Macedonian pharmaceutical bulletin, 68 (Suppl 1) 487 - 488 (2022)
Online ISSN 1857 - 8969
DOI:10.33320/maced.pharm.bull.2022.68.03.234
Short communication

Safety of Covid-19 vaccines: one-year post-marketing analysis

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Introduction

On December 12, 2019 a cluster of patients in Wuhan, Hubei Providence, China began to experience shortness of breath and fever (CDC, 2022). With the increasing number of patients developing pneumonia with unknown etiology on 30 January 2020, WHO declared the outbreak a public health emergency of international concern and on 11 March 2020, WHO characterized COVID-19 as a pandemic (WHO, 2019; 2020). SARS-CoV-2 is part of the coronavirus family, which include common viruses that cause a variety of diseases from colds to more severe (but rarer) diseases like severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) (CDC, 2020). One of the main ways to prevent the spread the disease along with social distancing, quarantines and wearing face masks, is applying vaccines. mRNA vaccines represent a promising alternative to conventional vaccine approaches because of their high potency, capacity for rapid development and potential for low-cost manufacture and safe administration (Pardi et al., 2018). The first two vaccines which received conditional marketing authorization (CMA) against COVID-19 were mRNA vaccines – Comirnaty (on 21 December 2020) and Spikevax (on 6 January 2021) (EMA, 2021). The viral vector-based vaccines against SARS-CoV-2 use a non-replicating harmless version of adenovirus as a way to deliver the genetic code of the S glycoprotein antigen, thus eliciting the targeted immune response (10). Jcovden and Vaxzevria are the two authorized vaccines of this type. The fifth authorized vaccine was Nuvaxovid which is protein-based and contains a version of a protein found on the surface of SARS-CoV-2 (the spike protein). For ensuring the safety of these medicinal products the marketing authorisation holders (MAHs) are expected to submit to European Medicines Agency (EMA) monthly summary safety reports (MSSRs) issued in addition to regular periodic safety update reports (PSURs) (Kelly, 2020).

Materials and methods

Scoping literature review was conducted on the information concerning safety of vaccines in the scientific databases. Identified articles were checked for duplication and screened first in the title and abstract screening phase, then those included were reviewed in full-text. As inclusion criteria we defined the articles to be written in English, with an abstract available, whereas exclusion criteria include lack of citations or low citation rate, articles published in a language other than English.

A critical analysis was performed on the information in MSSRs issued for the vaccines indicated for SARS-CoV-2 on the territory of the EU. The analysis begins with the publication of the first MSSR for Comirnaty on 29 January 2021 and ends approximately one year later with the publication of the last MSSRs for 2021 for all marketing authorised vaccines.

Results and discussion

To our knowledge this is the first summary analysis speculating on the safety of COVID-19 vaccines and risk-minimization measures taken after their marketing authorization in the EU.

According to grouping system organ class (SOC), which is the first of total five levels to the medical dictionary for regulatory activities (MedDRA) hierarchy, the adverse drug reactions (ADRs) can be collected in 27 different categories. For the period under review, 12 monthly reports were published for Comirnaty and 11 for Spikevax. In the MSSRs are reviewed 25 suspected ADRs, which are classified in 11 classes according to MedDRA. For 18 ADRs collected from 11 SOCs a causal association is proved with vaccine administration which has led to update in the product information (PI) during the post-authorisation period. The first MA for the vector vaccine was approved on 29 January 2021. Since then, 11 monthly reports have been published for Vaxzevria and

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10 for Jcovden (previously COVID-19 Vaccine Janssen), as this vaccine was approved a month later. In the MSSRs are reviewed 28 suspected ADRs and are classified in 11 classes according to MedDRA. For 22 ADRs collected from 9 SOCs a causal association is proved with vaccine administration which has led to update in the PI during the post-authorisation period.

MAHs of the vaccines sent seven direct healthcare professional communications (DHPCs) to healthcare professionals to inform them of any important new safety information about vaccines and any actions which they should take. Only one DHPC of the sent, affect mRNA vaccines and concerns the conditions of myocarditis and pericarditis.

For the vector vaccines disseminated DHPCs are six, four for Vaxzevria and two for Jcovden.

Most of the published literature focuses on the monitoring of a specific adverse reaction or specific target group with the causal relationship between the occurrence of ADR and administration of the vaccines.

There is conducted study with focus on cutaneous adverse effects of the available COVID-19 vaccines. The conclusion of the mentioned study is that injection-site reactions presenting on the skin are among the most frequent adverse events, most of them mild or moderate, usually self-limited. Serious adverse events like anaphylaxis are systemic adverse reactions with frequent cutaneous symptoms, which may be the first manifestation and the key for the diagnosis (Bogdanov et al., 2021). As can be seen from our study General disorders and administration site conditions and Skin and subcutaneous tissue disorders represent a total of 44% of all adverse reactions requiring update of mRNA vaccine product information while only 18% refer to viral vector-based vaccines. One of the possible reasons for the large difference in the percentages is the difference in the excipients. Polyethylene glycol, present in the mRNA vaccines, is the one suspected for the induction of allergic reactions (Rice et al., 2021).

Conclusion

The MSSRs allowed all new information collected after received of marketing authorization to be promptly reviewed and any need of update to be shared with the public in a timely manner. Over a period of one year, there are more than forty safety updates in the PI for COVID-19 vaccines, but still the benefits of vaccines continue to outweigh the risks.

Over the last year, the EMA has incorporated all available mechanisms and also created new regulatory approaches to provide European citizens with qualitative, safe and effective vaccines. Despite great efforts and a centralized approach, vaccination campaigns are lagging behind in some Member States. One of the main reasons for this is the different level of awareness among health professionals worldwide, which is also the subject of research by our team, and the lack of accessible and clear information for the general population.

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