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Evaluations of Audiovestibular Manifestations in Patients with Psoriasis

Psoriasisli Hastalarda Odyovestibüler Bulguların Değerlendirilmesi

Abstract

Objective: Sensorineural hearing loss can occur as a complication of autoimmune and inflammatory diseases. Although psoriasis is also a chronic inflammatory skin disease characterized by T-cell mediated hyper proliferation of the keratinocytes, the information about the relationship between audiological disorders is limited in the literature and the relationship with vestibular disorders has not been investigated before. In this study, we aimed to investigate the presence of audiovestibular disorders and their relationship with disease parameters.

Methods: Sixty-one patients with psoriasis and 61 healthy individuals were included in this prospective cross-sectional study. Those with possible etiologic factors that may lead to hearing and balance disorders were not included in the study. All participants were first performed a full ear, nose and throat examination. Subsequently, full audiological examination (pure audiometry, autoacoustic emission, stapes reflex, detection threshold of speech and discrimination) and electronystagmography tests were performed in the audiology laboratory where sound isolation was provided. Psoriasis severity was assessed by psoriasis area and severity index, body surface area and general evaluation of researcher.

Results: There were significant differences between patients and controls in terms of audiovestibular symptoms. According to audiograms, predominant bilateral sensorineural hearing loss was detected in high frequency in psoriasis patients. The vestibular abnormalities in patients with psoriasis were found to be more frequent than those in controls, only saccadic test values were observed as statistically significant.

Conclusion: Our study demonstrates that audiovestibular abnormalities are significantly associated with psoriasis. Therefore, patients with psoriasis should be evaluated for the co-occurrence of hearing loss or vestibular problems which might affect patients' quality of life.

Keywords: Psoriasis, hearing loss, vestibular dysfunction, audiometry, electronystagmography, sensorineural hearing loss

Öz

Amaç: Sensorinöral işitme kaybı, otoimmün ve inflamatuvar hastalıkların bir komplikasyonu olarak ortaya çıkabilmektedir. Psoriasis toplumda yaygın olarak görülmesine rağmen, odyolojik bozukluklar ile ilişkisi hakkında literatürdeki bilgiler sınırlıdır ve vestibüler bozukluklarla ilişkisi daha önce araştırılmamıştır. Biz de bu çalışmamızda, psoriasis hastalarında odyovestibüler bozuklukların varlığını ve hastalık parametreleri ile ilişkisini araştırmayı amaçladık.

Yöntemler: Altmış bir psoriasis hastası ile yaş ve cinsiyet uyumlu 61 sağlıklı gönüllü çalışmaya dahil edildi. İşitme ve denge bozukluğuna yol açabilecek olası etiyolojik faktörlere sahip olanlar çalışmaya dahil edilmedi. Tüm katılımcılara öncelikle tam bir kulak, burun ve boğaz muayenesi yapıldı. Takiben hastalara ses izolasyonu sağlanmış odyoloji laboratuvarında tam odyolojik tetkik (saf ses odyometri, otoakustik emisyon, stapes refleksi, konuşmayı alma ve ayırt etme eşiği saptanması) ve elektronistagmografi testleri yapıldı. Psoriasis hastalık şiddeti psoriasis alan ve şiddet indeksi, vücut yüzey alanı ve araştırmacının genel değerlendirmesi ile değerlendirildi.

Bulgular: Odyometrik testlerde hasta ve kontroller arasında anlamlı farklılık saptandı.

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Odyogramda kontrollere göre psoriasis hastalarında yüksek frekanslarda baskın bilateral sensörinöral işitme kaybı saptandı. Psoriasis hastalarında vestibüler testler kontrollere göre daha sık anormal saptandı, sadece sakkadik test değerleri arasında istatistiksel anlamlı olarak farklılık gözlendi.
Sonuç: Çalışmamızda psoriasis ile odyovestibüler sistem bozuklukları arasında anlamlı birliktelik saptandı. Bu nedenle, hastaların yaşam kalitesini etkileyebilen işitme kaybı ve vestibüler bozukluklar açısından psoriasis hastalarının kontrolü gereklidir.
Anahtar kelimeler: Psoriasis, işitme bozuklukları, vestibüler bozukluklar, odyometri, elektronistagmografi, sensörinöral işitme kaybı

Introduction

The inner ear is an important target of autoimmune and inflammatory attacks. Sensorineural hearing loss (SNHL) may occur as a complication of autoimmune and inflammatory diseases (1-3). Psoriasis is also an inflammatory skin disease characterized by T-cell mediated hyper proliferation of the keratinocytes (4). However, it has also recently been recognized as a chronic multisystem disease of variable course with inflammatory process, as with other rheumatologic inflammatory diseases. Hearing loss has been witnessed in variable rheumatologic diseases. Although psoriasis is a common disease, affecting approximately 2% of the general population, little is known about its effects on audiovestibular functions. The relation between psoriasis and SNHL has previously been examined in three studies (5-7). With the exception of Karabulut et al. (6), all studies demonstrated that aerial and bone-conduction threshold values in all frequencies were higher in patients with psoriasis. The only statistical significance between hearing loss and disease severity was found in the study of Güvenç et al. (5). None of these studies investigated the relationship between vestibular functions and psoriasis.

The aim of this study was to investigate the vestibular function in addition to the audiological functions and to identify the probable factors influencing audiovestibular functions in psoriasis patients.

Materials and Methods

A preliminary estimate of sample size for detecting the clinical difference of audiological impairment prevalence in psoriasis and in general population with effect size d=0.4, for which a study with a type 1 error of 0.05 and a type 2 error of 0.2 would require approximately 61 patients per group with two-sided significance testing. Consequently, 61 consecutive psoriasis patients, who were admitted to our psoriasis outpatient clinic between October 2015 and December 2015, and 61 consecutive healthy volunteers without a history of inflammatory rheumatic disease, were included in the study. Informed consent was obtained from all cases and controls. This study was approved by the Ethics Committee of the Faculty of Medicine of Akdeniz University (ethic commitee approval no: 70904504/71-11.02.2015).

The diagnosis of psoriasis was done according to clinical and histopathological findings. The demographic and clinical data of the patients, including disease severity, duration of the disorder, and previous therapies, were recorded. Psoriasis disease severity was evaluated either by Psoriasis Area and Severity Index (PASI) and body surface area (BSA), or investigator's global assessment (IGA) (8,9). IGA was used especially for palmoplantar plaque, palmoplantar pustular or inverse psoriasis in which PASI or BSA evaluation are inappropriate (10).

During the period of recruitment, patients with psoriasis and the control subjects were questioned about any history of previous audiovestibular disturbances, cranial trauma, exposure to noise, ear infection, metabolic disease, renal failure, ototoxic drug use, and familial history of hearing impairment. Those with a known cause, such as trauma, Meniere disease, other audiovestibular disorders, ear surgery, previous history of cardiovascular diseases, cerebrovascular complications, infections involving the inner ear, syphilis, barotrauma, acoustic schwannoma, or those in treatment with ototoxic drugs were excluded from the study. Participants who had severe cervical problems were excluded due to the inability to perform vestibular assessment.

All individuals were asked whether they had experienced hearing loss, vertigo, tinnitus, dizziness, or disequilibrium symptoms at the time of our study. All participants underwent complete ear, nose, and throat examination, including pneumatic otoscopy and automicroscopic examinations, as well as the following audiological tests: pure-tone audiometric test (0.25-1, 2-6 Hz) in a sound-isolated audiology laboratory, both aerial and bone conduction stimulus, and speech reception threshold (SRT) in terms of decibel hearing level. A speech discrimination test, tympanometry, and stapedius reflex threshold were also performed.

All participants were asked to perform electronystagmography (ENG). Only 30 patients and 30 control subjects agreed to participate due to the time-consuming nature of ENG tests. In ENG testing, spontaneous nystagmus, gaze-evoked nystagmus, oculographic tests (saccades; slow, smooth pursuit evaluation; and optokinetic stimulus) were completed, and positional nystagmus in supine, lying on the right, lying on the left, and cervical hyperextension positions (head hanging) were performed. After this, the cephalic rotational test in the supine position and the Dix-Hallpike test were administered. Finally, a bi-thermal water caloric test was performed.

Since the primary purpose of the vestibular apparatus is to control eye movements, the movements of the eyes used to examine the activity of the vestibular end-organs and their central vestibulo-ocular pathways (11). Oculographic tests and positional tests were performed with ENG device. In ENG testing, eye movements are recorded to analyze the vestibulo-ocular reflex as well as the saccadic, pursuit, optokinetic, and fixation visual systems. Electro-oculography,

employed in ENG, measures changes in the corneal-retinal potential via electrodes placed around the inner and outer canthi of the eyes to determine amplitude and velocity of the eye movements. Because of these oculographic tests nonvestibular eye movements, abnormalities would suggest vertigo of central origin (11).

The smooth pursuit test evaluates the ability to track a moving object with smooth eye movements and head still. Smooth pursuit is the most sensitive of the oculomotor tests but provides poor lesion site localization within the multiple pathways involved in pursuit generation. Abnormalities with pursuit are typically taken as an indication of possible vestibulo-cerebellar region involvement, the final common portion of the multiple pathways for pursuit production (12,13).

Saccade testing evaluates rapid movement of the eye used to place an object of interest on the most sensitive portion of the retina, the fovea. Saccade testing is not as sensitive as pursuit but when tested with different paradigms can provide for differentiating information concerning brainstem versus posterior cerebellar vermis involvement. Suggestions for possible frontal or parietal lobe involvement can also be obtained from saccade testing (13).

Optokinetic stimulation measures jerk nystagmus eye movements created by repeated objects moving across the subject's visual field and filling at least 80% of the visual field. Optokinetic stimulation is the least sensitive, probably owing to the combination of both smooth pursuit and saccade systems, allowing the optokinetic nystagmus to be generated by a combination of foveal and peripheral retinal stimulation. At present, it serves best as a cross-check with significant abnormalities seen during pursuit or saccade testing (13).

Irrigation of the external auditory canal with 30 °C cool and 44 °C warm water (caloric testing) can be used to identify any disturbance of peripheral vestibular function (horizontal canal) (13).

Statistical Analysis

Statistical analysis was performed using PASW Statistics 20 (IBM Corp. Released 2011. Armonk, NY: IBM Corp.). PASW 20 (SPSS/IBM, Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation, while categorical variables are given as percentages (%). The Kolmogorov-Smirnov test was used to verify the normality of the distribution of continuous variables. Statistical analysis of clinical data between the two groups consisted of unpaired t-tests for parametric data and Mann-Whitney U test analysis for nonparametric data, while the chi-square/Fisher's exact test were used for categorical variables. Differences were considered statistically significant when the probability value (p) was less than 0.05.

Results

Most of the patients with psoriasis were men (55.7%). The mean age of the patients at the time of our study was 47.20±16.40. The duration of the disease ranged from 2 to 540 months, with a mean of 125.79±131.53 months. There were no significant differences in terms of age and sex between the psoriasis patients and the healthy control subjects. Demographic and clinical findings of the patients and control subjects are shown in Table 1.

There were significant differences between the patients and control subjects in terms of audiovestibular symptoms. The values of the audiometric tests (pure-tone average, SRT, speech discrimination) yielded significant differences between patients and controls. All auditory differences are shown in Table 2.

The mean bone conduction and air conduction hearing thresholds were higher for all frequencies in the patients than in the control subjects (Table 3). The audiogram revealed a bilateral and symmetrical SNHL with predominant pattern of high frequency SNHL in patients with psoriasis compared to the control subjects (Table 3, 4).

Patients with psoriasis showed abnormal vestibular tests more commonly than the control subjects, while the values of the saccadic test yielded significant differences (Table 5).

No significant association was found between the presence of audiovestibular abnormalities and duration or severity of the disease (in terms of PASI, BSA, IGA). Additionally, there was no association between audiovestibular abnormalities

Table 1. Demographic, clinical, and laboratory findings of patients with psoriasis and control subjects

	Patients, n=61	Controls, n=61	p
Female/male	27/34	37/24	0.070
Mean age (years ± SD)	47.20±16.40	46.15±14.90	0.056
BMI	28.66±5.68	24.58±6.57	0.001
Patterns of psoriasis Plaque Guttate Inverse Erythrodermic Palmoplantar plaque	 43 (59.0%) 8 (13.1%) 4 (6.4%) 2 (3.2%) 13 (21.2%)		
Mean disease duration (months ± SD)	125.7±131.5		
PASI	4.07±7.91		
BSA	7.40±18.33		
Concomitant psoriatic arthritis	4 (6.6%)		
Nail psoriasis	22 (36.1%)		
Treatments Methotrexate Cyclosporine Topical treatments Acitretin UVB Adalimumab Ustekinumab No treatment	 19 (32.1%) 15 (24.5%) 8 (13.1%) 8 (13.1%) 4 (6.4%) 4 (6.4%) 2 (3.2%) 6 (9.8%)		
Mean duration of psoriasis treatment (months ± SD)	4.87±5.76		

BMI: Body mass index, PASI: Psoriasis area and severity index, BSA: Body surface area, UVB: Ultraviole B, SD: Standard deviation

Table 2. Auditory differences between patients with psoriasis and controls

	Patients, n=61 (%)	Controls, n=61 (%)	p
Individuals with abnormal audiovestibular symptoms			
Hearing loss	28 (45.9)	5 (8.2)	0.001
Tinnitus	18 (29.5)	3 (4.9)	0.001
Vertigo	19 (31.1)	2 (3.3)	0.001
Dizziness	12 (19.7)	2 (3.3)	0.005
Dysequilibrium	17 (27.9)	2 (3.3)	0.001
Abnormal tympanogram	10 (16.3)	0 (0.0)	0.001
Absence of stapedial reflex	6 (9.8)	1 (1.6)	0.114
PTA 0.25-1 kHz			
Right ear	17.30±7.58	14.87±2.07	0.713
Left ear	16.98±7.59	14.99±2.35	0.536
PTA 2-6 kHz			
Right ear	25.69±15.57	17.56±7.93	0.004
Left ear	26.20±15.72	18.19± 9.60	0.002
SRT, dB			
Right ear	20.08±8.68	16.23±2.84	0.011
Left ear	20.25±10.22	16.23±2.84	0.029
SDT, %			
Right ear	93.02±9.31	97.57±3.45	0.012
Left ear	92.80±9.91	97.31±4.05	0.011

PTA: Pure tone average, SRT: Speech reception treshold, SDT: Speech discrimination test, dB: Decibel

Table 3. Mean hearing thresholds for airway according to frequency

	Patients (dB ± ss)	Controls (dB ± ss)	p
Right ear			
250 Hz	21.72±7.01	19.92±2.50	0.324
500 Hz	18.36±7.89	15.57±1.85	0.096
1000 Hz	19.59±8.72	16.39±2.76	0.107
2000 Hz	21.31±13.69	14.75±6.86	0.015
4000 Hz	29.34±19.42	19.02±10.32	0.004
6000 Hz	38.61±22.71	26.89±13.27	0.004
Left ear			
250 Hz	21.15±6.48	20.00±2.74	0.901
500 Hz	18.20±8.32	15.98±2.20	0.527
1000 Hz	19.51±10.40	16.48±3.07	0.336
2000 Hz	21.89±14.98	15.82±7.76	0.020
4000 Hz	30.57±21.35	18.52±11.49	0.001
6000 Hz	41.31±23.09	29.59±15.82	0.004

dB: Decibel

and patterns of psoriasis, concomitant psoriatic arthritis, nail disease or use of anti-psoriatic drugs.

Discussion

Our study revealed significant differences between patients and control subjects in terms of audiovestibular symptoms and the values of audiometric tests. The mean bone conduction and aerial conduction hearing thresholds were higher

Table 4. Mean hearing thresholds for boneway according to frequency

	Patients (dB ± ss)	Controls (dB ± ss)	p
Right ear			
500 Hz	14.34±7.98	12.30±2.67	0.581
1000 Hz	15.08±8.78	12.62±3.94	0.445
2000 Hz	18.93±12.72	12.70±6.56	0.007
4000 Hz	24.34±16.49	17.13±9.72	0.031
Left ear			
500 Hz	13.93±7.02	12.54±3.49	0.479
1000 Hz	14.75±10.47	12.46±3.72	0.802
2000 Hz	17.46±12.83	13.28±7.12	0.096
4000 Hz	24.84±17.30	16.89±11.77	0.007

dB: Decibel

Table 5. Oculographic and vestibular test results of psoriasis patients and controls

	Patients, n=30 (%)	Controls, n=30 (%)	p
Abnormal vestibular test			
Spontaneous nystagmus	0 (0.0)	0 (0.0)	0.999
Gaze nystagmus	0 (0.0)	0 (0.0)	0.999
Positional nystagmus	4 (13.3)	1 (3.3)	0.353
Dix-Hallpike test	1 (3.3)	1 (3.3)	0.999
Abnormal caloric test	4 (13.3)	1 (3.3)	0.353
Abnormal oculographic test			
Smooth pursuit test	23 (76.7)	16 (53.3)	0.058
Saccadic test	16 (53.3)	3 (10.0)	0.001
Optokinetic test	5 (16.7)	2 (6.7)	0.424

for all frequencies like those seen in previously published data but not all frequencies have shown to be statistically significant. This difference was found to be statistically significant in high frequencies (2.4 and 6 kHz), similar to their results. Additionally, patients with psoriasis exhibited abnormal vestibular tests more commonly than the control subjects. To our knowledge, this is the first report that has specifically assessed the presence of electronystagmographic abnormalities in patients with psoriasis.

The relation between psoriasis and SNHL has been investigated in three studies (5-7). Also there are a few case reports and a retrospective study regarding sudden SNHL (SSNHL) in psoriasis patients (14-16). Güvenç et al. (5) assessed the hearing function of 51 psoriasis patients and 51 healthy volunteers in pure tone audiometry, and at all frequencies (airway and boneway) threshold values were found to be higher in the psoriasis patients compared to the control subjects. The values reached statistical significance at all frequencies except for right ear air conduction at 1000 Hz, bone conduction at 500 and 1000 Hz, left ear air conduction at 500 Hz, and bone conduction at 500 Hz ($p<0.05$). No significant relationship was found between hearing loss and age or disease duration. Significant relationship was found between PASI and hearing loss of medium-high frequencies. The authors suggested that hearing loss could not be due to age-related degeneration, because of its independence from age. And they suggested that they believe long-term low

levels of disease mediators don't have any effect to hearing loss because they didn't demonstrate any relation between hearing loss and disease duration. Relation between high PASI scores and hearing loss in medium and high frequencies (bone and airway) raises the thought that this could be related with high levels of proinflammatory cytokines, such as tumor necrosis factor alpha (TNF-α), in severe stages of the disease, and as a result of the creation of cochlear degeneration by such cytokines (5).

Karabulut et al. (6) assessed hearing loss in pure tone hearing thresholds and distortion product autoacustic emissions in 42 psoriasis patients and 60 healthy volunteers. No significant difference between groups was shown in the responses. Furthermore, neither SNHL nor distortion of cochlear cells were present. The authors suggested that increased frequency of hearing loss and vestibular disorders in chronic inflammatory and autoimmune diseases–could be due to the more prominent role of CD4 T cells instead of CD8 T cells which are prominent in psoriasis (6).

Finally, Aydın et al. (7) evaluated 41 psoriasis patients and 41 healthy control subjects with pure tone audiometry and transient evoked autoacoustic emission; no significant difference was found between the groups. However, it was observed that in the pure tone audiometry, hearing thresholds were higher at all frequencies in the psoriasis patients than the control subjects (7).

In a retrospective cohort study, Yen et al. (14) compared patients diagnosed with psoriasis from 2001 through 2006 with gender-, age-, and comorbidities-matched controls. They followed each patient until the end of 2011 and evaluated the incidence of SSNHL for at least 6 years after the initial psoriasis diagnosis. The study demostrated that the incidence of SSNHL was 1.51 times higher in the psoriasis cohort than in the control cohort (7.12 vs 4.73 per 10.000 person-years). As a result they suggested that psoriasis is significantly associated with a higher risk of developing SSNHL (14).

Psoriatic arthritis is a seronegative arthritis associated with psoriasis disease. In approximately 25% of patients with psoriasis, psoriatic arthritis can be observed. Psoriasis and psoriatic arthritis are considered as separate clinical entities by some clinicians, but the relationship between both diseases can't be ignored. Although there is no previous study evaluating vestibular functions in patients with psoriasis, some vestibular test abnormalities have been shown in patients with psoriatic arthritis similar to our study (16,17). Development of audiovestibular symptoms such as hearing loss, vertigo, tinnitus, imbalance, dizziness was shown to be significantly increased in the group of patients with psoriatic arthritis (16). As expected, the development of audiovestibular symptoms showed an increase with age, but had no relationship with disease duration (16). Audiometric examination revealed hearing loss in 60% of patients with psoriatic arthritis; a statistically significant difference (8.3% in the control group) was observed. Bilateral sensorineural high frequency hearing loss was the most frequent type. Oculographic abnormality in patients with psoriatic arthritis was observed more frequently than in the control subjects, but there was no statistically significant difference between the groups. Caloric test abnormalities in the evaluation of the vestibular system were found more frequently in patients with psoriatic arthritis compared to the control group. There was a significant correlation between the frequency of audiovestibular symptoms and the instant inflammation markers of patients. The authors suggested that chronic inflammation may play an important role in the development of abnormal audiovestibular findings in patients, because of its correlation with the inflammation markers of psoriatic arthritis (16).

In our study, thresholds at all frequencies for aerial and boneway were found to be higher in patients than in control subjects, similar to both Güvenç et al. (5) and Aydın et al. (7). This difference was found to be statistically significant in high frequencies (2.4 and 6 kHz), similar to their results. In addition, SRT was higher in psoriasis patients than in the control group, whereas the speech discrimination test was found to be lower.

Patients with psoriasis exhibited abnormal vestibular tests more commonly than control subjects, and the values of the saccadic test yielded significant differences. We observed abnormal caloric test and positional nystagmus in our patients. These tests are closely associated with the presence of hypofunction (canal paresis) of the inner ear (13). Therefore, these findings support a peripheral etiology for the audiovestibular impairment observed in patients with psoriasis. Not only vestibular tests but also oculographic tests were abnormal in our study. Smooth pursuit, opthokinetic and saccadic test abnormalities were more common in psoriasis patients than in controls. Abnormalities with these tests could be considered as an indication of possible vestibulo-cerebellar region involvement (13).

In the pathogenesis of immune mediated inflammatory diseases, TNF-α has been shown to play a critical role (18). Psoriasis, which responds well to TNF-α inhibitors in the treatment, also shows that TNF-α plays an important role in the aetiology of psoriasis. In addition, experimental studies investigating the role of TNF-α inhibitors in the immune-mediated inner ear disease demonstrated them to be effective in reducing inflammation and hearing loss in cochlear diseases (19). These findings support the hypothesis of the relationship between high levels of proinflammatory cytokines during severe psoriasis activity, and its association with cochlear degeneration postulated by Güvenç et al. (5). There were only four patients who used TNF-α inhibitors in our study, three of them whom median age was 20.3 had no audiovestibular impairment. Other patient who was 48 years-old had SNHL in high frequency. Due to small number of patients no significance could be shown between patients treated with and without TNF-α inhibitors.

Study Limitations

In terms of the limitations of our study, proinflammatory cytokines, which play important role in the pathogenesis of psoriasis, haven't been measured. In addition this study is not designed to determine the casuality.

Conclusions

Our current study demonstrates that audiovestibular abnormalities are significantly associated with psoriasis.

Taking into consideration that the cooccurance of hearing loss or vestibular problems cause discomfort and difficulty in daily life, awareness of this association and approaches for treatment can be helpful in enhancing patients' quality of life.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of the Faculty of Medicine of Akdeniz University (ethic commitee approval no: 70904504/71-11.02.2015).

Informed Consent: It was taken.

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Authorship Contributions

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