JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue

JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)

An International Scholarly Open Access, Peer-reviewed, Refereed Journal

EVALUATION AND ANALYSIS OF MECHANISM OF ACTION, EFFICIENCY AND SIDE EFFECTS OF COVID VACCINES

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ABSTRACT:

A respiratory virus called SARs-CoV-2 (COVID-19), which was originally discovered in Wuhan, China, in December 2019, causes respiratory distress as well as a systemic inflammatory response in the vasculature that is mediated by a cytokine storm. Despite the finest post-infective medical treatments now available, there have been 72 million infections and 1.6 million fatalities, yielding a mortality rate of 2.2%. Worldwide health officials now consider the development of a vaccine to be a top priority because of the COVID virus' quick spread and the resulting global pandemic. mRNA-1273 (Moderna), BNT162b2 (Pfizer/BioNtech), ChAdOx1 nCoV-19 (Astrazenac/Oxford), and rAd26)/rAd5 are three of the most promising vaccines. In this study, we address what is currently known about their mechanism of action, efficacy, and safety.

Keywords: Covid, Moderna, Pfizer, Astrazenac, Vaccine

INTRODUCTION:

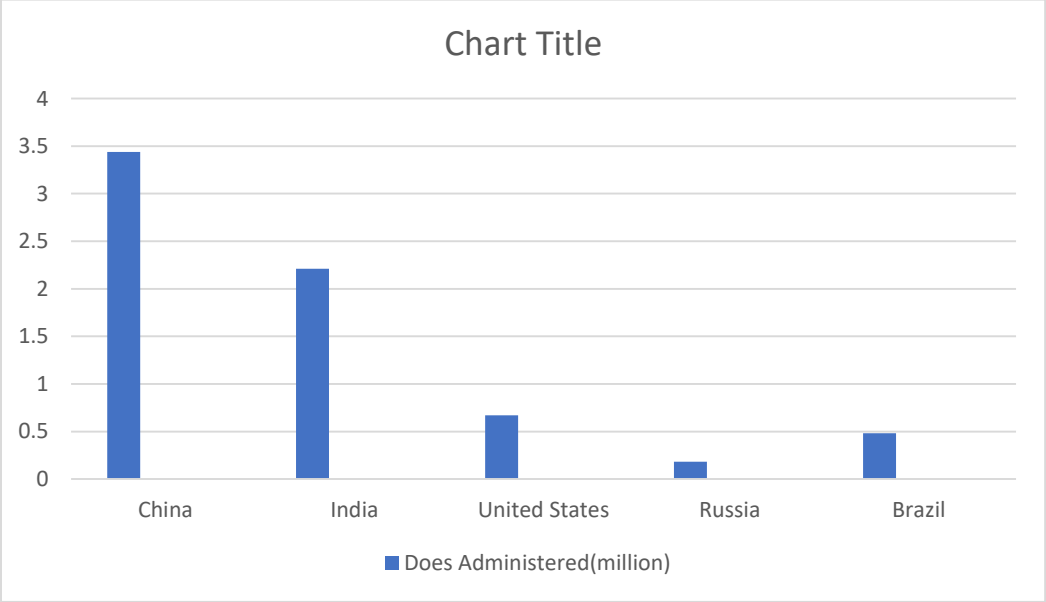
Globally, the coronavirus disease 2019 (COVID-19) pandemic has resulted in more than 30 million reported illnesses and 1 million fatalities. The severe acute respiratory syndrome coronavirus (SARS-CoV) 2 infection clinical spectrum includes asymptomatic infection to deadly and life-threatening disease. Globally, it is currently estimated that 20 million people have "recovered"; nonetheless, professionals are watching and reading reports of patients who have severe symptoms that have persisted and even significant end-organ failure as a result of SARS-CoV-2 infection. Since COVID-19 is a relatively new disease, many aspects of its clinical course, including any potential long-term health effects, are still unknown. (Del Rio, 2020)

Large, enclosed RNA viruses with medicinal and veterinary use include coronaviruses. Since a recently discovered coronavirus was discovered to be the primary cause of severe acute respiratory syndrome (SARS), interest in this viral family has grown. Coronaviruses use a number of unconventional tactics at the molecular level to carry out a complicated programme of gene expression. Ribosome frameshifting during genome translation, the synthesis of numerous subgenomic RNA species, and the assembly of progeny virions by a process that is particular to enclosed RNA viruses are all components of coronavirus replication. The creation of reverse genetic systems has aided in the advancement of research into these processes. (Masters, 2006)

Two subunits make up the SARS-CoV spike (S) protein; the S1 subunit has a receptor-binding domain that interacts with the host cell's angiotensin-converting enzyme 2 receptor, and the S2 subunit facilitates membrane fusion between the viral and host cell membranes. During SARS-CoV infection, the S protein is crucial for the generation of protective immunity, T-cell responses, and neutralising antibodies. (Du, 2009)

Main body

No. of vaccine does administered by china, India and USA (OUR WORLD IN DATA) https://ourworldindata.org/grapher/cumulative-covid-vaccinations



Name of the vaccine and launching date As per WHO

SR. NO.	NAME OF VACCINE	LAUNCHING DATE
1	The Pfizer/BioNTech Comirnaty vaccine	31 December 2020
2	The SII/COVISHIELD and AstraZeneca/AZD1222 vaccines	16 February 2021
3	The Janssen/Ad26.COV 2.S vaccine developed by Johnson & Johnson	12 March 2021
4	The Moderna COVID-19 vaccine (mRNA 1273)	30 April 2021
5	The Sinopharm COVID-19 vaccine	7 May 2021
6	The Sinovac-CoronaVac vaccine,	1 June 2021

7	The Bharat Biotech BBV152 COVAXIN vaccine	3 November 2021
8	The Covovax (NVX-CoV2373) vaccine	17 December 2021
9	The Nuvaxovid (NVX-CoV2373) vaccine	20 December 2021

1. The Pfizer/BioNTech Comirnaty vaccine

MECHANISM OF ACTION:

Long-term and widespread production of mRNA-encoding proteins, particularly RBD, in ACE2-expressing cells is indicated by the robust antigen expression that LNP-mRNA vaccines induced within cells and as secretory form for at least 160 h. They were also found in the lysosomes of the cells, suggesting that they may not be susceptible to lysosomal destruction. Additionally, animals who received prime and boost intradermal immunizations with 30 ng of LNP-mRNA had notable T follicular helper cell and GC B responses in draining lymph nodes, as well as a plasma cell response in splenocytes, especially for the mRNA that encodes the RBD. Additionally, observed cellular responses show that the vaccination induces Th1 CD4+ and CD8+ T cell responses. Humoral responses were also observed, demonstrating that the RBD mRNA-LNP vaccine induces strong RBD-specific IgG antibodies as well as potent neutralising antibodies against pseudotyped and live SARS-CoV-2 infection, with long-lasting high titers for 70 days after the second vaccination. In addition, it was discovered that RBD mRNA-LNP-induced antibodies can cross-react with SARS-CoV RBD and cross-neutralize SARS-CoV infection, offering defence against both coronaviruses. These antibodies can also potently disrupt binding between SARS-CoV-2 RBD and its ACE2 receptor, in a dose-dependent manner. Interesting, both vaccinations demonstrated 3 days of thermostability at 4°C and 25°C. Interestingly. (Mia Karam a b, 2022)

EFFICACY:

The secondary endpoint of the trial, vaccine effectiveness, was 73.2% (2-sided 95% CI: 43.8%, 87.6%) in children aged 6 months to 4 years who had no signs of past COVID-19 infection. This analysis was based on 21 cases in the placebo group (n=351) and 13 cases in the Pfizer-BioNTech COVID-19 vaccine group (n=794), all of which were diagnosed between March and June 2022. (BioNtech, 2022)

SIDE EFFECTS:

The most common and severe reported requested local reaction among vaccination recipients was pain or discomfort at the injection site. Following dosage 1, older age groups (2–4 years) than younger age groups (6–23 months) experienced pain/tenderness more frequently (30.8% vs 16.6%); a similar pattern was seen following doses 2 and 3 (31.0% vs 15.0% and 26.7% vs 16.0%, respectively). The second-most often reported local reaction was redness at the injection site. After dosage 3, older age groups experienced redness 10.9% more frequently than younger age groups (7.5%). Following either dose, there was less often reported injection site edema. After dose 2, redness and swelling were more typical than after doses 1 or 3. There were no local responses reported for grade 4. (prevention, 2022)

2. The SII/COVISHIELD and AstraZeneca/AZD1222 vaccines

MECHANISM OF ACTION

The whole structural surface glycoprotein (S protein) of the SARS-CoV-2 is carried by the adenovirus vector ChAdOx1 nCoV-19 used in the vaccine (AZD1222). The coding sequence for the S protein that ChAdOx1 nCoV-19

encodes is codon-optimized. ChAdOx1 nCoV-19 causes the host to mount a significant and effective T cell response. After vaccination, there was a significant rise in B cell activation, proliferation, and anti-IgA and anti-IgG antibodies to the SARS-CoV-2 virus.Instead of Th2 cytokines (IL-5 and IL-13), CD4 + T cells mostly produced Th1 cytokines (IFN-, IL-2, and TNF-). Importantly, it is demonstrated utilising a variety of methods that vaccination with ChAdOx1 nCoV-19 mostly elicits a Th1 response. Paracetamol was found to decrease reactogenicity and tolerance, making ChAdOx1 nCoV-19 safe, tolerant, and immunogenic. (Das, 2022)

EFFICACY:

When AZD1222 was administered as a half dose, followed by a full dosage spaced at least one month apart, one dosing regimen (n=2,741) demonstrated 90% vaccination efficacy, whereas another dosing regimen (n=8,895) shown 62% efficacy. Average efficacy was calculated using data from both dosage regimens (n=11,636), and it was found to be 70%. (AstraZeneca, 2022)

Side Effects:

Tenderness, discomfort, warmth, or itching where the injection is administered, overall malaise, weariness, chills, or fever, headache, feeling sick (nausea), joint pain, or muscle ache are all very common (may affect more than 1 in 10 persons). (India)

3. The Janssen/Ad26.COV 2.S vaccine developed by Johnson & Johnson

   MECHANISM OF ACTION:

   Ad26.COV2.S, the active ingredient, is a recombinant, replication-incompetent adenovirus serotype 26 (Ad26) encoding the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein. Adenovirus type 26's wild type virions are non-enveloped and range in size from 80 to 100 nm.Each encoding a single linear dsDNA molecule of about 35 kbp, which codes for the adenoviral proteins. The icosahedral protein structure that surrounds the dsDNA molecule is made up of the structural proteins II (hexon), III (penton), IV (fibre), VI, VIII, IX, and IIIa. The terminal protein and the core proteins V, VII, and X are directly connected to the DNA molecule. When the E1 gene is deleted, the vector cannot replicate in non-complementing cells, such as human cells. The virus can spread in Ad5 E1 complementing cell lines, such as HEK293, PER.C6 TetR, and HER96 cell lines. In addition, the Ad5 homologue has been substituted for the Ad26 E4 orf6 to enable the production ofreplication-incompetent Ad26 vectors in Ad5 E1 complementing cell lines, and a portion of the E3 gene region has been removed (E3) to make enough room in the viral genome for the insertion of foreign antigens. The generating cell line (PER.C6 TetR cells) silences the expression of the S antigen during the creation of the recombinant vector. Humans will express the S antigen after receiving the vaccine, which will trigger an immunological reaction. (agency)

EFFICACY

The COVID-19 Vaccine Janssen's efficacy against symptomatic SARS-CoV-2 infection was 67% in clinical trials (ENSEMBLE 1), 77% against severe/critical COVID-19 after 14 days and 85% after 28 days, and 93% against hospitalisations. Lower vaccination efficacy (VE) has been noted, nevertheless, as varieties of concern have emerged. In particular, against symptomatic infections, particularly those caused by SARS-CoV-2 variants of concern, such as the Omicron form, the ENSEMBLE 2 trial and subsequent investigations from South Africa revealed enhanced vaccine efficacy with two doses of vaccine given 2 months apart. (Organization, 2021)

SIDE EFFECTS

Signs of a severe allergic reaction can include: Difficulty breathing, Swelling of your face and throat, A fast heartbeat, A bad rash all over your body, Dizziness and weakness. (Johnson, 2021)

4. The Moderna COVID-19 vaccine (mRNA 1273)\

MECHANISM OF ACTION:

The mRNA-1273 vaccine from Moderna is an example of an mRNA vaccine, which essentially consists of strands of mRNA containing instructions for the cell on how to manufacture a spike protein that is unique to SARS-CoV-2 and then stimulates the immune response/produces antibodies to combat the virus. The SARS-CoV-2 full-length spike (S) protein is encoded by mRNA-1273, which has been altered to add two proline residues to the S protein (S2P) to stabilise it in a prefusion conformation. The CoV S protein is a prominent target for antibodies that block infection because it facilitates the attachment and entry of the virus into host cells (via fusion). (Moderna, 2021)

EFFICACY:

The Moderna vaccine has been proven to have a very high efficiency against serious illness, hospitalisations, and mortality after two doses and a first booster dose, but only a minor effectiveness against symptomatic illness.

SIDE EFFECT :

Pain and/or paresthesia at the injection site were the most prevalent local side effects following the first and second doses of the mRNA vaccination. (Moderns, 2022)

5. The Sinopharm COVID-19 vaccine

MECHANISM OF ACTION:

Cansino Biologics, the company that created Ad5-nCoV, used the same technology to create their ground-breaking Ebola vaccine. The vaccine is a genetically engineered viral immunisation that expresses COVID-19 spike protein using a replication-defective adenovirus type as its vector. In a manner similar to AZD1222, the vaccine gives cells genetic instructions regarding SARS-CoV-2 so they can produce the spike protein that sets off an immune response wherein SARS-CoV-2 specific antibodies are produced using a weakened adenovirus (common cold virus). (Zhu, 2020)

EFFICACY:

Two doses, given at intervals of 21 days, showed a 79% efficacy against symptomatic SARS-CoV-2 infection that appears 14 or more days after the second treatment, according to a significant multi-country Phase 3 trial. Hospitalisation was prevented by vaccination in 79% of cases. (Sinopharm, 2022)

SIDE EFFECT:

Pain at the injection site was the most prevalent adverse reaction following dosage one in 253 respondents (61.3%), and following dose two in 161 respondents (38.9%). 168 (40.6%) respondents reported overall tiredness, 99 (23.9%) myalgia/body pain, 93 (22.4%) low-grade fever, and 87 (21%) respondents reported headache. (Meo, 2023)

6. The Sinovac-CoronaVac vaccine,

MECHANISM OF ACTION:

CoronaVac is an inactivated vaccine that introduces the subject's body with the virus's dead cells after the infection has been contained with heat or chemicals. If the person later contracts the virus, the immune system will have learned from the dead antigens how to respond to living ones. In the instance of CoronaVac, the coronavirus was naturally inactivated with beta-propiolactone and contained SARS-CoV-2. (Zhang, 2021)

EFFICACY:

One of the most frequently used vaccinations in many nations even now is the Sinovac vaccine, a Chinese inactivated virus vaccine. The Sinovac vaccinations had an 83.5% success rate.

SIDE EFFECT:

350 (43.8%) participants reported fever as their most frequent side effect. Other frequent side effects included soreness and swelling at the injection site, which were experienced by 238 (29.8%) participants and 228 (28.5%) recipients, respectively. Fever was the most frequent adverse reaction following the second Sinovac dose, as reported by 262 (32.8%) subjects. (Chohan, 2023)

7. The Bharat Biotech BBV152 COVAXIN vaccine

MECHANISM OF ACTION:

The SARS-CoV-2 strain has been rendered inactive, thus the vaccine works by encouraging the immune system to create antibodies against it. Immunological stimulants (Alhydroxiquim-II), also referred to as vaccine adjuvants, are used in conjunction with the vaccination to enhance the immunological response and offer longer-lasting immunity.

EFFICACY:

Interim phase 3 clinical data indicate that it is a two-dose vaccine with a 78% effectiveness rate.

SIDE EFFECT:

In addition to body aches, stiffness, nausea, vomiting, fever, malaise, and headaches, COVAXIN side effects include discomfort, swelling, redness, and itching at the injection site. (Bharat Biotech, 2022)

8. The Covovax (NVX-CoV2373) vaccine

MECHANISM OF ACTION:

The vaccine combines spike proteins into a knucklebone-shaped nanoparticle that can be administered via injection along with its patented Matrix-M adjuvant, which has shown to have a potent and well-tolerated effect by promoting the entry of antigen-presenting cells into the injection site and enhancing antigen presentation in nearby lymph nodes, boosting immune response. (Keech, 2020)

EFFICACY:

In the first half of 2021, we conducted a phase 3 randomised, observer-blinded, placebo-controlled trial in Mexico and the United States to assess the effectiveness and safety of NVX-CoV2373 in adults (>18 years of age) who had not been exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Two doses of NVX-CoV2373 or a placebo were given to participants at random in a 2:1 ratio, 21 days apart.

SIDE EFFECT:

Tenderness and soreness at the injection site were the most often reported local side effects after each dose. (Dunkle, 2022)

9. The Nuvaxovid (NVX-CoV2373) vaccine

MECHANISM OF ACTION:

Purified full-length SARS-CoV-2 recombinant spike (S) protein that has been stabilised in its prefusion shape makes up Nuvaxovid. The addition of the saponin-based Matrix-M adjuvant makes it easier for innate immune system cells to activate, which heightens the intensity of the immunological response specific to the S protein. The two vaccine components trigger immunological responses from B- and T-cells against the S protein, including neutralising antibodies, which may help protect against COVID-19

EFFICACY:

The enrollment data for the study's two participating nations (the US and Mexico) correspond to the time when strains designated as Variants of Concern or Variants of Interest were predominately in circulation. For 61 of the 77 endpoint cases (79%), sequencing information was available. 48 of the 61 (or 79%) of them were deemed to be Variants of Concern or Variants of Interest. Alpha, Beta, and Gamma were the most frequent variations of concern, accounting for 31/61 cases (51%), whereas Iota and Epsilon made up the majority of the cases (13% and 5%, respectively). (Nuvaxovid, 2021)

SIDE EFFECT:

Reported pain, fatigue, headache, muscle pain, joint pain, fever, vomiting. (Novavax, 2022)

DISCUSSION: All of the vaccinations considered and compared here have the capacity to reduce infections or the occurrence of clinical symptoms. The fact that there is statistically no difference between the Moderna, AstraZeneca/Oxford, and Pfizer/BioNtech vaccines suggests that they are all equally effective in avoiding serious disease. The short time span was probably brought on by the need to find a vaccine quickly and the fierce battle for market dominance. The duration of the antibody response against the COVID-19 virus' S protein is yet unknown. Because COVID-19, an RNA virus, has a very unstable genome, it mutates quickly, much like the common cold to which it is related. There are currently at least six significant subtypes, and they appear to be geographically aggregating. China and Southeast Asia have Type I, Western Europe has Type II, the United States has a lot of Type IIIs, Japan has Type IVs, Australia has Type Vs, and South America has Type VIs.16 This implies that vaccinations created in one region of the world could not be as effective in other regions. The best estimate is 6 to 8 months, which means that these vaccinations must be given annually in a manner similar to how the flu shot is given. The effectiveness of the vaccines did not appear to depend on the technique employed, as both DNA- and mRNA-based vaccines appear to be equally effective. The adverse effects were mild but rather frequent. Surprisingly, aside from fever, where the DNA-based vaccines were more prevalent, the side effects of the mRNA vaccines were comparable to those of the DNA vaccines.

SUMMARY:

All four of the vaccines under consideration here appear to be successful in either preventing illness or its effects. Most notably, the COVID-19 vaccines from Moderna, AstraZeneca/Oxford, and Pfizer/BioNtech appear to be nearly equally effective at preventing serious illness. The Sputnik V vaccination is efficient at preventing infection, but there is no documented evidence that it can shield against serious illness. All four vaccines appear to be reasonably safe, with anaphylaxis being the most common but potentially fatal risk. Though these vaccines' phase III clinical studies will most certainly result in their approval, a benefit-cost analysis should be taken into account.First in queue for these vaccinations should be those who are most at risk, such as those over 60 or with moderate to severe chronic health issues. People with mild chronic diseases or those at moderate risk, such as health care workers or people 40 years of age and older, may also request vaccinations.

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