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Tinnitus cases after COVID-19 vaccine administration, one institution's observations

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ARTICLE INFO	A B S T R A C T					
Keywords: COVID-19 vaccine SARS-CoV-2 vaccine Pandemic Tinnitus	Objective: After the role out of the COVID-19 vaccine in the United States, there has been increase in case reports of tinnitus attributed to the vaccine reported. We present our institution's experience over the initial 13 month period the vaccines were available. Study design: Retrospective chart review. Setting: Tertiary academic otology and general otolaryngology practice. Patients: Patients who received a COVID-19 vaccine and a tinnitus diagnosis code. Interventions: Observation, steroids (oral and intratympanic), diagnostic imaging and audiometry. Main outcome measures: Patients who received a COVID-19 vaccine in the time frame of 12/1/2020–12/31/21 with a diagnosis of tinnitus, an audiogram, and at least one visit with one of our Otolaryngologists were included in the study. Twenty-seven of the 1254 patients identified met these criteria. The patients ranged in age from 41 to 84 years old including seven male and twenty female patients. Sixteen received the Pfizer vaccine, seven received the Moderna vaccine and four patients received the Janssen vaccine. Conclusions: No definite correlation could be established between COVID-19 vaccine and tinnitus. Any concurrent sudden hearing loss should be treated as usual with oral or intratympanic steroids. Health care providers should be aware of the tinnitus onset and if new or recent onset, to refer for prompt audiogram and Otolaryngology evaluation.					

1. Introduction

As the COVID-19 vaccines were offered in the United States, we began to see an increase in patients presenting to our academic medical center and in the otolaryngology community with audiovestibular complaints after receiving one of the vaccines that are currently in use in the US and around the world [1–8]. In particular, our medical center has seen almost double the number of patients (n = 1847) with tinnitus complaints in the thirteen months after the three COVID-19 vaccines (Pfizer BioNTech, Moderna and Janssen) became available in the United States compared with the number of patients seen for tinnitus in 2019 (n = 1017). Here we aim to describe our cases of tinnitus after COVID-19 vaccination mainly to raise awareness of this possibility and prompt referral for audiology and otolaryngology evaluation for possible concurrent sudden sensorineural hearing loss and treatment as appropriate.

2. Methods

Institutional review board approval was obtained for this retrospective review (IRB # 21-2401) The hospital electronic medical record database was searched using the International Classification of Diseases-10 (ICD-10) diagnosis codes for tinnitus (H93.11-.13, H93.19, H93.A1, H93.A2, H93.A9) and COVID-19 vaccines for time period 12/1/20-12/ 31/21 seen at an academic medical center identified 1254 patients. Patients were either referred by their primary care physician or selfreferred for tinnitus. Patients were identified as having possible covid vaccine related tinnitus if they reported tinnitus onset within four weeks of any COVID-19 vaccine dose, no other attributable cause was identified, had an audiogram after onset of symptoms and at least one visit with our Otolaryngologists. The timeframe of onset of tinnitus within four weeks of a COVID-19 vaccine was chosen as a reasonable timeframe for a patient and provider to rule out other possible explanations for the onset of their tinnitus (such as a noise exposure, new medication, etc.). The charts were then examined for any history of prior otologic disease,

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comorbidities (in particular anxiety or depression), medications, head trauma, or prior history of noise exposure. Any head imaging obtained was also reviewed for any evidence of thrombosis or retrocochlear pathology.

3. Results

After chart review, 27 cases were identified with self-reported tinnitus onset or worsening shortly after receiving a COVID-19 vaccination within 25 min to 4 weeks of a COVID-19 vaccine. All of the patients who self-attributed their tinnitus to receiving a COVID-19 vaccination reported onset within this 4 week time frame and one patient was specific enough to indicate "25 min." Seven male patients and twenty female patients ranging in age from 41 to 84 years with a median of 59 were identified. The majority of the patients self-identified as white, non-Hispanic, with one patient identified as Asian, one as Hispanic, and three as black, non-Hispanic. The majority of patients received the Pfizer vaccine (n = 16). Seven patients received the Moderna vaccine and four patients received the Janssen vaccine. The tinnitus descriptions are summarized in Table 1.

Tinnitus onset in the Pfizer patients was after the 2nd dose in 50 % (8/16) of the patients, 25 % (4/16) after the 1st dose, and unclear for the remainder. The majority of Moderna vaccine patients reported tinnitus onset after the first dose (4/7). Two patients reported onset after the 2nd Moderna dose and onset after 1st or 2nd dose was unclear for one patient.

Tinnitus was present or worsened in both ears for 48 % (13/27) of patients. Almost half of the Pfizer patients 44 % (7/16) experienced tinnitus only in the left ear while 13 % (2/16) experienced symptoms only in the right ear. Three patients reported pulsatile tinnitus. For the Moderna patients, 57 % (4/7) patients experienced bilateral tinnitus, 29 % (2/7) left sided tinnitus, and 14 % (1/7) right sided tinnitus. Two Janssen patients experienced bilateral tinnitus, one had left sided tinnitus and the other had right sided tinnitus. None of the Janssen or Moderna patients reported pulsatile tinnitus.

Associated audiovestibular complaints such as vertigo, dizziness, imbalance or hearing loss were noted by some of the patients (8/16 Pfizer patients, 3/7 Moderna patients and 1/4 Jansen patients). As the type of dizziness (vertigo, lightheadedness or imbalance) was not specified in every chart reviewed, these were all put into a general category of "dizziness" for the purposes of this study (Table 2). Of the Pfizer patients, three experienced dizziness at the onset of the tinnitus, four noted hearing changes and one patient noted both hearing change and dizziness. All but one had a sudden hearing loss or at least an asymmetric hearing loss on the audiogram. One patient reported asymmetric ear fullness but had normal audiogram. Of the Moderna patients, one patient noted dizziness, one noted hearing change, and one noted both hearing change and vertigo. Only one Janssen patient noted dizziness at the onset of the tinnitus. All of the dizzy patients reported symptoms as brief and intermittent or with improvement within the study period. The median pure tone average (PTA) at presentation for the entire cohort was 20 dB for each ear. The range for the right ear was 7 to 75 dB and the range for the left ear was 5 to 58 dB.

Seven patients received oral and/or intratympanic steroid injections for their tinnitus (4 Pfizer, 2 Moderna and 1 Janssen). Three of these patients reported improvement in the tinnitus with intratympanic steroids (of these patients, 2 also received oral steroids as well). Results of steroid treatment are summarized in Table 2. Patient # 8 reported improvement in tinnitus after one oral steroid treatment with improvement in hearing after the second course of oral steroids. Two patients reported worsening of tinnitus while on or after an oral steroid (Patient # 7 had been on prednisone for sinus inflammation during the time of vaccination and reported worsening of the tinnitus). The patient with a normal audiogram had been given an oral steroid by the primary care provider for sharp body pain after the vaccination. Interestingly, while patient 14 did experience improvement in her right tinnitus with oral and intratympanic steroid treatment, she also noticed improvement in her self-reported longstanding left sensorineural hearing loss (SNHL) from childhood after the steroid treatment. Presumably this is due to the oral steroid treatment as the intratympanic steroids were delivered to the ear experiencing the new tinnitus (her right ear).

Fourteen patients had recent head imaging (within the last 2 years) available for review. Seven of these patients had MRI Brain CN 8 protocol for asymmetric hearing loss which did not reveal any internal auditory canal (IAC) or cerebellopontine angle (CPA) masses. One of these patients also had an MRA head due to left pulsatile tinnitus which did not reveal any abnormality. Two patients had MRI Brain CN 8 protocol done for asymmetric tinnitus (one patient had a slight asymmetry in word recognition score but otherwise normal audiogram, the other patient had a stable symmetric bilateral snhl with left tinnitus) which was also negative. One patient had an MRI/A head for migraine headaches (this patient had bilateral tinnitus but a normal symmetric audiogram). Two patients had recent MRI brain imaging for other reasons (one done for vision loss, the other for ataxia) and two patients had a head CT done for evaluation of headache within the past 2 years that did not reveal any apparent brain masses or significant findings.

The most common comorbidities noted were asthma (7/27), allergic rhinitis (6/27), gastroesophageal reflux disease (5/27), hypertension (5/27) anxiety (5/27) and depression (4/27). Two patients had a diagnosis of anxiety only, three had a diagnosis of anxiety and depression and one had a diagnosis of depression only.

Compared to the rest of the cohort, patients with anxiety and/or depression diagnosis were more likely to have received a steroid treatment for their symptoms (3/6 or 50 % versus 4/21 or 25 % of the remaining cohort). Only one of these patients had a normal audiogram at the time of evaluation, the remainder all had asymmetric hearing loss. PTA and symptoms for patients with anxiety and/or depression are listed in Table 2. There were four females and two males in this group with an average age of 53 (range 44–62). All the patients except for one self-identified as white, non-Hispanic (the remaining patient self-identified as black, non-Hispanic). PTA median at presentation for this group was 25 dB for the right ear, 20 for the left ear.

Overall, our department has seen almost double the number of patients (n = 1847 of which 1254 were vaccinated during that time frame) with tinnitus complaints in the thirteen months after the three COVID-19 vaccines became available in the United States compared with the number of patients seen for tinnitus in a similar timeframe before the pandemic (December 1, 2018-December 31, 2019) (n = 1017 of which 642 were vaccinated in the first 13 months of vaccine availability).

4. Discussion

With this retrospective chart review, we aim to characterize patients presenting with tinnitus within four weeks of receiving a COVID-19 vaccine. The study relies on patient self-report of tinnitus onset after COVID-19 vaccination as not all patients in our clinics are specifically

Table 1	1
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Tinnitus characteristics after COVID-19 vaccination.

	Onset after 1st dose	Onset after 2nd dose	Unsure	Right	Left	Bilateral	pulsatile
Pfizer	4	8	4	2	7	7	3
Moderna	4	2	1	1	2	4	
Janssen	4			1	1	2	

Fable 2
Finnitus with other associated audiovestibular symptoms and treatment after COVID-19 vaccination

	Vaccine	Tinnitus description	Dizziness at presentation	Hearing loss/change perceived at presentation	Anxiety or depression comorbidity?	PTA presentation R dB	PTA presentation L dB	PTA after steroid R dB	PTA after steroid L dB	Treatment	Improved hearing after steroid?	Improved tinnitus after steroid?
1	Р	R worsening	0	+	A & D	32	20	22	17	Oral and intratympanic steroid	Improved then worsened	Mild
2	Р	bilateral constant	0	+		10	8			0		
3	Р	right constant	0	+	Α	75	17	47	12	Oral and intratympanic steroid	Improved	Mild
4	Р	L constant	0	+		25	30			0		
5	Р	R constant	+	0		17	12			0		
6	Р	R worsening	+	0		40	38			0		
7 ^a	Р	L worsening	+	0		12	15	12	15	Oral steroid for sinus inflammation	No change	Worsened
8	Р	left pulsatile	0	0	D	13	45	13	32	Oral steroid \times 2	Improved after second course	After first steroid course
9	Р	Bilateral	0	0	А	7	5			0		
10	М	L worsening	0			50	53			0		
11 ^a	М	R worsening	0	0	A & D	12	12	12	12	Oral steroid for ear pain	No change	Mild
12	М	R worsening	0	0		65	42	50	42	Oral steroids	Improved	Worsened
13	J	bilateral constant	0		A & D	37	22			0	-	
14	J	R constant	0	0		30	47	27	38	Oral and intratympanic steroid	Improved in non tinnitus ear (left)	Mild improvement in tinnitus ear (right)

P = Pfizer, M = Moderna, J = Janssen.

A = anxiety.

D = depression.

^a Patients audiograms at time of presentation to our institution. These patients did not have audiograms before steroid treatment given by outside provider.

asked this question or are aware of the possible association with COVID-19 vaccination with resulting recall bias. Six patients have some comorbidities such as anxiety or depression (2 with diagnosis of anxiety alone, 3 with diagnosis of anxiety and depression and 1 with depression alone) which may cause tinnitus exacerbation during times of stress coincidental to the timing of the COVID-19 vaccination. The general public had increased anxiety and uncertainty during the pandemic and the remaining patients without clinical diagnosis of anxiety or depression were still likely to experience these symptoms during the pandemic.

Despite these limitations, COVID-19 vaccination related SNHL and tinnitus has been observed and treated in similar fashion to other idiopathic sudden sensorineural hearing loss (SSNHL) and/or tinnitus. Patients with documented SSNHL did receive oral and/or intratympanic steroid injections. Some of the patients with tinnitus but without documented SNHL received oral and/or intratympanic steroids with mixed results. While all 3 patients that received intratympanic steroid (\pm oral steroids) showed initial improvement in tinnitus, the tinnitus eventually worsened again in one patient. Of the patients that received oral steroids alone, half reported improvement in symptoms and the other half reported worsening of symptoms. Certainly steroids are indicated for cases of documented SSNHL [9], however, it is difficult to recommend oral or intratympanic steroids for tinnitus alone based on this study.

Possible mechanisms of COVID-19 vaccine related tinnitus differ between the two types of vaccines. The Janssen vaccine is a viral vector vaccine that uses an adenovirus to deliver instructions to make the COVID-19 spike protein. The Pfizer and Moderna vaccines are mRNA vaccines. The Janssen vaccine has been associated with thrombosis and thrombocytopenia syndrome. The tinnitus experienced by these patients is possibly related to thrombotic events. During initial clinical trial, six cases of tinnitus were reported in the vaccine group and none in the placebo group. All cases were labeled as non-serious [10]. In the phase 3 trials only 15 cases of tinnitus were reported in the vaccine group and 4 in the placebo group (vaccine group, n = 21,894; placebo, n = 21,882). In this study, none of the patients with imaging available had evidence of recent infarct or thrombosis on imaging. The thrombotic events could have been too small and isolated to be picked up on imaging.

Tinnitus after second dose of mRNA vaccines may coincide with the onset of Immunoglobulin G (IgG) production, as IgG antibodies to vaccine protein antigens first appear 10 to 14 days after priming (11) and a larger systemic reaction really occurs. In this study, of the patients that received an mRNA vaccine, 8 noted symptoms after the first dose and 10 noted symptoms after the second dose. Perhaps this correlates with antibody response variabilities among individuals as some patients may get a vigorous enough antibody response after just one dose while many need 2 doses to get an adequate antibody response.

Prior studies of incidence of audiovestibular complaints after COVID-19 vaccine reported low incidences of hearing loss (1.82 % after Moderna and 1.49 % after Pfizer vaccine) or tinnitus (1.88 % after Moderna, 1.26 % after Pfizer vaccine) arguing that the low rates of reported symptoms suggests that COVID-19 vaccination has little to no effect on the audiovestibular system [11]. New or worsening symptoms are often noted in response to negative health-related information including vaccinations [12] even if ultimately found to be coincidental to vaccination. Often this is exacerbated by already existing anxiety or fear worsened by being in the COVID-19 pandemic which may explain the almost doubling of office visits to our center with a diagnosis of tinnitus. Tinnitus itself has been known to be more severe and/or frequent with co-existing anxiety disorders [13]. The incidence of bothersome tinnitus is also known to increase in the presence of anxiety and/or depression symptoms [14]. In addition, the severity of tinnitus has been shown to decrease with improvement in depression symptoms [15].

5. Conclusions

We report our institution's cases and treatment of COVID-19 vaccine and tinnitus. A correlation cannot be proven with this retrospective study with such few cases, however, patients will still present to their medical providers with tinnitus with and without hearing loss after a COVID-19 vaccination. In cases of sudden hearing loss, treatment with oral and/or intratympanic steroids within the recommended time frame should be considered based on prior clinical practice guidelines [9] as causation by COVID-19 vaccination has not been proven. Improvement in tinnitus after steroids is not clearly shown and providers should use their discretion in each individual case.

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Conflicts of interest

No conflicts of interest.

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