The Relationship Between Inhaler Use and Oral Problems in Patients with COPD and Affecting Factors: A Cross-Sectional Study

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Abstract

AIM: This study aimed to determine the relationship between inhaler drug use and oral problems in patients with chronic obstructive pulmonary disease and the affecting factors.

METHOD: The study has an analytical and cross-sectional design. The study was conducted between August 2020 and January 2021 with 208 patients with chronic obstructive pulmonary disease receiving treatment at a university hospital and using inhaler drugs. Research data were collected using a questionnaire and Eiler’s oral assessment guide. The data were analyzed using descriptive statistics, t-test and Pearson’s correlation test were used for dependent groups.

RESULTS: There was a positive significant correlation between the deterioration in the oral mucosa and the use of drugs containing ipratropium bromide + salbutamol and of combined drugs with budesonide effect (p < .05; p < .01). Eiler’s score was higher in patients receiving combined treatment of ipratropium bromide + salbutamol and corticosteroids (F= 4.80; p < .05). It was determined that there is a relationship between diabetes, heart diseases, cough, oxygen use, and oral problems.

CONCLUSION: A relationship was found between inhaler drug use and oral problems in patients with chronic obstructive pulmonary disease. Oxygen use, diabetes, heart diseases, and cough were also found to affect oral health.

Keywords: Chronic obstructive pulmonary disease, inhalers, oral health

Introduction

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by permanent respiratory symptoms and airflow limitation and is a leading cause of morbidity and mortality worldwide (Global Initiative for Chronic Obstructive Lung Disease [GOLD], 2021). Inhaler drug treatment has a key role in the treatment of COPD (Molimard et al., 2017). Bronchodilators, which are widely used in inhaler drug treatment, are a term used for drugs that increase forced expiratory volume in one second (FEV1) or alter other spirometric parameters and that generally lead to these effects by changing the airway smooth muscle tone (Günay et al., 2016).

Inhalation therapy is widely used in respiratory system diseases such as asthma and COPD. Especially in COPD, long-term and high-dose inhalation therapy is administered (Manger et al., 2017). Some inhaled drugs in oral drug therapy are taken by inhalation; however, most of them remain in the mouth or oropharynx. It was determined that only 10-20% of the drugs reach the lungs. Drug remaining in the mouth leads to the deterioration of the normal physiology of the oral mucosa (Gödara et al., 2011). Decreased secretion of saliva causes impairment in the oral mucosa and tooth decay. Low oral pH is an important factor in the formation of tooth deformities. The use of inhalers reduces oral pH. It was that the pH of saliva drops below 5.5 30 minutes after inhaler use (Kargul et al., 1998). The interaction of the drug content of inhaled drugs and saliva changes taste in patients (Dekhuijzen et al., 2016). Inhaler treatments also lead to oral ulceration and changes in the oral mucosa. In particular, corticosteroid-containing inhaler drugs cause erythema and the formation of candidiasis in the buccal mucosa, oropharynx, and lateral parts of the tongue and also an increase in dry mouth and cough (DeRossi et al., 2010). One of the problems seen in patients using inhalers is dry mouth. Beta-2 agonists, anticholinergics, and corticosteroid-containing inhalers can cause dry mouth (Barnes, 1995). Dry mouth leads to problems such as difficulty in swallowing, burning sensation and pain in the mouth, and instability of prostheses in the mouth. A dry mouth may cause oral fissures, ulcers, and a decrease in epithelial tissue in the future (Regezi et al., 2008).

Inhaler drugs, which are frequently used in the treatment of COPD, affect the quality of life of patients, especially in terms of nutrition and swallowing; therefore, patients use different drugs due to oral problems. This study aimed to examine the relationship between inhaler drug use and oral problems in patients with COPD and the affecting factors. There is a need for studies that will focus on oral problems in patients with COPD using inhaler drugs in a wide framework. In this...
respect, it is thought that the present study will contribute to the field. The study was aimed to determine the relationship between inhaler drug use and oral problems in patients with COPD and the affecting factors.

Research Questions
1. Is there a relationship between inhaler drug use and oral problems in patients with COPD?
2. What are the factors affecting oral problems that develop in patients with COPD using inhalers?

Methods
Study Design
This study was an analytical and cross-sectional design.

Sample
Patients who received treatment due to the diagnosis of COPD between December 2020 and April 2021 and who were using inhalers were included in the study. In the study, the sample size was calculated based on the study conducted by Rodríguez et al. (2018) to evaluate oral health risks in patients with pneumonia and asthma receiving inhaler therapy. In the analysis based on the data of this study, the effect size was found to be .217 using t-test in G*Power 3.1.9.2 with a power of .80, α of .05, and sample size of 126. The minimum number of individuals to be included in the study sample was calculated as 128 in G*Power 3.1.9.2 with an effect size of .30, α of .05, and power of .80 assuming a t-test. A total of 208 (18 years and over) patients were included in the study with the improbable (random) sampling method, considering the possible loss of cases.

The inclusion criteria of the study were as follows:
- Being diagnosed with COPD
- Using inhalers
- 18 years and over

The exclusion criteria of the study were as follows:
- Not receiving inhaler drug treatment during the data collection period
- Being unable to undergo oral examination (patients who cannot open their mouths enough for oral assessment, patients who were unfavorable to remove their masks if they wore a CPAP mask)

Data Collection
Data were collected using a data collection form developed by the researcher according to the literature (Dekhuijzen et al., 2016; Godara et al., 2011; Molimard et al., 2017) and Eiler’s oral assessment guide.

Data Collection Tools
The data collection form consists of 26 questions including information about the patient’s demographic characteristics (age, gender, marital status, educational status, etc.), other current diseases, diet, inhaler drugs used, duration and frequency, respiratory pattern, the status of receiving oxygen therapy, and the presence of hemoptysis, cough, and secretion.

Eiler’s oral assessment guide
Eiler’s oral assessment guide is widely used in the assessment of oral health. The scale was developed by Eilers et al. (1988) and consists of five items. These items are the lips, mucous membrane, tongue, teeth, and saliva. Each item is scored between 1 and 4 and the total score of the oral assessment scale varies between 4 and 20. On the oral assessment scale, a score below 5 indicates a normal oral mucosa; a score of 6-10 indicates mild dysfunction; a score of 11-15 indicates moderate dysfunction; and a score of 16-20 indicates severe dysfunction.

Statistical Analysis
The data obtained from the study were analyzed using the Statistical Package for Social Sciences (SPSS IBM Corp., Armonk, New York, USA) version 25. The Kolmogorov-Smirnov test was used to test whether the data showed normal distribution or not. In the analysis of the data, all the data fit the normal distribution. The data were analyzed using descriptive statistics (e.g., mean, number, and percentage). The t-test and Pearson’s correlation test were used for dependent groups. The p-value was taken as .05 in the study.

Ethical Considerations
The research protocol was approved by Aydın Adnan Menderes University Ethics Committee (Approval Date: November 14, 2019, Number: 50107718-050.99). Written permission was taken from Aydın Adnan Menderes University Research and Application Hospital to collect the research data. Written and verbal information was given to the participants and their consent was taken. The study was conducted in accordance with the principles of the Declaration of Helsinki, by underlining that participants’ personal details would remain confidential and that they might leave the study at any time they liked.

Results
Of the participants, 35.6% were female, the mean age was 69.12 ± 9.87, and 11.5% were single. Table 1 shows the other demographic characteristics of the patients.

Among the patients, 56.7% were fed with a special diet due to their chronic diseases. Of them, 27.9% had a diabetic diet, 26.4% had a hypertension diet, and 2.4% had one of the other diets. The daily fluid intake of the patients was between 450 mL and 4000 mL and they consumed an average of 644.09 mL of fluid. Of the patients, 7.2% had nausea, 2.9% had vomiting, and 7.2% had difficulty in swallowing. Of the patients, 35.1% had tachypnea, 13.9% underwent hyperventilation, 1% underwent hypoventilation, and 5.6% had wheezing during respiration. Of the patients, 49.5% had secretions, 67.8% had cough complaints, 38.0% had dyspnea, and 21.6% had chest pain.

Inhaler drugs used by the patients were coded: ipratropium bromide + salbutamol effective (anticholinergics,
Among the patients, 33.7% had missing teeth and 77.9% used inhaler drugs with a nebulizer. 17.8% used dry powder inhaler drugs, whereas 82.2% used in 3 doses, and 2.4% used in 1 dose. Among the patients, 52.9% used inhaler drug in 6 doses, 24.1% used in 4 doses, 10.6% used in 2 doses, 6.8% used in 8 doses, 3.4% used in 3 doses, and 2.4% used in 1 dose. Among the patients, 17.8% used dry powder inhaler drugs, whereas 82.2% used inhaler drugs with a nebulizer.

Of the patients, 70.2% had dry mouth, 15.4% had deterioration in the oral mucosa, and 37.5% had redness in the mouth. Among the patients, 33.7% had missing teeth and 77.9% used dental prostheses.

There was no correlation between dryness in the oral mucosa and inhaler drugs ($p < .05$) whereas a positive significant correlation was found between the deterioration in the oral mucosa and the use of drugs containing ipratropium bromide + salbutamol and combined treatment of ipratropium bromide + salbutamol and drug with budesonide effect ($p < .05; p < .01$). A positive significant correlation was determined between the redness in the oral mucosa and the oxygen level ($p < .05$) (Table 2).

The mean Eiler’s oral assessment scale score of the patients included in the study was 10.90 ± 2.59. In the oral health assessment of the patients according to this scale, it was determined that 53.4% had mild dysfunction, 39.4% had dysfunction, and 6.7% had severe dysfunction. Table 3 shows the results of the ANOVA test between the patients’ mean Eiler’s oral assessment scale scores and the inhaler drugs they used. A statistically significant difference was found between the Eiler’s scores of patients using ipratropium bromide and combined treatment of salbutamol + corticosteroid ($F = 4.80; p < .05$) (Table 3).

Table 4 presents the relationship between oral problems seen in patients and chronic diseases, cough, secretion, chest pain, and oxygen use. There was a positive significant correlation between dryness in the oral mucosa and diabetes mellitus (DM) and cough, between deterioration in the oral mucosa and cardiac diseases and secretion, and between redness in the oral mucosa and secretion ($p < .05$). Of the patients 77.4% received oxygen. Of these patients, 37.8% took oxygen at a rate of 2 L/min, 32.2% at a rate of 4 L/min, and 24.2% at a rate of 5 L/min. These patients received oxygen by nasal cannula, whereas other patients (5.8%) who received oxygen of 6 L or above used oxygen masks.

**Discussion**

This study was conducted with 208 individuals aged between 40 and 94 to determine the relationship between inhaler drug use and oral problems in patients with COPD and reveal the affecting factors. The obtained data can provide a better understanding of the relationship between inhalers and oral health.

In the study, it was seen that there was a positive significant correlation between the deterioration in the oral mucous membrane and using drugs containing ipratropium bromide + salbutamol and combined treatment of ipratropium bromide + salbutamol and drugs with budesonide effect. Moreover, the majority of patients had dry mouth. It was emphasized that anticholinergic drugs cause dry mouth by reducing saliva secretion (Gupta et al., 2006) and that anticholinergic drugs are the most common cause of the decrease in saliva amount (Scully, 2003). About 10-20% of inhaler drugs reach the lungs and the remaining dose stays in the oropharynx. It was reported that drugs remaining in the oropharynx, especially those containing steroids, cause local lesions in this region and in the mouth (Barnes, 1995). Similar findings in this study suggest that inhaler drugs cause deterioration in the oral mucous membrane. In the 2021 report, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) reported that drugs containing anticholinergics cause dry mouth (Global Initiative for Chronic Obstructive Lung Disease [GOLD], 2021). It can be stated that the reason for the dry mouth in the patients included in the study was the oxygen.
used together with inhaler drugs. It was reported that long-term use of beta-2 agonists is associated with decreased saliva production and reduces salivary secretion by 26% (Ryberg et al., 1991). It can be suggested that a dry mouth may cause deterioration in the mucous membrane. Regezi et al. (2008) revealed that dry mouth causes oral fissures, ulcerations, and a decrease in epithelial tissue with the prolongation of inhaler drug use (Regezi et al., 2008).

In this study, there was a statistically significant difference between the Eiler's scores of patients using combined drugs containing ipratropium bromide, salbutamol + corticosteroids. Eiler's scale evaluates the oral health of the patient holistically and an increase in the mean scale score indicates that the oral dysfunction increases. Similar to in this study results, Dekhuijzen et al. (2016) reported that the combined use of these drugs affects oral health negatively and that the number of daily doses increases various oral deteriorations. Considering that more than half of the patients in this study used six doses of inhaler per day, it can be suggested that the daily drug dose also affects oral health.

It was found that there was a positive significant correlation between dryness in the oral mucosa and DM and cough, between deterioration in the oral mucosa and cardiac diseases and secretion, and between redness in the oral mucosa and secretion. Hong et al. (2016) found that the prevalence of periodontitis was significantly higher in adults with DM (43.7%) than in those without DM (Hong et al., 2016). In a study conducted with DM patients with cardiac diseases, the prevalence of periodontitis and tooth loss was found to be high (Han et al., 2021). Furthermore, it was reported that glyemic processes affect saliva and increase dental cavities in diabetic patients (Jawed et al., 2011; Yeh et al., 2012). In the findings obtained

| Table 2. | Pearson Correlations Between Patients’ Oral Problems and Inhalers and Drug Doses |
|-----------|--------------------------------------------------------------------------------|
| Dryness in the Oral Mucosa | Deterioration in the Oral Mucosa | Redness in the Oral Mucosa |
| **Inhaler Drugs** | **r** | **p** | **r** | **p** | **r** | **p** |
| Drug A | .21 | .769 | .410 | .043 | .048 | .492 |
| Drug B | -.05 | .473 | .129 | .063 | .092 | .187 |
| Combined treatment with A + B | -.047 | .496 | -.228 | .001 | -.104 | .135 |
| Drug C | .102 | .142 | .067 | .337 | .016 | .813 |
| Drug D | .056 | .424 | .080 | .248 | .121 | .082 |
| Combined treatment with A + B + D | .019 | .784 | .036 | .609 | .063 | .369 |
| Combined treatment with A + D | .063 | .363 | .068 | .328 | .125 | .073 |
| Drug dose | .044 | .529 | .080 | .254 | .098 | .160 |

Note: Drug A = ipratropium bromide + salbutamol; Drug B = budesonide; Drug C = salbutamol; Drug D = corticosteroid. *p < .05 **p < .01

| Table 3. | Results of the ANOVA Test Between the Inhaler Drugs Used by Patients and Eilers’s Mean Scores |
|-----------|----------------------------------------------------------------------------------|
| **Inhaler Drugs** | **Inferor** | **Non-user** | **F/p** |
| Drug A | User | 11.16 ± 2.90 | 8-19 | 0.08/0.36 |
| Non-user | 10.80 ± 2.45 | 7-21 |
| Drug B | User | 10.76 ± 2.04 | 7-15 | 0.09/0.76 |
| Non-user | 10.92 ± 2.66 | 8-21 |
| Drugs A + B | User | 10.78 ± 2.53 | 8-21 | 0.66/0.41 |
| Non-user | 11.07 ± 2.67 | 7-19 |
| Drug C | User | 11.80 ± 2.04 | 10-14 | 0.60/0.43 |
| Non-user | 10.88 ± 2.60 | 7-21 |
| Drug D | User | 11.59 ± 2.36 | 8-16 | 3.18/0.07 |
| Non-user | 10.76 ± 2.62 | 7-21 |
| Drugs A + B + D | User | 11.66 ± 2.41 | 8-16 | 1.38/0.24 |
| Non-user | 10.84 ± 2.60 | 7-21 |
| Drugs A + D | User | 13.00 ± 2.30 | 10-16 | 4.80/0.03 |
| Non-user | 10.83 ± 2.57 | 7-21 |

Note: Drug A = ipratropium bromide + salbutamol; Drug B = budesonide; Drug C = salbutamol; Drug D = corticosteroid. *p < .05

| Table 4. | Pearson Correlations Between Patients’ Oral Problems and Chronic Diseases, Cough, Secretion, Chest pain, and Oxygen Use |
|-----------|------------------------------------------------------------------|
| **Dryness in the Oral Mucosa** | **Deterioration in the Oral Mucosa** | **Redness in the Oral Mucosa** |
| **r** | **p** | **r** | **p** | **r** | **p** |
| DM | .138 | .046 | .062 | .372 | .059 | .398 |
| HT | .101 | .146 | .010 | .883 | .032 | .645 |
| Cardiac Disease | -.078 | .260 | -.137 | .046 | .037 | .600 |
| Secretion | .120 | .085 | .137 | .048 | .187 | .007 |
| Cough | .158 | .023 | -.048 | .489 | .071 | .306 |
| Dyspnea | -.118 | .089 | .078 | .262 | -.035 | .617 |
| Chest Pain | .011 | .880 | .002 | .972 | -.008 | .788 |
| Oxygen Use | .151 | .030 | -.056 | .419 | .042 | .546 |
| Oxygen Level (L/min) | -.118 | .091 | -.132 | .058 | .167 | .016 |

Note: DM = diabetes mellitus; HT = hypertension. *p < .05.
from this study, a correlation was found between cough and secretion and oral mucosal problems. Phlegm and cough are common symptoms in patients with COPD. Cough generally aims to eliminate phlegm (Başıyı̇t, 2010). The bacteria and infectious agents that phlegm contains may vary depending on its characteristics. Purulent phlegm seen in patients with COPD is yellow or green. It often indicates a bacterial respiratory tract infection. It contains mucus, bacteria, and inflammatory cells (Görgün & Yıldız, 2016). The relationship between phlegm, cough, and oral problems in the patients included in this study can be explained by the fact that these bacterial formations in phlegm may cause problems in the mouth.

A positive significant correlation was found between oxygen use and dry mouth and between oxygen level and redness in the oral mucous membrane. Likewise, it was reported that oxygen use reduces salivary secretion and that non-humidified oxygen use reduces salivary secretion by 2.3 folds (Güneş et al., 2012). It was stated that high-flow oxygen therapy affects the swallowing reflex negatively (Sanuki et al., 2017) and causes dry mouth (Sotello et al., 2015).

Study Limitations

This study has some limitations. The effect of other drugs used by patients on oral health is unknown. In addition, since the daily dose of inhaler drugs given to patients was generally similar, no clear findings regarding the relationship between drug dose and oral health could be obtained. Furthermore, the study results are limited to the inhaler drugs examined in the study. The results cannot be generalized for other inhaler drugs used in COPD.

Conclusion and Recommendation

In the study, it was determined that there is a relationship between the use of anticholinergics-beta adrenergics alone and in combination with glucocorticosteroids and the deterioration of the oral mucous membrane. Eiler’s scores of those using combined drugs containing ipratropium bromide, salbutamol + corticosteroid were found to be higher. It was determined that there is a relationship between diabetes, cardiac diseases, cough, and oxygen use and oral problems. It is seen that patients with COPD using inhalers encounter problems regarding oral health. It is important to assess the oral health of these patients and provide effective oral care to prevent potential problems.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Aydın Adnan Menderes University. (Approval Date: November 14, 2019, Number: 50107718-050.99).

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