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ORIGINAL ARTICLE

Vestibular Evoked Myogenic Potential Responses in Patients with Systemic Lupus Erythematosus

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Abstract

Introduction: To evaluate vestibular evoked myogenic potential (VEMP) test responses in patients with systemic lupus erythematosus (SLE).

Methods: Thirty patients who were followed up for SLE in rheumatology clinic were referred for the cVEMP test. A complete head and neck examination, neurotological examination, pure tone audiometry, and tympanogram test were performed for all patients. Seven patients with neurotological, acute and chronic otitis media, hearing the loss in pure audio audiometry, abnormal tympanogram, head and neck trauma, and disease and drug use history that could affect the vestibular system were excluded. Thirty healthy controls without medical therapy and systemic disease history that could affect the vestibular and auditory system and with normal pure tone audiometry and normal tympanogram were included in the study. Both the patient and healthy control groups were tested for cVEMP from 100 dB to 85 dB stimulation. The amplitude and latency values of cVEMP responses of the control group and SLE group were compared.

Results: No response was obtained in five patients in the SLE group, whereas all frequency responses were obtained in all the controls. There was a decrease in the amplitudes and latency prolongation in the SLE group compared to the control group.

Discussion and Conclusion: Autoimmune diseases have been previously shown to contribute to the pathophysiology of endolymphatic hydrops. SLE is an autoimmune disease and can lead to saccular hydrops, which can be demonstrated by the cVEMP test.

Keywords: Endolymphatic hydrops; systemic lupus erythematosus; VEMP.

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease affecting many organs and systems, such as skin, joints, lungs, and kidneys [1, 2]. Sensory neural hearing loss, tinnitus, and vestibular findings can be seen in patients with SLE, although otitic diseases are not among the diagnostic criteria [1, 2]. Vestibular symptoms are common in patients with SLE; in a questionnaire study, vestibular symptoms, such as vertigo, were significantly higher in patients with SLE than in the controls [3, 4]. The vestibular sensorial epithelium is located in the saccular macula, utricular macula, and crista ampullaris in each semicircular canal. The peripheral sensory epithelium comprises type 1 and type 2 hair cells along with supporting cells [5, 6]. Histopathological studies have shown that type 1 hair cell density in saccule, utricle, and semicircular canal in patients with SLE decreased significantly compared

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to the control group, but there was no difference in type 2 hair cell density [7]. Some causes of endolymphatic hydrops are trauma, viral infections, and autoimmune diseases [8]. In our study, we aimed to reveal the presence of saccular hydrops by the cVEMP test in the autoimmune disease SLE.

Materials and Methods

Thirty-seven patients who were followed up for SLE in the rheumatology clinic were referred to us for the cVEMP test. A complete head and neck examination, neurotological examination, pure tone audiometry, and tympanogram test were performed on all patients. Seven patients with neurotological, acute and chronic otitis media, hearing loss in pure tone audiometry, abnormal tympanogram, head and neck trauma, and disease and drug use history that could affect the vestibular system were excluded. Thirty healthy controls and 30 patients with SLE were included in the study. Of the 30 patients with SLE, 28 were female and 2 were male. The mean age of the patients was 41.05±4.96. Of the 30 healthy controls, 25 were female, five male. All patients included in the study were subjected to a bilateral cVEMP test at 500 Hz frequency. The cVEMP test was performed starting from 100 dB stimulation to 85 dB stimulation level. In the study, stimuli at 100 dB were taken into consideration. The amplitudes and latencies of the cVEMP responses in the 100 dB stimulus of the SLE group were compared between the control group and the control group. The study was approved by the local ethics committee (Protocol number: B.10.1.TKH.4.34.H.GP.0.01/58).

Stimulus Design and Recording Setup (cVEMP Recording)

The stimulus profile was gated with 2 ms rise time, 2 ms fall time, 2 ms plateau time, and 5.1 Hz repetition rate with 500 Hz tone burst. Frequencies were presented 50–150 times with the aim of average responses. The signal of EMG was bandpass-filtered (10–750 Hz) and recorded between the range of 10 ms before stimulus start and 60 ms afterward. VEMP recordings were performed using an Eclipse EP 25 VEMP evoked potential system (Interacoustics AS, Assens, Denmark). The impedance of electrodes was ≤3 kΩ.

Statistics Analysis

IBM SPSS Statistics 22 (SPSS IBM, Turkey) programs were used for statistical analysis. Power analysis was performed to determine the minimum sample width required to compare two groups and two ratios. The normal distribution suitability of the parameters was evaluated by the Shapiro–Wilks test. Student t-test was used to compare the descriptive statistical methods (mean, standard deviation) as well as the two-group comparisons of the parameters with normal distribution in the comparison of quantitative data. Significance was assessed at $p<0.05$ level.

Results

Thirty SLE patients and 30 healthy volunteers were included in the study. There were 30 patients and 30 healthy controls. Of the 30 patients, 28 were female and two were male. The age of the patients ranged from 27 to 48 years, and their mean age was 41.05±4.96 (Table 1).

Of the 30 healthy controls, 26 were female, and 4 were male. The age of the healthy controls ranged from 26 to 49 years, and the mean age was 41.6±5.18 (Table 1).

The right and left 100 dB nHL P13 and N23 latency values in the control group were significantly lower than those in the SLE group ($p<0.05$) (Table 2).

Table 1. Demographic characteristics of patients

Patients with SLE	**Sex**	**Age mean±SD**
Female	28	41.05±4.96
Male	2	
Control group	**Sex**	**Age mean±SD**
Female	26	41.6±5.18
Male	4	

SD: Standard deviation; SLE: Systemic lupus erythematosus.

Table 2. Evaluation of study parameters between groups

	Healthy group Mean±SD	**SLE group Mean±SD**	**p**
Right 100 dB P13 Latency	13.5±0.27	16.62±0.7	0.001*
Right 100 dB N23 Latency	23.39±0.35	26.97±0.72	0.001*
Right 100 dB P13-N23 Amplitude	161.21±42.95	90.69±20.44	0.001*
Left 100 dB P13 Latency	13.46±0.29	16.95±0.51	0.001*
Left 100 dB N23 Latency	23.32±0.3	26.26±0.24	0.001*
Left 100 dB P13-N23 Amplitude	139.93±21.25	78.28±15.38	0.001*

Student t Test; *$p<0.05$; dB: Decibel.

The right and left 100 dB P13-N23 amplitude values in the control group were found to be significantly higher than those in the SLE group ($p<0.05$) (Table 2).

Discussion

SLE is an autoimmune connective tissue disorder affecting many organs and systems. The etiology of this disease is not entirely known, and clinical and laboratory findings are diverse and variable [9]. SLE tends to show relapses and remissions, and it may present with symptoms not specific to the disease, such as fatigue, fever, muscle aches, and weight loss, as well as organ and system symptoms that are specific to the disease [9]. SLE is a complex disease, usually involving severe clinical manifestations and organ involvement [10].

The 500 Hz frequency cVEMP test is the most sensitive indicator to detect changes [11]. High levels of circulating DNA-anti-DNA immune complexes exceed the clearing capacity of the reticuloendothelial system (RES), and these immune complexes then accumulate in various tissues, including the glomerulus, causing local damage there [12]. Autoimmune inner ear diseases can be primary or secondary [13]. While primary diseases are limited to the inner ear, many non-specific autoimmune diseases, such as SLE, rheumatoid arthritis, Sjogren syndrome, polyarteritis nodosa, Vogt Koyanagi Harada syndrome, chronic lymphocytic thyroiditis, Cogan syndrome, Behçet syndrome, sarcoidosis, granulomatosis with polyangiitis, ulcerative colitis, and relapsing polychondritis, affect other organs and tissues as well as the inner ear [14, 15]. Vestibular complications are quite common in patients with SLE [16]. One study showed that the incidence of abnormal findings on electronystagmography in patients with SLE was significantly higher than that in healthy controls [17]. Another study showed that pediatric patients with SLE also had vestibular disorders, as confirmed by videonystagmography and computerized dynamic posturography [18]. Derebey at al. [19] showed that circulating immune complexes pass through to the endolymphatic sac circulation and stria vascularis, leading to increased inflammation and permeability and impaired fluid balance. Takeda et al. [20] performed a study examining plasma arginine vasopressin (p-AVP). Endolymphatic area showed increased p-AVP levels and increased endolymphatic volume when endolymphatic p-AVP increased. In this study, guinea pigs were sensitized with an allergic stimulus. Histological evaluation was performed at various points and also post-provocation. Cross-sectional area was used when endolymphatic volume changes were compared to animals injected with saline. In a second experiment, subjects were given oral administration of pranlukast hydrate, a leukotriene antagonist. Before antigen exposure, subjects were given saline and compared with subjects who were given pranlukast. EH was observed in each turn of cochlea after antigen exposure in subjects not given pranlukast as a prophylactic, whereas, EH was not seen in the animals given pranlukast. p-AVP levels were elevated in the sensitized group; however, among those pre-medicated with pranlukast, p-AVP levels were significantly lower. This study showed that a systemic immunological disease affects the inner ear and that prophylactic treatment can suppress it.

A strong association between SLE and balance disorder has been suggested, but vestibular system involvement in patients with SLE has not been fully examined [21]. The morphologic, physiologic, and developmental characteristics of vestibular sensory cells (type 1 and type 2 hair cells) are remarkably different [22, 23].

It has been found that there is a significant difference between type 1 and types 2 hair cell loss in patients with SLE. It is thought that this condition is caused by the important physiological differentiation of type 1 and type 2 cells [7]. Histopathological studies on SLE specimens have shown that type 1 hair cells are significantly affected and that a systemic diseases such as SLE can lead to vestibular system involvement. Demonstration of vestibular type 1 hair cell loss may provide a pathological basis to explain balance problems that patients with SLE encounter [7]. Histopathologically, the intensity of type 1 and type 2 hair cells was not significantly correlated with the age of the patient or the duration of SLE [7]. Based on this information, we aimed to decipher asymptomatic findings of saccular hydrops in SLE. Patients in the SLE group were in remission and did not have vestibular symptoms. Since the cVEMP test allows us to obtain a better and more effective response at high stimulation and at 500 Hz frequency in order to determine saccular hydrops, we assessed the patients at a frequency of 500 Hz and stimuli at 100 dB. Previous histopathological and videonystagmography studies have demonstrated that structures related to balance are affected in both symptomatic and asymptomatic ears of patients with SLE. In our study, we found that latency is prolonged and amplitude decreased in patients with SLE.

Conclusions

SLE can affect the vestibular system in the inner ear, and this can be demonstrated by the VEMP test.

Ethics Committee Approval: The study was approved by the local ethics committee (Protocol number: B.10.1.TKH.4.34.H.GP.0.01/58).

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Conflict of Interest: None declared.

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