

Otolaryngology adverse events following COVID-19 vaccines

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Abstract. – OBJECTIVE: Since the outbreak of COVID-19 pandemic, the international scientific community aimed at developing a vaccine to protect against the infection and prevent serious forms of the disease. To date, various adverse events of COVID-19 vaccines have been reported, mostly mild to moderate.

MATERIALS AND METHODS: In this short communication, we reviewed available literature and described the most frequent otolaryngology adverse events reported after COVID-19 vaccination.

RESULTS: The most frequent adverse events following COVID-19 vaccine described in the literature are represented by audiovestibular symptoms, such as tinnitus, sudden sensorineural hearing loss, vertigo, and dizziness. Other side effects include facial nerve palsy, epistaxis, and oral manifestations (*lichen planus*, bleeding, ulcers, and vesicles).

CONCLUSIONS: COVID-19 vaccine is of utmost importance in limiting the spread of SARS-CoV-2. Otolaryngology-related side effects have been described, but none was severe or life threatening. The mechanisms underlying these effects are still mostly unknown.

Key Words:

COVID-19, Vaccines, Adverse events, Otolaryngology.

Introduction

The progressive spread of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has caused dramatic effects on national health care systems^{1,2}. Since then, the scientific community aimed at developing a vaccine to protect against the infection and prevent serious forms of the disease³. The first COVID-19 vaccine approved by European Medicines Agency (EMA) in December 2020 was developed by BioNTech Manufacturing GmbH (Mainz, Germany) and Pfizer Inc (New York, NY, USA). Afterwards, several vaccines have been developed: messenger RNA (mRNA) vaccines (mRNA-1273, Moderna) or

vaccines made using human and primate adenovirus vectors, like Ad26.COV2.S (Janssen - Johnson & Johnson) and ChAdOx1 nCov-19 (Oxford/AstraZeneca)⁴.

To date, various side effects of COVID-19 vaccines have been reported, mostly mild to moderate. This is the first article that reviews and comments the most frequent otolaryngology adverse events reported after COVID-19 vaccination.

Materials and Methods

Audiological and Vestibular Adverse Events

A few audiological and vestibular adverse events of COVID-19 vaccine have been reported in the literature. The audiovestibular post-vaccination adverse events reported in the Italian Drug Agency (AIFA) and in the UK Medicines and Healthcare Products Regulatory Agency (MHRA) databases include vertigo, dizziness, and tinnitus, with an overall incidence of 0.15% for AIFA and 0.41% for MHRA⁵.

Parrino et al⁶ reported three cases of tinnitus after BNT162b2 mRNA-vaccine injection with normal hearing at the pure tone audiometry and no abnormalities at brain MRI.

Formeister et al⁷ described several cases of sudden sensorineural hearing loss (SSHL) reported in the Centers for Disease Control and Prevention (CDC) Vaccine Adverse Events Reporting System (VAERS) in the United States. Among a total of 86,553,330 vaccines doses, they described 40 cases (0.000046%) of SSLH with temporal association (onset of SSLH within 3 weeks from the vaccination) and high credibility of reporting (documentation of audiological findings or steroid treatment). Of them, 28 cases occurred after Pfizer vaccine and 12 cases after Moderna.

Jeong et al⁸ described 3 cases of SSLH after vaccination (2 after Pfizer-BioNTech and one after Oxford-AstraZeneca).

Table I. Audiological and vestibular adverse events reported in the literature after COVID-19 vaccination. SSHL: Sudden Sensorineural Hearing Loss.

Author	Vaccine	Tinnitus	SSHL	Vertigo	Dizziness
Ciorba et al ⁵ according to MHRA	Pfizer-BioNTech	153 (0.09%)	71 (0.04%)	1,406 (0.84%)	-
	Oxford-AstraZeneca	113 (0.17%)	25 (0.04%)	885 (1.33%)	-
	Moderna	12 (0.10%)	10 (0.09%)	90 (0.80%)	-
Ciorba et al ⁵ according to AIFA	Pfizer-BioNTech	1257 (0.49%)	335 (0.14%)	985 (0.38%)	-
	Oxford-AstraZeneca	3,727 (0.47%)	24 (0.08%)	78 (0.26%)	-
	Moderna	110 (0.37%)	724 (0.09%)	2,175 (0.27%)	-
Parrino et al ⁶	Pfizer-BioNTech	3	-	-	-
Formeister et al ⁷	Pfizer-BioNTech	-	28 (0.3%)	-	-
	Moderna	-	12	-	-
Jeong et al ⁸	Pfizer-BioNTech	-	2	-	-
	Oxford-AstraZeneca	-	1	-	-
Di Mauro et al ⁹	Pfizer-BioNTech	-	-	23	-
	Oxford-AstraZeneca	-	-	5	-
	Moderna	-	-	4	-
	Janssen-Johnson	-	-	1	-
Wichova et al ¹⁰	Pfizer-BioNTech	15	25	5	8
Kadali et al ¹¹	Pfizer-BioNTech	16 (1.99%)	-	20 (2.49%)	-

Di Mauro et al⁹ reported 30 patients with acute vertigo and 3 patients with dizziness occurring within 48 hours after COVID-19 vaccination. Among them, 9 cases had benign paroxysmal positional vertigo and in 7 cases there was no clinical evidence of vestibular or central impairment.

Wichova et al¹⁰ reported 25 patients with SSHL, 15 with tinnitus, 8 with dizziness and 5 with vertigo. Another study¹¹ performed to investigate the side effects of the Pfizer-BioNTech vaccine among healthcare personnel shown vertigo-like symptoms in 20 cases and tinnitus in 16 cases. Table I details the audio-vestibular disorders after COVID-19 vaccination reported in literature.

The pathophysiological mechanisms of audio-vestibular alterations after COVID-19 vaccination are unclear. Generally, reported cases present a history of atopy and autoimmune disorders; pathogenesis could therefore involve a hypersensitivity reaction, an abnormal autoimmune response and a vasculitis or vascular ischemia directing to the cochlea or vestibular system^{12,13}.

Table II. Facial nerve palsy reported in the literature after COVID-19 vaccination.

Author	Vaccine	Facial nerve palsy
Baden et al ¹⁴	Pfizer-BioNTech	4/38,000 (0.0105%)
Baden et al ¹⁴	Moderna	3/30,420 (0.0098%)
Falsey et al ¹⁵	Oxford-AstraZeneca	3/12,021 (0.025%)

Facial Nerve Palsy

Unilateral facial nerve palsy has been reported after COVID-19 vaccine. During the trial for Pfizer-BioNTech, 4 cases of facial palsy in a population of 38,000 persons (0.0105%) were reported by the FDA¹⁴. In Moderna vaccine phase 3 trials, 3 cases of Bell's palsy were reported in the arm of vaccine involving 30,420 participants (0.0098%)¹⁴. During the clinical trial for Oxford-AstraZeneca, 3 cases were reported among 12,021 participants (0.025%)¹⁵. Other cases have been reported afterwards; generally, patients were treated with high doses of steroids with the full recovery of facial function after 3-6 months¹⁶⁻¹⁸.

The pathogenesis of these events is unclear; it could be caused by the reactivation of latent dormant virus, as shown for the influenza and meningococcal vaccines^{19,20}.

Table II shows the results of phase 3 trials regarding facial nerve palsy after COVID-19 vaccination.

Other Adverse Events

Table III lists other otolaryngology adverse events reported in the literature after COVID-19 vaccine. They include epistaxis and oral cavity alterations.

A large population cohort study²¹ investigated bleeding episodes after COVID-19 vaccination and reported an incidence of nose bleeding of 0.3% after the first dose and 0.5% after the second dose of mRNA vaccines (Pfizer-BioNTech or Moderna). The incidence of epistaxis after adenovectored vaccines (Oxford-AstraZeneca) was

Table III. Other otolaryngology adverse events after COVID-19 vaccination.

Author	Vaccine	Epistaxis
Trogstad et al ²¹	Pfizer-BioNTech	9 (0.3%) first dose
	Moderna	15 (0.5%) second dose
	Oxford-AstraZeneca	106 (2.1%) first dose
Sharda et al ²⁴	Pfizer-BioNTech	<i>Lichen planus</i> (1 patient)
Riad et al ²⁵	Pfizer-BioNTech	Burning or bleeding gingiva 17/522 (3.3%) Blisters 11/522 (2.1%) Ulcers 10/522 (1.9%) Vesicles 8/522 (1.5%)

2.1%; the difference between these two vaccines was statistically significant²¹. The study hypothesized that both mRNA and adeno-vectored vaccines may cause an immune-mediated platelet destruction and thrombocytopenia²².

Some case reports²³ of cutaneous *lichen planus* have been reported after vaccination; among them, only one case regarded the oral cavity in a 35-year-old female without history of *lichen planus* or other dermatological pathologies after Pfizer-BioNtech vaccine²⁴.

Other side effects in the oral cavity after Pfizer-BioNtech vaccines have been reported by Riad et al²⁵; they included burning or bleeding gingiva (3.3%), blisters (2.1%), ulcers (1.9%) and vesicles (1.5%). In small number of cases angular cheilitis, halitosis and xerostomia have been reported. Generally, these events occurred 1-3 days after the vaccination.

Conclusions

COVID-19 vaccine is of utmost importance in limiting the spread of SARS-CoV-2. As of today, more than 10 billion doses have been administered worldwide and only a limited number of side effects have been reported. In the otolaryngology field, adverse events included audiovestibular alterations, facial palsy, and epistaxis. However, in no case they were severe or life threatening. The mechanisms underlying these effects are still mostly unknown.

Conflict of Interest

All authors declare no conflicts of interest.

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