

Impact of inhalation therapy on occurrence of oral manifestations in patients with bronchial asthma, in Jeddah, Saudi Arabia

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Abstract

Background: Inhalation therapy for asthma includes cortisol and bronchodilators. High dosage and long duration of inhalation therapy has been linked with several adverse effects on the oral tissues.

Objectives: To explore the oral manifestations associated with the use of inhalation therapy among patients with asthma in Jeddah city.

Method: This was a cross sectional study; the non-probability convenient sampling method was used to select 215 subjects (99 with Doctor diagnosed asthma and 116 without asthma), from the outpatient clinics of two private hospitals. Data were collected using interview questionnaire, the standard 5th ed. WHO survey on oral manifestations, measurement of vital signs and anthropometric parameters, as well as clinical oral examination. Data were analyzed using SPSS version 22, and Logistic multinomial regression was used to study the Odds ratio and its 95% confidence interval between the variables. Level of significance for the study was 0.05. Results: The majority of patients with asthma (95%) used inhalation therapy, without use of spacers. Ulceration, pigmentation and candidiasis of the tongue, buccal mucosa and palate were

significantly more encountered among patients with asthma compared to those without asthma ($p < 0.001$, 0.002 and 0.046 respectively). Xerostomia and salivary gland affection, also, were significantly more encountered among patients with asthma compared to those without asthma ($p < 0.000$, and 0.002 respectively). Patients with asthma were 7.7 times more likely to develop tongue disorders (OR: 7.7, $p < 0.013$), 3 times more likely to develop buccal mucosal disorders (OR: 3, $p < 0.039$), and 15 times more likely to develop palate disorders (OR: 15, $p < 0.004$) compared to subjects without bronchial asthma.

Conclusion: Use of inhalation therapy in patients with asthma was significantly associated with increased occurrence of oral health problems. Health education programs about proper use of inhalers and oral hygiene should be implemented by primary health care personnel.

Key words: Inhalation therapy, Asthma, Oral manifestations, Jeddah.

Introduction

Asthma is a chronic inflammatory airway disorder, (1) where its occurrence is linked to several factors, such as sociodemographic constitution, environmental and occupational exposure, personal and genetic characteristics, and the morbid condition of the patient (2 - 10). Asthma is characterized by episodic attacks of cough, shortness of breath and wheezing (11, 12). Headache, body aches, vomiting and nasal symptoms are also reported by patients with asthma (13-18). Symptoms of insomnia and tremors were reported by uncontrolled asthma patients, who were put on high doses of systemic medications (19 – 22). Beta2 agonists, and cortisol (mainly inhalation therapy), are the standard treatment for asthma, in addition to anticholinergic drugs and antileukotrienes (23– 32). The health of the oral cavity is essential for good general health (33). Growth of bacteria in the oral cavity, on the teeth and mucosa, is affected by the variety of surfaces it provides bacteria with. These different bacterial populations are influenced by the integrity of the soft-tissues, oral hygiene, saliva, diet, and the host's immune and inflammatory responses (34). Bronchial asthma is one of the major systemic diseases which produces dental caries. Salivary production and secretion are associated with the prolonged use of β_2 agonists, inhaled corticosteroids, and antihistamines. The reduction in saliva can affect the natural process by which the mouth maintains its chemical balance and the protective function of cleaning the mouth. Reduced salivary flow provides a favorable environment for the growth and multiplication of microorganisms, such as Lactobacilli and Streptococcus mutans, causing dental caries (35). Ig E-mediated allergic reactions are typical in asthma, and thus the increase in salivary Ig E values could reflect the extent of these reactions on the oral mucosa. Similar reactions are also assumed to be a pathogenic mechanism in periodontal disease.(36). Candida Albicans causes deep-seated or superficial infections in patients under treatment with antibiotic or corticosteroid drugs (37). The present study was conducted to explore the clinical patterns of asthma, and its treatment regimens, and explore the impact of inhalation therapy on the occurrence of oral health problems.

Subjects and Methods

It was a cross sectional study, and the sampling method was a non-probability convenient one.

Sample size was determined using G*power software, where $\alpha = 0.05$, Power = 0.95 effect size = 0.3, and degree of freedom= 5 (38). The minimal sample size required was 194 subjects; thus, 215 subjects were enrolled in the present study (99 with Doctor diagnosed asthma and 116 without asthma), from the outpatient clinics of two private hospitals. Data were collected using interview questionnaire which provided information on the personal and clinical aspects of the subjects. Each subject was asked a medical history questionnaire to know if he/she was diagnosed by a doctor as having asthma or not. Each subject was asked the standard 5th ed. WHO survey on oral manifestations (39). Measurement of vital signs and anthropometric parameters, as well as clinical oral examination was done on every subject. Data were analyzed using SPSS version 22, and Logistic multinomial regression was used to study the Odds ratio and its 95% confidence interval between the variables. Level of significance for the study was 0.05.

Availability of the data: the raw data is available at the research center of ISNC and all results of the data are included in the paper.

Results

Total number of patients with doctor diagnosed asthma was 99, while those without asthma were 116 subjects. The mean age of patients with asthma was 50 years (SD: 10.2), while mean age of the control subjects was 48.2 years (SD: 7.4). This difference was not statistically significant ($t = - 1.47$; $p < 0.143$). No significant differences were found between normal subjects and patients with asthma in gender or educational level ($p > 0.05$). A greater proportion of patients with asthma were unemployed compared to the normal subjects (52.5% and 31.0% respectively; $p < 0.006$). A greater proportion of patients with asthma were smokers compared to the normal subjects (41.4% and 27.6% respectively; $p < 0.033$). A lower proportion of patients with asthma used to rinse their mouth frequently compared to the normal subjects (73.7% and 86.2% respectively; $p < 0.022$). A greater proportion of patients with asthma suffered from diabetes, hypertension and ischemic heart diseases (33.3%, 38.4%, and 14.1% respectively), compared to the normal subjects (19.8%, 13.8%, and 3.4% respectively); $p < 0.025$ (Table 1).

Table 1: Distribution of studied subjects by having asthma and personal and clinical characteristics

Variable	Categories	Doctor diagnosed asthma				Total		X ² (p-value)
		No		Yes		N	%	
		N	%	N	%			
Gender	Female	47	40.5	47	47.5	94	43.7	1.051 (0.305)
	Male	69	59.5	52	52.5	121	56.3	
Educational Level	< University	65	56	71	71.7	136	63.3	5.652 (0.17)
	≥ University	51	44	28	28.3	79	36.7	
Occupational	Unemployed	36	31.0	52	52.5	88	40.9	10.206 (0.006)
	Manual	49	42.2	29	29.3	78	36.3	
	Clerical	31	26.7	18	18.2	49	22.8	
Smoking habit	Non-Smoker	84	72.4	58	58.6	142	66.0	4.554 (0.033)
	Smoker	32	27.6	41	41.4	73	34.0	
Rinse the mouth frequently	No	16	13.8	26	26.3	42	19.5	5.284 (0.022)
	Yes	100	86.2	73	73.7	173	80.5	
Brush teeth frequently	No	32	27.6	42	42.4	74	34.4	5.210 (0.022)
	Yes	84	72.4	57	57.6	141	65.6	
Use dental floss 2 times day	No	92	79.3	70	70.7	162	75.3	2.128 (0.145)
	Yes	24	20.7	29	29.3	53	24.7	
Use mouth wash 2 times per day	No	76	65.5	68	68.7	144	67.0	0.243 (0.622)
	Yes	40	34.5	31	31.3	71	33.0	
Use of fluoride	No	36	31.0	40	40.4	76	35.3	2.052 (0.152)
	Yes	80	69.0	59	59.6	139	64.7	
Suffer from Diabetes Mellitus	No	93	80.2	66	66.7	159	74.0	5.058 (0.025)
	Yes	23	19.8	33	33.3	56	26.0	
Suffer from Hypertension	No	100	86.2	61	61.6	161	74.9	17.173 (0.000)
	Yes	16	13.8	38	38.4	54	25.1	
Suffer from Ischemic heart disease	No	112	96.6	85	85.9	197	91.6	7.962 (0.005)
	Yes	4	3.4	14	14.1	18	8.4	
Suffer from GERD	No	106	91.4	84	84.8	190	88.4	2.217 (0.136)
	Yes	10	8.6	15	15.2	25	11.6	

Table 2 reveals the oral manifestations of the studied subjects having bronchial asthma. Angular stomatitis was significantly more encountered among patients with asthma compared to those without asthma ($p < 0.001$). Ulceration, pigmentation and candidiasis of the tongue, buccal mucosa and palate were significantly more encountered among patients with asthma compared to those without asthma ($p < 0.001$, 0.002 and 0.046 respectively). Xerostomia and salivary gland affection were significantly more encountered among patients with asthma compared to those without asthma ($p < 0.000$, and 0.002 respectively).

Table 2: Distribution of studied subjects by having asthma and oral Manifestations (continued next page)

Variable	Categories	Doctor diagnosed asthma				Total		X ² (p- value)
		No		Yes		N	%	
		N	%	N	%			
Arrhythmia	YES	1	.9	5	5.1	6	2.8	3.454 (0.063)
	NO	115	99.1	94	94.9	209	97.2	
Angular stomatitis	YES	116	100	90	90.9	206	95.8	11.006 (0.001)
	NO	0	0.0	9	9.1	9	4.2	
Tongue	No	113	97.4	80	80.8	193	89.8	22.439 (0.001)
	Ulceration	0	0.0	2	2.0	2	.9	
	Pigmentation	0	0.0	8	8.1	8	3.7	
	Candidiasis	0	0.0	5	5.1	5	2.3	
	Geographical tongue	0	0.0	2	2.0	2	0.9	
	Taste changes	1	0.9	0	0.0	1	0.5	
	Fissured tongue	2	1.7	2	2.0	4	1.9	
Buccal mucosa	No	110	94.8	82	82.8	192	89.3	8.062 (0.045)
	Ulceration	3	2.6	8	8.1	11	5.1	
	Pigmentation	2	1.7	6	6.1	8	3.7	
	Candidiasis	1	0.9	3	3.0	4	1.9	
Periodontium	No	25	21.6	18	18.2	43	20.0	14.450 (0.002)
	Gingivitis	69	59.5	43	43.4	112	52.1	
	Bleeding Gum	0	0.0	7	7.1	7	3.3	
	Recession of the gum	22	19.0	31	31.3	53	24.7	
Palate	No	114	98.3	84	84.8	198	92.1	14.961 (0.002)
	Ulceration	2	1.7	4	4.0	6	2.8	
	Pigmentation	0	0.0	1	1.0	1	0.5	
	Candidiasis	0	0.0	10	10.1	10	4.7	
Teeth	No	4	3.4	7	7.1	11	5.1	7.240 (0.299)
	Caries	25	21.6	15	15.2	40	17.6	
	Attrition	0	0.0	2	2.0	2	0.9	
	Pockets	4	3.4	1	1.0	5	2.3	
	Missing	2	1.7	2	2.0	4	1.9	
	Staining	1	0.9	0	0.0	1	0.5	
	More than one defect	80	69.0	72	72.7	152	70.7	

(Table 2: Distribution of studied subjects by having asthma and oral Manifestations continued)

Pockets	No	53	54.7	32	32.3	85	39.5	40.543 (0.000)
	Mild	50	43.1	24	24.2	74	34.4	
	Moderate	13	11.2	16	16.2	29	13.5	
	Severe	0	0.0	27	27.3	27	12.6	
Teeth affected	No	4	3.4	9	9.1	13	6.0	6.968 (0.138)
	UA	29	25.0	20	20.2	49	22.8	
	UP	47	40.5	50	50.5	97	45.1	
	LA	10	8.6	6	6.1	16	7.4	
	LP	26	22.4	14	14.1	40	18.6	
Lips	No	114	98.3	90	90.9	204	94.9	7.095 (0.069)
	Cheilosis	1	0.9	6	6.1	7	3.3	
	Candidiasis	0	0.0	2	2.0	2	0.9	
	Ulceration	1	0.9	1	1.0	2	0.9	
Xerostomia	NO	116	100	87	87.9	203	94.4	14.892 (0.000)
	YES	0	0.0	12	12.1	12	5.6	
Salivary glands	No	116	100	91	91.9	207	96.3	9.736 (0.008)
	Inflammation	0	0.0	7	7.1	7	3.3	
	Stones	0	0.0	1	1.0	1	0.5	

Table 3 displays that the majority of the patients with asthma (71.7%) used systemic and inhalation medicine; 22.2% used inhalation medicine only. About one third of the patients (34.3%) used both bronchodilators and cortisol as systemic drugs; while 23.2% used SABA alone as systemic drugs. About one fifth of the patients (22.2%) did not use systemic drugs for treatment of asthma. About 94% of the patients received inhalation therapy for asthma; SABA was the medicine usually used in the inhalation therapy (76.8%). The majority of the patients did not use spacers with the inhalers (96%); and the majority of the patients use the inhalers PRN (72.7%). Most of the patients used the inhaler once or twice per day (45.5% and 37.4% respectively). About 86% of the patients did not receive health education by the treating doctor about oral hygiene, and the majority of the patients did not practice regular oral hygiene measures after using the inhalers (79%). Headache and cough were commonly encountered among patients with asthma.

Table 3: Clinical characteristics of patients with asthma (continued next page)

Variable	Categories	Number	Percent
Medication used	Nothing	2	2.0
	Systemic	2	4.0
	Inhalation	22	22.2
	Systemic and inhalation	71	71.7
Systemic drugs	No	22	22.2
	Cortisol syrup	9	9.1
	Cortisol lab	3	3.0
	Cortisol injection	2	2
	SABA	23	23.2
	LABA	3	3
	Cortisol and bronchodilator	34	34.3
	LTA	3	3
Inhalation therapy	No	6	6.1
	MDI	37	37.4
	Powder	25	25.3
	Nebulizer	31	31.3
Medicine in the inhalation Therapy	No	3	3
	Budesonide	1	1
	Fluticasone	2	2
	LABA	13	13.1
	SABA	76	76.8
	LAMA	2	2
	SAMA	2	2
Dose of cortisol	No	13	13.1
	Mild	51	51.5
	Moderate	32	32.3
	High	3	3
Use of spacer	No	96	96
	Yes	4	4
Use of the inhaler	Regular	27	27.3
	PRN	72	72.7
Frequency of administration	00	4	4.0
	1,00	45	45.5
	2,00	37	37.4
	3,00	10	10.1
	5,00	1	1.0
	6,00	1	1.0
	20,00	1	1.0
Advised by Doctor on oral hygiene	No	85	85.9
	Rinse mouth	13	13.1
	Brush teeth	1	1.0

Table 3: Clinical characteristics of patients with asthma (continued)

Practice oral hygiene after inhalation	No	78	78.8
	Rinse mouth	17	17.2
	Brush teeth	2	2.0
	Mouth wash	2	2.0
Complaint	No	27	27.3
	Headache	16	16.2
	Dizziness	5	5.1
	Insomnia	5	5.1
	Cough	25	25.3
	Hoarseness of voice	4	4.0
	Sore throat	2	2.0
	Runny or stuffy nose	9	9.1
	Nausea	1	1.0
	Vomiting	3	3.0
	Dry mouth and throat	1	1.0
	Diarrhea	1	1.0

Table 4 reveals that patients with doctor diagnosed asthma were 7.7 times more likely to develop tongue disorders (OR: 7.7, $p < 0.013$), and 3 times more likely to develop buccal mucosal disorders (OR: 3, $p < 0.039$) compared to subjects without bronchial asthma.

Table 4: Multinomial Logistic regression of tongue disorders and buccal mucosal disorders and bronchial asthma and other personal and clinical characteristics

Variables	Tongue disorders			Buccal mucosa disorders		
	B	P	Exp (B)	β	P	Exp(B)
Intercept	6.031	.000		.959	.472	
Age in years	-.068	.013	934	.021	.424	1.021
Doctor diagnosed asthma (yes=1, no=0)	2.044	.004	7.724	1.111	.039	3.036
Gender (male=1, female=0)	-.453	.461	.636	-.517	.334	.596
Educational level (yes=1, no=0)	-1.448	.078	.235	.104	.842	1.110
Smoking habit	.183	.776	1.200	.705	.189	2.023
Rinse the mouth frequently (yes=1, no=0)	-1.077	.144	.341	-.844	.182	.430
Brush teeth frequently (yes=1, no=0)	1.181	.126	3.258	.007	.991	1.007
Use dental floss ≥ 2 times/day (yes=1, no=0)	-.157	.823	.854	.161	.790	1.175
Use mouth wash \geq 2 times/day (yes=1, no=0)	1.105	.102	3.019	-.009	.988	.991
Use of fluoride (yes=1, no=0)	-1.171	.085	.310	-1.010	.070	.364

Table 5 shows that patients with doctor diagnosed asthma were 15 times more likely to develop palate disorders (OR: 15, $p < 0.004$) compared to subjects without bronchial asthma.

Table 5: Multinomial Logistic regression of periodontium disorders and palate disorders, and bronchial asthma and other personal and clinical characteristics

Variables	Periodontium disorders			Palate disorders		
	B	P	Exp (B)	β	P	Exp (B)
Intercept	- .856	.454		7.188	.000	
Age in years	-.010	.651	.90	-.056	.072	.945
Doctor diagnosed asthma (yes=1, No=0)	.084	.821	1.088	2.711	.004	15.038
Gender	-.019	.961	.981	1.252	.110	3.499
Educational level (yes=1, No=0)	-.228	.545	.796	-1.738	.081	.176
Smoking habit	.547	.192	1.728	-1.756	.055	.173
Rinse the mouth frequently (yes=1, No=0)	-.907	.115	.404	-2.303	.007	.100
Brush teeth frequently (yes=1, No=0)	.501	.244	1.650	1.688	.072	5.408
Use dental floss 2 times per day or more (yes=1, No=0)	-.214	.638	.807	.260	.760	1.297
Use mouth wash 2 times per day or more (yes=1, No=0)	-.175	.676	.839	.913	.329	2.491
Use of fluoride (yes=1, No=0)	-.173	.668	.841	-2.296	.013	.101

Discussion

The purpose of this study was to explore the impact of use of inhalation therapy in patients with asthma on the health of the oral cavity. Previous studies revealed that women had increased occurrence of bronchial asthma compared to men, educational level may influence asthma control, and (4) asthma is a common occupational lung disease (3-5). However, in the present study no significant associations were found between asthma and gender, educational level, or occupation of the subject. Air pollution, and second-hand smoking (SHS) exposure represents significant risk factors for asthma (6). In the present study, we found a significant link between smoking and occurrence of asthma. Growth of bacteria in the oral cavity, on the teeth and mucosa, is affected by the variety of surfaces it provides bacteria with. These bacteria are affected by the condition of the oral hygiene, soft-tissues, diet and saliva, as well as the host's immune and inflammatory responses (33, 34). The present study revealed that patients with asthma are significantly less likely to brush their teeth, rinse the mouth, use dental floss or use fluorides. This is consistent with findings from a previous study. (40). Previous studies reported significant association between asthma and occurrence of diabetes mellitus, hypertension and coronary heart disease. (7 – 9). This is consistent with findings from the present study. Gastro-esophageal reflux disorder (GERD), is significantly associated with asthma (10). However in the present study asthma was not significantly associated with GERD. Asthma should be considered as a potential etiology in any patient with chronic cough, because asthma is a common condition that is commonly associated with cough (12). In addition, migraine-type and tension-type headaches are more common in patients with asthma, compared to the overall population (11-13). The present study revealed that headache and cough were commonly encountered among patients with asthma. This is in line with another study (11). The present study revealed that ulceration, pigmentation and candidiasis of buccal mucosa and palate; as well as bleeding gum and gingival recession were significantly more common in patients with asthma compared to those without asthma. This was in line with a previous study, which revealed that, the amount of *Candida* organisms was found to be high in the oral cavity of patients with asthma due to the immunosuppressive effect of the inhaled cortisol (43).

High doses of systemic medications for asthma lead to salivary glands affection with resultant xerostomia, inflammation and stone formation which may increase dental caries (19 – 22). Beta2 agonists, and inhaled cortisol reduce secretion of saliva and increase dental caries, attrition and dental erosion (45, 46). This is consistent with findings from the present study.

ICSs, the mainstay of asthma treatment, lead to a reduction in both airway inflammation and airway hyper-responsiveness (29). In the present study the majority of the patients with asthma (71.7%) used systemic medication and inhalation of cortisol, while 22.2% used

inhalation medicine only. Patients diagnosed with asthma should be prescribed a short-acting, beta-2 agonist "rescue" inhaler (29). This is consistent with findings from the present study. Previous studies revealed that the use of spacer with the MDI (an additional reservoir placed between the mouthpiece of the MDI and the mouth of the patient) or a valved holding chamber (VHC) (a reservoir with a one-way valve permitting airflow into, but not out of, the patient's mouth) prior to inhalation increased the amount of inhaled medicine to different generations of the airways (31). However, in the present study, the majority of the patients did not use spacers with the inhalers (96%); and the majority of the patients use the inhalers PRN (72.7%). Previous studies revealed that clinical trials have shown that the "as-required," or PRN, use of inhaled combinations of a corticosteroid and a rapid-onset β_2 -agonist provides clinical advantages over the traditional PRN inhaled rapid-onset β_2 -agonists alone in patients with different degrees of asthma severity (32). In the present study most of the patients used the inhaler of β_2 -agonist only, once or twice per day (45.5% and 37.4% respectively). Dental practitioners should be aware of the correlation between asthma and oral health. They should educate their patients to follow precautionary measures to prevent adverse effects on oral tissues (42). In the present study we found that 85% of the doctors did not advise the asthmatic patients to maintain oral hygiene.

Conclusions

The majority of patients with asthma use inhalation therapy, but they do not use inhalers. Oral clinical disorders e.g. ulceration, pigmentation and candidiasis, in the tongue, buccal mucosa, and palate as well as xerostomia are significantly associated with inhalation therapy for asthma. Oral hygiene practice by patients with asthma was low. The health care practitioners should focus on health education of patients with inhalation therapy, about importance of proper practice of oral hygiene.

Limitations of the study:

This study was a convenient non-probability one, and used an online questionnaire so the representation of the data to the population can't be assured. However, this was an exploratory study and showed no marked variations in the characteristics of the studied subjects, and the results are similar to those obtained globally.

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