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CLINICAL STUDY

GUSTATORY AND OLFACTORY DYSFUNCTION AND QUALITY OF LIFE IN PATIENTS WITH LUNG CANCER

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SUMMARY

Objective: The aim of this study was to investigate the olfactory and gustatory dysfunction and their effects on quality of life in patients with lung cancer.

Methods: A total of 40 patients with newly diagnosed lung cancer and a control group of 40 healthy individuals were enrolled in this study. The Sniffin" Sticks test was used to evaluate their olfactory function, and taste strips were used for their gustatory function. The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30), Patient-Generated Positive Global Assessment (PG-SGA), and Beck Depression Inventory (BDI) were applied to all patients.

Results: There was a statistically significant decrease in the odor and taste scores of the patients compared with the control group ($p < 0.001$). The mean score of the patients in EORTC-QLQ-C30 general health status subscale was 58.3 ± 21.8 (moderate). The odor threshold was significantly correlated with the EORTC-QLQ-C30 general health scores ($r = 0.31$; $p = 0.004$) and physical functioning scores ($r = 0.32$; $p = 0.041$). Furthermore, 45% of the patients had moderate and severe malnutrition according to PG-SGA classification. Symptoms related to nausea ($p = 0.015$), fatigue ($p = 0.001$), and appetite loss (p ? 0.001) were more significant in the patients with moderate and severe malnutrition.

Conclusion: Patients with lung cancer have lower taste and smell scores compared with healthy individuals. On the other hand, better olfaction is associated with higher functionality, which may indicate that olfactory changes can affect a person's overall health.

Keywords: Cancer, taste, smell, quality of life

AKCİĞER KANSERLİ HASTALARDA KOKU VE TAT DİSFONKSİYONU VE YAŞAM KALİTESİ

ÖZET

Amaç: Bu çalışmanın amacı, akciğer kanserli hastalarda koku alma ve tat alma işlev bozukluğunu ve bunların yaşam kalitesine etkilerini araştırmaktır.

Materyal-Metod: Yeni tanı almış akciğer kanseri olan 40 hasta ve 40 sağlıklı bireyden oluşan kontrol grubu bu çalışmaya dahil edildi. Koku işlevlerini değerlendirmek için Sniffin "Sticks testi kullanıldı ve tat alma işlevi için tat şeritleri kullanıldı. Tüm hastalara kanserin tedavisi ve araştırması için Avrupa örgütü yaşam kalitesi ölçeği (EORTC-QLQ-C30), hasta bazlı subjektif global değerlendirme (PG-SGA) ve Beck depresyon ölçeği (BDI) uygulandı.

Bulgular: Hastaların koku ve tat skorlarında kontrol grubuna göre istatistiksel olarak anlamlı azalma vardı ($p <0,001$). EORTC-QLQ-C30 genel sağlık durumu alt ölçeğindeki hastaların ortalama puanı 58,3 ± 21,8 (orta) idi. Koku eşiği, EORTC-QLQ-C30 genel sağlık puanları ($r = 0.31$; $p = 0.004$) ve fiziksel işlevsellik puanları ($r = 0.32$; $p = 0.041$) ile anlamlı şekilde korelasyon gösterdi. Ayrıca PG-SGA sınıflandırmasına göre hastaların% 45'inde orta ve şiddetli beslenme bozukluğu vardı. Orta ve şiddetli beslenme bozukluğu olan hastalarda bulantı ($p = 0,015$), yorgunluk ($p = 0,001$) ve iştah kaybı (p ? 0,001) ile ilgili semptomlar daha belirgindi.

Sonuç: Akciğer kanseri olan hastalar, sağlıklı bireylere göre daha düşük tat ve koku puanlarına sahiptir. Öte yandan, daha iyi koku alma, daha yüksek işlevsellikle ilişkilidir, bu da koku alma değişikliklerinin bir kişinin genel sağlığını etkileyebileceğini gösterebilir.

Anahtar Sözcükler: Kanser, tat, koku, yaşam kalitesi

INTRODUCTION

Lung cancer is the most common type of cancer in the world [1]. An understanding of cancer-induced chemosensory changes will give healthcare professionals strategic power to manage important parameters, such as nutritional status and weight loss status, in the disease and treatment process [2]. Thus, it is important to recognize the changes that occur in such a common cancer. Lung cancer patients often complain of chemosensory changes in subjective evaluation studies [3,4]. Taste and smell abnormalities (TSA) are common in cancer patients. They have been assumed to be related to malnutrition by affecting the eating behavior of the patient. Malnutrition and weight loss are also considered as risk factors for mortality and morbidity in patients with cancer [3,5,6]. Therefore, TSA evaluations in cancer patients are often emphasized, as they may reduce the quality of life and psychological well-being [3,4,7].

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The pathologic mechanisms of TSA caused by cancer are not fully understood. The chronic inflammatory process in cancer can affect both the peripheral chemoreceptors and central areas which contribute to modulation resulting in TSA [8]. Former studies show that TSA may vary in individuals, in a spectrum from declines to the complete loss of taste and smell [9]. Most studies on cancer and TSA have focused on the effects of chemotherapy and radiotherapy while very few studies have evaluated the situation in cancer patients who have not yet received treatment and/or have been newly diagnosed. These are usually quantitative evaluations [6].

To our knowledge, this is the first study to assess the quantitative characteristics (such as taste and smell) and qualitative characteristics (such as quality of life) of patients with lung cancer have not been jointly. In the present study, our primary objective was to investigate the taste and smell dysfunction of patients with lung cancer and its effect on the quality of life in these patients.

MATERIAL and METHODS

Participants

The study group was composed of 40 newly diagnosed patients with lung cancer who have not yet received any treatment (n=30 non-small cell lung cancer, n=10 small cell lung cancer; 28 male (70%), 12 female (30%); 60.7±8.9 (41-78) and 40 age and sex matched healthy individuals 23 male [(%), 17 female (42%); mean age 57.6± 7.3 years (42-71).

After local ethical committee consent was obtained (KAEK 051), this prospective study was conducted in a group of newly diagnosed lung cancer patients, who were admitted to the medical oncology clinic of a tertiary center between September 2019 and March 2020. This study was performed in humans in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national) and with the 1975 Declaration of Helsinki, as revised in 2008. The study population inclusion criteria were diagnosis with primer lung cancer, agreement to participate in the study with written consent.

The exclusion criteria were diagnoses of acute rhinosinusitis and neurological disorders. Sociodemographic data, such as sex, age and medical history, were questioned. The height, body weight, and body mass indexes (BMI) were measured. All patients were given the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30), Patient-Generated Positive Global Assessment (PG-SGA), and Beck Depression Inventory (BDI)

Olfactory test

All participants underwent bi-rhinal orthonasal olfactory testing using the Sniffin" Sticks test battery (Burghart Messtechnik, Germany), which consists of specially produced pen-like instruments that dispense different odors. It tests an individual's odor threshold (OT), odor discrimination (OD), and odor identification (OI). Total (TDI) scores from these three measurements were evaluated. The participant was accepted as normosmic if TDI score was ≥30.5, hyposmic if TDI score was 16.5?30.5, and functionally anosmic if TDI score was <16.5 [10].

Gustatory test

The four basic flavors; namely, sweet, bitter, sour, and salty, are absorbed by 8-cm-long strips of paper with four concentrations (n = 16 solution) and applied on different sides of the tongue at various concentrations. The following concentrations are used for the taste strips: sweet: 0.4, 0.2, 0.1, and 0.05 g/ml sucrose; sour: 0.3, 0.165, 0.09, and 0.05 g/ml citric acid; salty: 0.25, 0.1, 0.04, and 0.016 g/ml sodium chloride; bitter: 0.006, 0.0024, 0.0009, and 0.0004 g/ml quinine hydrochloride. True and false determinations of the different taste concentrations were recorded, and taste perception was evaluated over 16 points [11].

EORTC-QLQ-C30 (version 3)

This scale consists of 30 questions and three sections which are general health status scale, functional scale, and symptom scale. Each domain is scored on a 0-100 scale; higher scores for the first two scales are accepted better, whereas higher scores for the symptom scale represent worse symptoms [12,13].

PG-SGA

In this method, the patient's medical history and physical examination findings were used together in nutritional evaluation. The PG-SGA nutritional status is classified into three subgroups; A (well nourished), B (suspicion of malnourishment or moderately malnourished), or C (severely malnourished) [14]. The nutritional intervention requirement was defined as follows: there is no need for nutritional intervention (0-1 point); the patient and his family require nutritional education (2-3 points); the patient requires nutritional intervention (4-8 points); the patient requires critical intervention and symptom control (≥ 9 points). High scores were indicative of malnutrition [15].

BDI

The BDI is a 21-item self-assessment scale. The results were classified as normal (1-10 points), mild mental distress (11-16 points), borderline clinical depression (17-20 points), medium depression (21-30 points), serious depression (31-40 points), or very serious depression (40 points and above) [16].

Statistical analysis

Statistical analysis was performed using the software Statistical Package for the Social Sciences (SPSS) version 20 (SPSS Inc., USA). Descriptive analysis results were presented as means ± standard deviations. The $\chi 2$ test was used for the categorical variables, and the findings were expressed as observation counts and percentages. Mann-Whitney U test was used to analyze the variables between groups while the relations between the olfactory and gustatory scores and the parameters were assessed using Spearman's rank correlation analysis. Multiple logistic regression analyses were used to determine the effect of the independent categorical variables on the dependent variables. A two-sided p value less than 0.05 was considered significant.

RESULTS

The demographical and clinical characteristics of the patient group are shown in Table 1. The two groups were similar by means of gender and age (p = 0.24 and p = 0.06, respectively). Multiple logistic regression analyses showed that smoking as a sole factor did not have a significant effect on loss of olfactory and gustatory functions.

Olfactory and taste tests

The difference in the olfactory and gustatory test scores of the patients and the control group was significant (p <0.001) when compared to the control group (Table 2). Patients had hyposmia by 83% (n = 34) and hypogeusia by 20% (n = 8).

EORTC-QLQ-C30

The mean score of the patients on the EORTC-QLQ-C30 General Health Status Subscale was 58.3 ± 21.8 (moderate). The patients obtained the highest score from the cognitive function (86.2 ± 19.2) and the lowest score from the physical function (66.8 ± 26.2) in the functional scale section. In the symptom scale section, the three most common symptoms were insomnia (43.3 ± 33.9), fatigue (43.1 ± 31.9), and pain (34.6 ± 30.5) (Table 3). Olfactory test (OT) results were significantly correlated with EORTC-QLQ-C30 general health scores (r = 0.31, p = 0.004) and physical functioning scores (r = 0.32, p = 0.041). Fatigue (r=0.63, p <0.001) and nausea (r=0.53, p <0.001) were significantly correlated with appetite loss.

PG-SGA

The scores indicating the requirement for nutritional intervention assessment are shown in Table 4.

Of the patients evaluated, 55% (n = 22) were well nourished (A), 40% (n = 16) were moderately malnourished (B), and 5% (n = 2) were severely malnourished (C) according to PG-SGA classification. There was no difference between Groups A, B and C in terms of the olfactory and gustatory test scores (p > 0.05). The symptoms related to nausea (p = 0.015), fatigue (p = 0.001), and appetite loss (p ? 0.001) were more severe in patients with moderate and severe malnutrition.

BDI

The BDI mean score was 9.6 ± 3.4. Twenty-two patients (55%) were considered normal, and 18 patients (45%) were experiencing mild mental stress. Olfactory and gustatory

scores of the patients showed no correlation with their" BDI results.

Table 1. The demographical and clinical characteristics of the patient group (n=40)

Age (years) (mean±SD) (min-max)	60.7±8.9 (41-78)
Gender (F/M) n (%)	12 (30%) /28 (70%)
BMI (kg/m^2) (mean±SD) (min-max)	26.2±6.2 (18.1-44.3)
Weight (kg) (mean±SD) (min-max)	71.1±15.8 (42-108)
Smoking n (%)	
Current smoker	7 (17%)
Former smoker	28 (70%)
Never have smoked	5 (13%)
Alcohol n (%)	
Current	0
Former	6 (15%)
Never	34 (85%)
Tumor Type n (%)	
NSCLC	30 (75%)
SCLC	10 (25%)
Disease Stage	
I-II	5 (13%)
III-IV	35 (87%)
Comorbidity	
HT	5 (12%)
DM	1 (3%)
HT+DM	2 (5%)
COPD	5 (12%)
None	27(68%)

Abbreviations: SD, standart deviation; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; HT, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease

Table 2. Olfactory and gustatory test scores of the patients, compared to the scores of the control group

	Study group (n=40) *mean±SD*	**Control group (n=40) *mean±SD***	***p***
OT	5.1±1.4	7.7±1.7	**<0.001**
OD	10.3±1.3	13.1±1.1	**<0.001**
OI	10.6±2.1	13.3±1.2	**<0.001**
TDI	26.1±4.1	34.3±3.1	**<0.001**
Sweet	2.9±0.8	3.3±0.5	**0.038**
Salty	2.9±0.9	3.4±0.5	**0.018**
Sour	2.8±0.8	3.3±0.4	**0.004**
Bitter	2.9±0.8	3.4±0.5	**0.002**
Total Taste Score	11.4±2.4	13.4±1.1	**<0.001**

Abbreviations: OT, odor threshold; OD, odor discrimination; OI, odor identification;

TDI: Threshold, Discrimination; Identification; SD: standart deviation

Table 3. EORTC QLQ-C30 scores

EORTC QLQ-C30		
	Items	mean±SD
Global health status	29-30	58.3±21.8
Physical functioning	1-5	66.8±26.2
Role functioning	6-7	75.4±25.9
Emotional functioning	21-24	75.3±26.2
Cognitive functioning	20,25	86.2±19.2
Social functioning	26-27	77.1±29.1
Fatigue	10,12,18	43.1±31.9
Nausea and vomiting	14-15	13.3±27.5
Pain	9,19	34.6±30.5
Dyspnea	8	22.5±30.6
Insomnia	11	43.3±33.9
Appetite loss	13	25.8±39.6
Constipation	16	15.8±32.9
Diarrhea	17	4.2±17.2
Financial difficulties	28	23.3±31.3

Abbreviations: EORTC QLQ-C30; European Organization For Research and Treatment of Cancer Quality of Life

Table 4. Patients in need of nutritional intervention obtained by the PG SGA

PG SGA scores	n (%)
2-3	16 (40%)
4-8	11 (28%)
≥9	13 (32%)

Abbreviations: PG SGA; Patient-Generated Subjective Global Assessment

DISCUSSION

This study showed that; olfactory and gustatory functions have been affected in patients with newly diagnosed lung cancer. Although the reasons for the loss of smell and taste in cancer patients are not fully understood, some findings have revealed that malignancy itself may cause these changes in cancer patients [17-19]. One of the suggested explanations for TSA is increased inflammation [20]. Cancer cells that proliferate rapidly in advanced cancer are known to increase inflammation with the release of cytokines [21] and increased inflammation negatively affects the regeneration of smell and taste cells [9,22]. Another factor which has been explained to cause olfactory and taste disturbance is tobacco use which is also one of the main reasons of lung cancer [23,24]. Coherently, our patient group included heavy smokers. Therefore, we checked the effect of smoking via logistic regression analysis. However, the analysis revealed that smoking may be associated with loss of odor and taste, but this may not be the only cause of TSA. Ultimately, the relationship between cancer and chemosensory change can be influenced by multiple factors[6].

There are levels of smell loss caused by cancer, such as decreased sense of smell or odor distortion [9]. We detected hyposmia in 83% (n=34) of our patients, but there was no functional anosmia, parosmia, or phantosmia. Although the most frequently reported taste changes are increased or decreased bitter taste [6], various sensitivity changes have been reported in other basic tastes [7]. All taste scores of our patients were lower than those of the controls, hypogeusia was detected in 20% (n=8) of the patients.

The quality of life in lung cancer patients is lower than that in the healthy population. Fatigue, appetite loss, and respiratory problems negatively affect these patients" quality of life [25]. In our study, the changes in the quality of life of the patients were evaluated with the EORTC-QLQ-C30 the general health status subscale were moderate (58.3 ± 21.8).

Insomnia, fatigue, and pain were the most common cause of discomfort on the symptom scale. For successful cancer treatment, a patient must maintain appropriate nutritional behavior. Factors that reduce food intake, such as nausea, vomiting, and deterioration in smell and taste perception, can disrupt nutrition. Nutrition and chemosensory dysfunctions are interrelated conditions in cancer patients. Patients with more chemosensory complaints have lower energy intake, higher rates of weight loss, and lower quality of life [7]. Lung cancer leads to weight loss and malnutrition more prominently in those patients [26]. Nutritional evaluations with PG-SGA are used safely, and such studies reveal that malnutrition is common in patients with lung cancer; furthermore, 25.1%?40% of patients have severe malnutrition and thus need urgent nutritional support [26,27]. Our results, consistent with the literature showed that 45% of lung cancer patients had moderate to severe malnutrition and had more severe symptoms related to nausea, fatigue, and appetite loss. In the present study, nausea and fatigue, , were found to be correlated with loss of appetite [28] while changes in loss of smell and taste were not significantly related. Interestingly, in our study, odor thresholds were correlated with EORTC-QLQ-C30 general health scores and physical

functionality scores. This fact may be explained by the presence of chemosensory factors.

Depression has been defined in 33% of patients with lung cancer, and the prevalence of depression has been told to be higher in patients with small-cell-type carcinomas [29]. In a meta-analysis, depression is indicated as one of the risk factors for mortality in cancer patients [30]. In our study, 45% of the patients had mild mental distress, but there was no difference in the BDI scores between the cancer subtypes. Besides, chemosensory parameters and BDI scores were not significantly related.

There are two major limitations in this study that could be addressed in future researches. First one is the relatively low number of patients at different stages of cancer. Second one is the deficiency of monitoring the eating habits of the patients more definitively.

CONCLUSION

This study showed that patients with lung cancer experience taste and smell abnormalities.

Even though this situation does not correlate with chemosensory changes in patients with poor nutritional status, factors such as appetite and nausea affect nutrition. These results are important to lead the the clinicians, establish a correct nutrition program to sufficiently nourish the cancer patients.

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