TÜRKİYE'DE BULUNAN VİTİLOGOLU HASTALARIN İŞİTMELERİNİN DEĞERLENDİRİLMESİ

An Evaluation of the Hearing Examinations of Vitiligo Patients in Turkey

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ÖZET

Amaç: Vitiligo, depigmente makula ve belirgin melanosit yıkımıyla karekterize edinsel, idiopatik, otoimmün bir hastalıktır. Çalışma vitilogo hastalarında olası odyolojik anormallikleri saptamak için planlandı. Konvansiyonel odyolojik testlerle (saf ses eşiği) ve transient otoakustik emisyon (TEOAE) ile vitiligo hastalarında koklear fonksiyonları ölçtük ve kontrol grubuyla karşılaştırdık.

Materyal ve Metot: Vitiligolu 32 hasta cinsiyetçe benzer 32 sağlıklı kişi çalışmaya alındı. Odyometrik ve TEOAE testleri hasta ve kontrol grubunda yapıldı. Odyometrik ölçümler ses geçirmeyen kabinde saf ses odyometriyle yapıldı. Saf ses eşikleri 250-6000 Hz'de her kulak için ölçüldü.

Bulgular: Odyometrik bulgular vitiligolu hastalar ve kontrol grubu arasında 250-6000 Hz arası saf ses eşiklerinde fark olmadığını ortaya koydu. Vitiligolu hastalarda saf ses odyogramda sensörinöral işitme kaybı yoktu. Vitiligolu hastalarda saf ses odyometride değişiklik olmasa da transient otoakustik emisyon değerlerindeki düşmelerin dış tüy hücrelerini etkilediği düşünülebilir.

Sonuç: Konvansiyonel odyometri ile birlikte TEOAE testleri koklear disfonsiyonun erken tanısında güvenilir testlerdir. Vitiligolu hastalarda hastalığın ilerlemesi ve erken fark edilmesi açısından odyolojik incelemenin rutin olarak yapılması gerektiğini düşünüyoruz.

Anahtar kelimeler: *Vitiligo; Odyometri; Transient uyarılmış otoakustik emisyon; Koklear disfonksiyon.*

ABSTRACT

Objective: Vitiligo is an acquired, idiopathic autoimmune disease characterized by depigmented maculae and marked with melanocyte destruction. The study was performed to detect possible audiological abnormalities in vitiligo patients. We aimed to use conventional audiological tests (pure tone threshold) and altered cochlear function, by measuring and analyzing transient evoked otoacoustic emission (TEOAE) testing any subclinical auditory abnormalities of in patients with vitiligo, compared with controls.

Materials and Methods: Thirty-three patients with vitiligo and 32 age- and sex-matched healthy control cases were included in this study. Audiometric and TEOAE testings for both ears were performed for both patients and controls. Audiometric examinations were performed using a pure tone audiometer in a silent cabin. Pure tone thresholds were determined for each ear at frequencies of 250 – 6000 Hz for air conduction.

Results: Findings of the audiometric tests indicate that there was no difference between vitiligo and control group cases in pure tone threshold values between 250 and 6000 Hz. There was not sensorineural hearing loss on pure-tone audiogram in patients with vitiligo. Although there is no change in pure tone audiometry in vitiligo patients, it is considered that reductions in transient evoked otoacoustic emission values began to affect the outer hairy cells.

Conclusion: Conventional audiometry with TEOAE testing are reliable tests for the early detection of cochlear dysfunction. All patients with vitiligo required routine monitoring and audiological assessments for early identification and monitoring of changes as the disease progresses.

Key words: *Vitiligo; Audiometry; Transient evoked otoacoustic emission; Cochlear dysfunction.*

INTRODUCTION

Vitiligo is a common, acquired disorder resulting from destruction of functional melanocytes. It has a worldwide occurrence of 0.3-1.0%. Functional melanocytes in patients with vitiligo disappear by a mechanism that has not yet to be identified. In general, there have been three hypotheses to explain vitiligo: the immune, the neural and the autocytotoxic hypotheses (1).

Melanocytes are found not only in the skin but also in the uveal tract, the inner ear, the retinal pigment epithelium and the leptomeninges. Due to this reason mechanisms causing the loss of skin melanocytes can also affect other organs that contain melanocytes (2).
The inner ear is one of the important region in which melanocytes are located. Many authors have reported that melanin-containing cells in the inner ear protected cochlea against various stress, particularly loud noise (3). Although some studies determined that hearing was affected in patients with vitiligo (4), several studies reported that hearing wasn't affected (5,6).

Most patients with vitiligo are asymptomatic for audiological abnormalities. Therefore, we aimed to use conventional audiological tests and altered cochlear function, by measuring and analyzing transient evoked otoacoustic emission (TEOAE) any subclinical auditory abnormalities of in vitiligo patients, compared with controls.

METHODS

A total of 33 vitiligo patients, all of whom had been referred to the Department of Dermatology of Medical Center Hospital, and 32 healthy control subjects were enrolled in the present prospective study. The age of onset, duration, family history of vitiligo were recorded. Patients were also investigated for blood hemoglobin and glucose levels, total and differential leukocyte counts, erythrocyte sedimentation rate, antinuclear antibodies and thyroid autoantibodies. After the thorough dermatological examination patients were classified into three disease groups: acral, segmental and generalized. In addition, the vitiligo patients divided into 2 groups according to presence or absence of lesions around the ears. The percentage of the body surface involved with disease was estimated by using the 'rule of nines'(7). The control group included sex- and age-matched normal individuals, with no history of otitis media or inner ear diseases, no exposure to excessive noise. After physical examination, all subjects underwent pure-tone audiometry and TEOAE tests. We excluded patients with definitive ear diseases (e.g., tympanic perforation or chronic otitis media), familial hearing loss, chronic noise exposure, head trauma, or metabolic, neurological, vascular or autoimmune disease.
Clinical and tympanometric examination was made for exclusion of middle-ear pathologies. Audiometric and TEOAE examinations for both ears were performed for both patients and controls. Audiometric examination; audiometry was performed using a pure-tone audiometer (clinical audiometer model AC40; Interacoustics, Copenhagen, Denmark) in a silent cabin. Pure-tone thresholds were determined for each ear at the frequencies of 250-6000 Hz for air conduction. The extent of hearing impairment was assessed according to the International Standard Organization hearing threshold parameters (normal: inability to hear at minus 10-20 dB; mild deafness: inability to hear at 27 -40 dB; moderate deafness: inability to hear at 41-55 dB).

In both groups, the parameters of the TEOAE amplitudes, stimulus stability, stimulus intensity, and reproducibility were recorded (8).
All subjects provided written informed consent; our study was approved by the Local Ethic Board at Medical Faculty of University.

Statistical analysis
Pure-tone audiometry andTransient Evoked Otoacoustic Emission results were compared between the vitiligo and control group using Student's t-test and Pearson's correlation coefficient. All statistical analyses were performed using SPSS software (version 12.0; SPSS Inc.; Chicago, IL). A p value < 0.05 was the threshold of significance.

RESULTS

In total, 33 patients with vitiligo (11Male, 22 Female) and 32 healthy, sex and age-matched controls (10 Male, 22 Female) were randomly enrolled. Mean ± SD age was 23.0±12.3 (range 8–47) for the patients with vitiligo, and 25.9±12.5 (range 5–48) for the controls. There was no statistical difference for the age distribution between the vitiligo and control groups or between male and female participants.

The mean duration of illness was identified as 5.15 ± 4.20 (1-20) years in vitiligo group. Of the patients, 16 (48.5%) had acral, 16 (48.5%) had generalized and 1 (3.0%) had segmental distribution. Twenty one patients (63.6%) did not have vitiligo lesions in the periauricular area, but 12 (36.4%) did. Ten patients (30.3%) had the disease in their family history. Percentage disease involvement ranged between the minimum 9% (4 patients) and the maximum 81% (5 patients).

There was not sensorineural hearing loss on pure-tone audiogram in patients with vitiligo. Findings of the audiometric tests indicate that there was no difference between vitiligo and control group cases in pure tone threshold values between 250 and 6000 Hz (Table 1). No significant correlation was established between hearing and presence or absence of periauricular involvement, body involvement percentages, familial vitiligo history and positive autoantibody values.

Amplitude (1.0, 1.4, 2.0, 2.8 and 4.0 Hz frequency), Stimulus, Reproducibility and Stability values of the patients and the control group were measured through the use of TEOAE test. Reduction of transient evoked otoacoustic emission amplitude values of 1.4, 2.0 and 2.8 kHz were found significant in the right ear (9.42±8.56 vs 14.83±6.37 p=0.027, 9.68±9.60 vs 15.65±5.73 p=0.014 and 9.48±8.13 vs 16.08±6.82 p=0.009, respectively), while 2.0 kHz amplitude value was significant in the left ear (8.86±7.30 vs 15.55±6.08 p=0.004). As of reproducibility values, both right and left ears produced responses above 50% and therefore both were accepted as positive. Stimulus and stability values were not found significantly different (Table 2).

Table 1: Audiometric signs in patient and control groups (Pure-Tone Thresholds (dB-HL)

	Right ear		Left ear		Right ear	Left ear	Significance
Frequency (Hz)	**Patients**	**Control group**	**Patients**	**Control group**	**p**	**p**	
250	14,87±4,02	15.75±5.44	14,63±4,06	14.50±4.26	0.507	0.908	NS
500	12,81±4,05	11.25±3.93	11,84±4,43	11.50±2.85	0.174	0.755	NS
1000	12,15±2,74	10.75±4.66	11,54±3,80	10.25±4.12	0.173	0.250	NS
1500	11,45±3,75	10.35±3.55	9,96±3,67	9.45±3.83	0.295	0.626	NS
2000	10,75±5,46	9.75±4.12	8,75±4,66	8,00±2,99	0.481	0.608	NS
4000	11,63±5,39	11.25±5.82	10,45±7,00	11.00±3.47	0.807	0.747	NS
6000	17,03±6,72	16.50±6.50	19,09±9,95	17.00±5.71	0.779	0.396	NS
NS=not significant.							

Table 2: Transient Evoked Otoacustic Emission values in the patient and control groups.

Amplitude Frequency (Hz)	Right ear		Left ear		Right ear	Left ear
	Patients	Control group	Patients	Control group	p	p
1.0	5.56±6.19	11.00±8.66	3.31±3.50	11.24±15.36	0.053	0.086
1.4	9.42±8.56	14.83±6.37	9.90±4.94	12.62±6.40	0.027*	0.191
2.0	9.68±9.60	15.65±5.73	8.86±7.30	15.55±6.08	0.014*	0.004*
2.8	9.48±8.13	16.08±6.82	11.46±6.96	13.91±6.90	0.009*	0.299
4.0	8.97±8.47	13.54±7.88	10.26±8.78	12.38±6.68	0.099	0.392
Stimulus	80.29±5.69	79.72±20.71	77.11±8.52	81.34±12.77	0.926	0.295
Reproductivity	76.27±22.5	92.09±7.56	73.18±20.13	89.33±11.88	0.001	0.002
Stability	99.90±0.83	99.33±2.66	100.27±1.61	97.52±13.88	0.488	0.519

*Statistically significant difference between vitiligo patients and controls($p < 0.05$).

DISCUSSION

Alphonse Corti was the first researcher who mentioned the presence of pigment cells in the inner ear. There are many melanocytes in the human cochlea, particularly in the modiolus, in the osseous spiral lamina, in Reissner's membrane and in the vascular stria; melanocytes are found especially in highly vascularized areas of apparently important secretory or metabolic function (9,10). The exact role of melanin is unknown but is thought to be vasomotor function in the inner ear. According to Savin, (11) cells containing pigments are adhered to blood vessel walls, that are regions of intense metabolite exchanges. For this author, melanin facilitates the passage of substances from one side to the other, thus protecting the balance of the cell membrane. Because of the important role of melanin in the inner ear, hearing is affected in systemic disorders that affect pigmented areas (eyes, skin and hair) such as the Vogt-Koyanagi and Waardenburg syndromes (9,10).

Otoacoustic emissions (OAEs) are spontaneous acoustical signals that are produced by outer hair cells of theorgan of Corti and can be elicited by acoustic stimulation. OAEs are simple, efficient, and objective. For clinical applications, OAEs are evoked by using either transient (transient evoked otoacoustic emissions (TEOAEs) or tone pairs (distortion product otoacoustic emissions (DPOAEs) of sound envelopes.

TEOAEs are highly sensitive to cochlear pathology in a frequency-specific way. TEOAEs can be recorded in almost all persons who have up to 20 to 30 dB hearing level (dB HL) of hearing threshold (12). Angrisani et al. (9) reported that twenty-one (87.5%) of 24 patients with vitiligo had normal pure tone audiometries, two had unilateral hearing loss between 3000 Hz and 8000 Hz, and one had moderate cochlear loss in the left ear; thus, 12.5% of patients had hearing loss. Fourteen (66.7%) of 21 patients with normal audiometries presented partial (at 4 KHz) or absent TEOAE, suggesting cochlear dysfunction. Eleven (64.7%) of 17 patients in which TEOAE were absent had bilateral failure, and six (35.2%) patients had unilateral failure.

Aslan et al. (8). reported that hearing thresholds at 0.25, 4, 8, 10, and 12.5 kHz were found to be increased in vitiligo patients. Significant reduction in the amplitudes of TEOAEs was found only at 4 kHz in the vitiligo group. In our study, a change was found not in the pure tone audiometry, but in TEOAE. We think this may be due to the fact that although high-frequency audiometry was used in other studies, we evaluated hearing only up to 6000 Hz. In TEOAE, a significant change was established at 1.4 and 2.8 kHz in the right ear, and significant results were obtained at 2.0 kHz in both right and left ears (amplitudes were decreased compared with control group).

In addition, although pure tone audiometry is normal in vitiligo patients. It is considered that reduction in TE-OAE amplitudes began to affect the outer hairy cells in the inner ear.

Tosti et al. (4) found hearing loss in 16 % of patients with vitiligo; they strengthened the hypothesis that part of the melanocytes was damaged by auto-immunity which is the one of accepted etiological theories of vitiligo. In an another study; Fleissig et al. (13) showed that; vitiligo patients demonstrated a significantly higher prevalance of sensorineural hearing loss. Aydogan et al.(1) examined the audiological thresholds between 250 and 8000 Hz and the electrophysiological potentials in 57 patients with vitiligo and 50 healthy controls. These authors found that 14% of vitiligo patients reported mild sensorineural dysacusis, of which six had bilateral hearing loss and two had unilateral hearing loss. They reported that their findings were similar to other data and suggested that melanin might have an important role in modulating the transduction of auditory stimuli in the inner ear andin maintaining the function and structure of the auditory system.

Ardic et al. (3) studied 29 vitiligo patients, applying audiometry from 250 Hz to 16 KHz. This author found pure tone thresholds between 4 000 Hz and 10 000 Hz in the vitiligo group, which was significantly worse compared with the control group. Male patients presented hearing loss at higher frequency ranges than female patients, which was statistically significant. They reported that vitiligo is a significant hearing loss factor, and males are more affected than females.

Some studies (1,5,13-16) did not find any correlation between loss of hearing and disease duration, while others (3,8,17) did. Nawaf Al-Mutairi et al. (5) examined the audiological abnormalities in 197 patients developing vitiligo after the age of 40. Audiometric examinations were done using a pure tone audiometer. The majority of patients showing hypoacusis had sensorineural type of impairment (30 patients). There was no statistically significant difference between the healthy group. They concluded that in contrast to the association noticed in early onset vitiligo, late onset vitiligo does not seem to be significantly associated with audiological abnormalities. In accordance to another study; high frequency sensory neural was detected in 8 patients of total 21 vitiligo patients (16). In this study, as has previously been shown by Sharma and colleagues and Fleissig and colleagues there was no correlation between duration of disease and visual abnormalities. They explained this situation as the possibility that otic melanocytes are affected as the beginning of disease and than stabilized.

Sharma L. et al (15). evaluated hearing in vitiligo patients and they found hypoacusis in 34 vitiligo patients (18.89%). Thirty four patients suffered from deafness, which was not associated with the duration of the disease. Deafness was significantly more common in the patients with generalized involvement. Therefore, the authors speculated that the melanocytes being generalized might be playing a role in this condition.Akay et al.(17) aimed to to establish the clinical and epidemiological profile of vitiligo in Turkey. Audiometry was performed in 53 vitiligo patients and sensorineural hypoacusis was found in 20 patients (37.7%). Nine of these patients showed unilateral minimal hearing loss and the other 11 bilateral hearing loss. Their results demonstrate that vitiligo is a part of systemic autoimmune process and audiological examination should be performed in all patients examinated for hypoacusis.

Although no significant correlation was found between hearing and presence of periauricular involvement, body involvement percentage, familial history of vitiligo and positive autoantibody values in our study, there was a significant correlation between disease duration and left ear 1500, 2000 and 4000 Hz. Our findings show that TEOAE are a sensitive test for detecting cochlear dysfunction before symptoms become manifest, despite normal audiometries. TEOAE results were significant. Our findings support this statement, adding that conventional audiometry with TEOAE testing are reliable tests for the early detection of cochlear dysfunction. Our study thus strengthens the hypothesis that vitiligo is a significant factor for altered cochlear function.

One limitation of our study should be mentioned. Neither distortion product otoacoustic emissions (DPOAEs) were performed nor high frequency audiometry assessed in the present study. High frequency audiometry and DPOAEs could have been used in the audiological assessment instead of conventional audiometry and TEOAEs. But the structure of our hospital was not appropriate to these assessments because of technical deficiencies.

The mechanism destroying the melanocyte in the skin could also affect other melanocytic organs. It is believed that, loss of epidermal melanocytes and melanin-containing cells in the inner ear lead to sensorineural hearing loss in vitiligo (2). Also vitiligo patients appear to be more predisposed to cochlear dysfunction, as shown by the significance of otoacoustic emissions, although pure tone audiometry was within normal limits in most of the sample.We believe that even if most of the patients with vitiligo are usually asymptomatic in hearing, all vitiligo patients required routine monitoring and audiological assessments by specialists for early identification of cochlear dysfunction and monitoring of changes as the disease progresses. Also further large-scale clinical trials which include high frequency audiometry and DPOAEs may provide statistically significant values and allow clarification of the relationships between hearing loss and prognostic factors in vitiligo.

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