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The impact of vaccination against SARS-CoV-2 infection on vestibular function and central compensation

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Abstract

Aim: The aim of this study was to evaluate the effects of SARS-CoV-2 vaccines on vestibular system. In addition, in this study we aimed to investigate the possible protective effects of vaccination on the vestibular system in people who recovered Covid-19.

Materials and Methods: Totally, 77 subjects were divided into four groups, and evaluated using computerized dynamic posturography (CDP), vestibular evoked myogenic potentials (VEMPs) and video head impulse test (v-HIT). The groups were as follows; Group 1; who had SARS-CoV-2 infection at least one year ago and have not been vaccinated at all. Group 2; who had SARS-CoV-2 infection at least one year ago and were vaccinated 5 times (2 doses of Sinovac and 3 doses of Biontech). Group 3; who had no known SARS-CoV-2 infection, and were vaccinated 5 times (2 doses of Sinovac and 3 doses of Biontech). Group 4; who had no known SARS-CoV-2 infection, and have not been vaccinated at all.

Results: The SOT values of (Covid-Vaccine-) group were better than the (Covid+Vaccine-) group ($p=0.001$), and no other significant difference was found between the groups ($p>0.05$). The v-HIT gains of the groups were not significantly different ($p>0.05$). On o-VEMPs, there was elongation in the N1 and P1 latencies in (Covid+Vaccine-) group compared to (Covid-Vaccine+) group. The amplitudes decreased in (Covid+Vaccine-) compared to (Covid-Vaccine-) ($p<0.05$). According to c-VEMP results, vaccination led to elongation in the P1 latencies and increased the P1-N1 amplitudes ($p<0.05$).

Conclusion: Both SARS-CoV-2 viral infection and vaccination may impact on vestibular system. The impact of vaccination seems on the saccule level. However, vaccination may limit or diminish the impact of SARS-CoV-2 on equilibrium, possibly by facilitating the central compensation.

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Introduction

Since December 2019, the new type of coronavirus, SARS-CoV-2, has become a serious world health problem. The virus could lead to fever, dry cough, sore throat, headache, shortness of breath, diarrhea, anosmia, taste changes, vomiting and abdominal pain [1–5]. However, neurological and vascular impact of the virus has been a major concern.

Although SARS-CoV-2 is primarily targeting the respiratory and circulatory systems, mounting data suggests that up to 30% of patients may experience neurological signs [6, 7]. Covid-19 individuals have had a variety of neurological symptoms including loss of consciousness, headaches, dizziness and vertigo [3, 6, 8]. The impact of SARS-CoV-2 on vestibular system was also reported previously [9].

The central and peripheral balance related systems enable to stabilize gaze during head movement, control the posture in the gravity field and adjust the position of the head on the body. This is performed by the integration of information conveyed from the visual, vestibular and proprioceptive systems.

The receptors of peripheral vestibular system are semicircular canals, utricle and saccule. The semicircular canals are sensitive to angular movements while the utricle and saccule are sensitive to linear movements [10]. The video head impulse test (vHIT) enables the evaluation of each

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semicircular canal separately, and gives information about the superior and inferior nerves [11]. The ocular vestibular evoked potentials (o-VEMP) provide information about the utricle and superior vestibular nerve, and the cervical vestibular evoked potentials (c-VEMP) provide information about the function of the saccule and inferior vestibular nerve [12]. The computerized dynamic posturography (CDP) help to evaluate the central and peripheral problems related to equilibrium [13, 14].

The use of messenger ribonucleic acid (mRNA) based vaccines becomes a novel method in the treatment of various infectious diseases and cancers due possibly to high efficacy, low side effects and low access costs [15]. World Health Organization (WHO) validated several SARS-CoV-2 vaccines for use [16]. Among these vaccines are Sinovac's CoronaVac vaccine, and the mRNA vaccines like BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna) [17, 18].

Recent studies suggest that the vaccines may have adverse effects such as redness, swelling and pain at the vaccine shot area, and headache, fatigue, muscle pain, fever, itching, nausea, vomiting, joint pain, chills, and also anaphylactic shock in rare cases [19]. Although, there are some reported cases of hearing loss and vertigo [17, 20] there is no comprehensive study that evaluates the possible protective effects of the vaccines on vestibular system.

The objective of this study was to evaluate the effects of SARS-CoV-2 vaccines on vestibular system. In addition, in this study we aimed to investigate the possible protective effects of vaccination on the vestibular system in people who recovered Covid-19.

Materials and Methods

The study was approved by the Ethical Committee of the University. An informed consent was taken from 77 subjects who participated in the study between November 2021 and March 2022. The ages of subjects ranged from 20 to 59 (mean 34±11,1) years. There were 41 males and 36 females. The SARS-CoV-2 positivity or negativity was confirmed according to specific PCR tests. The vestibular evaluations were performed two months after the last vaccination. The subjects were divided into four age and gender matched groups as follows;

Group 1 (Covid+Vaccine-) comprised of 37 subjects who had SARS-CoV-2 infection at least one year ago, and have not been vaccinated at all.

Group 2 (Covid+Vaccine+) comprised of 10 subjects who had SARS-CoV-2 infection at least one year ago, and were vaccinated against SARS-CoV-2 virus 5 times (2 doses of Sinovac and 3 doses of Biontech).

Group 3 (Covid-Vaccine+) comprised of 10 subjects who had no known SARS-CoV-2 infection, and were vaccinated 5 times against SARS-CoV-2 virus (2 doses of Sinovac and 3 doses of Biontech).

Group 4 (Covid-Vaccine-) or controls comprised of 30 subjects who had no known SARS-CoV-2 infection, and have not been vaccinated at al.

Vestibular evaluation

The subjects in the groups were evaluated using c-VEMP, o-VEMP, vHIT and CDP tests. The c-VEMPs recorded from the sternocleidomastoid muscle in response to an auditory stimulus and represented the inhibitory vestibulocollic reflex. It showed the ipsilateral saccule and inferior vestibular nerve's function. The o-VEMPs recorded from the inferior oblique muscle in response to an auditory stimulus, and the test reflected the functioning of the superior vestibular nerve and the contralateral utricle [21]. The VEMP (Interacoustics Eclipse, Denmark) tests applied with 7.1 rate and 500 Hz Tone Burst stimulus at 100 dB nHL and 2 waves were recorded for each ear. Both O-VEMP and C-VEMP tests were assessed by their amplitudes (Microvolt) and latencies (milliseconds).

The v-HIT identified saccades in response to high-acceleration head movements and quantified vestibulo-ocular reflex (VOR) gains to offer information about each semicircular canal. This test showed the functions of semicircular canals, vestibular and ocular motor nuclei in the brainstem, and extra-ocular muscles [22]. The vHIT (Otometrics ICS Impulse v-HIT, Denmark) applied to the participants for each semicircular canal. The average values of the 20 responses used for the analysis to measure each semicircular canal gain.

CDP was used to measure the relative contributions of sensory systems to postural regulation in the upright position. The test could reveal the existence of postural instability and assisted in determining which sensory system was affected. The CDP sensory organization test (SOT) was used to evaluate the sensory inputs maintaining postural stability and monitored central compensatory state. The subject's capacity to analyze and coordinate information from the somatosensory, visual, and vestibular systems was also assessed by the SOT. Individuals were tested under six different situations (eyes open/closed, sway/fix referred visual surround, and sway/fix referenced support surface) throughout three trials [23]. SOT (Natus Smart Balance Manager, California, USA) analysis has done based on composite scores. However, visual, vestibular, somatosensorial and preference scores were also evaluated.

Statistical analysis

Data were processed using the SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA) computer software. Descriptive statistics of all parameters were made. The

Table 1. SOT composite score statistics of the groups on CDP.

Group	Groups compared	P value
Covid + Vaccine -	Covid + Vaccine +	NS
	Covid - Vaccine +	NS
	Covid - Vaccine -	**.001**
Covid + Vaccine +	Covid - Vaccine +	NS
	Covid - Vaccine -	NS
Covid - Vaccine +	Covid - Vaccine -	NS

Table 2. VEMP statistics.

		o-VEMP			c-VEMP		
Group	Groups compared	N1 latency	P1 latency	N1-P1 amplitude	P1 latency	N1 latency	P1-N1 amplitude
Covid + Vaccine -	Covid + Vaccine +	NS	NS	NS	NS	**.023**	**.000**
	Covid - Vaccine +	**.000**	**.008**	NS	NS	**.001**	**.000**
	Covid - Vaccine -	NS	NS	**.000**	NS	NS	**.000**
Covid + Vaccine +	Covid - Vaccine +	NS	NS	NS	NS	NS	**.000**
	Covid - Vaccine -	NS	NS	NS	NS	**.003**	**.000**
Covid - Vaccine +	Covid - Vaccine -	NS	NS	NS	NS	**.000**	**.000**

normal distribution of the data was evaluated with the Shapiro – Wilk test, assuming a significance value of $p<0.05$.

ANOVA tests were used to evaluate the equilibrium status of the groups after Covid 19 and/or vaccination and to determine the possible effects. For further comparisons, Tukey HSD was used when the variances were homogenous, and Tukey HSD was used when the variances were not homogenous. Tamhane was used. Independent Samples T Test was used as a parametric test among variables with normal distribution, especially in the investigation of the protective effect of vaccination between the groups. Mann-Whitney U test was used as a nonparametric test between variables that did not show normal distribution. The significance value was accepted as $p<0.05$. The GPower* analysis of statistical measurements demonstrated that the actual power was 0.95.

Results

The SOT composite score values of (Covid-Vaccine-) group were better than the (Covid+Vaccine-) group ($p=0.001$) whereas there was no significant difference between the other groups ($p>0.05$), suggesting negative impact of SARS-CoV-2 infection on SOT composite score results and protective effect of vaccine independent of SARS-CoV-2 infection (Figure 1) (Table 1). The v-HIT results that shows VOR gains of the groups were not significantly different for each semicircular canals ($p>0.05$), suggesting that the semicircular canals were spared independent of infection or vaccination. There was elongation in the N1 and P1 latencies of o-VEMPs in (Covid+Vaccine-) group compared to (Covid-Vaccine+) group. There was also amplitude decrease in (Covid+Vaccine-) group compared to (Covid-Vaccine-) group ($p<0.05$). There was no difference between the other comparisons. The results may suggest

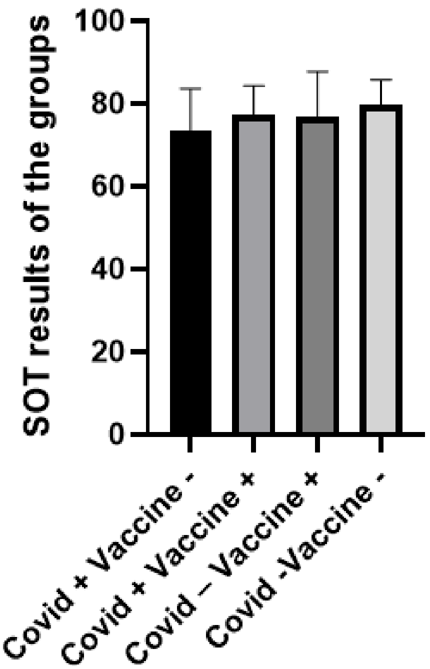

Figure 1. SOT composite score results of the groups.

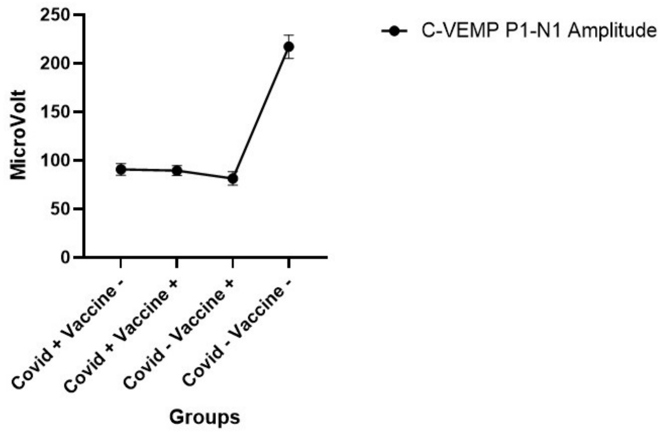

Figure 2. C-VEMP amplitudes of the groups.

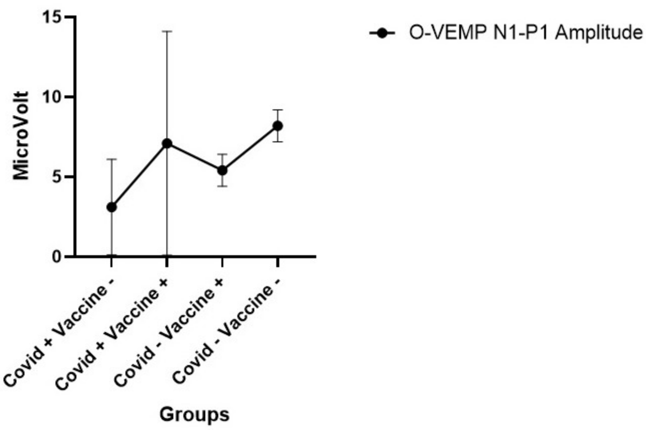

Figure 3. O-VEMP amplitudes of the groups.

a protective effect of vaccine in the subjects exposed to viral infection (Figure 2 and Figure 3). According to c-VEMP results, vaccination lead to elongation in the P1 latencies and increased the P1-N1 amplitudes. The negative impact of vaccination on c-VEMP results was more prominent than in SARS-CoV-2 infection (Table 2).

Discussion

The SARS-CoV-2 infection may cause balance problems. At least ten percent of the patients infected with SARS-CoV-2 virus may define some sort of balance problems like vertigo or dizziness [24, 25]. The objective vestibular test batteries like VEMPs and v-HIT tests also showed a variety of abnormalities attributable to SARS-CoV-2 infections [9, 26–28]. Decreased SOT scores were also reported on CDP testing, which has been considered one of the important tools used to evaluate equilibrium and vestibular compensation [29].

According to one of the recent studies, almost one-fourth of the patients had dizziness after vaccination against SARS-CoV-2 [20]. A case of vestibular neuritis was also reported three days after SARS-CoV-2 vaccination [18]. A vestibular hypofunction was also reported in the patients who had vestibular symptoms after vaccination [29].

The SOT scores on CDP in our study, the subjects who had no SARS-CoV-2 infection nor its vaccine scored better than the subjects who had the viral infection without vaccination. We thought that these findings were compatible with previous results. That is, the viral infection could have a negative impact on equilibrium. However, the SOT scores in the vaccinated groups were similar to controls. Therefore, we may suggest that vaccination may have a protective role in central compensation of equilibrium. It may also be speculated that this protective role of vaccination might be independent of previous SARS-CoV-2 infection.

In our study, the v-HIT results of the groups were not significantly different, suggesting that semicircular canals in the inner ear are spared in SARS-CoV-2 infection, and there is no impact of vaccination on the results.

According to o-VEMP test results, the N1 and P1 latencies elongated in (Covid+Vaccine-) group compared to (Covid-Vaccine+) group. There was decreased amplitudes in (Covid+Vaccine-) group compared to (Covid-Vaccine-) group. These results also suggest the negative impact of SARS-CoV-2 infection on vestibular system, and protective role of vaccination.

Despite the aforementioned findings, c-VEMP results in this study revealed a negative impact of vaccination on vestibular system. This impact of vaccination was more prominent compared to SARS-CoV-2 infection. This condition may explain dizziness problems, if any, experienced by the subjects who were either vaccinated or infected with SARS-CoV-2 virus. In the present study, although vHIT responses were not affected, the effects observed in VEMP responses suggest that contrary to our expectations, Covid infection causes peripheral organ involvement rather than nerve involvement, but the effects of vaccines cannot be fully interpreted due to the low sample size and the use of different vaccines. However, in the light of overall vestibular test results, it is plausible to say that vestibular abnormalities occurring in SARS-CoV-2 infections could be compensated better by means of vaccination. Despite its protective role on equilibrium, especially in the central compensation, the vaccines could impact on saccule in the inner ear.

Conclusion

In conclusion, both SARS-CoV-2 viral infection and vaccination may impact on vestibular system. The impact of vaccination seems on the saccule level. However, vaccination may limit or diminish the impact of SARS-CoV-2 virus on equilibrium, possibly by facilitating the central compensation.

Ethical approval

The study was approved by the Ethical Committee of the Istanbul Medipol University(E-10840098-772.02-785).

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