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Chapter

Side Effects of the COVID-19 Vaccines

Irina Magdalena Dumitru

Abstract

Vaccination against COVID-19 was one of the most important discoveries in the fight against the pandemic and saved millions of lives. As with any vaccine, side effects have been reported, but the benefit of vaccination is much more important and should be considered. The most common side effects are mild to moderate, especially at the injection site, as well as self-limiting; non–life-threatening systemic reactions and severe reactions after vaccination are rare. In this chapter, the author will describe all types of side effects related to COVID-19 vaccines, information obtained from Web of Science, PubMed, Medline, Embase, Cochrane Library, Centre for Disease Control Prevention (CDC), cdc.gov database, and Vaccine Adverse Event Reporting System (VAERS).

Keywords: COVID-19, vaccine, protection, side effects, allergic reactions

1. Introduction

The occurrence of side effects after vaccination is a normal phenomenon; most side effects are local reactions and systemic effects are usually rare [1].

The safety of COVID-19 vaccines has been closely monitored during clinical trials, but even now, during their use, both local and systemic adverse reactions occur immediately after administration and delayed reactions [1].

Several types of COVID 19 vaccines have been used or are being used (Table 1):  

2. Common side effects

The most common local effects after vaccination are pain, redness, and swelling at the injection site [3]. In a study conducted in the Czech Republic, on 922 health workers, local pain was reported in 89.8% of cases, after the administration of Pfizer-BioNTech COVID-19 vaccine [4]. Side effects after the second shot may be more intense than the ones experienced after the first shot [3].

Tiredness, headache, muscle aches, chills, joint pain, and fever (more common after the second dose) were also reported [5].

In his paper published in 2021, Meo et al. [6] analyzed the most recent and eloquent data on the side effects of the 2 RNA vaccines, Pfizer-BioNTech COVID-19
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Trade-name</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer–BioNTech COVID-19</td>
<td>Comirnaty</td>
<td>mRNA vaccine</td>
</tr>
<tr>
<td>Moderna COVID-19</td>
<td>Spikevax</td>
<td>mRNA vaccine</td>
</tr>
<tr>
<td>Janssen COVID-19</td>
<td>Johnson &amp; Johnson COVID-19</td>
<td>Viral vector vaccine</td>
</tr>
<tr>
<td>Oxford–AstraZeneca COVID-19</td>
<td>Vaxzevria, Covishield</td>
<td>Viral vector vaccine</td>
</tr>
<tr>
<td>Sinopharm BIBP COVID-19</td>
<td>BBIBP-CorV</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>CoronaVac COVID-19</td>
<td>Sinovac COVID-19</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>Gam-COVID-Vac</td>
<td>Sputnik V</td>
<td>Viral vector vaccine</td>
</tr>
<tr>
<td>NVX-CoV2373</td>
<td>Novavax COVID-19</td>
<td>Protein subunit vaccine and a virus-like particle vaccine, though the producers call it a &quot;recombinant nanoparticle vaccine&quot;</td>
</tr>
<tr>
<td>BBV152</td>
<td>Covaxin</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>ADS-mCOV</td>
<td>Covidecia</td>
<td>Viral vector vaccine</td>
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<tr>
<td>CIGB-66</td>
<td>Abdala</td>
<td>Subunit vaccine</td>
</tr>
<tr>
<td>ZF2001</td>
<td>Zifivax</td>
<td>Subunit vaccine</td>
</tr>
<tr>
<td>FINLAY-FR-2</td>
<td>Soberana 02</td>
<td>Conjugate vaccine</td>
</tr>
<tr>
<td>Covivac</td>
<td></td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>VLA2001</td>
<td>Valneva COVID-19 vaccine</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>QazCovid-in</td>
<td>QazVac</td>
<td>Inactivated virus vaccine</td>
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<tr>
<td>Minhai COVID-19 vaccine</td>
<td>KCONVAC</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>COViRan Barekat</td>
<td></td>
<td>Inactivated virus-vaccine</td>
</tr>
<tr>
<td>Chinese Academy of Medical Sciences COVID-19 vaccine</td>
<td>Covidful</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>IMBCAMS COVID-19 vaccine</td>
<td></td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>MVC-COV1901</td>
<td>Medigen</td>
<td>Protein subunit vaccine</td>
</tr>
<tr>
<td>ZyCoV-D</td>
<td></td>
<td>DNA plasmid based COVID-19 vaccine</td>
</tr>
<tr>
<td>FAKHRAVAC</td>
<td>MIVAC</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>COVAX-19</td>
<td>Spikogen</td>
<td>Protein subunit vaccine</td>
</tr>
<tr>
<td>Razi Cov Pars</td>
<td></td>
<td>Protein subunit vaccine</td>
</tr>
<tr>
<td>Turkovac</td>
<td>ERUCOV-VAC</td>
<td>Inactivated virus vaccine</td>
</tr>
<tr>
<td>Sinopharm CNBG COVID-19 vaccine</td>
<td></td>
<td>Recombinant protein subunit vaccine</td>
</tr>
<tr>
<td>Corbevax</td>
<td></td>
<td>Protein subunit vaccine</td>
</tr>
<tr>
<td>FINLAY-FR-1A,</td>
<td>Soberana Plus</td>
<td>Conjugate vaccine</td>
</tr>
<tr>
<td>CoVLP</td>
<td></td>
<td>Virus-Like Particle vaccine</td>
</tr>
<tr>
<td>Noora</td>
<td></td>
<td>Protein-based vaccine</td>
</tr>
</tbody>
</table>

*Type of vaccine that uses a copy of a molecule called messenger RNA (mRNA) to produce an immune response.*
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and Moderna, data published in the Web of Science (Clarivate Analytics), PubMed, EMBASE, World Health Organization (WHO), Food and Drug Authorities (FDA) USA, Local Ministries, Health Institutes, and Google Scholar. It was found that the most common reactions caused by administration of the first dose vaccine of Pfizer-BioNTech COVID-19 were pain, swelling, redness, fever, fatigue, headache, chills, vomiting, diarrhea, muscle pain, joint pain, lymphadenopathy, shoulder injury, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, syncope, and right leg paresthesia [7]; and pain, swelling, redness at the site of vaccine, fever, fatigue,
headache, chills, vomiting, arthralgia, myalgia, and urticaria after the first dose of Moderna vaccine (Figure 1) [7]. Moderate or severe reactions have been reported after the second dose of vaccine, and facial swelling and Bell's palsy have also been reported [8].

Also, the most common reactions after administration of the most commonly used vaccines are shown in the Table 2 [2].

### 3. Allergic reactions

Most side effects were mild and moderate, and severe allergic reactions were rare [10]. In patients who have experienced severe side effects after receiving the first dose of mRNA vaccines, dose 2 has not been given. Also, no other dose was given to patients who experienced severe allergic reactions after COVID 19 Janssen or Oxford-AstraZeneca vaccines [10].

Documented hypersensitivity to polyethylene glycol (PEG) is a contraindication to the COVID-19 Pfizer vaccine, severe allergic reaction has been observed in about 10 cases per million doses of vaccine administered [11].

According to the Center for Disease Control (CDC), the 15-minute postvaccination monitoring recommendation is certified by the fact that most allergic reactions

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Side effects prevalence</th>
<th>Common Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer-BioNTech COVID-19</td>
<td>&lt; 1 in 10 people</td>
<td>Pain and swelling at the injection site, tiredness, headache, muscle aches, chills, joint pain, and fever</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 in 1000 people</td>
<td>Temporary one-sided facial drooping and allergic reactions such as hives or swelling of the face</td>
</tr>
<tr>
<td>Moderna COVID-19</td>
<td>&lt; 1 in 10 people</td>
<td>Pain at the injection site, fatigue, headache, myalgia (muscle pain), arthralgia (joint pain)</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 in 1000 people</td>
<td>Delayed cutaneous reactions at injection site resulting in rash-like erythemas</td>
</tr>
<tr>
<td>Janssen COVID-19</td>
<td>&lt; 1 in 10 people</td>
<td>Pain and swelling at the injection site, redness, headache, tiredness, muscle pain, nausea, coughing, joint pain, fever, and chills</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 in 100 people</td>
<td>Sneezing, tremor, throat pain, rash, sweating, muscle weakness, pain in the arms and legs, backache, weakness, and feeling generally unwell</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 in 1000 people</td>
<td>Hypersensitivity (allergy), and itchy rash</td>
</tr>
<tr>
<td>Oxford-AstraZeneca COVID-19</td>
<td>&lt; 1 in 10 people</td>
<td>Vomiting, diarrhea, fever, swelling, redness at the injection site, and low levels of blood platelets</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 in 100 people</td>
<td>Enlarged lymph nodes, decreased appetite, dizziness, sleepiness, sweating, abdominal pain, itching, and rash</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 in 1000 people</td>
<td>Hypersensitivity (allergy)</td>
</tr>
</tbody>
</table>

Table 2. The most common reactions after administration of Pfizer-BioNTech, Moderna, Janssen, and Oxford-AstraZeneca vaccines [2].
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(71%) occur during this period, especially in patients with a history of allergic events (81%) [11]. Anaphylaxis after COVID-19 vaccination is rare with rates of 4.7 cases/million Pfizer-BioNTech vaccine doses administered and 2.5 cases/million Moderna vaccine doses administered [12]. In cases where anaphylaxis has been reported, it has occurred within the first 15 minutes of receiving the vaccine, especially at the first dose of vaccine, usually in people who have reported allergic reactions or anaphylaxis in their medical history [13].

4. Myocarditis and pericarditis

Myocarditis and pericarditis after COVID-19 vaccination are rare. Most cases have been reported after receiving Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines), particularly in male adolescents and young adults [14]. Most of them (95%) had mild or moderate manifestations, self-limiting in most cases, and did not require hospitalization for more than four days [15, 16]. Myocarditis has been reported more often after the second dose, usually within a week of vaccination [14].

According to the Vaccine Adverse Event Reporting System (VAERS), a significant number of cases of myocarditis have been reported in young people, after the administration of mRNA vaccine, especially the second dose, with favorable evolution under specific treatment and hospitalization [17].

Related to the age group, most cases were reported in young people in the 16–17 age group (105.9 cases per one million doses) [17], followed by the 12–15 age group (70.7 cases per one million doses) and 18–24 age group (52.4 cases per million doses) [17].

In the study published in August 2021 by Diaz et al., myocarditis occurred a median of 3.5 days (IQR, 3.0–10.8 days) after mRNA vaccination, the median age was 36 years (IQR, 26–48 years), all were discharged after a median of 2 days (IQR, 2–3 days), and there were no readmissions or deaths [18].

Pericarditis developed especially after the second immunization, median onset was 20 days (IQR, 6.0–41.0 days) after the vaccination, median age was 59 years (IQR, 46–69 years median stay in hospital was 1 day (IQR, 1–2 days), no deaths were reported [18].

5. Thrombosis with thrombocytopenia syndrome (TTS)

Thrombosis with thrombocytopenia syndrome (TTS) has been associated with the administration of the Janssen COVID-19 vaccine [19]. TTS is rare and has occurred in approximately 4 cases per one million doses administered [19]. A review of reports indicates a causal relationship between the Janssen COVID-19 vaccine and TTS [20, 21].

The following features were found in relation to TTS [20, 21]:

- All side effects have been reported after the first dose of the Janssen COVID-19 vaccine (none after booster doses).
- Median time from vaccination to symptom onset: 9 days (range 0–18 days).
• 48% are women aged <50 years.
• Median age: 44.5 years (range 18–70 years).
• 83% in White non-Hispanic persons.
• 54% have a cerebral venous sinus thrombosis (CVST).

Venous thrombosis risk factors in U.S. TTS cases following Janssen COVID-19 vaccination are [20, 21]: obesity (46%), hypertension (30%), diabetes (13%), and systemic estrogen therapy (6%).

Thrombotic adverse events have also been reported following the administration of the Oxford-AstraZeneca COVID-19 vaccine, especially in younger women [19, 22]. Analysis of VigiBase reported embolic and thrombotic events after vaccination with Oxford-AstraZeneca, found a related incidence of 0.21 cases per 1 million vaccinated-days [23].

The following characteristics were found in cases with TTS in connection with AstraZeneca COVID-19 vaccination [19]:

• TTS developed 5 to 24 days after initial vaccination.
• Women younger than 50 years of age, some of whom were receiving estrogen replacement therapy or oral contraceptives.
• Patients were known to have had previous thrombosis or a preexisting prothrombotic condition.
• A high percentage of the patients had thromboses at unusual sites (cerebral venous sinus thrombosis or thrombosis in the portal, splanchnic, or hepatic veins).
• The median platelet counts at diagnosis were approximately 20,000 to 30,000 per cubic millimeter (range, approximately 10,000 to 110,000).

6. Guillain-Barré Syndrome (GBS)

Guillain-Barré syndrome (GBS) in people who have received the Janssen COVID-19 vaccine is a very rare side effect and was reported during the 42 days following vaccination, especially in men ages 50 years and older [24].

Based on a recent analysis of data from the Vaccine Safety Datalink, the rate of GBS was 11 times higher following Janssen COVID-19 vaccination compared to Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) [25].

In a study, conducted by Miguel García-Grimshaw and published in August 2021, on more than 3 million people who received mRNA vaccines, GBS was very rare, with incidence of 0.18/100,000 administered doses, within 30 days from first dose vaccine administration [26]. No cases were reported after second dose administration [26]. The presence of a concomitant trigger in most of our cases suggests a lack of mechanistic connection between mRNA vaccines and GBS [26].
6.1 Delayed type reactions

Delayed hypersensitivity reactions after the administration of vaccines for COVID-19 have been reported, a median of 7 days after the first vaccine dose, mainly after administration of mRNA vaccines [27]. Delayed large local reactions were noted as well urticaria, morbilliform eruptions, erythromelalgia, erythema multiforme, vasculitis, petechiae, pityriasis-rosea-like exanthems, or persistent maculopapular exanthema [28, 29]. Angioedema and liver damage were also described [28, 29].

6.2 Very rare side effects

A number of very rare side effects have been reported with various vaccines:

- A rare autoimmune neurologic disorder characterized by ascending weakness and paralysis after Janssen COVID-19 vaccination [30]
- Ocular adverse effects like facial nerve palsy, abducens nerve palsy, acute macular neuroretinopathy, central serous retinopathy, thrombosis, uveitis, multiple evanescent white dot syndrome, Vogt-Koyanagi-Harada disease reactivation, and new-onset Graves’ Disease [31]
- Reactive arthritis (ReA) after CoronaVac vaccination [32]
- Auto-immune hepatitis following Covishield vaccination [33]
- Sudden sensorineural hearing loss after Oxford-AstraZeneca Covid-19 vaccination [34]
- Bullous pemphigoid rash following Moderna [35]
- Interstitial lung disease after BNT162b2 mRNA COVID-19 vaccine [36].

7. Conclusions

COVID-19 vaccines are safe and effective; most side effects are mild and moderate and resolve in a few days. Severe reactions after vaccination are rare; however, the benefit of vaccination is much greater than the risk.
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[34] Jeong J, Choi HS. Sudden sensorineural hearing loss after COVID-19 vaccination. International