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Evaluation of hearing loss and tinnitus in Behcet's disease

Ahmet Karadağ[1] · Mujde Karadağ[2] · Adem Bora[3] · Emrullah Hayta[4] · A. Bahadır Çetin[5] · Sevil C. Doğan[1] · Kasım Durmuş[3] · E. Elif Altuntaş[3]

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Abstract

Objective The aim of this study is to evaluate sensorineuralhearing loss (SHNL) and tinnitus in patients with Behcet's disease (BD), while also determining the association between the clinical symptoms of BD and the disease duration with the development of hearing loss.

Materials and methods The study included 44 patients with BD and 42 healthy volunteers as the control group. The level of tinnitus-induced annoyance and the effects of tinnitus on daily life were evaluated with Visual Analog Scale (VAS) and the Tinnitus Reaction Questionnaire (TRQ). The hearing levels of all participants were measured with high-frequency audiometry and transient auto-acoustic emission tests.

Results The patients with BD were significantly more affected by SNHL and tinnitus than the controls ($p < 0.05$). The correlation between disease duration and age among those with SNHL was statistically significant ($p < 0.05$). No association was found between the clinical findings and SNHL and tinnitus ($p > 0.05$) in the BD patients.

Conclusion In the present study, high-frequency SNHL was found to be common in among the patients with BD. SNHL in BD is positively correlated with the patients' age of the and the disease duration.

Keywords Behcet's disease · Hearing loss · Audiometry · Tinnitus

Introduction

Behcet's disease (BD) is a chronic, remitting and inflammatory disease affecting mainly the mucocutaneous system, the eyes and joints, and the vascular and central nervous systems [1]. The incidence of BD differs from region to region, being particularly common in the Mediterranean region, and in the Middle East and Far East [2]. Vasculitis and secondary autoimmunity developing in response to the accumulation of immune complexes in small and intermediate blood vessels, have been identified in recent clinical studies as playing a major role in the pathogenesis of BD, although the exact mechanism of BD is still unknown [3, 4]. BD may present with clinical signs and symptoms in many different

✉ Ahmet Karadağ
dr_ahmetkaradag@hotmail.com

Mujde Karadağ
dr_mujdekaradag@hotmail.com

Adem Bora
adembora@yahoo.com

Emrullah Hayta
dremay@gmail.com

A. Bahadır Çetin
drbahadir38@hotmail.com

Sevil C. Doğan
drsevilceyhan@gmail.com

Kasım Durmuş
kasimdurmus58@gmail.com

E. Elif Altuntaş
ealtunta@yahoo.com

1 Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

2 Department of Otolaryngology, Sivas Numune Hospital, Sivas, Turkey

3 Department of Otolaryngology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

4 Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Acıbadem University, İstanbul, Turkey

5 Department of Ophthalmology, Sivas Numune Hospital, Sivas, Turkey

organ systems [5, 6]. In recent studies, vestibular system involvement was identified in rheumatoid diseases accompanied by vasculitis, and hearing loss developed secondary to this may be common [7, 8]. Incidences of SNHL due to vestibular system involvement have been reported in a range of 12–80% in studies of BD [9–11], and T-cell mediated immune response secondary to vasculitis has been suggested as playing a role in the involvement of the vestibular system [12, 13].

Although there are a few studies in literature reporting hearing loss due to inner ear involvement in BD, many of these included no control group [14, 15], meaning that the association between hearing loss and clinical findings, and between the duration of BD and tinnitus, as in other vestibular system pathologies, is covered inadequately. In the present study we investigate hearing loss and tinnitus in BD, and analyze the association between hearing loss and the clinical findings and disease duration in BD.

Materials and methods

The study was conducted between December 2016 and December 2017 and included 44 patients with BD who were in remission and who met the diagnostic criteria [16] defined by the International Behcet's Disease Study Group, as well as 42 healthy controls. The exclusion criteria applied in this study included disorders that could cause SNHL (e.g. diabetes, hypertension, endocrinological disorders, liver and kidney function disorders, malignancy, syphilis, neuro-Behcet's disease and congenital cochlear malformation), neurological and hematological diseases, receiving chemotherapy or radiotherapy, prior ear surgery, perforated tympanic membrane, acute or chronic middle-ear infection, working in a noisy environment, using ototoxic or immunosuppressive drugs (other than colchicine), history of noise trauma and hearing loss, less than 18 years or more than 60 years of age, and accompanying vascular or autoimmune diseases.

The gender, age, duration of disease, medications for the treatment of BD and clinical findings (oral and genital ulcers, ocular lesions, skin lesions, arthritis, vascular pathologies and pathergy test results) seen during the course of the disease of the patients with BD included in the study were recorded. The same physician performed a detailed ear, nose and throat examination on all participants, and the same audiometrist performed hearing tests. Both health professionals were blinded to the identity of the study participants. All subjects included in the study (BD and controls) were asked about the presence of tinnitus. Those who confirmed the presence of tinnitus were further tested with the Visual Analog Scale (VAS) and the Tinnitus Reaction Questionnaire (TRQ) in order to evaluate the level of tinnitus-induced annoyance and the effects of tinnitus on daily life, respectively.

The study was approved by the human Ethics Committee of our University, and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from every study participant.

Audiometric measurements

The threshold levels of the air and bone transmissions of patients with BD and the healthy individuals were measured using a clinical audiometry device (INTERACOUSTICS AC 40 Clinical Audiometer), calibrated according to ISO standards. All audiological tests were performed with the other ear masked. Pure tone hearing thresholds at frequencies of 0.25, 0.5, 1, 2, 4, 6, 8 and 12 kHz were measured. A pure tone hearing threshold of between 0 and 20 dB is classified as normal hearing, 21–40 dB as slight hearing loss, 41–60 dB as intermediate, 61–80 dB as severe 80–100 dB as deep and more than 100 dB as total hearing loss [17]. In the following stage, a transient evoked optoacoustic emission (TEOAE) test was applied to all patients using a TEOAE device. (Maico, ERO scan analyzer, GmbH Salzufer, 13/14, 10,587, Berlin Germany). During the test, disposable props were used to close the ear canal. When the testing was complete, if there was a response to TEOAE (hearing better than 30 dB), the result was noted as a "PASS" on the screen, and as "REFER" in the event of no response (hearing loss range of 30 dB or more). The screening test was repeated on the ear for which a "REFER" was noted. A stimulant was applied in form of a click in the frequency range 0.7–4 kHz and at an 83 dB/SPL ($\pm$3 dB) degree of density. The test was recorded in each session separately for the right and left ears, and the results were recorded one-by-one in the frequency band width of 1.5–4 kHz and in the 1.5, 2, 2.5, 3, 3.5 and 4 kHz frequencies for TEOAE. In the 1.5–4 kHz band width, an average amplitude of TEOAE below 6 dB was considered no response to OAE.

Tinnitus reaction questionnaire (TRQ)

Patients scoring 60 and above in this test, comprising 26 questions, answered on a scale of 0–4, are considered to be under major stress, which helps in the identification of those who can and those who cannot cope with tinnitus. It further evaluates complaints related to tinnitus and its effects on the patient's career and leisure time, along with compliance problems [18]. The TRQ used in the study was translated from English to Turkish by a professional translator with a good command of both languages, and with the recommendations and advice of two different otorhinolaryngologists

who are proficient English speakers. After the completion of the Turkish translation of the TRQ, a pilot study was carried out to test the comprehensibility of the questionnaire. The garnered data was analyzed by a statistician, and a Cronbach's Alpha coefficient of 0.886 was calculated. The statistical analysis carried out on the pilot study showed the questionnaire to be "highly reliable", and it was thus concluded to be appropriate for use in the present study.

Visual analog scale (VAS)

VAS has been adopted by various branches of medicine and has many variations. It has previously been adjusted and applied in many studies, given its ability to indicate the level of discomfort experienced by a patient due to tinnitus [19]. VAS measures the subjective perception of annoyance of the patient on a scale of 0–10, in which 0 reflects "No annoyance at all" and 10 reflects "Very much annoyed". We applied VAS to measure the tinnitus-induced annoyance on a scale of 0–10, over the previous week. The purpose of using VAS was explained in detail to the patients in the study, and they were informed how the scale was to be used to assess to what extent tinnitus (buzzing/ringing in the ears) affected their daily lives. The respondents were asked the question, "To what extent has tinnitus (buzzing/ringing in your ears) annoyed you within the last week? Please mark on the scale". The TRQ uses a Likert-type scale, has been found to be 'highly reliable' in previous calculations. Therefore, Spearman's correlation coefficient test was used to determine the reliability of scores obtained from VAS according to TRQ ($r=0.859$, $p<0.001$) The VAS value was considered to be reliable, and was thus used for the present study.

Statistical analyses

Analyses were conducted with the IBM SPSS Statistics 22 (IBM Corp., Armonk, NY, USA). A Kolmogorov–Smirnov test was applied to all data; and a Student's *t* test and a Pearson's correlation test were used for the evaluation of the data, since the parametric test hypotheses were matched, and a Chi-square test was used for the evaluation of categorical data. Data was expressed in the tables as number, percentage and mean ± standard deviation, and a p value of <0.05 was considered statistically significant.

Results

The study was completed 44 BD patients and 42 healthy controls. No statistically significant difference was found between the sociodemographic characteristics of the groups, including age and gender ($p>0.05$). The socio-demographic data of both groups is presented in Table 1. The disease duration and the clinical findings of patients with BD included in the study are presented in Table 2. A hearing test was performed on both groups using TEOAE, and the test result was REFER in nine individuals in the patient group and one individual in the control group. The differences in TEOAE were statistically significant between the BD and control groups ($p<0.05$). A pure-tone hearing test revealed that several individuals had hearing loss at two or more frequencies. The hearing loss between the 4000 and 6000 Hz frequencies in the group with BD was statistically significant

Table 2 Clinical manifestations in Behçet's patients

	BD (n = 44) Mean ± SD
Disease duration (month)	109.31 ± 54.38
	n (%)
Oral ulcers	44 (100)
Genital ulcers	30 (68.2)
Oculer lesions	22 (50)
Arthritis	23 (52.3)
Skin lesions	26 (59.1)
Pathergy positive	31 (70.5)
Vascular lesions	7 (15.9)

BD Behcet disesase, *n* number of patients, *SD* standard deviation

Table 1 Socio-demographic data of the patients with Behcet's disease and the control group

	BD ($n=44$) Mean ± SD	Control ($n=42$) Mean ± SD	p value
Age (years)	40.13 ± 8.82	39.59 ± 8.27	0.770
	n (%)	*n* (%)	
Gender			
Female	26 (59.1)	23 (54.8)	0.685
Male	18 (40.9)	19 (45.2)	

BD Behcet disesase, *SD* standard deviation, *n* number of patients

when compared to the control group ($p < 0.05$). Tinnitus was present in 12 (27.3%) patients in the group with BD, while there was no tinnitus in the control group. The comparison of the groups in terms of SNHL is presented in Fig. 1, and the hearing loss at in different frequencies identified from the pure tone audiogram is presented in Table 3. SNHL was bilateral in 29 patients and unilateral in two patients in the BD group; and SNHL was bilateral in four and unilateral in four individuals in the control group. Disease duration and age were statistically significantly different among patients with and without SNHL in the group with BD ($p < 0.05$). However, no statistically significant difference was found in the disease duration and age among patients with and without SNHL in the group with BD ($p > 0.05$). The results of a comparison of the patients with BD and with and without SNHL in terms of disease duration and age are presented in Table 4. No association was found between the clinical findings of BD and SNHL or tinnitus ($p > 0.05$). In patients with BD, the mean VAS score indicating the degree of tinnitus-induced annoyance, was 3.08 ± 1.24 (minimum-maximum 1–5). Furthermore, the mean TRQ score measuring the level of stress caused by tinnitus in the patients was 22.91 ± 16.28 (minimum-maximum 5–60), and which indicates that tinnitus causes stress in patients with BD.

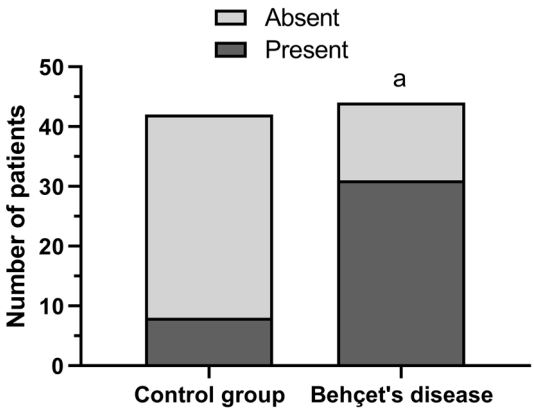

Fig. 1 Percentages of subjects with sensorineural hearing loss in control and Behcet's disease groups. [a]$p < 0.05$ vs. control group. In patients with Behcet's disease, sensorineural hearing loss is more pronounced

Discussion

In the present study, 44 patients with BD and 42 age-matched healthy controls were subjected to hearing tests and an evaluation of tinnitus. Hearing loss was detected in

Table 3 Percentage of patients with sensorineural hearing loss assessed with pure-tone audiometry in the control and Behcet's disease groups

	21–40 dB			41–60 dB			61–80 dB		
	Controls ($n = 42$)	BD ($n = 44$)	Significance	Controls ($n = 42$)	BD ($n = 44$)	Significance	Controls ($n = 42$)	BD ($n = 44$)	Significance
250 Hz									
Right ear	2 (4.8%)	7 (15.9%)	NS						
Left ear	2 (4.8%)	6 (13.6%)	NS						
500 Hz									
Right ear	2 (4.8%)	1 (2.3%)	NS						
Left ear	2 (4.8%)	1 (2.3%)	NS						
1000 Hz									
Right ear					1 (2.3%)				
Left ear					1 (2.3%)				
2000 Hz									
Right ear		2 (4.6%)							
Left ear		2 (4.6%)							
4000 Hz									
Right ear	1 (2.4%)	10 (23%)	0.008*	1 (2.4%)	2 (4.6%)	NS			
Left ear	2 (4.8%)	8 (18.1%)	NS	1 (2.4%)	2 (4.6%)	NS			
6000 Hz									
Right ear	3 (7.1%)	18 (40.9%)	0.001*	1 (2.4%)	7 (15.9%)	NS		1 (2.3%)	
Left ear	3 (7.1%)	17 (38.6%)	0.001*	1 (2.4%)	7 (15.9%)	NS		1 (2.3%)	

According to results of chi-square test, Behcet's disease caused significant sensorineural hearing loss in high frequencies

BD Behcet's disease, *dB* decibel, *NS* non-significant

*$p < 0.05$ Data are expressed as number (percentage)

Table 4 Comparison of disease duration and the age of patients with Behçet's disease with and without hearing loss

	Patients with SNHL ($n=31$) Mean ± SD	Patients without SNHL ($n=13$) Mean ± SD	p value
Disease duration (month)	120.65 ± 56.48	82.31 ± 38.75	0.031*
Age (years)	42.23 ± 8.74	35.15 ± 7.06	0.009*

SNHL sensorineural hearing loss, *SD* standard deviation, *n* number of patients

*$p<0.05$

31 patients (70.4%) in the BD group and in eight patients (19%) in the control group, suggesting that. SNHL is more common among patients with BD than in healthy subjects. That said, although the present study found SNHL to be the second most common clinical finding with a positive pathergy test in patients with BD, no relationship was identified between SNHL and the clinical findings of BD. Furthermore, the rate of abnormal TEOAEs was found to be higher in those with BD when compared to the healthy controls. In addition, the mean age of the patients with BD and with SNHL was found to be higher than that of patients with BD without SNHL, which was compatible with the results reported previously in literature [14, 20–23]. Also, disease duration in patients with BD and with SNHL was found to be longer than in patients with BD without SNHL. This finding differs from those of previous studies in literature [11, 14, 20]. Tinnitus was identified in 12 patients (27.3%) with BD, whereas no case of tinnitus was identified in the control group. This finding indicates that the rate of tinnitus is higher in patients with BD than in healthy subjects. Our study also showed that tinnitus is a cause of annoyance in patients with BD and also a source of stress. This finding indicates that tinnitus unfavorably affects the daily lives of patients with BD. This is the first study in literature to establish such findings.

Hearing loss in BD was first demonstrated by Alajouanine et al. [24], and the frequency of hearing loss was found to be high in BD in later clinical studies. Bakhshaee et al. [25], identified hearing loss at high frequencies in 59.2% of patients with BD, while in their study, Sonbay et al. [10], reported SHNL at a rate of 23% in the BD, particularly at high frequencies. In their studies, Sota et al. [14], and Cınar et al. [11], reported a rate of 63% for SHNL in the BD. The percentage of SNHL at high frequencies was found to be 84.5% in BD in another clinical study [26]. Similar to the studies mentioned above, SNHL was found to be 70.4% at high frequencies in the presence of BD in the present study. Sota et al. [14], and Bakhshaee et al. [25], in their studies, found that SNHL was the fourth most common clinical finding in BD after oral ulcers, ocular lesions and skin lesions. Andreoli et al. [23], found in their study that SNHL was the third most common finding in cases of BD. Similar to the mentioned studies, it was found in the present study that SNHL was the third most common clinical finding after oral ulcers and pathergy in BD.

Choung et al. [22] found no correlation between the clinical findings of BD and SNHL in their study, and this is supported by another clinical study that found no link between the clinical findings of BD and SNHL [27]. Ak et al. [20], also found no correlation between the clinical findings of BD and SNHL in their clinical study of patients with BD. Similar to the studies mentioned above, no association was found between the clinical findings of BD and SNHL in the present study either. Yarıktas et al. [28] in their clinical study found a difference in the age of patients with BD with and without SNHL, but no difference in disease duration between the patients with BD with and without SNHL. Similarly, Ak et al. [20] in their clinical study reported a difference in the age of patients with BD with and without SNHL, but found no difference in disease duration between patients with BD with and without SNHL. Kemal et al. [28] in their clinical study found no difference in disease duration between the patients with BD with and without SNHL. Similar to the studies stated above, a difference was found in the age of the patients with BD with and without SNHL in the present study, while in contrast to the studies above, a difference in disease duration was noted between the patients with BD with and without SNHL that may be attributable to the longer disease duration in the present study.

TEOAE measurements reflect the physiological status of the outer hair cell in the cochlea, and an abnormal TEOAE measurement may indicate a cochlear pathology. Aslan et al. [26], found that the rate of abnormal TEOAE measurements was higher in BD patients when compared to healthy controls and these findings mirrored those of another clinical study [29].

The limitations of the present study include its small patient population, the lack of ear Magnetic Resonance Imaging or histopathological evaluations, the cross-sectional nature of the study, and the fact that no patients with active BD were included in the study.

In conclusion, SNHL is more frequent in patients with BD, and significant differences can be seen in age and disease duration in patients with BD with and without SNHL. Furthermore, no correlation has been identified between the clinical findings of BD and SNHL; the frequency of tinnitus is higher among patients with BD when compared to the healthy controls; tinnitus is a matter of annoyance and affects the daily life activities of patients with BD negatively. Therefore that BD patients with tinnitus should undergo therapy for tinnitus. It can thus be suggested that the addition of an ear nose and throat examination to the treatment and follow-up plans of patients with BD would be beneficial.

Further studies are needed to evaluate hearing loss and tinnitus in BD.

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Compliance with ethical standards

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