

Evaluation of olfactory function in Behçet's disease

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Abstract

Objective: Behçet's disease (BD) is a chronic, relapsing type of vasculitis of unknown etiology and is characterized by oral and urogenital ulcers and ocular inflammation with cutaneous, musculoskeletal, vascular, and nervous system manifestations. Few cases involving the nasal mucosa have been reported in the literature, and the true prevalence of BD remains unknown. Neurological involvement associated with BD might play a more important role in causing olfactory dysfunction than mucosal involvement, but sufficient clinical data are not available on the effect of BD on olfaction in adults. We therefore evaluated the olfactory function of patients diagnosed with BD.

Material and Methods: Patients were chosen from among a consecutive patient group population who visited the internal medicine rheumatology polyclinic and otolaryngology departments of Ondokuz Mayıs University Hospital. A total of 50 patients (both males and females) aged 18 to 60 years with a diagnosis of BD and 46 healthy controls (matched to the study group in terms of age and gender) were included. BD was diagnosed based on the criteria defined by the International Study Group for BD. A complete clinical history was taken for and a physical examination was performed in all participants. Patients with other rheumatic diseases; obstructive nasal pathologies leading to conductive-type olfactory dysfunction (e.g., septum deviation or nasal polyp); advanced systemic disease (e.g., hypertension or malignancy); a history of antithyroid, antihistamine, antidepressant, or steroid medication use within the past month; or who were current smokers, had an active upper respiratory infection, or had a history of otolaryngologic operations were excluded. The results of the "Sniffin' Sticks" (SS) olfactory test were compared between the two groups.

Results: The mean age of the 50 BD patients was 35.3±10 years; that of the 46 health controls was 36.9±11 years. There was no significant group difference in age or gender distribution ($p>0.05$). Odor identification and overall scores were significantly lower in the BD group than in the control group. There were no significant differences in odor discrimination scores between the BD and control groups ($p>0.05$).

Conclusion: To our knowledge, this is the first study to evaluate olfactory function in patients diagnosed with BD using the SS test. Odor identification was more impaired in BD patients than in healthy controls, but there was no group difference in odor discrimination. BD patients should also be assessed for the involvement of olfactory function and may require treatment due to a malfunction of the olfactory system that affects the quality of life.

Keywords: Behçet's disease, olfactory function, Sniffin' Sticks test



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Introduction

Behçet's disease (BD) is a chronic, relapsing type of vasculitis of unknown etiology and is characterized by oral and urogenital ulcers and ocular inflammation with cutaneous, musculoskeletal, vascular, and nervous system manifestations (1). Few cases involving the nasal mucosa have been reported in the literature, and the true prevalence of BD remains unknown (2). Neurological involvement associated with BD might play a more important role in causing olfactory dysfunction than mucosal involvement, but sufficient clinical data are not available on the effect of BD on olfaction in adults (3). We therefore evaluated the olfactory function of patients diagnosed with BD.

Material and Methods

Study design

The study commenced after obtaining approval from the Clinical Trials Ethics Committee Ondokuz Mayıs University (2015/109) and written informed consent from each subject. All investigations were conducted in accordance with the Declaration of Helsinki on biomedical studies involving human subjects. Patients were chosen from among a consecutive patient group population who visited the internal medicine rheumatology polyclinic and otolaryngology departments of Ondokuz Mayıs University Hospital. A total of 50 patients (both males and females) aged 18 to 60 years with a diagnosis of BD and 46 healthy controls (matched to the study group in terms of age and gender) were included. BD was diagnosed based on the criteria defined by the International Study Group for BD (4). A complete clinical history was taken for and a physical examination was performed in all participants. Patients with other rheumatic diseases; obstructive

nasal pathologies leading to conductive-type olfactory dysfunction (e.g., septum deviation or nasal polyp); advanced systemic disease (e.g., hypertension or malignancy); a history of antithyroid, antihistamine, antidepressant, or steroid medication within the past month; or who were current smokers, had an active upper respiratory infection, or had a history of otolaryngologic operations were excluded. All participants then underwent the olfactory test.

Olfactory testing

The "Sniffin' Sticks" (SS) (Burghart GmbH; Wedel, Germany) test was applied in addition to routine systemic and otolaryngologic examinations, conducted by blinded researchers. Odor thresholds for identification and discrimination were determined for 12 common odors. Odorants were presented using commercially available felt-tip pens. During odor presentation, the pen caps were removed by the experimenter for 3-4 s, and then the tip of the pen was placed at a distance 15-25 mm from the participant's nostrils. Using a multiple forced-choice paradigm, subjects identified individual odors from among four different verbal descriptions, after an interval of at least 30 s to prevent olfactory desensitization (5). The subjects were free to sample the odors as frequently as was required to make a decision. The test result was given by the summed score of all correctly identified odors. The maximum score for each subtest (discrimination and identification) was 12, resulting in a maximum composite score of 24.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows software package (SPSS Inc.; version 15.0, Chicago, IL, USA). Parametric values are provided here as the means±SDs; nonparametric values are given as percentage values. To compare continuous parametric variables, the Student's t-test or analysis of variance was used; to compare nonparametric continuous variables, the Mann-Whitney U test was used. Categorical data were compared using the chi-square test. A p value < 0.05 was taken to indicate statistical significance.

Results

The mean age of the 50 BD patients was 35.3±10 years, compared to 36.9±11 years for the 46 control group patients. There was no significant group difference in age or gender distribution (p>0.05; Table 1). The demographic characteristics of the BD patients are presented in Table 1. Odor identification and total scores were significantly lower in the BD group compared to the control group (Figure 1, 2).

There were no significant differences in odor discrimination scores between the BD and control groups (p>0.05). The descriptive data for the olfactory test parameters of each group are presented in Table 2.

Discussion

In our study, we revealed that odor identification was more impaired in BD patients than in healthy controls. Therefore, BD patients should also be assessed for the involvement of olfactory function and may require treatment due to a malfunction of the olfactory system affecting the quality of life.

Olfactory receptor neurons directly interact with the external environment in a manner that differs from other neurons, i.e., they possess a unique ability to regenerate. However, neural development and differentiation within

the olfactory system is yet to be completely explained (6). Although frequently neglected by clinicians and patients, the olfactory sense is of utmost importance to humans, because it contributes significantly to safety and the quality of life. Olfactory impairment is associated with a decreased taste perception; therefore, taste

Table 1. Demographic characteristics of Behçet's disease

	(n=50)
Oral ulceration, n (%)	50 (100)
Genital ulceration, n (%)	36 (72)
Eye lesions, n (%)	13 (26)
Skin lesions, n (%)	48 (96)
Arthritis, n (%)	15 (30)
Neurological involvement, n (%)	4 (8)
Vasculer involvement, n (%)	20 (40)

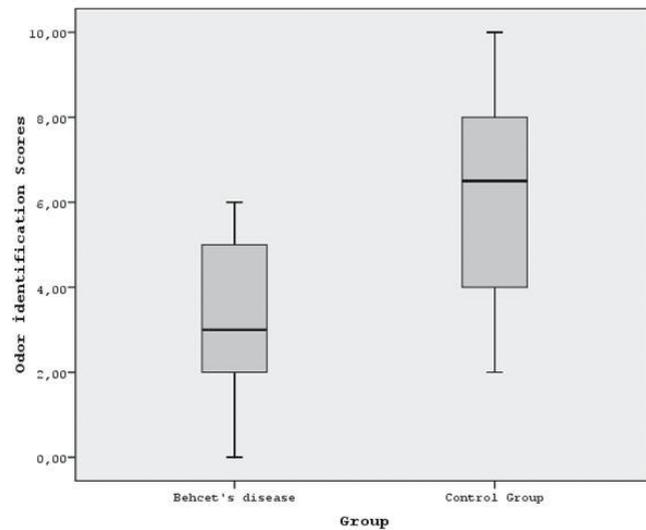


Figure 1. Odor identification scores in Behçet's disease and control groups

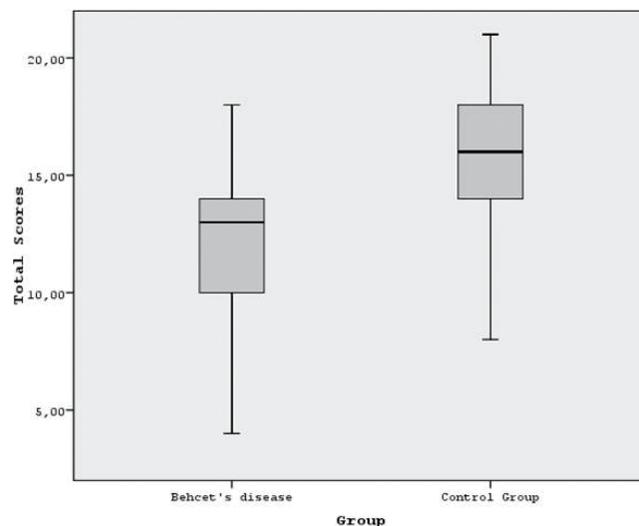


Figure 2. Total scores in Behçet's disease and control groups

Table 2. Descriptive statistics of results from Behçet's disease group and healthy control group olfactory testing results

	Behçet's disease group	Healthy control group	p
Odor identification score	3.2±1.7	6.2±2.1	p<0.001*
Odor discrimination score	8.8±2.1	9.4±1.6	p=0.15
Total score	12±3.4	15±3.1	p<0.001*
Female/Male	21 (42%)/29 (54%)	21 (46%)/25 (54%)	p=0.72
Mean Age	35.3±10	36.9±11	p=0.453

*Statistically significant

perception is strongly influenced by olfaction (7). Smell and taste play a role in stimulating gastric excretions in the context of normal digestive physiology, and also serve as an early-warning system against harmful substances (8, 9).

Olfactory dysfunction has been confirmed in various neurological and psychiatric diseases, such as schizophrenia and depression, endocrine disorders (hypothyroidism, diabetes), and neurodegenerative diseases (Alzheimer's, Parkinson's, multiple sclerosis) (10, 11). Olfactory dysfunction is also involved in various autoimmune diseases, such as systemic lupus erythematosus (SLE) (12).

Behçet's disease represents a multisystem vasculitis characterized by mucosal aphthosis, primarily in the oral and genital mucosa. To the best of our knowledge, there is no previous report of olfactory function disorder developing due to neurological or nasal mucosal factors in BD patients. A previous study evaluated olfaction using a butanol threshold and odor identification tests. (3). Numerous smell disorder tests are available, the most widely used of which are the University of Pennsylvania Smell Identification Test (UPSIT) and the Connecticut Chemosensory Clinical Research Center Test (CCCRC) in North America, and the SS test in Europe and Australia (also used in the present study) (13-15).

The SS test has been used previously to assess olfactory performance in a Turkish population, but the odor identification results obtained using this test may vary due to local and cultural factors (16, 17). We evaluated the olfactory function of BD patients using this test.

Olfactory dysfunction may denote neurological involvement in BD. In a previous study (3), patients with skin and eye involvement were included. In this study, patients' olfaction was evaluated using the butanol threshold or odor identification tests, and it was found that olfaction scores were significantly lower in patients

with BD and slightly higher in patients with nasal mucosal findings. In our study, neurological involvement was present in four patients but, in all patients, there was no mucosal involvement.

We used the SS test as it has proven applicability in the Turkish population. Odor identification and total scores were significantly lower in BD patients than in healthy controls, but there was no group difference in odor discrimination scores. To our knowledge, this is the first study to assess olfaction using the SS test in BD patients. Olfactory dysfunction and nasal mucosal involvement have been observed in various autoimmune diseases, such as Wegener granulomatosis, Churg–Strauss syndrome, systemic lupus erythematosus, Sjögren's syndrome, and systemic sclerosis (18-22). However, at present, an insufficient number of studies have assessed olfaction in BD patients. Further studies are required to assess whether olfactory disorder in BD develops due to nasal mucosa or neurological factors. We believe that our study provides a useful starting point for future studies, which should use larger samples to investigate olfactory function.

To our knowledge, this is the first study to evaluate olfactory function in patients diagnosed with BD using the SS test. The results revealed diminished olfactory identification in BD patients. BD patients should also be assessed for the involvement of olfactory function and may require treatment due to a malfunction of the olfactory system that affects the quality of life.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ondokuz Mayıs University School of Medicine.

Informed Consent: Written informed consent was obtained from who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - L.A.; Design - L.A.; Supervision - M.S., M.Ö.; Resources - R.K, E.G; Materials - S.Ö, E.G; Data Collection and/or Processing - S.Ö,

E.G; Analysis and/or Interpretation - L.A., L.A.; Literature Search - L.A.; Writing Manuscript - L.A.; Critical Review - M.S., M.Ö.; Other - S.Ö., E.G.

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