

Assessment of nasal mucociliary activity in patients with Behçet's disease

I OZBAY¹, C KUCUR¹, F TEMİZTURK², Y OZKAN², C KAHRAMAN³, F OGHAN¹

Departments of ¹ORL, ²Physical Therapy and Rehabilitation, and ³Internal Medicine, Dumlupınar University, Kutahya, Turkey

Abstract

Objective: To investigate nasal mucociliary clearance in patients with Behçet's disease.

Methods: Thirty patients with Behçet's disease, diagnosed on the basis of criteria defined by the International Study Group for Behçet's Disease, and 30 healthy individuals were recruited. In both groups, individuals with conditions that could affect nasal mucociliary clearance were excluded. Nasal mucociliary clearance time was evaluated using saccharin tests. The time between placement of a saccharin tablet and the tasting of the saccharin was measured and recorded as the saccharin clearance time.

Results: The mean nasal mucociliary clearance time was significantly longer in the Behçet's disease patients than in the control subjects ($p < 0.001$). Furthermore, there was a positive correlation between Behçet's disease duration and nasal mucociliary clearance time ($p < 0.001$, $r = 0.882$).

Conclusion: The results suggest that nasal mucociliary clearance time is longer in Behçet's disease patients than in control subjects, and is positively correlated with disease duration.

Key words: Nasal Mucosa; Behçet Disease; Saccharin

Introduction

A Turkish dermatologist named Hulusi Behçet defined Behçet's disease, in 1937, as a triple symptom complex of recurrent aphthous ulcers, genital ulcers and uveitis.¹ Behçet's disease is a chronic, relapsing condition that affects small vessels in multiple systems of the body, with a large spectrum of clinical manifestations involving the vascular, ocular, mucocutaneous, gastrointestinal, musculoskeletal and central nervous systems. The most common clinical features of Behçet's disease in the ENT region include oral, laryngeal and oropharyngeal mucosal ulcerations, and morbidities related to scar formation during the healing process.²

Nasal mucociliary clearance is defined as the capability of the respiratory mucosa to deport foreign particles by ciliary activity and maintain the moisture of the mucosal surfaces by inducing mucous gland secretions. Nasal mucociliary clearance can be assessed by determining the time taken for the elimination of inhaled or inspired aerosols.³ A normal result for the saccharin clearance test is clearance of saccharin in 7–15 minutes; those with a saccharin clearance time of more than 20 minutes are considered to have abnormal mucociliary clearance.^{4,5} A taste disorder should be excluded if the nasal mucociliary clearance of saccharin is over 60 minutes. One study reported a

relationship between disturbed nasal mucociliary clearance and certain rhinological pathologies including sinusitis, allergic rhinitis and nasal polyposis.⁶

A relationship between sinonasal diseases, including chronic rhinosinusitis and olfactory dysfunction, and Behçet's disease has been shown in some studies.^{7,8} However, no study has reported the effects of Behçet's disease on nasal mucociliary clearance. Therefore, we undertook this novel study to determine whether disturbed nasal mucociliary clearance is a contributing pathophysiological factor for the sinonasal manifestations of Behçet's disease.

Materials and methods

Participants

We recruited 30 patients with Behçet's disease diagnosed on the basis of criteria defined by the International Study Group for Behçet's Disease.⁹ The criteria were the presence of oral ulceration, plus any two of the following: genital ulcerations; typical, defined eye lesions; typical, defined skin lesions; or a positive pathergy test result, suggestive of Behçet's disease in the absence of other possible explanations. All patients were examined using a 0-degree endoscope; none had evidence of nasal cavity disorders

such as ulcers, sinusitis or polyps. We also recruited 30 healthy individuals who were negative for all these criteria.

We excluded individuals in both groups who had conditions that could affect nasal mucociliary clearance, such as current upper respiratory tract infection, allergic rhinitis and major septal deviation, and those with a history of previous nasal surgery, smoking and/or trauma. We also excluded patients with a prolonged saccharin clearance time, beyond 60 minutes, or a taste disorder.

Nasal mucociliary clearance

The nasal mucociliary clearance time was evaluated using saccharin tests. The tests were performed at an otorhinolaryngology clinic by the same clinician, who was blinded to the groups. Measurements were obtained at a temperature of 20–24 °C and at a relative humidity of 45–60 per cent. The subjects were instructed to blow their noses, and to refrain from food or liquid intake 1 hour before the test; they were encouraged to rest for 30 minutes before testing.

With the subject in an upright position, a saccharin tablet with an approximate diameter of 1.5 mm (one-quarter of a saccharin tablet) was placed 1 cm posterior to the anterior border of the medial aspect of the lower concha using bayonet forceps. During the test, subjects were requested to maintain their position, and asked to refrain from deep breathing, coughing, talking, sniffing or sneezing. They were instructed to swallow at 30-second intervals and to indicate when they tasted the saccharin. The time between placement of the saccharin tablet and the tasting of the saccharin was measured by a chronometer and recorded as the saccharin clearance time.

Ethical considerations

The protocol of this study was approved by the local ethics committee. All subjects in the study provided written and oral informed consent.

Statistical analysis

All statistical analyses were performed using SPSS software, version 19 (SPSS, Chicago, Illinois, USA). Normality was assessed using the Shapiro–Wilk test. Data are expressed as means \pm standard deviations. The independent samples *t*-test and Kruskal–Wallis test were used to examine differences between groups. Correlation analysis was conducted using Pearson's test. A *p* value of less than 0.05 was considered statistically significant.

Results

A total of 60 individuals completed the study. The Behçet's disease group included 19 women and 11 men, with a mean age of 41.3 ± 13.3 years (range, 19–74 years). The control group included 18 women and 12 men, with a mean age of 46.7 ± 13.7 years (range, 18–71 years). There were no significant

differences between the patient and control groups in terms of age ($p = 0.122$) or gender ($p = 0.795$; Table I).

The mean nasal mucociliary clearance time in the Behçet's disease and control groups was 13.4 ± 3.3 minutes (range, 8–19 minutes) and 9.0 ± 1.8 minutes (range, 6–13 minutes), respectively (Table I), being significantly longer in the former than in the latter group ($p < 0.001$; Figure 1).

The mean duration of Behçet's disease was 8.53 ± 6.77 years (range, 1–22 years), and this was positively correlated with nasal mucociliary clearance time ($p < 0.001$, $r = 0.882$; Figure 2).

Discussion

The incidence of Behçet's disease is high in the countries located along the ancient Silk Road, stretching from Asia to the Mediterranean countries. It is therefore very common not only in Turkey (80–370 cases per 100 000 inhabitants) but also in Japan, Korea and China.¹⁰ ENT specialists in Turkey frequently encounter Behçet's disease patients because this condition is associated with several otorhinolaryngological manifestations.

Morales-Angulo *et al.* identified the ENT manifestations in 33 Behçet's disease patients and found oral ulcers to be the most common (97 per cent), followed by oropharyngeal ulcers (24 per cent) and audiovestibular symptoms (high-frequency sensorineural hearing loss, vertigo and bilateral vestibular hypofunction; 15 per cent).¹¹ One patient showed symptoms compatible with vestibular neuritis as the first manifestations, indicating the onset of neuro-Behçet's disease. In 12 per cent of patients, the presence ofodynophagia secondary to oropharyngeal lesions, initially interpreted as acute or recurrent tonsillitis, was the first manifestation, alone or in association with cutaneous or ocular lesions.

Behçet's disease also affects the nasal mucosa. The prevalence of nasal mucosal involvement in Behçet's disease patients was investigated by Shahram *et al.*¹² Of 400 patients, 67 reported a history of nasal mucosal involvement, although not all of the patients

TABLE I
DEMOGRAPHIC DATA AND MEAN NASAL MUCOCILIARY CLEARANCE TIME IN BEHÇET'S DISEASE AND CONTROL GROUPS

Variable	Control group*	Patient group*	<i>p</i>
Age (mean \pm SD; years)	46.7 \pm 13.7	41.3 \pm 13.3	0.122
Sex (% female)	60.0	63.3	0.795
Nasal mucociliary clearance time (mean \pm SD; minutes)	9.0 \pm 1.8	13.4 \pm 3.3	<0.001 [†]

**n* = 30. [†]Indicates significant difference. SD = standard deviation

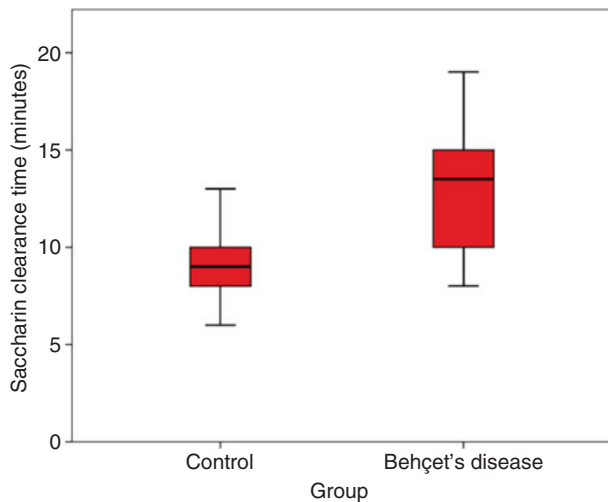


FIG. 1

Mean nasal mucociliary clearance time in the Behçet's disease and control groups.

had nasal involvement at the time of the study. Nasal mucosal involvement included: a history of mucosal ulcers, in 51 patients; pain, in 49 patients; burning, in 32 patients; obstruction, in 11 patients (bilateral in 1 patient); itching, in 7 patients; epistaxis, in 6 patients; and post-nasal discharge, in 5 patients. The most common nasal symptom was dysosmia, which was observed in 15 patients. Other nasal symptoms included: obstruction, in 10 patients; ulcers, in 2 patients; pain, in 2 patients; a burning sensation, in 1 patient; and discharge, in 1 patient. None of these 31 patients with nasal symptoms reported a history of epistaxis or nasal itching. Abnormal signs were present in only 16 patients; these included nasal cartilage deformity (in six patients), unilateral nasal obstruction (in four patients), post-nasal discharge (in three patients), non-aphthous ulcers (in three patients) and crusted ulcers (in two patients).

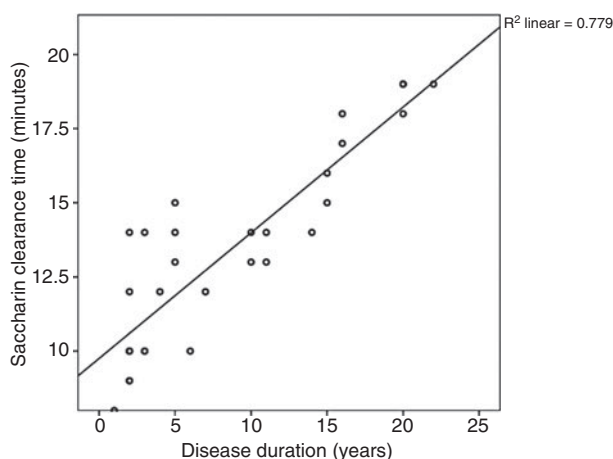


FIG. 2

Correlation between the duration of Behçet's disease and nasal mucociliary clearance time.

Veyseller *et al.* investigated the effects of Behçet's disease on olfactory function, nasal mucosa and nasal symptoms.⁷ Endoscopic evaluation revealed nasal mucosal lesions in 16 of 30 Behçet's disease patients. The lesions were not specific for Behçet's disease, and were mainly located in Little's area, the medial surface of the inferior turbinate and, less commonly, the nasal septum. They were mostly hyperaemic, crusting erosions, and ulcerations with occasional haemorrhage. The authors also evaluated olfactory function and found that olfactory dysfunction was associated with Behçet's disease. They claimed that nasal symptoms were associated with the presence of nasal lesions, although they did not find a correlation between nasal findings and olfactory function.

Verim *et al.* evaluated the frequency of chronic rhinosinusitis in Behçet's disease patients and healthy controls, and found prevalence rates of 23.2 per cent and 2.7 per cent, respectively, with a statistically significant difference between groups.⁸

Mucociliary clearance is the primary defence mechanism of the respiratory tract. Potentially harmful particles are retained by the mucus covering, and ciliary motion deports them from the nasal cavity to the nasopharynx.¹³ Evaluation of the nasal mucociliary clearance rate is a credible index for the clearance function of the upper and lower respiratory tracts. Prolonged nasal mucociliary clearance time is considered to indicate disturbed nasal mucociliary clearance.⁴ This may give rise to long-term respiratory tract diseases, and sinonasal and middle-ear infections.¹⁴ The saccharin test is a simple and safe method for investigating nasal mucociliary clearance.

This study evaluated the effects of Behçet's disease on nasal mucociliary clearance. We found that nasal mucociliary clearance time was prolonged in patients with Behçet's disease compared to controls, but was still within the normal range reported in the literature (under 20 minutes).^{4,5} Moreover, we found that the mean duration of Behçet's disease was positively correlated with nasal mucociliary clearance time. We hope that this preliminary study will encourage other larger studies to be undertaken.

- Nasal mucociliary clearance time is prolonged in Behçet's disease patients compared with that in healthy individuals
- Nasal mucociliary clearance time is correlated with Behçet's disease duration
- Clinicians should closely monitor patients with Behçet's disease for evidence of respiratory tract diseases, and sinonasal and middle-ear infections

Nasal mucociliary clearance time is affected by diverse factors, including: temperature; moisture; partial oxygen pressure and pH (acidity); cigarette smoke

and various inhalation agents; anatomical barriers such as a deviated septum; adenoid hypertrophy; and systemic diseases such as viral infections, chronic sinusitis, chronic and allergic rhinitis, cystic fibrosis, chronic bronchitis, and diabetes mellitus.^{15–17} Therefore, we excluded patients with any such conditions from our study.

This study is, to our knowledge, the first to evaluate nasal mucociliary clearance in Behçet's disease patients. Nevertheless, the results should be considered as preliminary given that the sample size was relatively small. An important limitation of the study is the lack of a pathophysiological evaluation of the subjects' nasal mucosae. Other limitations follow from known problems of the saccharin test. The test depends on the sensation of taste. In addition, it does not provide objective information that can be subjected to quantitative analyses.¹⁸ In contrast, rhinoscintigraphy, in which the velocity of radioactive material placed in the nasal cavity is measured by gamma cameras, provides more definitive results.^{19,20} However, it involves exposure to a low dose of radiation.²¹

Conclusion

Our findings, which require confirmation, suggest that nasal mucociliary clearance time is prolonged in Behçet's disease patients, and is correlated with the duration of Behçet's disease. Clinicians should closely monitor these patients for respiratory tract diseases, and sinonasal and middle-ear infections.

References

- Behçet H. Oral relapsing, aphthous ulcers of the mouth, eye and genitalia caused by a virus [in German]. *Dermatol Wochenschr* 1937;**105**:1152–7
- Webb CJ, Moots RJ, Swift AC. Ear, nose and throat manifestations of Behçet's disease: a review. *J Laryngol Otol* 2008;**122**:1279–83
- Uysal IO, Gokakın AK, Karakus CF, Devenci K, Hasbek Z, Sancakdar E. Evaluation of nasal mucociliary activity in iatrogenic hypothyroidism. *Eur Arch Otorhinolaryngol* 2013;**270**:3075–8
- Asai K, Haruna S, Otori N, Yanagi K, Fukami M, Moriyama H. Saccharin test of maxillary sinus mucociliary function after endoscopic sinus surgery. *Laryngoscope* 2000;**110**:117–22
- Lale AM, Mason JD, Jones NS. Mucociliary transport and its assessment: a review. *Clin Otolaryngol* 1998;**23**:388–96
- Habesoglu M, Demir K, Yumusakhuyulu AC, Yilmaz AS, Oysu C. Does passive smoking have an effect on nasal mucociliary clearance? *Otolaryngol Head Neck Surg* 2012;**147**:152–6
- Veyseller B, Dogan R, Ozücer B, Aksoy F, Meric A, Su O *et al*. Olfactory function and nasal manifestations of Behçet's disease. *Auris Nasus Larynx* 2014;**41**:185–9
- Verim A, Cebeci F, Baser E, Calim ÖF, Kadioğlu D, Kocagöz GD. Prevalence of chronic rhinosinusitis in the setting of Behçet disease. *J Craniofac Surg* 2015;**26**:186–90
- International Study Group for Behçet's Disease. Criteria for diagnosis of Behçet's disease. *Lancet* 1990;**335**:1078–80
- O'Neill TW, Rigby AS, Silman AJ, Barnes C. Validation of the International Study Group criteria for Behçet's disease. *Br J Rheumatol* 1994;**33**:115–17
- Morales-Angulo C, Vergara Pastrana S, Obeso-Agüera S, Acle L, Gonzalez-Gay MA. Otorhinolaryngological manifestations in patients with Behçet disease [in Spanish]. *Acta Otorrinolaringol Esp* 2014;**65**:15–21
- Shahram F, Zarandy MM, Ibrahim A, Ziaie N, Saidi M, Nabaei B *et al*. Nasal mucosal involvement in Behçet disease: a study of its incidence and characteristics in 400 patients. *Ear Nose Throat J* 2010;**89**:30–3
- Soylu Özler G, Akbay E, Akkoca AN, Karapınar OS, Şimşek GÖ. Does menopause effect nasal mucociliary clearance time? *Eur Arch Otorhinolaryngol* 2015;**272**:363–6
- Sun SS, Hsieh JF, Tsai SC, Ho YJ, Kao CH. The role of rhinoscintigraphy in the evaluation of nasal mucociliary clearance function in patients with sinusitis. *Nucl Med Commun* 2000;**21**:1029–32
- Sakakura Y, Ukai K, Majima Y, Murai S, Harada T, Miyoshi Y. Nasal mucociliary clearance under various conditions. *Acta Otolaryngol* 1983;**96**:651–4
- Maurizi M, Paludetti G, Todisco T, Almdori G, Ottaviani F, Zappone C. Ciliary ultrastructure and nasal mucociliary clearance in chronic and allergic rhinitis. *Rhinology* 1984;**22**:233–40
- Wanner A. Allergic mucociliary dysfunction. *Laryngoscope* 1983;**93**:68–70
- Di Giuda D, Galli J, Calcagni ML, Corina L, Paludetti G, Ottaviani F *et al*. Rhinoscintigraphy: a simple radioisotope technique to study the mucociliary system. *Clin Nucl Med* 2000;**25**:127–30
- Nuutinen J. Asymmetry in the nasal mucociliary transport rate. *Laryngoscope* 1996;**106**:1424–8
- Soane RJ, Carney AS, Jones NS, Frier M, Perkins AC, Davis SS *et al*. The effect of nasal cycle on mucociliary clearance. *Clin Otolaryngol* 2001;**26**:9–15
- Polat C, Dostbil Z. Evaluation of the nasal mucociliary transport rate by rhinoscintigraphy before and after surgery in patients with deviated nasal septum. *Eur Arch Otorhinolaryngol* 2010;**267**:529–35

Address for correspondence:

Dr Isa Ozbay,
Department of Otolaryngology,
Medicine Faculty of Dumlupınar University,
Kutahya, Turkey

Fax: +90 274 231 6673

E-mail: isaozbay@gmail.com

Dr I Ozbay takes responsibility for the integrity of the content of the paper

Competing interests: None declared