Vestibular-Evoked Myogenic Potential Responses in Patients with Allergic Rhinitis

Alerjik Rinit Hastalarında Vestibüler Uyarılmış Miyojenik Potansiyel Yanıtları

Ahmet BAKİ[1], Muhammet YILDIZ[2]

[1]Ümraniye Training and Research Hospital Ear, Nose and Throat Clinic, Istanbul, Turkey
[2]Rize State Hospital Ear, Nose and Throat Clinic, Rize, Turkey

Correspondence Address
Yazışma Adresi

Ahmet BAKİ
Ümraniye Eğitim ve Araştırma Hastanesi Kulak Burun Boğaz Hastalıkları Kliniği, İstanbul, Turkey
E-mail: dr.ahmet170@gmail.com

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Ahmet BAKİ
ORCID ID: 0000-0003-2851-0849
Muhammet YILDIZ
ORCID ID: 0000-0002-1771-7345

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ABSTRACT

Objective: To evaluate cervical vestibular-evoked myogenic potential (cVEMP) test responses in patients with allergic rhinitis (AR).

Material and Methods: Fifty patients with an AR diagnosis and anamnesis, physical examination, and skin prick test results were divided into two groups as mild to moderate-severe AR. Twenty-five healthy control subjects with a negative skin prick test were also included in the study. There were 25 subjects each in the healthy control group, mild AR group and moderate-severe AR group. Bilateral cVEMP test was administered using 100 dB nHL stimulation at 500 Hz frequency. The latency and amplitude values were compared between the control group and mild AR group, control group and moderate-severe AR group, and mild AR group and moderate-severe AR group.

Results: The right-left P13 and N23 latency values of the healthy control group were statistically significantly lower than those of the mild AR group and moderate-severe AR group. The right-left P13 and N23 latency values of the mild AR group were statistically significantly lower than those of the moderate-severe AR group. The right and left P13-N23 amplitude values in the healthy control group were found to be statistically significantly higher than in the mild and moderate-severe AR group. The right and left P13-N23 amplitude values of the mild AR group were statistically significantly higher than those of the moderate-severe AR group.

Conclusion: In patients with allergic rhinitis without vestibular complaints, the cVEMP test may detect saccular dysfunction. Further studies with larger groups are needed to verify our findings.

Key Words: Allergic rhinitis, Cervical vestibular-evoked myogenic potential, Endolymphatic hydrops

ÖZ

Amaç: Alerjik rinit (AR) hastalarında servikal vestibüler uyarılmış miyojenik potansiyel (cVEMP) test yanıtlarını değerlendirmek.

Gereç ve Yöntemler: Anamnez, fizik muayene ve deri prick testi sonuçları birleştirilerek AR tanısı konulan 50 hasta hafif ile orta-ağır AR olan hastalar olarak iki gruba ayrıldı. Çalışmaya deri prick testi negatif olan 25 sağlıklı kontrol grubu dahil edildi. Yirmi beş sağlıklı kontrol grubu, 25 hafif AR grubu ve 25 orta-ağır AR grubu vardı. Bilateral cVEMP testi, 500 Hz frekansta 100 dB nHL stimülasyonu ile uygulandı. Kontrol grubu ile hafif AR grubu, kontrol grubu ile orta-ağır AR grubu, hafif AR grubu ile orta-ağır AR grupları arasında latans ve amplitüd değerleri karşılaştırıldı.

Bulgular: Sağlıklı kontrol grubunun sağ-sol P13 ve N23 latans değerleri, hafif AR grubu ve orta-ağır AR grubuna göre istatistiksel olarak anlamlı derecede düşüktü. Hafif AR grubunun sağ-sol P13 ve N23 latans değerleri orta-ağır AR grubuna göre istatistiksel olarak anlamlı derecede düşüktü. Sağlıklı kontrol grubundaki sağ ve sol P13-N23 amplitüd değerleri, hafif ve orta-ağır AR grubuna göre istatistiksel olarak anlamlı derecede yüksek bulundu. Hafif AR grubunun sağ ve sol P13-N23 amplitüd değerleri orta-ağır AR grubundan istatistiksel olarak anlamlı derecede yüksekti.

Sonuç: Alerjik riniti olan ve vestibüler şikayetleri olmayan hastalarda cVEMP testi sakküler disfonksiyonu saptayabilir. Bulgularımızı doğrulamak için daha büyük gruplarla daha fazla çalışmaya ihtiyaç vardır.

Anahtar Sözcükler: Alerjik rinit, Servikal vestibüler uyarılmış miyojenik potansiyel, Endolenfatik Hidrops

INTRODUCTION

Allergic rhinitis (AR) is an inflammatory disease of the nasal mucosa associated with an allergen, and is accompanied by nasal discharge, nasal obstruction and sneezing symptoms (1). AR is classified according to its duration and severity (2). The symptoms of AR are classified as intermittent when they occur less than four days per week or continue for less than four weeks, and as persistent when they occur more than 4 days per week or continue for longer than 4 weeks (2). AR is defined as mild when there are no symptoms such as sleep disturbance, disruption of daily activities, disruption of sports and hobbies, and loss of school and labor. If one or more of these parameters are present, it is defined as moderate to severe AR (2).

Meniere disease (MD) is a disorder of the inner ear that causes vertigo attacks, fluctuating hearing loss, tinnitus, and aural fullness. A characteristic pathological finding of MD involves endolymphatic hydrops (EH) in the inner ear (3). Trauma, infection, autoimmune and other causes are accused in the etiopathogenesis (4). The presence of immunoreactive H1, H2, and H3 receptors has been demonstrated, and may be the target of an allergic reaction in the endolymphatic sac cells (5). Studies have recently shown that allergies are also involved as one of the etiologic causes of MD (6).

In recent years, the cVEMP test has been used to detect EH besides the anamnesis, physical examination, pure tone audiometry, electrocochleography and imaging methods such as magnetic resonance imaging (MRI) (7,8). In patients with EH, it has previously been demonstrated that cVEMP responses cannot be obtained in 54% of the affected ears (9). The aim of our study was to investigate the cVEMP responses in patients with AR, taking into account the role of allergic diseases in the etiopathogenesis of EH.

MATERIALS and METHODS

A complete head and neck examination, neurological examination, pure tone audiometry, tympanogram and skin prick tests were performed in 85 patients who complained of nasal obstruction, nasal discharge, sneezing, and itching. A total of 35 patients whose signs were incompatible with the anamnesis, physical examination and skin prick test, or who had neurological and otologic disease such as acute and chronic otitis media, hearing loss in pure tone audiometry, or an abnormal tympanogram were excluded from the study. Fifty AR patients diagnosed by anamnesis, physical examination and skin prick test results were divided into 2 groups as mild and moderate-severe AR according to the classification of Allergic Rhinitis and its Impact on Asthma. Twenty-five healthy control groups with negative skin prick tests were also included in the study. In total, 75 cases were included in the study with 25 patients in each group. The bilateral cVEMP test was administered to all patients. The latency and amplitude values were compared between the control and mild AR groups, control and moderate-severe AR groups, and mild AR and moderate-severe AR groups. In the skin prick tests of the patients, allergens against at least two allergen substances such as house dust mite, grass mixture, adhesive grass, mushroom mixture, wild mix, hazelnut, cat feather, whole egg, cocoa, tomato, banana, and chicken were detected. Informed consent was obtained from all patients, and the study was approved by the Local Ethics Committee (B.10.1.TKH.4.34.H.GP.0.01/51).

cVEMP Recording:

The tests were performed by a single researcher in a quiet room. Electrodes were placed on the forehead (ground electrode), on the central parts of each sternocleidomastoid muscle (SCM) (active electrodes), and on the sternal part of the SCM (reference electrode). The measurements were taken while participants were in the sitting position. Monaural stimuli were given, respectively, to the right and left ear, and ipsilateral electromyographic activity of the SCM was recorded. During the test, the impedance of the electrodes was <500 Ω. A tonal stimulus (500 Hz) was administered to both sides (100 dB) to test for cVEMPs in both ears. The cVEMP responses (an initial positivity [p13] followed by negativity [n23]) were recorded for each test. P13-N23 interpeak latencies and amplitudes were measured.

Stimulus Design and Recording Setup:

The cVEMP values were obtained from the subjects by using bilateral air conduction tone bursts with stimulus frequencies of 500 Hz to test the right and left ears. The stimulus profile was adjusted to produce a 2 ms rise, a 2 ms plateau, and a 2 ms fall time with a repetition rate of 5.1 Hz. A frequency of 500 Hz was presented 50–150 times to obtain average responses. A cVEMP evoked potential system (Eclipse EP 25; Interacoustics AS, Assens, Denmark) was used for cVEMP recordings. The impedance of electrodes was ≤ 3 kΩ. An EMG feedback system (Interacoustics Eclipse; Interacoustics AS, Assens, Denmark) was used for recording muscle responses between 50 and 200 μV. Muscle responses were recorded from 10 ms before the stimulus onset to 60 ms afterward. To improve reliability and reduce interpatient variability, the test was performed twice, and cVEMP amplitudes were normalized by dividing raw amplitudes by the background EMG activity.

Statistics: The IBM SPSS Statistics Version 22 (IBM Turkish Limited Company, Istanbul, Turkey) program was used for statistical analysis. The normal distribution suitability of the parameters was evaluated by the Shapiro-Wilk test. Descriptive statistical methods (mean, standard

deviations, and median value) were calculated. When the groups were evaluated together, nonparametric data were assessed by the Kruskal-Wallis test. P values were confirmed by the Bonferroni test. The Mann-Whitney U test was used in the comparison of nonparametric data between groups. Significance was assessed at the p <0.05 level.

RESULTS

There were 50 AR patients (30 females and 20 males) and 25 controls (15 females and 10 males). The mean age was 34.56±5.5 in the patient group and 36.08±5.07 in the control group. No statistical significance was found between the groups for age and gender distribution (p=0.45).

cVEMP responses were obtained in all cases in the control group and mild AR group. However, in patients with moderate to severe AR, cVEMP responses were not obtained in five patients.

The right and left 100 dB P13 latency values of the healthy control group were statistically significantly lower than those of the mild AR group and moderate-severe AR group (p<0.001) (Table I). The right and left 100 dB P13 latency values of the mild AR group were statistically significantly lower than those of the moderate-severe AR group (p<0.001) (Table I).

The right and left 100 dB N23 latency values of the healthy control group were statistically significantly lower than those of the mild AR group and moderate-severe AR group (p<0.001) (Table I). The right and left 100 dB N23 latency values of the mild AR group were statistically significantly lower than those of the moderate-severe AR group (p<0.001) (Table I).

The right and left 100 dB P13-N23 amplitude values in the healthy control group were found to be statistically significantly higher than in mild and moderate-severe AR (p<0.001) (Table I). The right and left 100 dB P13-N23 amplitude values of the mild AR group were statistically significantly higher than those of the moderate-severe AR group (p<0.001) (Table I).

DISCUSSION

AR is an inflammatory disease caused by nasal mucosal IgE in atopic individuals (10). It is the most common allergic disease in the United States, while it is the fifth most common chronic disease (11). The incidence of AR in the population ranges from 10 to 20% (11). In the pathophysiology of AR, sensitization that results with the formation of IgE occurs following the first encounter with the allergen. In the second encounter with an allergen, an early AR response occurs, while a late response occurs as a result of repeated allergic stimulation and increasing regulatory materials in the environment. Subsequently, specific eosinophils migrate from the circulation to the inflammation regions. The cytokines secreted from cells in the area of inflammation increase the lifespan of inflammatory cells and result in chemotaxis. As a result of these inflammatory events, a hypersensitive mucosal response develops and allergic individuals become susceptible to allergenic substances (12).

While MD is one of the most common causes of EH, its relationship with allergy has been elaborated on in the literature. Derebery and Berliner explained the relationship between allergy and MD by three theories (12). The first theory is that endolymphatic sac has fenestrated blood vessels that allow mast cell degranulation and inflammation by allowing the passage of antigens. The second theory is that circulating immune complexes pass through the endolymphatic sac circulation and stria vascularis, leading to increased inflammation and permeability and impaired

Table I: Comparison of parameters between groups.

	Groups			p
	Healthy Group	**Mild AR Group**	**Moderate-Severe AR Group**	
	Mean±SD/ Median	**Mean±SD/ Median**	**Mean±SD/ Median**	
Right 100 dB P13 Latency	14.9±0.80/14.86	16.45±1.31/16.65	18.37±1.69/18.33	**0.001***
Right 100 dB N23 Latency	22.6±1.35/22.88	24.99±1.54/25	27.24±1.41/27	**0.001***
Right 100 dB P13-N23 Amplitude	168.61±52.01/179.4	96.92±28.3/91.2	79.93±33.66/68.65	**0.001*** **0.019****
Left 100 dB P13 Latency	14.91±1.11/14.96	16.54±1.21/16.33	18.61±0.99/18.67	**0.001***
Left 100 dB N23 Latency	23.79±1.26/23.73	26.39±1.08/26.33	28.16±1.04/28.29	**0.001***
Left 100 dB P13-N23 Amplitude	158.54±51.37/151.6	115.11±35.76/99.11	88.45±20.68/79.38	**0.001***

Mann-Whitney U test*, p <0.001, **SD:** Standard Deviation, **P13:** The first positive peak wave, **N23:** The first negative peak wave, **dB:** decibel, **AR:** Allergic Rhinitis. **p value calculated from the comparison of mild AR and moderate-severe AR groups.

fluid balance. The third theory is the theory of viral antigen-allergic interaction; viruses can increase allergic symptoms by causing histamine release and trigger T-cell migration into the endolymphatic sac, and can also cause damage to epithelial surfaces. It has been shown that both inhaled and food allergens can cause MD (13). The severity and frequency of MD attacks have been shown to be reduced in patients who receive immunotherapy and remove food allergens from the diet (13).

Abnormalities in VEMP responses have been documented in MD, cVEMP peak-to-peak amplitudes are reduced, a finding attributed to a hydropic sacculus (14,15). Katayama et al. also studied the relationship between the visualization of EH in MRI with an intratympanic injection of gadolinium and cVEMP in patients with MD (16). They found that EH was significantly associated with the disappearance of cVEMP. In our study, cVEMP responses were found to be impaired as the severity of AR increased. cVEMP test responses showed latency prolongation and decreased amplitudes in the AR patients.

Takeda et al. performed a study that guinea pigs were actively sensitized with an allergic stimulus and changes of the endolymphatic space were investigated histologically at various time points after the provocation (17). The animals in the control group received no sensitization but only distilled water. EH was observed 12, 24, and 36 hours after the last sensitization and their cross-sectional areas of the scala media were significantly larger than that of the control group. In a second experiment, animals were actively sensitized and provoked in the same manner. Before antigen exposure, subjects were given distilled water and compared with subjects given oral administration of pranlukast (a leukotriene receptor antagonist). EH findings were observed in each turn of the cochlea after antigen exposure in subjects who were not given pranlukast prophylactically, whereas EH was not seen in the animals given pranlukast. This study showed that a systemic immunological disease affects the inner ear and prophylactic treatment can suppress it.

Singh et al. (18) performed pure audio audiometry and otoacoustic emission tests on AR patients who did not have a hearing loss complaint and found high-frequency hearing loss and abnormal otoacoustic emission responses. These abnormalities, which are determined by audiologic tests, were attributed to EH caused by allergic reactions and the release of toxic molecules into the inner ear. The adverse effects of AR in the inner ear were demonstrated both in experimental studies and in clinical trials. In this study, we evaluated cVEMP responses in AR patients and we obtained abnormal cVEMP responses in the study group compared to the control group.

In conclusion, the cVEMP test can detect saccular dysfunction before the occurrence of vestibular symptoms in AR patients and may be an indicator that can develop later in patients with AR with Meniere-like findings in the cVEMP test. The fact that the number of patients was low and the present hydrops findings are not supported by other imaging results and test batteries is a limitation of our study.

CONCLUSION

cVEMP abnormalities were detected in patients with AR in this study. Saccular dysfunction was detected by the cVEMP test in patients with allergic rhinitis without vestibular complaints.

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