



CONTEMPORARY ASPECTS OF TYPES OF VACCINES TO PREVENT SARS-COV2 INFECTION

СОВРЕМЕННЫЕ АСПЕКТЫ ТИПОВ ВАКЦИН ДЛЯ ПРЕДОТВРАЩЕНИЯ SARS COV2 ИНФЕКЦИИ

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Abstracts. *This article deals with the brief review of current available vaccines to prevent SARS-CoV2 infection in people of both genders and different ages, mainly adults.*

Key words: *vaccine, COVID-19, prevention, protection, immunoprophylaxis.*

Introduction.

Infectious diseases had followed the existence of humankind, and question of the non-susceptibility to them was the focus of scientists since the Louis Pasteur times. Nowadays the special field of medicine as the vaccinology appeared and is a very fast developing in XXI century.

SARS-CoV2 infection became real serious emergent infectious disease with worldwide distribution and nowadays with more than 120 mln people cases over the world. Statistics every day is changing to the side of prevalence and high morbidity in spite of present partially specific drugs like the remdesivir, lopinavir and some others that can inhibit viremia in the blood and on the epithelial mucosas.

With the pandemic of COVID-19 since 2020 until now and still ongoing, people all over the world are still waiting for a vaccine to prevent effectively the illness. The initial focus of scientific accelerated international efforts for bringing an effective vaccine to the market as soon as possible was on novel platform technologies that promised speed but had limited history in the medical institution or clinic.

This current review aimed to analyse and describe modern vaccines against COVID-19 and some thoughts about the best one vaccine to prevent SARS-CoV2 infection should be.

Main part.

Effective prevention of COVID-19 is a crucial importance question for millions of people around the world, especially risks groups and vulnerable people. There are almost all countries has already started mass scale immunization against SARS-CoV-2 infection, Ukraine and India too. Speed of vaccination is still slow, and, unfortunately, COVID 19 morbidity level is still very high in both countries. One of the reason of such situation, on the main author's opinion, is also lack of information and deficiency of trust to these new vaccines. Up to now, we have different anti



SARS-CoV2 vaccines by the type and principal structure:

1. mRNA Based

- Pfizer-Biotech
- Moderna

2. Viral-vector Based

- a) Oxford-AstraZeneca (Covishield)
- b) Cansino
- c) Janssen
- d) Gamaleya RI/Sputnik V

3. Protein Subunit

- NovaVax
- Chinese AOS

4. Whole virus

- SinoVac
- Bharat Biotech (Covaxin)
- Sinopharm X 2
- Medicago Inc

Now we described these different types more detailed as manufacturers had characterized them.

mRNA Based: nucleic acid vaccines use genetic material – either DNA or RNA – to provide cells with the instructions to make the antigen. In the case of COVID-19, this is usually the viral spike protein. Once this genetic material gets into human cells, it uses our cells' protein factories to make the antigen that will trigger an immune response. The advantages of such vaccines are that they are easy to make, and cheap. Since the antigen is produced inside our own cells and in large quantities, the immune reaction should be strong. A downside, however, is that so far, no RNA or DNA vaccines have been licensed for human use, which may cause more hurdles with regulatory approval. In addition, mRNA vaccines need to be kept at ultra-cold temperatures, -70°C or lower, which could prove challenging for countries that don't have specialised cold storage equipment, particularly low- and middle-income countries. ⁽¹⁾

Pfizer - BNT162b1 is a codon-optimized mRNA vaccine that encodes for the trimerized SARS-CoV-2 RBD, a critical target of the virus nAb. The vaccine portrays an increased immunogenicity due to the addition of T4 fibrin-derived foldon trimerization domain to the RBD antigen. The mRNA is encapsulated in 80 nm ionizable cationic lipid nanoparticles, which ensures its efficient delivery. The Phase 1/2 clinical trials have revealed elevated RBD-specific IgG antibodies levels with a geometric mean concentration to be as high as 8 to 46.3 times titer of convalescent serum. Whereas, the geometric mean titers of the SARS-CoV-2 neutralizing antibodies were found to be 1.8 to 2.8 times the convalescent serum panel. Moderate and transient local reactions and systemic events were observed with no adverse effect. However, the data analysis did not evaluate the safety and immune responses beyond 2 weeks following the administration of the second dose [2].

Moderna. It is a vaccine composed of synthetic mRNA encapsulated in Lipid nanoparticle (LNP) which codes for the full-length, pre-fusion stabilized spike



protein (S) of SARS-CoV-2. It has the potential to elicit a highly S-protein specific antiviral response. Furthermore, it is considered to be relatively safe as it is neither made up of the inactivated pathogen nor the sub-units of the live pathogen. The vaccine has got a fast-track approval from FDA, to conduct the Phase II trials. The company has released the interim phase I antibody data of eight participants who received various dose levels. The participants of the 25 µg dose group gave results comparable to the convalescent sera. Whereas, in participants who received the 100 µg dose, the levels of nAb essentially surpassed the levels found in convalescent sera. The vaccine was found to be predominantly safe and well tolerated in the 25 µg and 100 µg dose cohorts, while three participants experienced grade 3 systemic symptoms after the administration of the second dose of 250 µg dose levels.

Viral-vector / Recombinant Based: viral vector vaccines also work by giving cells genetic instructions to produce antigens. But they differ from nucleic acid vaccines in that they use a harmless virus, different from the one the vaccine is targeting, to deliver these instructions into the cell. One type of virus that has often been used as a vector is adenovirus, which causes the common cold. As with nucleic acid vaccines, our own cellular machinery is hijacked to produce the antigen from those instructions, in order to trigger an immune response. Viral vector vaccines can mimic natural viral infection and should therefore trigger a strong immune response. However, since there is a chance that many people may have already been exposed to the viruses being used as vectors, some may be immune to it, making the vaccine less effective [4, 5].

Oxford-AstraZeneca (Covishield) - ChAdOx1 recombinant adenovirus vaccine was developed using codon optimized S glycoprotein and synthesized with the tissue plasminogen activator (tPA) leader sequence at 5'end. The sequence of SARS-CoV-2 coding for amino acids and the tPA leader and was propagated in the shuttle plasmid. This plasmid is responsible for encoding the major immediate early genes of the human cytomegalovirus along with tetracycline operator sites and polyadenylation signal from bovine growth hormone between the Gateway® recombination cloning site. The adenovirus vector genome is constructed in the bacterial artificial chromosome by inserting the SARS CoV2 S gene into the E1 locus of ChAdOx1 adenovirus genome. The virus was then allowed to reproduce in the T-Rex 293 HEK (human embryonic kidney 293) cell lines and purified by the CsCl gradient ultracentrifugation. The absence of any sub-genomic RNA in the intramuscularly vaccinated animals from the pre-clinical trials is indicative of the escalated immunity against the virus. The previous studies have suggested that a single shot should marshal the immune response.

Cansino is a recombinant, replication defective adenovirus type-5 vector (Ad5) expressing the recombinant spike protein of SARS-CoV-2. It was prepared by cloning an optimized full-length gene of the S Protein along with the plasminogen activator signal peptide gene in the Ad5 vector devoid of E1 and E3 genes. The vaccine was constructed using the Admax system from the Microbix Biosystem. The phase I clinical trials have established a positive antibody response or seroconversion. A four-fold increase in the RBD and S protein-specific neutralizing antibodies was noted within 14 days of immunization and peaked at day 28, post-vaccination.



Furthermore, the CD4 + T cells and CD8 + T cells response peaked at day 14 post-vaccination. However, the pre-existing anti-Ad5 immunity partly limited both the antibody and the T cell responses. The study will further evaluate antibody response in the recipients who are between the age of 18 and 60, and received one of three study doses, with follow-up taking place at 3- and 6-months post-vaccination.

Protein Subunit vaccines use pieces of the pathogen (mostly fragments of protein) to trigger an immune response. Doing so minimises the risk of side effects, but it also means the immune response may be weaker too. This is why they often require adjuvants, to help boost the immune response.

NovaVax - NVX-CoV2373 is a nano-particle based immunogenic vaccine which is based upon the recombinant expression of the stable pre-fusion, coronavirus S-Protein. The protein was stably expressed in the baculovirus system. The company plans to use the Matrix-M adjuvant to enhance the immune response against SARS-CoV2 spike protein by the induction of high levels of neutralizing antibodies. In the animal models, a single immunization resulted in the high level of anti-spike protein antibodies, which blocked the hACE2 receptor binding domain and could elicit SARS-CoV-2 wild type virus-neutralizing antibodies.

Whole Virus vaccines use whole viruses to trigger an immune response, and there are two main approaches to getting them. Live attenuated vaccines use a weakened form of the virus that can still replicate without causing illness. Inactivated vaccines use viruses whose genetic material has been destroyed so they cannot replicate, but still trigger an immune response. Both types use well-established technology and pathways for regulatory approval, but live attenuated ones may risk causing disease in people with weak immune systems and often require careful cold storage, making their use more challenging in low-resource countries. Inactivated virus vaccines can be given to people with compromised immune systems but might also need cold storage. Let's describe the most important vaccines from this group.

Covishield is ChAdOx1 nCoV19 corona virus recombinant vaccine, manufactured by Serum Institute of India Pvt Ltd, and is known now as AstraZeneca, by type is monovalent, single recombinant, replication-deficient chimpanzee adenovirus (ChAdOx1) vector encoding the S glycoprotein of SARS-CoV2. Produced by genetically modified HEK 293 cells. Mechanism of action – local expression of S glycoprotein of SARS-CoV-2, that can neutralize antibody and cellular immune responses. Should be administered as 2 doses (0,5ml each) four weeks apart (from four to twelve) intramuscularly in deltoid muscle, with protective efficacy 70,42%. Official contraindication is hypersensitivity to any component of it, and precautions – hypersensitivity, concurrent illness, thrombocytopenia and/or coagulopathy, immunocompromised host, pregnant and lactating mother. Very common adverse reactions are headache, myalgia, arthralgia, nausea, local pain.

Covaxin is whole-virion inactivated SARS-CoV-2 vaccine BB152 manufactured by Bharat Biotech BSL-3 facility is 100% indigenous, by the type of vaccine is whole-virion inactivated (BB152) with strain-NIV-2020-770, strength - 6mcg in 0,5 ml dose for the both genders and age group ≥ 18 years old with two doses (0,5 ml each) four weeks apart, intramuscularly, and seroconversion 86-96%. Storage at refrigerator temperature. This vaccine is interacted with antimalarial – chloroquine



and corticosteroids [11-15].

Pfizer Vaccine – BNT162B2-Manufactured by Pfizer-BioNtech, with generic name – Tozinameran and brand name – Comirnaty. By the type of vaccine – is nucleoside-modified mRNA (modRNA) which encodes part of the the spike protein found on the surface of the SARS-CoV-2 coronavirus (COVID-19), triggering an immune response against infection by the virus protein. Mechanism of action is based upon mRNA that carries instructions for making the virus's spike protein recognised as foreign by the immune system so antibodies, B cells and T cells are activated. This vaccine is available for age group above 16 years old and with two doses (0,3 ml each) three weeks apart, intramuscular route and declared protective efficacy up to 95%. Peculiarities of storage – temperature below -80° to -60° C (as frozen form till ready to use) and thawing from +2° to +8°C or room temperature up to 25°C.

Moderna – manufactured by “Moderna” by National Institute of Allergy & Infectious Disease (NIAD), Biomed Advanced Research and Development Authority (BARDA). This is type of vaccine – nucleoside-modified messenger RNA (mod RNA) compound “Mrna-1273” encode prefusion stabilized spike (S) protein naturally present on the surface of SARS-CoV-2 particles.

- Drug delivery System: -PEGylated lipid nanoparticle (LNP);
- Mechanism of action – mRNA that carries instructions for making the virus's spike protein, recognised as foreign by the immune system so antibodies, B cells and T cells are activated.
- Age group - ≥ 18 years old;
- Dosage - 2 doses (0,5 ml each) four weeks apart;
- Route – intramuscular;
- Site - deltoid muscle;
- Contraindications - severe allergic reaction, pregnant, lactating mother;
- Adverse reactions – facial swelling, Bell's palsy;
- Common reactions - pain at the injection site, tiredness, headache, muscle pain, chill, joint pain, lymphadenopathy, nausea, vomiting, fever.

Eligible for vaccination are following to prevent SARS-CoV2 infection [3, 8, 9]:

Persons who are at maximum risk of getting infected with COVID-19 infections and population at high-risk would be vaccinated first:

1. Health Care Workers (HCWs): health care providers and workers in health care settings (public and private).

2. Frontline Workers (FLWs): personnel from state and central police organisation, armed forces, home guards, prison staff, disaster management volunteers, civil defence organisation, municipal workers and revenue officials engaged in surveillance and containment activities.

3. Population ≥ 50 years of age and < 50 years with co-morbidities like diabetes, hypertension, cancer, lung diseases etc. This prioritization is not sequential. These priority groups may be vaccinated simultaneously depending on the availability of the vaccine.

Side effects that have been reported with the COVID-19 vaccine include:

- Injection site pain;
- Injection site swelling;
- Injection site redness;



- Injection site itching;
- Stiffness in the upper arm;
- Weakness in injection arm;
- Body ache;
- Headache;
- Fever after six to twelve hours;
- Malaise;
- Weakness;
- Rashes;
- Nausea;
- Vomiting.

Signs of a severe allergic reaction can include difficulty in breathing, swelling of your face and throat, a fast heart beat, rash all over the body, dizziness and weakness.

Recent studies has been demonstrated cases of thrombosis after shot of AstraZeneca, Pfizer, Moderna vaccines as these vaccines had been injected to the most of population in different countries, including Ukraine, Republic of India and USA, Canada, European countries. Unfortunately, there is no one very safe anti COVID19 vaccine nowadays. I hope that soon, in the near one-two year's humankind may create herd immunity against old and new coronavirus strains due to natural epidemic process and self-regulation of this parasitic system in modern 2021.

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No conflicts of interests.

Аннотация. Статья про короткий обзор современных доступных вакцин для профилактики SARS-Cov2 инфекции у людей обоих полов и разного возраста, взрослых преимущественно.

Ключевые слова: вакцина, COVID-19, превенция, защита, иммунопрофилактика.