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Original Article

# The evaluation of nose functions in chronic obstructive pulmonary disease

Ozge Caglar[1], Pinar Mutlu[2], Arzu Mirici[2], Sibel Oymak[3], Sefa Derekoy[1]

[1] 18 Mart University Faculty of Medicine, Department of Otorhinolaryngology, Canakkale,Turkey
[2] 18 Mart University Faculty of Medicine, Department of Pulmoner Diseases, Canakkale, Turkey
[3] 18 Mart University Faculty of Medicine, Department of Public Health, Canakkale, Turkey



**Abstract**

**Aim:** The aim of this study was to assess the nasal and olfactory functions of patients with chronic obstructive pulmonary disease (COPD).

**Material and Methods:** This prospective study included patients followed-up with COPD in the pulmonary diseases clinic. Patients with COPD without any nasal disease or systemic disease were included in the study. After routine ear nose throat examination was performed, patients with no nasal pathology had the saccharin test and Sniffin' Sticks tests applied. The control group consisted of volunteers that were living in the same region. The same tests applied to the control group too and the results were compared.

**Results:** There were no significant differences between patient group and control group in terms of categorical variables such as gender, age, smoking status, living area... It was found that the odor functions of COPD patients were significantly affected when compared with the control group. Odor test results were significantly lower in the patient group (p: 0.0001). In addition, mucociliary function was decreased in COPD patients.

**Conclusions:** It was found that the smell and mucociliary functions of COPD patients were worse than the individuals of the same age and this situation had a significant effect on the quality of life of the patients.

**Keywords:** Rhinology; olfactory function; sniffin sticks; mucociliary function; COPD

## INTRODUCTION

The prevalence of olfactory dysfunction in the general population is a controversial issue and is often not fully predictable. Odor loss is quite common in patients with sinonasal problems such as chronic rhinosinusitis (1). Pathology is based on two pathophysiological mechanisms of olfactory dysfunction observed in chronic rhinosinusitis patients, which may either be loss of transmission type (swollen or hypertrophic mucosa) or loss of sensation (directly affecting olfactory sensory neurons) (2-3).

The sense of smell is the least understood sense in the body. Today, many studies have been carried out to evaluate olfactory functions and the conditions affecting these functions (4). Two types of tests are used for odor measurement; psychophysical (subjective) tests and electrophysiological (objective) tests. Psychophysical tests include the odor threshold test, odor differentiation test and odor identification test. Electro-olfactogram (EOG) and odor-stimulated brain potential (OSBP) measurement tests are electrophysiological (objective) tests (5). The Sniffin' Sticks test is widely used in Europe and Turkey. This test has advantages such as long shelf life, reusability and short application time. Determination of odor threshold, odor discrimination and odor identification can be performed with this method. These tests show that this test is also suitable for Turkish people (6) .

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease that is characterized persistent respiratory symptoms and airflow limitation that is due to airway or alveolar abnormalities usually caused by exposure to noxious particles or gases (7).

It is widely known that there is a relationship between

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**Corresponding Author:** Ozge Caglar, 18 Mart University Faculty of Medicine, Department of Otorhinolaryngology, Canakkale,Turkey
**E-mail:** ozgecaglar@comu.edu.tr

rhinitis and asthma, because 90% of asthmatic patients have rhinitis and allergic rhinitis, while about 30% of patients with rhinitis and allergic rhinitis develop asthma (8).

Different study groups have supported the idea that COPD is a disease that affects the whole of the airway (9).

For this reason, the aim of this study is to evaluate upper respiratory symptoms in a well-defined COPD cohort. Also, no studies published so far have evaluated the sense of smell of COPD patients and have not used the Sniffin' Sticks test to do so.

In this study, mucociliary functions of nose and also odor threshold, odor discrimination, odor identification values were evaluated using the 'Sniffin' Sticks' test in COPD patients.

## MATERIAL and METHODS

The study was approved by the Institutional Ethics Committee of 18 Mart University School of Medicine (18920478-050.01.04/E.21041, 17.02.2017). This study was made in accordance with the Declaration of Helsinki.. Only participants over the age of 18 were included in the study and all experiments were conducted with the written approval of each participant. 40 patients with COPD and 34 volunteers were included in our study. The post-bronchodilator FEV1 of all patients was <80% lower than the predicted value by age, height and sex, and the FEV1 / FVC ratio was less than 0.7. The diagnosis of COPD is based on at least 10 pack-years of smoking history, symptoms suggestive of COPD, physical examination findings, radiographic findings, and spirometric measures. Spirometry was performed according to the guidelines of the American Thoracic Society-European Respiratory Society using the spirometer system Masterscope JLAB V5.22.1.50 (Cardinal Health, Germany, Hoechberrg, 2006). The forced expiratory volume (FEV1), forced vital capacity (FVC) and FEV1/FVC ratio were calculated. All spirometric measurements were made by same technician. Patients were included in the study provided that the expected value of the post-bronchodilator FEV1 / FVC ratio was less than <0.7 according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD-2019) guidelines.

Respiratory function tests were performed by the respiratory function test nurse with a spirometry device in our clinic's pulmonary function test laboratory using Masterscope JLAB V5.22.1.50 (Cardinal Health, Germany, Hoechberg, 2006). The patients' height and weight were measured and recorded with precision measurements. The spirometer was calibrated daily. Patients were checked for short-acting bronchodilator six hours before spirometry, long-acting bronchodilator 12 hours before, and theophylline 24 hours before. The patients rested very well. Before spirometry, the test was explained verbally and visually. The patient's nose was covered with a ratchet, and a cardboard spirometry mouthpiece was used. When spirometry was performed, the patient was asked to breathe normally and calmly three times before breathing deeply enough to be able to hold their breath for a few seconds, and then to breathe out for at least 6 seconds at a time without interruption quickly and strongly. At least three technically acceptable maneuvers were performed for the test and higher FEV1 or FEV1 / FVC values were accepted. Subsequently, the patient received 400 mcg of the short-acting beta-2 agonist salbutamol inhaler, and after 15 minutes the test was repeated and the reversibility response was assessed.

Patients with COPD first underwent a full ENT examination, and care was taken that patients did not have nasal pathology or any disease that could affect the sense of smell like superior-anterior septal deviations. Patients that had been prescribed short-term oral corticosteroids within the last 6 months or had sinonasal surgery within the last 12 months were excluded from the study. Patients with allergic rhinitis were excluded from the study. In addition, patients with systemic diseases (diabetes mellitus or rheumatologic disease) that could affect the sense of smell were excluded from the study. To assess the mucosal status each participant underwent nasal endoscopy performed by same ear, nose and throat specialist. The saccharin test was performed to determine the mucosal clearance of the patients. ¼ saccharin was placed under the lower turbinates of the patients, and the time to the taste area was calculated. Participants were instructed to only drink water and avoid smelling products an hour before the test.

34 patients without any lung or other disease were included in the study as a control group. The control group was selected from the same age, same gender and smokers as the study group. Patients who had history of major head trauma, oral or topical steroid use, acute bacterial or viral infection and sinusitis, nasal surgery, and allergic rhinitis were not included in the study.

The "Sniffin Sticks" odor test and saccharin test were performed on all patient and control groups.

This study was conducted in the ENT clinic of the university hospital, with nothing to affect the patients' sense of smell.

Firstly, saccharin test was performed on both groups. The saccharin test placed one- fourth of saccharin in the lower part of the lower concha of the patients, and the taste duration of the patient was accepted as mucociliary activity. Then the odor test was applied.

### Application of Sniffin' Sticks Test

The Sniffin' Sticks test (Burghardt, Wedel, Germany) was performed with 3 sets of 16 scent pens each. Odor threshold, odor discrimination and odor identification functions were evaluated. During these procedures, the patient's eyes were covered with a mask and odorless gloves were used.

In the odor threshold test, the lowest concentration odor value that a person can sense is taken as the threshold

value. In the test, 3 fragrance pens including 2 solvent and n-butanol odors were used. The patient's eyes were closed and the highest concentrations of scent pens were initially sniffed by the patient. This smell should be detected more than the other smells. Three pens were presented to the patient, starting with the triple ballpoint pen containing the lowest odor concentration, and proceeding to the pen with the highest odor concentration. The patient had to find the lowest concentration that he could distinguish from the pen twice. The lowest concentration that the patient perceived was determined as the peak value. By repeating this process, the lowest values and smell values that could not be smelt were found and recorded.

In the odor differentiation test, the patient was asked to close their eyes and a triple pen containing 16 odors was presented with 1 and 2 identical fragrances and the patient was asked to find the different smell. The sum of the correct answers was taken as the odor discrimination score.

In the odor identification test, 16 items with different odors were presented and the patient was given a list of 4 options to choose from. The sum of the correct answers was accepted as the value for odor identification.

The sum of the three tests (ex-discriminant-identification) was used to calculate the final TDA-score (showing the final odor test result) with no more than 48 points (each subtest added a maximum of 16 points). The normosmia composite score was 30.5 points or more for TDI score, while hyposmia was from 16.5 and 30.5 points and functional anosmia was below 16.5 points.

### Statistical Analysis

Analysis of the data was completed using SPSS Package Program version 20.0. Frequency, percentage, mean, standard deviation, median, minimum, and maximum values were used in the presentation of descriptive data. The normal distribution of the variables was determined by the Shapiro-Wilk test according to the number of patients in the groups. When the sample size and normal distribution fitness tests were examined, nonparametric tests were preferred for the analysis methods. Mann Whitney U test was used to compare age and continuous variables between groups. Chi-square test was used to compare categorical variables between patient and control groups. The cases with P-value below 0.05 were considered statistically significant.

The relationship between age and continuous variables related to smell was examined with the Spearman correlation analysis. In the evaluation of the correlation, the following interpretations were made strong relationship between 0.00-0.24: weak, 0.25-0.49: medium, 0.50-0.74: strong, 0.75-1.00: Very strong.

## RESULTS

The average age of our study group was 64.26±9.27 years (Median: 66.00 Min: 38.00-Max: 81.00).

The comparison between patient and control groups according to demographic and clinical characteristics is presented in Table 1. There were no significant differences between groups in terms of categorical variables such as gender, age, and smoking status.

In the patient group, the median values of odor threshold value, discrimination, detection and test scores were significantly lower than the control group. When we looked at the results of saccharin test, it was observed that there was a prolongation in the patient groups but this was not statistically significant (Table 2).

**Table 1. Comparison of patient and control groups according to categorical variables**

| | Patient group (n=40) | | Control group (n=33) | | |
|---|---|---|---|---|---|
| **Variables** | **n** | **%** | **n** | **%** | **p** |
| **Gender** | | | | | |
| Male | 35 | **87.5** | 27 | **81.8** | 0.530 |
| Female | 5 | 12.5 | 6 | 18.2 | |
| **Age (year)** | 64.9±9.1 | 66.5 (40.0-81.0) | 63.5±9.5 | 65.0 (38.0-80.0) | |
| **Smoking** | | | | | |
| Yes | 32 | 80.0 | 23 | 69.7 | 0.457 |
| No | 8 | 20.0 | 10 | 30.3 | |
| **Additional Disease (not systemic)** | | | | | |
| Yes | 12 | 30.0 | 8 | 24.2 | 0.775 |
| No | 28 | 70.0 | 25 | 75.8 | |
| **Alcohol** | | | | | |
| Yes | - | - | - | - | - |
| No | 40 | 100.0 | 33 | 100.0 | |

%: column percentage, p: Chi-square test

**Table 2. Comparison of patient and control group in terms of continuous variables**

| | Patient group (n=40) | | Control group (n=33) | | |
|---|---|---|---|---|---|
| **Variables** | **Mean ±Standard deviation** | **Median (Min-Max)** | **Mean ±Standard deviation** | **Median (Min-Max)** | **p** |
| **Age (year)** | 64.9±9.1 | 66.5 (40.0-81.0) | 63.5±9.5 | 65.0 (38.0-80.0) | 0.553 |
| **FEV 1** | %60-70 | | | | |
| **FEV1/FVC** | <0.7 | | | | |
| **Odorthreshold value** | 2.5±1.8 | 2.0 (0.0-6.5) | 5.7±1.2 | 5.5 (3.5-8.5) | **0.0001** |
| **Odor discrimination** | 5.4±3.3 | 5.0 (0.0-11.0) | 10.8±1.6 | 11.0 (8.0-14.0) | **0.0001** |
| **Odor identification** | 6.4±3.5 | 7.0 (0.0-11.0) | 11.8±1.6 | 12.0 (9.0-15.0) | **0.0001** |
| **Test total scor** | 14.4±7.5 | 14.5 (0.0-26.5) | 28.4±3.8 | 27.5 (22.5-37.5) | **0.0001** |
| **Duration of illness** | 114.9±138.5 | 54.0 (2.0-480.0) | - | - | - |
| **Sakarin test result** | 16.9±4.5 | 16.0 (10.0-25.0) | 16.1±4.1 | 15.0 (7.0-25.0) | **0.449** |

Min: Minimum, Max: Maximum, p: Mann Whitney U Test

### Correlation analysis results

In our patient group, Spearman correlation analysis was used to examine whether or not continuous variables were changing together. There was a medium negative correlation between age and continuous variables of discrimination, determination and test total score. (p = 0.009, p = 0.017, 0.005, respectively). It was found that as the age increased, the measurements related to olfactory decreased inversely. There was a strong positive correlation between odor threshold, discrimination, identification and test total score (p <0.001).

There was no correlation between duration of smoking and age, duration of illness and other continuous variables. There was medium negative correlation between saccharine test result and discrimination and test total scores (r = -0.331, p = 0.037, r = -0.370, p = 0.019, respectively). As the test total score, the discrimination measurement values increased, the saccharin measurement value decreased.

## DISCUSSION

Epidemiologic studies suggest that 75% of COPD patients have nasal pathologic symptoms and that more than 1/3 of patients with sinusitis have lower airway symptoms such as COPD. It is not surprising that rhinitis or sinusitis coexist with COPD, since the upper and lower respiratory tracts are similar in terms of inflammation and both regions have similar exposure to allergens and irritants. Possible mechanisms of combined upper and lower respiratory tract dysfunction include nasal-bronchial reflex, inflammation caused by cigarette smoking, mouth respiration resulting from nasal obstruction, and pulmonary aspiration of nasal content. Patients with chronic sinusitis usually have nonspecific bronchial hyper responsiveness suggesting neural reflex. Postnasal drainage of nasal inflammatory mediators during sleep can also increase airway sensitivity at a lower rate. Nasal and sinus disease in COPD patients are also associated with dysfunctional respiratory function (10).

Diseases of the upper and lower respiratory tract are often considered separately and treated by different specialists (11). However, evidence suggests that upper respiratory symptoms are common (12) in COPD patients, and it is often accompanied by inflammation of the nose (13). In addition, nasal symptoms in COPD reduce quality of life (14) and are associated with treatment failure during these exacerbations (15).

Histologically, the upper and lower airways are very similar. The nasal and bronchial airways are covered with ciliated epithelium and include submucosal blood vessels, mucosal glands and basal progenitor cells .The main physiological difference between the upper and lower airways is that control of the upper respiratory tract openings is predominantly by vascular tone, whereas the lower airway opening is also controlled by smooth muscle (16).

The nose is important for heating, humidifying and filtering the inspired air. When air reaches to the larynx, the air temperature is about 32 °C and the humidity is about 98%. Nasal turbinates have a very convenient shape and structure for these functions. The total airway is available in excess of half of the resistance, which enhances healing function (17). Allergens and irritants provoking bronchial vasomotor and secretory responses have a similar effect on the nasal and sinus airways.

COPD is usually associated with increased neutrophil activity (18) and mucus hypersecretion (19). Nihlen and colleagues (20) measured secreted, exudative and granuloid activation of the nasal mucosa of COPD patients and matched control subjects with or without nasal symptoms, and showed that both COPD and nasal complaints are more common.

Effective treatment of rhinosinusitis may reduce pulmonary aspiration of sinus or nasal secretions, including microorganisms, inflammatory cells and cytokines. Several studies have shown that treatment of the upper airway alone may also improve accompanying lower airway disease (21).

Based on this, we thought that the sense of smell may also be affected in patients with COPD. The sense of smell plays an important role in everyday human life and loss of smell function is often expressed as a serious decrease in quality of life. The main causes of olfactory disorders are head trauma, upper respiratory tract infections, sinonasal diseases, head trauma and toxic exposure.

In this study, we also investigated how lower respiratory tract disease actually affects the upper respiratory tract of patients and changes the sense of smell which may affect quality of life. In this case we used the Sniffin' Sticks test, which I thought was the most appropriate to gather data. This work is preliminary research and we selected the control group with the same features to eliminate all the causes that may affect the sense of smell. In addition, we found that mucociliary functions were also decreased in COPD patients, but not statistically significant.

**Limitation of study**

We have had to exclude most of the patients for many reasons, such as being very old, not being able to perform the odor test and having system diseases that may affect odor function. Therefore, the number of study population remained limited Further studies can be done with larger patient groups

## CONCLUSIONS

In COPD patients, nasal functions, especially olfactory function and mucosiliary function, are highly affected. Therefore these patients must be assessed by an ENT specialist, and necessary measures must be taken to ensure that the sense of smell can be preserved.

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*Ozge Caglar: ORCID:0000-0001-8737-2891*
*Pinar Mutlu: ORCID: 0000-0002-7496-0026*
*Arzu Mirici: ORCID: 0000-0002-7189-9258*
*Sibel Oymak: ORCID: 0000-0001-7979-8892*
*Sefa Derekoy: ORCID: 0000-0002-7037-8901*

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