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Pulmonary function test: A critical domain in oral submucous fibrosis patients

Vishal Mehrotra, Sheenam Sambyal, Gauri Mishra¹, Kriti Garg, Rahul Srivastava, Saman Ishrat

Abstract:

INTRODUCTION: The study aims to measure and compare pulmonary function tests (PFTs) in oral submucous fibrosis (OSMF) patients (smokers/nonsmokers) and normal individuals.

MATERIALS AND METHODS: The study population included 150 participants that comprised 50 nonsmoker OSMF patients, 50 OSMF patients who smoke as well, and 50 patients with no deleterious habits. Spirometer was used to assess PFT.

RESULTS: Results showed that a significant *P* value was obtained for forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁), FEV₁/FVC, peak expiratory flow rate (PEFR), and maximum voluntary ventilation (MVV) and also for the predicted values of FEV, FEV₁, FEV₁/FVC, PEFR, and MVV in OSMF (smokers/nonsmokers) study groups.

CONCLUSION: Thus, the decrease in pulmonary function can be an alarming sign for restrictive type of pulmonary disease.

Keywords:

Areca nut, arecoline, oral submucous fibrosis, pulmonary function test, smokers, spirometer

Introduction

Oral submucous fibrosis (OSMF) is an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. OSMF has also been referred as idiopathic scleroderma of mouth, idiopathic palatal fibrosis, sclerosing stomatitis, and juxta-epithelial fibrosis. This premalignant condition is characterized by submucosal fibrosis that affects most parts of the oral cavity, progressive trismus due to rigid lips, cheeks, pharynx, and upper third of the esophagus leading to dysphagia.^[1,2]

This premalignant condition is predominant in South East Asia, specifically in Indian subcontinent.^[3] Since the last few years, there has been an increase in prevalence (>6%) of OSMF.^[4] Males are more

affected (male:female ratio is 4.9:1), most commonly in the age group of 20–40 years.^[5]

Areca nut is a seed that grows most commonly in tropical Pacific, Asia, and parts of East Africa. Areca nut is available commercially as various freeze-dried products, for example, pan masala, gutka, and mawa (areca and lime); these products have a higher concentration of areca nut per chew.^[6]

Areca nut and gutka chewing are the principal risk factors for the development of OSMF. The areca alkaloids result in fibroblast proliferation and inhibition of collagen phagocytosis.^[7] The arecoline which is one of the most important constituents of betel nut results in elevated collagen synthesis by OSMF fibroblasts in contrast to normal fibroblasts (clonal

Department of Oral
Medicine and Radiology,
Rama Dental College,
Kanpur, Uttar Pradesh,
India, ¹Department of
Dentistry, Government
Medical College, Jalaun,
Uttar Pradesh, India

Address for correspondence:

Dr. Sheenam Sambyal,
Department of
Oral Medicine and
Radiology, Rama
Dental College, Kanpur,
Uttar Pradesh, India.
E-mail: sambyalsn121@
gmail.com

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selection). Tannins and catechins in the betel nut result in stabilization of collagen structure. The high copper content in areca nut plays a key role in stimulation of fibroblasts. The various other mechanisms mentioned in the literature which are associated with development of fibrosis include an increase in expression of fibrogenic cytokines, upregulation of COX-2 inflammatory changes, and stabilization of extracellular matrix. It is also believed that immunological factors and nutritional deficits also play a role in pathogenesis of OSMF.^[8]

Arecoline is considered as the principal etiological factor, but the addition of peroxy nitrite (a reaction product of cigarette smoking) and nicotine acted as a synergistic effect on the arecoline-induced cytotoxicity and glutathione depletion, thus patients with habit history of areca nut chewing along with cigarette are at high risk of malignant transformation.^[8]

In the literature, it has been documented that the areca nut metabolite arecoline causes aggravation of disease in asthmatics by increasing bronchoconstriction in a dose-dependent manner.^[9]

Pulmonary function test (PFT) serves as an important tool in diagnosing and measuring the severity of various respiratory diseases and thus serves as a key adjuvant to the patient history, various noninvasive imaging modalities, and other invasive procedures, for example, bronchoscopy. Spirometric values vary according to age, height, sex, and body size.^[10,11]

This study was conducted to evaluate the changes in pulmonary function values among normal controls and OSMF patients with and without smoking habit.

Materials and Methods

Study design and setting

The present cross-sectional study was conducted in a private dental college in Kanpur city during the period of August 2020 to January 2021.

Study participants and sampling

The present study included 150 participants between the age group 20 to 60 years and were further categorized into three groups:

Group I consisted of fifty participants who were clinically diagnosed with OSMF and had a habit of chewing betel nut but were non-smokers, Group II comprised of fifty participants who were clinically diagnosed with OSMF and had a habit of chewing betel nut and smoking tobacco and Group III consisted of fifty healthy participants with no deleterious habits (e.g. betel nut chewing/ tobacco smoking).

Spearman's correlation test was performed to calculate the sample size, and mean/standard deviation was calculated for the analysis directly from the MedCalc statistical software version 20.026.

Data collection and technique

The inclusion criteria in this study consisted of patients: not using bronchodilators, non-smoker, not performing any strenuous exercise at the day when the spirometer test was conducted; and those not consuming alcohol or eating a large meal before 4 hours of the procedure. Lastly, the patients should be wearing comfortable, loose clothes during the procedure.

The exclusion criteria consisted of patients suffering from any acute and chronic systemic illness including respiratory diseases or allergy, those under any type of medicinal treatment for OSMF or any other systemic illness, and finally, patients who consume alcohol.

PFTs were measured using computerized spirometer model no. "SPIRO-232," P.K. Morgan Medical Ltd. The participant was asked to stand in front of the spirometer and was asked to open his mouth. The mouthpiece of these spirometers was introduced into his mouth, and he was asked to close the lips around the mouthpiece tightly. Immediately, after the deep inspiration, he was asked to blow out the air as fast as possible into the mouthpiece. PFTs done were as follows: forced vital capacity (FVC) (L), forced expiratory volume in 1 s (FEV1) (L), FEV1/FVC%, peak expiratory flow rate (PEFR) (L/min), and maximum voluntary ventilation (MVV) (L/min). The MedCalc statistical software version 19.7.2 (MedCalc Software Ltd. 64-bit version 2020 Belgium) was used to calculate *P* value (*P* value significant at $P < 0.05$).

Ethical consideration

An ethical clearance was taken from the institutional ethical committee before the commencement of the present study.

Results

There was no significant difference between the mean ages of the three study groups, and majority of the OSMF patients were of age range 35–42 years. A significant *P* value ($P = 0.0011$) for OSMF (nonsmokers) in the age group of 18–26 years and *P* value ($P = 0.0080$) for OSMF (smokers) in the age group of 27–34 years were obtained [Table 1].

Furthermore, a significant *P* value was obtained for FVC, FEV1, FEV1/FVC, PEFR, and MVV and also for the predicted values of FEV, FEV1, FEV1/FVC, PEFR, and MVV in OSMF study groups [Table 2].

Table 1: Age-wise stratification of patients

Age	OSMF (nonsmokers) patients (n=50)	OSMF (smokers) patients (n=50)	Controls (n=50)	P
18-26	12	10	20	Nonsmokers (0.0011)
27-34	6	11	10	Smokers (0.0080)
35-42	20	16	9	
43-50	12	13	11	
Mean	34.88	34.76	31.18	
SD	6.314	8.147	4.589	

SD=Standard deviation, OSMF=Oral submucous fibrosis

Table 2: Pulmonary function test values for normal and oral submucous fibrosis patients

Pulmonary function test	Mean	SD	P
FVC			
OSMF (nonsmokers)	3.019	0.478	0.0001
OSMF (smokers)	2.984	0.551	0.0001
Normal	3.689	0.297	
FEV1			
OSMF (nonsmokers)	2.457	0.799	0.0001
OSMF (smokers)	2.873	0.687	0.0001
Normal	3.694	0.357	
FEV1/FVC			
OSMF (nonsmokers)	92.874	4.128	0.0032
OSMF (smokers)	96.547	3.791	0.0048
Normal	88.474	5.886	
PEFR			
OSMF (nonsmokers)	7.995	1.658	0.0018
OSMF (smokers)	7.228	1.547	0.0027
Normal	8.965	1.449	
MVV			
OSMF (nonsmokers)	87.869	24.218	0.0001
OSMF (smokers)	88.694	23.879	0.0001
Normal	104.658	16.273	
Predicted FVC			
OSMF (nonsmokers)	3.886	0.4128	0.0012
OSMF (smokers)	3.447	0.203	0.0062
Normal	4.215	0.278	
Predicted FEV1			
OSMF (nonsmokers)	3.014	0.194	0.0221
OSMF (smokers)	2.869	0.218	0.0369
Normal	3.891	0.146	
Predicted FEV1/FVC			
OSMF (nonsmokers)	82.964	3.258	0.0001
OSMF (smokers)	83.214	3.002	0.0001
Normal	89.645	1.426	
Predicted PEFR			
OSMF (nonsmokers)	8.554	0.221	0.0001
OSMF (smokers)	8.964	0.314	0.00012
Normal	9.021	0.617	
Predicted MVV			
OSMF (nonsmokers)	127.698	17.896	0.0021
OSMF (smokers)	123.658	18.964	0.0084
Normal	139.54	19.614	

MedCalc statistical software has been used to calculate P value, P value is taken significant at P<0.05. SD=Standard deviation, OSMF=Oral submucous fibrosis, FVC=Forced vital capacity, FEV1=Forced expiratory volume in 1 s, PEFR=Peak expiratory flow rate, MVV=Maximum voluntary ventilation

Discussion

Sushruta – the ancient Indian medical text – describes a condition termed “VI-DARI” under mouth and throat diseases as “progressive narrowing of mouth, depigmentation of oral mucosa, and pain on taking food.”^[12] All these are the characteristic features of Oral submucous fibrosis. However, it was only in 1952 when Joshi^[13] described the condition as “submucous fibrosis” and Schwartz^[14] described it as “atrophica idiopathica mucosae oris” that the condition came to be recognized in modern medical literature. However, in the 1960s and 1970s, only sporadic cases of OSF were seen, more often in older females. The prevalence of OSF kept on increasing. In 1980, Pindborg^[15] estimated about 250,000 cases of OSF in India which is now estimated to have increased to two million cases – an eight-fold increase in <15 years.^[16] This sharp rise in the prevalence of OSF could be attributed to increased popularity of various chewing habits – especially of pan masala. Various brands of pan masala are available in India, the exact ingredients being kept a guarded trade secret. They are attractively packaged both in tins and sachets and aggressively advertised. It has found social acceptance and has come to be recognized as a symbol of modernity and high status.^[17]

PFTs are an important tool in the investigation and monitoring of patients with respiratory pathology.^[10] Spirometry is the most frequently used measure of lung function and is a measure of volume against time. It is a simple, least technique-sensitive, and quick procedure to perform: patients are asked to take a maximal inspiration and then to forcefully expel air for as long and as quickly as possible.^[18]

Spirometry provides the following measurements:

- FVC is the maximal volume of air that can be forcibly expelled from the lungs from a position of maximal inhalation. It indicates lung volume
- FEV1 is the maximal volume of air exhaled in the 1st s of an FVC maneuver. In individuals with normal lung function, this is 75%–80% of FVC. FEV1 reflects the mechanical properties of the large- and medium-sized airways

- Forced expiratory ratio (FEV1/FVC or FER %) is the ratio of FEV1 to FVC, expressed as a percentage. It assists with distinguishing obstruction from possible restriction when FEV1 is reduced. If restriction is suspected, further testing with static lung volumes may be required^[19]
- PEFr is the maximum flow rate generated during a forceful exhalation, starting from full-lung inflation. PEFr primarily reflects large airway flow and depends on the voluntary effort and muscular strength of the patient.^[20]

PEFr measures the airflow through the bronchi and thus the degree of obstruction in the airways. Peak expiratory flow is typically measured in units of liters per min (L/min). Peak flow readings are higher when patients are well and lower when the airways are constricted.^[21]

In the present study, the sample size consisted of 150 participants which were subdivided into three groups. Group I consisted of fifty participants who were clinically diagnosed with OSMF and had a habit of chewing betel nut but were non-smokers, Group II comprised of fifty participants who were clinically diagnosed with OSMF and had a habit of chewing betel nut and smoking tobacco and Group III consisted of fifty healthy participants with no deleterious habits (e.g. betel nut chewing/ tobacco smoking). For these study groups, PFT was performed using a spirometer.

A similar study was conducted by Nivsarkar *et al.*, with a study group of 100 participants. Group 1 consisted of 50 patients with a habit of chewing betel nut and Group 2 consisted of participants with no deleterious habits. Pulmonary function test in this study were measured using computerized spirometer.^[22] Nivsarkar *et al.* in their study found that there were a decrease in values of FVC, FEV1, PEFr, MVV, and their predicted values and an increase in FEV1/FVC ratio and its predicted value although this relation was not found to be significant.^[22] The results obtained in the present study shows statistically significant changes in FVC, FEV1, FEV1/FVC, PEFr, and MVV and their predicted values in Group I and Group II study subjects which is in contrast to the results obtained from the study mentioned above.

Datta and Yanga studied Melanesian males of age range 18–40 years and found that betel nut chewers had significantly reduced FVC and FEV1. The results of this study were similar to our study where significant reduction in values of FVC and FEV1 was observed in patients with OSMF.^[23]

Kiyangi and Saweri looked at the effects of betel nut in healthy individuals with no history of asthma and found no changes in FEV1. The result in our study was contrary

to the above as FEV1 values were significantly reduced in our study.^[24]

Taylor *et al.* also tested arecoline inhalation in healthy individuals. Even though there was more bronchoconstriction found in asthmatic people (six of seven patients), one of six healthy individuals developed bronchoconstriction, concluding that arecoline causes constriction of bronchial smooth muscles, thereby causing difficulties in respiration, particularly in patients with respiratory tract disorder.^[25] The result obtained from the research by Taylor *et al.* can be the cause of changes in the lung function test by spirometry in our study.

Wang *et al.* study sample size consisted of 600 asthma patients and 1200 controls which were studied to investigate the connection between asthma and betel nut use. They found that a higher arecoline level was associated with worse lung function FEV1 ($\rho = -0.359$, $P = 0.004$) and FVC ($\rho = -0.309$, $P = 0.02$) in the male asthma group and concluded that betel nut chewing results in esophageal inflammation and fibrosis that may result in aggravation of asthma (an obstructive lung disease).^[26,27] A similar result was obtained in our study too where lung function was compromised in patients with OSMF (smokers/nonsmokers).

Deng *et al.* in their study stated areca nut chewing as a risk factor for bronchospasm and chest discomfort and reported adverse clinical manifestations following initial or heavy betel nut use as bronchoconstriction, aggravation of asthma, and even respiratory failure.^[28,29] A similar result was obtained in our study too, where spirometry measurements showed significant changes in the lung function test, thereby favoring the concept of obstructive lung changes in OSMF patients (smokers/nonsmokers).

Limitation and recommendation

This study is one of the pioneer studies in which PFT is measured in OSMF patients with or without habit of smoking. A small sample size and a short period over which the study was conducted form the limitation of the present study. To validate the result of the present study, we recommend a larger sample size and a prolonged duration period of the study are required.

Conclusion

The habit of chewing areca nut is increasing worldwide. The addictive nature of areca nut is causing various oral and systemic problems in all age groups. Areca nut chewers are predisposed to asthma as it causes bronchoconstriction and decreased FEV. It is found in our study that the PFT is decreased in OSMF

patients (smokers/nonsmokers) compared to normal controls. The decrease in pulmonary function can be a warning sign for obstructive and restrictive type of pulmonary disease. More studies analyzing association between OSMF patients and patients with pulmonary disorders shall be conducted on a wider scale to further validate the results.

Future scope

OSMF leads to various systemic and oral complications, of which obstructive lung diseases are among the malignant ones. This study highlights the significant changes in PFTs in OSMF patients. Thus, further studies on the larger sample size are required to validate the results.

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Conflicts of interest

There are no conflicts of interest.

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