccine formulated with a Toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) or Alum (Algel). Efficacy is 81.0%.
10. **NVX-Cov2373:** Composed of stable profusion, full-length S protein made form VLP nanoparticle technology, given with saponin-based adjuvant, Matrix-M^{TM}. Efficacy is 96.4%.
11. **Epivac Corona:** The vaccine contains small portions of viral proteins known as peptides. Efficacy is 100%
12. **Covishield** contains adenovirus. Efficacy is 70%.

All the vaccines are administered intramuscularly (i/m).

4. MODE OF ACTION OF COVID-19 VACCINES

A. **mRNA Vaccines:** BNT 162b2 is a lipid nanoparticle (LNP) which is formed from a modified nucleoside messenger RNA (mRNA) vaccine which encodes the receptor binding domain (RBD) of the SI protein. The RBD is constructed on a T4-fibritin -derived fold on trimerization base, which helps to guide antigen folding into the native trimeric state. The N-methyl pseudo-uridine (m1 ψ) nucleoside modification offers it some protection from its inherent immunity. It is enclosed in a capsule with LNP which offers it some protection from being broken down by enzymes and creates room for a proficient uptake by the cells. A very high coronavirus neutralizing antibody titers with strong T cell responses was demonstrated by BNT 162b2 in the phase one of the clinical trial. [15,16,17].

Table 1. Covid-19 vaccine platforms, attributes and doses (14)

Platform	Attributes	Doses	Vaccine candidate (Manufacturer).
Mrna	Fast development speed, low-to-medium manufacturing scale.	2	BNT-162b2 (Pfizer, BioNTech mRNA-1273 (Moderna).
DNA	Fast development speed; low to medium manufacturing scale	2	INO-4800 (Inovio)
Viral vector	Medium to fast development; high manufacturing scale	1 or 2	AZD-1222Ad5 Cov (Astrazeneca; Oxford University Ad26.Cov2.S (Johnson&Johnson)
Protein subunit	Medium-to-fast development, high manufacturing scale.	2	NVX-Cov2373 (Novavax)
Whole virion inactivated	Ability to quickly produce large amount of vaccine	2	Covaxin; BBV152 (Ocugen and Bharat Biotech).

B. **Non-Replicative Vector Vaccines:** ChAdOx1-S, which is currently known as AZD1222, employs a different viral vector, an adenovirus derived from the chimpanzee. The interaction with already formed antibodies which acts against the adenoviruses The possible interaction with preformed antibodies against adenoviruses are minimized by the use of chimpanzee vector while the viral multiplication is blocked by the EI deletion. The E3 deletion also promotes the introduction of larger genetic cargo into the viral vector. The added sequence encodes for the full-length S protein with a tissue plasminogen activator signal sequence. The S protein sequence is codon-optimized. In the phase 1 clinical trial, the results showed no severe side effects with efficient humoral and cellular immune responses, [19,20, 21].

C. **Inactivated vaccines:** BBIBP-CorV is a propionolactone inactivated SARS-Cov-2 vaccine. The inactivated virus was isolated from a patient in the Jinyintan Hospital in Wuhan (HBO2 Strain). The virus was cultivated in a standard Vero cell line for propagation. In the phase 1 and 2 clinical trials, a strong humoral response was observed in 100% of the group that received the vaccine [20,21,22,23].

D. **Subunit Vaccines:** NVX-Cov 2373 is a recombinant SARS-Cov-2 (rSARS-Cov-2) nanoparticle vaccine constructed from the full-length (including the trans-membrane domain) and wild-type SARS-COV-2 spike glycoprotein. The vaccine was designed with a special adjuvant called Matrix-M^{TM}.

Matrix-M^{TM} an adjuvant based on saponin extracted from Quillaja saponaria Molina tree induces high and prolonged and extended levels of broadly reacting antibodies backed by a balanced THI and TH2 type of response type. Despite the fact that the mechanism of action of Matrix-M adjuvant is yet to be identified comprehensively, the adjunct enhances a fast and substantial effect on the drainage by the cells to the lymph nodes located locally. This creates an enabling environment for the activating cells which include activating cells like T cells, B cells, Natural Killer cells, neutrophils, monocytes and dendritic cells. Previous studies done on vaccines have also demonstrated good effects that are not dependent on dose with encouraging level of safety for the vaccines [15,16,17].

5. ADVERSE EFFECTS OF COVID-19 VACCINES

The pharmacovigilance department of the various ministeries of health worldwide should be positioned to address the problems of adverse drug events in the population following immunization (Minsterio da Sauda (BR), 2020; Ministerio da Saude da Saude (BR), 2021). The majority of the adverse drug events from immunization with coronavirus vaccine are usually due to the factors relating to the components of the vaccine candidates both in patients with the first exposure and those already vaccinated previously [10,14].

Some serious side effects are associated with the administration of some of the recently developed vaccine components. These events may be so severe as to warrant immediate admission into the emergency departments of the hospital to prevent permanent damage to the systems of the affected individuals. Delay in instituting some interventions and resuscitation may result in death or severe disability in the affected clients [10].

Amongst the adverse events encountered in coronavirus vaccine administration is a phenomenon referred to as immunization errors. This error may be due to the deployment of non-professionals in the administration of the vaccines to the intending clients. There is therefore, need for proper training of personnel, adequate supervision of personnel and installation of proper equipment and materials for the immunization process. First class cold chain system should also be maintained for the appropriate preservation of the vaccines [14].

In a study conducted by Roberta Barros da Silva [22], inappropriate use of immunological and biological products were found to facilitate the occurrence of some immunization errors in the treatment of some patients in the population. The study however revealed a low incidence of immunization errors (0.74 IT per 100,000 doses) in the community receiving immunization against coronavirus disease [10,11].

Immunization error may often be stratified into various levels: error in the process of production can be classified as production error. This is an error emanating from non-compliance with good manufacturing practices and ethics that may ultimately lead to compromise in the quality of the vaccines. There may also be errors arising

from the cold chain (there is poor storage and movement of the vaccine to the intended destination. Unintended errors may also occur from poor handling of the vaccine products and administration error may also occur because of non-sterile injection, improper reconstitution of the vaccine during the process of administration to the patients. There is also the possibility that the intended injection may be given in the wrong site. Some personnel with inadequate training may inadvertently overlook some of the contraindications and expiry dates of the vaccines while administering the vaccines to the population [19,24]. Extravasation and administration of the vaccine in pregnant women outside the priority group was the most significant immunization error identified in some of the studies done in the population.

According to the center for disease control (CDC) report 2021 [25], during December 21, 2020 to January 10, 2021, the administration of 4,041396 first doses of Moderna covid-19 vaccine (2,465,411 to females (61%), 1,450,966 to males (36%) and 125019 to persons whose sex was not recorded (3%) was reported to CDC. During the same period, reports of 1266 (0.03%) adverse events following the inoculation of the initial dose of the Moderna coronavirus disease vaccines had been submitted to Vaccine Adverse Events Reporting System (VAERS). Out of the 1266 reports submitted to the vaccine adverse events reporting system, one hundred an eight cases were shortlisted for future analysis with a view to establishing the probability of hypersensitivity reactions with consequent anaphylaxis [25,26].

In a study done to study the impact of vaccines derived from messenger RNA nucleotide and viral vectors amongst German health workers, Klugar et al [27], it was revealed that all the local side effects from the vaccines occurred mainly in clients receiving the vaccine developed from messenger RNA nucleotide. The coronavirus vaccine developed from viral vectors showed little or no local side effects in the patients that received the vaccine. The study showed that about 78.3% and 70.4% of the clients that received the messenger RNA-derived coronavirus vaccine manifested a minimum of one local side effect in the study (χ^2= 3.421, sig = 0.064).in summary, it was discovered that the most prevalent local side effect in the study was pain in the injection site (75.6%). This was followed by swelling in the injection site (18%) and then finally erythematous patches in the injection site (10.4%). The study showed that patients that recieved vaccines derived from messenger RNA manifested more side effect of injection site erythema than clients that received vaccines derived from viral vectors (χ^2 = 3.993; Sig. 0.046) respectively.

In a reverse of the findings, clients that received coronavirus vaccines derived from viral vectors manifested more systemic side effects than clients that received vaccines derived from messenger RNA nucleotide. A minimum of one side effect was manifested by 87.2% of the group that received vaccines derived from viral vectors. Among the group that received messenger RNA-based vaccines, 61% developed a minimum of one systemic side effect in the study (χ^2 = 30.522; sig < 0.001), respectively. The study revealed that on the whole, that headache and general fatigue were the commonest side effects experienced systemically (53.6%). Next was pain in the muscles (33.2%). Feeling of chills (23%) and pains in the joints (21.2%) were the next in line in terms of the systemic side effects of the vaccines [27,28].

There were statistically significant differences in the both local and systemic side effects in the groups that received different vaccine products (messenger RNA-based and viral vector-based) in various studies done across the globe. Hemorrhage from the gums of the teeth (4.3%) , vesicular eruptions in the mouth (6.3%), foul smelling from the mouth (3.7%), numbness in the mouth (2.2%), swelling of the mucous membrane of the mouth and ulcers in the mouth (2.2%) were the most common oral side effects encountered by the clients that received the vaccines. It was also observed that the differences between the viral vector-based vaccine group and mRNA-based vaccine group were statistically significant (χ^2 97.782, 106,419, 27.506, 27.292, 63.907, 16.161 and 47.501, sig. < 0.001, < 0.001 and < 0.001, < 0.001 <0.001 and < 0.001, respectively). The majority of the side effects affecting the mouth was found to manifest in the groups within the first seven days of receiving the vaccines [27,28,29].

In other studies conducted to assess the side effects of the various coronavirus vaccines, it was observed that dermatological lesions (3.5%) were also experienced by the clients that received both messenger RNA-based vaccines and vaccines derived from viral vectors. Generalized rash was the commonest dermatological manifestation (2.8) observed in

the groups that received the vaccines followed by urticaria (0.7) and swelling in the mucous membrane of the throat (0.7%). Skin lesions were more in the group that received the viral-vector derived vaccine (5.6%) than in the group that received the mRNA-based vaccines. The skin of the face was the most affected site (57.1%) next was the upper limb (38.1%); 19% of the clients had dermatological lesions in the lower limbs [26,28,29].

Over three thousand five hundred reports of side effects from clients that received coronavirus vaccines were registered with the center for disease control in the united states of America in the month of June of 2021 [21]. Major features manifested were severe abdominal pains, convulsions abnormal heartbeats and signs mimicking cerebrovascular accidents (CVA). Some of the clients with severe signs and symptoms were admitted in the emergency rooms of the hospital with some patients complaining of severe respiratory distress [24,25].

Over three thousand five hundred reports of side effects from clients that received coronavirus vaccines were registered with the center for disease control in the united states of America in the month of June of 2021 [21]. Major features manifested were severe abdominal pains, convulsions abnormal heartbeats and signs mimicking cerebrovascular accidents (CVA). Some of the clients with severe signs and symptoms were admitted in the emergency rooms of the hospital with some patients complaining of severe respiratory distress [24,25].

Well over one thousand case reports of inflammation of the heart muscles and the pericardium were reported to the Vaccine Adverse Events Reporting system following the inoculation with mRNA-based coronavirus vaccine produced by Moderna and Pfizer-BioNtech pharmaceutical companies in the United States of America (USA) according to the CDC reports in April, 2021. This necessitated the revision of the patient and provider fact sheet by the Food and Drug Administration (FDA) in USA [30].

Severe adverse effect of anaphylactic shock was reported in some patients that received the Pfizer coronavirus vaccine which was authorized in the United Kingdom (UK) on the 2nd of December, 2020. This reaction occurred within the first twenty four hours of being inoculated with the vaccine. The anaphylactic shock was mainly due the polyethylene glycol component of the Pfizer vaccine [31]. Within 24 hours of the administration of the first dose of the Pfizer vaccine (authorized in the UK on the 2nd of December, 2020), 3 cases of suspected anaphylaxis and were treated with adrenaline. A single case report has confirmed that polyethylene glycol (PEG) can cause severe anaphylaxis to the Pfizer vaccine [30,31].

The Food and Drug Administration (FDA) of the United states of America also approved the use of Pfizer coronavirus vaccines as an emergency in the United states of America on the 11th of December, 2020). More than 1.8 million people received the first doses of the vaccine in the United states with over 4393 adverse drug reactions recorded in the population and submitted to the Vaccine Adverse Event Reporting System (VAERS). Anaphylactic reactions occurred in twenty one people while six people showed dermatological side effects [32,33].

A component of the Astrazeneca coronavirus vaccine known as Polysorbate 80 (PS80;Tween 80) is a product of polyethoxylated sorbitan and oleic acid. Polyethylene glcol and PS80 also contained in the Pfizer vaccine are implicated in the aetiology of the anaphylactic reactions due to hypersensitivity experienced by the patients receiving these vaccines [34,35,36,37].

5. CONCLUSION

The health regulation body in the world, World health organization (WHO), the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have approved twelve coronavirus vaccines globally. The spontaneous appearance of various mutant variants of the coronavirus has continued to constitute a great source of worry in the control efforts for the coronavirus pandemic. Some of the vaccines are formulated from nucleoside-modified mRNA while some are formulated from an adenovirus derived from the chimpanzee. Others are recombinant nanoparticle vaccines. Adverse reactions to the coronavirus vaccines can be due to immunization errors and components of the immunological and biological products. The adverse reactions include: injection site pains, fever, anaphylaxis, urticaria, myocarditis, pericarditis, thrombotic events and bleeding tendencies.

ACKNOWLEDGEMENT

We acknowledge the support we enjoyed from the university Librarian and the support staff during the literature search for this work.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Attia S, Howaldt HP. Impact of COVID-19 on the dental community: Part I Before Vaccine (BV). Clin. Med. 2021;10:288.
2. Leidner AJ, Murthy N, Chesson HW, Biggerstaff M, Stoecker C, Harris AM, Acosta A, Dooling K, Bridges CB. Cost-effectiveness of adult vaccinations: A systematic review. Vaccine. 2019;37:226-234. [PubMed]
3. Gavi the Vaccine Alliance. There are Four Types of COVID-19 Vaccines: Here's How They Work. #VaccinesWork; 2021.
Available:https://wwvv.gavi.org/vaccineswork/there-are-four-types-covi.d-19-vaccines-heres-how-they-work
Access on 29 July 2021
4. European Medicines Agency (EMA). Authorised COVID-19 Vaccines. COVID-19; 2021.
Available:https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronaviras-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#authorised-covid-19-vaccines-section
Access on 29 July 2021
5. Bettini, E, Locci M. SARS-CoV-2 mRNA vaccines: Immunological mechanism and beyond. Vaccines. 2021;9:147. [PubMed]
6. Dong Y, Dai X, Wei Y, Zhang L, Zheng M, Zhou F. A systematic review of SARS-CoV-2 vaccine candidates. Signal Transduct. Target. Ther. 2020;5:237.
7. Divya S, Fahima Sheerin SMH, Chindhiha S, Selvakumar K. Worldmeter coronavims update (live). Int. J. Recent Acad. Res. 2020;2:610-614.
8. Paul-Ehrlich-Institute. Coronavims und COVID-19; 2021.
Available:https://www.pei.de/DE/newsroom/dossier/coronavims/coronavirus-inhalt.html
Access on 7 July 2021
9. Nohl A, Afflerbach C, Lurz C, Brune B, Ohmann X, Weichert V, Zeiger S, Dudda M. Acceptance of COVID-19 vaccination among front-line health care workers: A nationwide survey of emergency medical services personnel from Germany. Vaccines. 2021;9:424. [PubMed]
10. Ministerio da Saude (BR), Secretaria deVigilancia em Saude, Departamento de Imunizacoes e DoengasTransmissfveis. Manual deVigilancia Epidemiologica de Eventos Adversos Pos-Vacinacao. Brasilia, DF; 2020.
11. World Health Organization. Council for International Organizations of Medical Sciences. Definition and application of terms for vaccine pharmacovigilance: report of ClOMS/WHO Work Group on Vaccine Pharmacovigilance. 2012. Geneva: WHO/ClOMS.
12. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and namingit SARS-CoV-2. Nat Microbiol. 2020;5(4): 536-544.
13. Dai L, Gao GF. Viral targets for vaccines against COVID-19. Nat Rev Immunol. 2021;21(2):73-82.
14. World Health Organization. GACVS COVID-19 Vaccine Safety subcommittee meeting to review reports of deaths of very frail elderly individuals vaccinated with Pfizer BioNTech COVID-19 vaccine, BNT162b2. Geneva: WHO; 2021
Available:https://www.who.int/news/item/22-01-202l-gacvs-review-deaths-pfizer-biontech-covid-19-vaccine-bnt162b2
Access on 2021 Feb 22
15. Sharma O, Sultan AA, Ding H, Triggle CR. A review of the progress and challenges of developing a vaccine for COVID-19. Front Immunol. 2020;1:585354.
16. Chung YH, Beiss V, Fiering SN, Steinmetz NF. COVID-19 vaccine frontrunners and their nanotechnology design. ACS Nano. 2020;14(10):12522-12537.
17. Lee P, Kim CU, Seo SH, Kim DJ. Current status of COVID-19 vaccine development: Focusing on antigen design and clinical trials on later stages. Immune Netw. 2021;21(l):e4.
18. McGill COVID19 Vaccine Tracker Team. Vaccines Candidates by Trial Phase; 2021.

Available:https://covid19.trackvaccines.org/vaccines/?fbclid=IwAR0rJdUx1T1j9TalYCJzwvnqm6MWluN2wwWtnuDP0GW6YvKLh3nW-Ex0ZKU.
Access on 27 June 2021

19. Jordan R, Barrett JR, Belij-Rammerstorfer S, et al. Phase ½ trial SARS-Cov-2 vaccine ChAdox1 nCov-19 with a booster dose induces multifunctional antibody responses. Nat Med. 2021;17(2):279-288.
20. Folegatti PM, Ewer KJ, Aley PK et al. Safety and immunogenicity of the ChAdOxl nCov-19 vaccine against SARS-Cov-2: a preliminary report of a ½, single-blind, randomized controlled trial. Lancet. 2020; 396(10249):467-478.
21. Xia S, Zhang Y, Wang Y et al. Safety and immunogenicity of an inactivated SARS-Cov-2 vaccine, BBIBP-CorV: A randomized double-blind, placebo-controlled phase ½ trials. Lancetninfect Dis. 2021;21(1):39-51.
22. Silva RBD, Silva TPRD, Sato APS, Lana FCF, Gusmão JD, Souza JFA, Matozinhos FP. Adverse events following immunization against SARS-CoV-2 (covid-19) in the state of Minas Gerais. Rev Saude Publica. 2021;55:66.
DOI:10.11606/s1518-8787.2021055003734
PMID: 34706042; PMCID: PMC8522717
23. Oliver S, Gargano J, Marin M, et al. The Advisory Committee on Immunization Practices' interim recommendation for use of Moderna COVID-19 vaccine-United States, December 2020. MMWR Morb Mortal Wkly Rep. 2021;69:1653-1656.
24. Ramasamy MM, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOxl nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): A single-blind, randomised, controlled, phase 2/3 trial. Lancet. 2021:396:1979-1993.
Available:https://doi.org/10.1016/S0140-6736(20)32466-l
25. Centers for Disease Control and Prevention (). Allergic reactions including anaphylaxis after receipt of the first dose of moderna COVID-19 vaccine—United States, December 21,2020-January 10; 2021.
Available:https://www.cdc.gov/mmwr/volumes/70/wr/mm7004el. html
Access on 8 Jul 2021
26. Moderna. Moderna announces primary efficacy analysis in phase 3 COVE study for its COVID-19 vaccine candidate and filing today with U.S. FDA for emergency use authorization: Moderna, Inc; 2020.
27. Klugar M, Riad A, Mekhemar M, Conrad J, Buchbender M, Howaldt HP, Attia S. Side Effects of mRNA-Based and Viral Vector-Based COVID-19 Vaccine among German Healthcare Workers. Biology (Basel). 2021;10(8):752.
DOI: 10.3390/biology10080752
PMID:34439984;PMCID:PMC8389568
28. Anderson EJ, Rouphael NG, Widge AT, Jackson LA, Roberts PC, Makhene M, et al. Safety and immunogenicity of SARS-coV-2 mRNA-1273 vaccine in older adults. N Engl J Med. 2020;383(25):2427-38.
Available:https://doi.org/10.U)56/NEJMoa2028436
29. Widge AT, Rouphael NG, Jackson LA, Anderson EJ, Roberts PC, Makhene M, et al. Durability of responses after SARS-coV-2 mRNA-1273 vaccination. N Engl J Med; 2020.
Available:https://doi.org/10.1056/NEJMc2032195
30. United States Food and Drug Administration. Pfizer-BioNTech COVID-19 vaccine; 2021.
Available:https://www.fda.gov/emergcncy-prepa redness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine
Access on 3 Jul 2021
31. Sellaturay P, Nasser S, Islam 5, Gurugama P, Ewan P. Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine. Clin Exp Allergy; 2021.
Available:https://doi.org/10.1111/cea.13874
32. MMWR2 allergic reactions including anaphylaxis after receipt of the first dose of Moderna COVID-19 Vaccine - United States. December 21, 2020-January 10, 2021. MMWR Morb Mortal Wkly *Rep.* 2021;70(4):125-129.
33. Shimabukuro T, Nair N. Allergic reactions including anaphylaxis after receipt of the first dose of Pfizer-BioNTech COVID-19 vaccine. JAMA. 2021;325(8):780.
34. Wenande W, Garvey LH. Immediate type hypersensitivity to polyethylene glycols: A review. CEA. 2016;46:907-922.
Lu IN, Rutkowski K, Kennard L, et al. Polyethylene glycol may be the major allergen in depot medroxyprogesterone

acetate. J Allergy Clin Immunol Pract. 2020;8:3194-3197.
35. Kennard L, Rutkowski K, Mirakian R, Wagner A. Polyethylene glycol: not just a harmless excipient. J Allergy Clin Immunol Pract. 2018;6:2173.
36. Stone CA, Yiwei L, Relling MV, et al (2019). Immediate hypersensitivity to polyethylene glycols and polysorbates: more common than we have recognized. JACI Pract. 2019;7:1533-1540.
37. Li PH, Wagner A, Thomas I, et al (2020). Steroid allergy: clinical features and the importance of excipient testing in a diagnostic algorithm. J Allergy Clin Immunol Pract. 2018;6:1655-2166.
Rutkowski K, Wagner A, Rutkowski R. Immediate hypersensitivity reactions to steroids and steroid containing medications. Curr Opin Allergy Clin Immunol;20:362-366.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/103259