

Reported orofacial adverse effects of COVID-19 vaccines: The knowns and the unknowns

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Abstract

Introduction: Adverse events associated with vaccine administration can manifest in the oral cavity and orofacial region. Hence, the aim of this study was to compare the orofacial adverse effects of two recently authorised COVID-19 vaccines, namely BNT162b2 and mRNA-1273.

Methods: Publicly available data on BNT162b2 and mRNA-1273 vaccines were accessed from the relevant regulatory authorities in the United States, Canada, European Union and United Kingdom. Both patient/recipient information and health-care professional fact sheets for each of these drugs were manually searched to find their orofacial adverse effects.

Results: Adverse events affecting the orofacial region were reported for both vaccines. These were rare and included acute peripheral facial paralysis (Bell's palsy), facial swelling, and swelling of the lips, face or tongue associated with anaphylaxis. There was heterogeneity in the acknowledgement of vaccine-related adverse events in North America compared with Europe.

Conclusion: Globally, there are inconsistencies in the description of adverse effects presenting in the orofacial region of the COVID-19 vaccines BNT162b2 and mRNA-1273. We believe that awareness of these orofacial manifestations will improve recognition, management and reporting of vaccine-related adverse effects.

KEYWORDS

Bell's palsy, BNT162b2, COVID-19, mRNA-1273, side effects, Vaccine

1 | INTRODUCTION

Adverse drug reactions (ADRs) and medication-related events are potentially life-threatening consequences of the use of medicines, including vaccines. By and large, the benefits of vaccination clearly outweigh the risks—vaccines prevent between 2 and 3 million deaths from infectious diseases every year.¹ It is important, however, that adverse events are recognised and managed in a timely fashion to minimise the possible harm. To this aim, dentists and other health

professionals should be prepared to detect orofacial ADRs as being drug-induced.

Over the past decade, the scientific community and the vaccine industry have been asked to respond urgently to epidemics of H1N1 influenza, Ebola, Zika viruses, and this has resulted in an acceleration of vaccine-development programmes worldwide.² Recently, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a virus that causes coronavirus disease 2019 (COVID-19), has emerged as a highly pathogenic agent and has spread globally. The development of effective and

safe vaccines against this virus has been extremely fast.³ Of the many candidates, currently two RNA-based COVID-19 vaccines have been granted emergency use and marketing authorisation by the relevant regulatory agencies in North America and Europe and are being used worldwide. A third vaccine (AZD1222, Oxford–AstraZeneca) has currently been approved for use in the UK. Initial efficacy and safety data for both BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) vaccines have been published^{4,5} and product monographs including relevant information from the trials are available.

As vaccination campaigns kick off worldwide, and with several billion doses predicted to be administered in the near future,⁶ it is likely that a sizeable number of adverse events will be observed. Hence, the aim of this study was to research and compare the reported orofacial adverse effects of two COVID-19 vaccines. Dentists' knowledge of these orofacial manifestations will improve recognition, management and reporting of vaccine-related adverse effects.

2 | MATERIALS AND METHODS

Product monographs, Product Information (PI) and Consumer Medicine Information (CMI) for the BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) vaccines were accessed from the following regulatory authorities: US Food and Drug Administration (FDA), Health Canada, European Medicines Agency (EMA)/European Commission and UK's Medicines and Healthcare products Regulatory Agency (MHRA). Details and relevant websites are reported in Table S1. Reported side/adverse/undesirable effects concerning the orofacial region were extracted and tabulated.

3 | RESULTS

3.1 | Terminology

Information leaflets intended for use of non-healthcare professionals were referred to as Fact sheet for the recipients and caregivers (US), Patient Medication Information (Canada), Information for the user (EU) and Information for UK recipients (UK). Product Information for healthcare professionals was identified as Fact sheet for vaccination providers (US), Health Professional Information (Canada), Summary of product characteristics (EU) and Information for Healthcare Professionals (UK) (Table S1).

3.2 | Differences in reporting orofacial adverse effects between countries

Both vaccines were associated with potential orofacial adverse effects. Rare (up to 1 in 1000 people) but serious allergic reactions causing swelling of the face, lips or tongue were reported (Tables 1 and 2). Description of localised orofacial adverse effects including

TABLE 1 List of orofacial adverse effects of BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) vaccines as reported in the information to patients/users

Vaccine	Country/region	Reported orofacial adverse effects
BNT162b2	United States	Swelling of face and throat
mRNA-1273	United States	Swelling of face and throat
BNT162b2	Canada	Swelling of the face, tongue or throat
mRNA-1273	Canada	Swelling of the face, tongue or throat
BNT162b2	EU	Rare: temporary one sided facial drooping ^a
mRNA-1273	EU	Swelling of your lips, face, or throat Rare: temporary one sided facial drooping (Bell's palsy); swelling of the face (in patients who have had facial cosmetic injections)
BNT162b2	United Kingdom	Rare: temporary one sided facial drooping ^a
mRNA-1273	United Kingdom	Very rare: swelling of the face or tongue Rare: temporary one sided facial drooping (Bell's palsy); swelling of the face (in patients who have had facial cosmetic injections)

^aSevere allergic reaction (unknown frequency) was reported without explicitly referring to orofacial manifestations.

facial drooping (Bell's palsy) was found, however these were not disclosed in the information for patients in US and Canada (Table 1). Swelling of the face in patients who have had facial cosmetic injections occurred exclusively with the mRNA-1273 vaccine but was only reported in the product information available in EU and UK.

3.3 | Consistency of product information for users and healthcare professionals

For EU and UK consumers, temporary one sided facial drooping/acute peripheral facial paralysis (Bell's palsy) and facial swelling were reported in the product information to both patients (Table 1) and healthcare professionals (Table 2). Conversely, US and Canada vaccine fact sheets for patients did not report these side effects. Bell's palsy was also not acknowledged in the Health Professional Information of Canada.

4 | DISCUSSION

Our study shows that COVID-19 vaccines have possible, albeit rare, orofacial side effects including Bell's palsy, facial swelling, and

Vaccine	Country/region	Reported orofacial adverse effects
BNT162b2	United States	Bell's palsy (facial paralysis)
mRNA-1273	United States	Bell's palsy, facial swelling (vaccine recipients with a history of injection of dermatological filler)
BNT162b2	Canada	None
mRNA-1273	Canada	Facial swelling
BNT162b2	EU	Rare: acute peripheral facial paralysis
mRNA-1273	EU	Rare: acute peripheral facial paralysis; facial swelling
BNT162b2	United Kingdom	Rare: acute peripheral facial paralysis
mRNA-1273	United Kingdom	Rare: facial paralysis; swelling of the face (in patients who have had facial cosmetic injections)

TABLE 2 List of orofacial adverse effects of BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines as reported in the information to healthcare providers^a

^aSevere allergic reactions were reported for all drugs without explicitly reporting orofacial symptoms such as swelling of the face or tongue.

swelling of the lips, face or tongue associated with anaphylaxis. There appear to be inconsistencies in the description of these effects in the information provided to patients and healthcare professionals. For example, patient information leaflets in North America do not report orofacial side effects except those related to allergic reactions.

In addition to systemic ADRs with orofacial manifestations such as anaphylaxis, both vaccines were associated with acute peripheral facial paralysis. Specifically, of the 73 799 volunteers (36 901 effectively receiving at least one vaccine dose) taking part in the two large phase 3 vaccine trials,^{4,5} eight cases of suspect Bell's palsy were reported, with a total of seven in the groups receiving a vaccine and one in placebo groups. The FDA concluded that currently available information was insufficient to determine a causal relationship with the vaccine because the cases in the vaccine groups did not differ from the frequency that is expected in the general population.⁷ This may explain why this adverse effect was not reported in the information to users in the US.

There were two serious adverse events of facial swelling occurring only in the mRNA-1273 vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported 1 and 2 days after vaccine injection and was likely related to vaccination according to MHRA (UK).⁸ However, no mention was made of this reaction in package leaflets in the US and Canada.

In general, we found that description of ADRs was more difficult to find in the US versions of product information sheets. Conversely, information for healthcare professionals in Europe and the UK reported a tabulated list of adverse reactions and their frequency, and were classified according to MedDRA system organ class.

Unlike previous studies,⁹ we assessed orofacial drug-related adverse effects as reported both in the registered drug company full product information/monograph as well as in the package leaflet containing patient/consumer information. We believe that this is a more comprehensive approach and, in agreement with this view, our

study found that some information was not explicitly disclosed to users. It is to note that diseases were included in our list only when the orofacial manifestations were explicitly stated, therefore, it is likely that the occurrence of oral ADRs was underreported. For example, common ADRs such as muscle pain, joint pain and enlarged lymph nodes may have manifested in the head and neck region and hence were not captured in the available reports.

In conclusion, we found that both BNT162b2 and mRNA-1273 COVID-19 vaccines are associated with orofacial ADRs and that there is heterogeneity in the description of these adverse effects worldwide.

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The author declares no conflicts of interest.

AUTHOR CONTRIBUTION

Nicola Cirillo, conceptualization; data curation; formal analysis; investigation; methodology; writing-original draft.

PEER REVIEW

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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