

Association between Oral Submucosal Fibrosis and Habitual Gutka and Pan Usage

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Abstract: Oral sub mucous fibrosis (OSF) is a precancerous condition caused by the use of areca nut in various forms. There are few reports on areca nut use and OSF in Chabahar, south Iran. In this descriptive, analytical and cross-sectional study 397 users of Pan / Gutka (products contain areca nut) were studied to survey the oral submucosal fibrosis. The criterion of diagnosis of OSF in this study was the limitations of mouth opening and stiff fibrotic bands within the mucosa. Information about the amount of consumption, kind of substance used, and duration of consumption was mentioned in the questionnaire. Data were analyzed and studied by, SPSS 14, c hi-square test. Of 397 Pan (Areca nut) / Gutka consumers (391 men and 6 women), 70 participants (17.63%) men and one woman (0.25%) were affected by OSF. The risk of OSF in Gutka consumers (20%) was more than pan users (17.54%). Duration, dose and frequency of consumption were significantly associated with OSF occurrence ($p < 0.05$). Recent study indicated strong relationship between consumption of products containing areca nut with OSF. [Masoomeh Shirzaii, Maryam Hormozy, Javid Dehghan Haghighi, Mani Javadimehr. **Association between Oral Submucosal Fibrosis and Habitual Gutka and Pan Usage.** *Life Sci J* 2013;10(4):204-209] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 27

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Introduction:

Oral sub-mucosal fibrosis (OSF) is a precancerous, chronic, progressive condition of the oral, often seen in Indian migrants and inhabitants of South East Asia (1). The lesion is characterized by sub mucosal fibrosis, reduced levels of vasculature and mucosal atrophy. All its features include: stomatopyrosis, oral mucosal pallor and mucosal rigidity that caused limitation in opening of the mouth, also tongue protrusion and flexibility of cheek. Dysphasia occurs in severe cases. Experimental (in vitro) and epidemiological studies showed chewing areca nut (areca catechu) is an important etiological factor causing OSF (2).

Various Areca nut products such as betel quid (areca nut+ betel leaf + Slaked lime) with or without tobacco and pan that is easily available. In Indian there are region differences in consumption of various products of areca nut. The nut contains alkaloid and arecoline that is a very strong stimulus for synthesis of collagen by fibroblasts (3). Consumption of products containing areca nut (pan, Gutka) spread at an early age resulting in increased occurrence OSF in young adults (4). Many consumers' products containing areca nut and tobacco

and ...can play an important role in the initiation and progression of this precancerous condition (3).

There are few epidemiological studies about the consumption of different products of areca nut (such as pan and Gutka) and OSF occurrence, in Iran, and there are not studies related to the occurrence of OSF complications in Chabahar (South East of Iran), Therefore in this study, occurrence of OSF and related factors to its have been evaluated.

Methods:

This cross-sectional, descriptive and analytical study conducted on 397 consumers of Areca nut products including pan and Gutka in Chahbahar, Iran (2009). Samples were collected by multistage random method from visitors to Health Centers in the city and were examined by means of Head Light and Dental Mirror for the occurrence of OSF by an oral medicine specialist. This study was performed in a particular time section (approximately six months). Information form including demographic, types of oral habits, amount of consumption, duration usage (month), consumption frequency(daily), type of substance consumed (pan, Gutka,) was completed for each individual. They were enrolled for at least a year for the consumption of pan or Gutka alone or

together simultaneously. Subjects who sometimes were taking these products (less than two times in a month) and also those who were using tobacco products as well as cigarettes and hookah, were excluded from this study.

OSF clinical diagnosis criteria were include: restrictions on opening of the mouth, existence of fibrosis band in buccal / labial mucosa, lack of elasticity in buccal / labial mucosa (1,3,5). Clinical diagnosis was confirmed by biopsy in some cases (that clinical diagnosis was difficult). Dense submucosal layer and vascular collagen in connective tissue, chronic inflammation of cells with different numbers and epithelial atrophy were the criteria of diagnosis. (1). the amount of opening of the mouth was assessed based on inter incisal distance (mm). OSF was divided into three clinical stages considering the amount of opening of the mouth as follows :(6)

Stage I: Mouth opening \geq 45 mm.

Stage II: Restricted mouth opening 20-44 mm.

Stage III: Mouth opening $<$ 20 mm.

All the subjects participated consciously and without coercion in this study. Patients were allowed if desired, be excluded from the study. Information about every person would remain confidentially and all patients had given their consent.

Statistical analysis

All the data obtained based on the existing information form were analyzed according to the statistic computer program SPSS 14 and chi –square test.

Results:

In this study were studied 397 consumers of pan /Gutka (391 man 98.5%) and 6 women (1.5 %) with age limitations of 8-48 years and mean age of 20.22 years. Prevalence of OSF in the statistically studied community was equivalent to 17.63% (70 cases) which 69 (17.38%) were men and one woman (0.25%) The mean age of OSF patients was 25.5 \pm 8.04 and the average of healthy subjects was 24.9 \pm 14.65. The number of patients that chewed pan was 359 (90.4 %). Substance consumptions distribution in studied subjects was shown in Table 1.

Table 1: Distribution frequency of substance consumption in studied subjects.

Substance Used	OSF	Normal	Total	P-Value
	n%	n%	n%	
Pan	63(17/55)	296(82/45)	359(100)	
Gutka	6(20)	24(80)	30(100)	0.95
Pan + Gutka	1(12/5)	7(87/5)	8(100)	

In this study, the prevalence of OSF in different age groups did not differ much with each other (P=0.27).Age distribution in studied subjects were shown in table 2.

Table 2: age Distribution of studied subjects.

Age of initiation in this study was very low (10-20 years) and 35.76% of individuals in this age group started to consume pan / Gutka.

In present study, there are significant correlation between duration consumption and occurrence of OSF (p<0.001), so that shown in table 3.

Table 3: Distribution frequency of time duration consumption in studied

It has been shown in this study that the consumption frequency of these substances is as great as possible during the day; the incidence rate of sub-mucosal fibrosis is greater. So that, by taking two times a day, three cases (0.75%) and three times a day 18 cases (4.5%), and more than three times a day, 43 cases (10.83%) were suffering from OSF. Table 4

Table 4: Comparison of frequency of substance consumption per day in OSF and normal subjects

There were 26 cases in Stage I (37.1%), 35 cases in Stage II (50%) and 9 cases in Stage III (12.9%). In the present study there was a significant correlation between occurrence of OSF with consumption frequency of pan and Gutka, So that most patients with OSF were in a group that consumed pan and Gutka more than three packages a day Table 5.

Table 5: Comparison amount of consumption per day in OSF and normal subjects

All the OSF signs and symptoms were developed in 40 (57.1%) patients, such as restriction on mouth opening, stiffness of mucosa, fibrotic bands in the area under labial/buccal mucosa, simultaneously. The most commonly affected region in 44 cases (62.8%) was the buccal mucosa. 130 subjects (32.7%) consumed pan as mouth freshener and 101 cases (25.4%) of this article consumed this as an exciting material. There was not significant correlation between the sex and morbidity variable of OSF. OSF prevalence in men and women in the study are presented in Table 6.

Table. 6: Sex Distribution frequency in studied subjects

Table 2: age Distribution of studied subjects

Age group	OSF		normal		total	
	n	(%)	n	(%)	n	(%)
Age of initiation in this study was very low (10-20 years) and 35.76% of individuals in this age group started to consume pan / Gutka.						

Table 3: Distribution frequency of time duration consumption in studied Subjects

10-20 yr	24	6.04	118	29.72	142	35.76
21-30 yr	35	8.81	159	40.05	194	48.86
31-40 yr	5	1.25	37	9.31	42	10.57
41-50 yr	6	1.51	11	2.77	17	4.28
>50yr	0	0	2	0.5	2	0.5

Duration consumption	OSF		normal		total	
	n	(%)	n	(%)	n	(%)
0-6	0	0	41	10.32	41	10.32
6-12	0	0	60	15.12	60	15.12
12-24	0	0	81	20.40	81	20.40
>24	70	17.63	145	36.53	215	54.16

Table 4: Comparison of frequency of substance consumption per day in OSF and normal subjects

Usage frequency	OSF		normal		total	p-value
	n	(%)	n	(%)		
1 time	0	0	108	27.20	108	0<0001
2 time	3	0.75	84	21.16	87	21.91
3 time	18	4.53	43	10.84	61	15.37
>3 time	43	10.84	98	24.68	141	35.52

Table 5: Comparison amount of consumption per day in OSF and normal subjects

	OSF		normal		total	
	n	(%)	n	(%)	n	(%)
1 package	1	0.25	107	26.95	108	27.2
2 package	5	1.26	83	20.9	88	22.17
3 package	16	4.03	45	11.33	61	15.37
>3 package	48	12.09	92	23.17	140	35.26

Table 6: Sex Distribution frequency in studied subjects

Gender	Affected		normal		total	
	n	(%)	n	(%)	n	(%)
male	69	17.65	322	82.35	391	100
female	1	25	5	75	6	100

Discussion:

Oral Sub-mucosal fibrosis is a pre-cancerous condition that often occurs in South East Asia inhabitants and Indian migrants. Areca nut product consumption is a common habit in these individuals and there exist a strong relationship with morbidity of sub-mucosal fibrosis. (3)

Several etiological factors have been proposed for the occurrence of OSF, include: a set of local factors, such as: capsacin, spicy food, and areca nut. In addition to local factors, systemic factors also played a major role in creating OSF include: chronic anemia, vitamin B-complex deficiency and genetic susceptibility. (3, 5, 7)

Areca nut chewing in various forms is common in India, the incidence of OSF is increasing, so that 250 000 cases in 1980 and 2 million in 1993 (have been reported). Consumption of products containing areca nut is common in countries like The South East Asia, India, Bangladesh and Pakistan (3). In Iran, the taking of areca nut in cities that are located near the border with Pakistan, for example Chabahar, is common. In current study, occurrence of OSF in the pan / Gutka users was studied. This is the first study reported in this field in South East of Iran. In the present study, occurrence of OSF in pan / Gutka consumers was equivalent to 17.63%, while the prevalence of OSF in the studies of Reichart, et al (2008) in Vietnam (8) and Sarswathi (2006) in South India (9) were equivalent to 13% and 0.55 %, respectively which is less than present study and also in the study of Jacob (2004) in Kerala, India (10) 56% cases were affected by OSF, that this result is more than our results. It appears, factors such as frequency consumption of these substances, compounds that are added to these products (tobacco, catechu, and...) differences in diet and total influence of genetic factors and regional differences are effective influences in the incidence of OSF., in total, the rate of incidence of OSF in Chabahar population is higher than elsewhere in Iran, due to easy access to products containing areca nut and cultural factors. This city is very near to Pakistani border town and areca nut derivatives are transferred through the border into the country and are available for very low prices to the people residing in this region. Also, Natives of this region due to lack of adequate knowledge on the consumption of disadvantages of this substances, they have the habit of chewing areca nut products, but this material is rarely used in other parts of Iran. In many studies, the distribution frequency of age and sex in OSF patients was very wide. In some studies in India, the occurrence of OSF is more common in women but, sinor (1990) in his another study done in this country, has showed the occurrence of this complication is more common in men (11). The ratio of affected males to females in the study of Kumar (2007) was reported as 6:1. (6), and in the study of Ranganathan (2004), it was reported as 9. 9:1(3). OSF in this study was more prevalent in men (17.6 %), and 0.25% in female. In the present study, 84.6% subjects were within the limited age range of 10 -30 years, and 50% of patients with OSF were in the 21-30 years age group. In the study performed by Kumar (6) (2007), 50% of his subjects were in 20-29 years age group, but in the study of Pindborg (1980) (12), most patients were in the 60-69 years age group. Owing to, consumption of pan at too young stage, occurrence of OSF in this age group is very high. This bad habit is common from primary school young age children in

Chabahar, and even distribution of this substance in school campus is acceptable. Moreover, diversity of products of areca nut is cheap and easy to access and to these reasons consumption of these substances is observed at an early age (6, 4). Another important point in this study was that, although with increasing age, declined prevalence of OSF, but most elder people consuming areca nut were affected by OSF. It appears with increase in cumulative risk factors and affective local factors and increase in duration of consumption and type of material consumed, frequency of usage provide the ground for creating OSF in the elderly. Epidemiologic studies on Indian immigrants in South African has shown that chewing areca nut is considered as an important risk factor for OSF (12,13). In recent years, consumption of commercial products containing areca nut, like Pan, and Gutka in India, Pakistan and the border areas adjacent to these countries has increased and many of the OSF patients have a history of prolonged chewing pan (4,14).In the current study, the prevalence of OSF in Gutka consumers was (20%) more than the consumers of Pan (17.54 %), but the study performed by Kumar (2007) in Chennai, 81% affected by sub-mucosal fibrosis were patients taking Pan (6). Shah (1998) has reported that chewing pan compared to betel quid for a shorter period will lead to OSF (14). Kumar during his study (2007) on 75 patients with OSF concluded that this generation of OSF in betel quid consumers was 10 years, betel nut six years and pan, five years (6).The probability of the occurrence of OSF in pan consumers for a short time more. In the current study, duration of use associated with the occurrence of OSF,it was clear so that all patients had the experience of consumption more than two years this result was consistent with study of Rajalalitha et al (2005)(15). The study of Shah et al, unlike present study, has showed there is no clear relationship of duration of consumption with the incidence of OSF(14). In recent study, 68.5% patients were seen in a group that consumed more than three packages of substance daily, and There exist significant correlation between incidence rate of OSF with the frequency and amount consumed, and type of substance used daily. Maher et al also reported that amount consumed daily had stronger risk factor for OSF incidence than period of consumption (16). Rajalalitha et al and **Ajit Auluck** et al opinion that, amount of areca nut in betel quid and the frequency and duration of chewing betel quid are clearly related to the development of OSF (13, 15). The study of Jacob (2004) in India also showed consumption dose, frequency and duration had a positive effect in creating OSF. (10). Results of this study showed the probability of occurrence of OSF in people who consumed pan and Gutka repeatedly during the day was more, and there existed significant

relationship between these two *variables*. Kumar during his study (2007) tried to achieve similar results. (6) Shah (1998) has reported, the consumption frequency of Pan, was a stronger risk factor for OSF occurrence and period of consuming has less importance(14), but, in present study all patients with OSF who had been taking pan and Gutka for more than 24 months, showed direct correlation between dose and the occurrence of OSF. In the study of Jacob (2004) in India, it was also reported that the dose, frequency and duration of consumption had a positive effect in creating OSF(10). Maher (1994) and Shah during a study (1998) concluded that the increasing the consumption of products containing areca nut, increased the prevalence of OSF.(16,14) limitations in opening of the mouth, white, pallor and stiff mucosa and fibrotic bands within the mucosa are complications and classical symptoms of OSF. In present study, severe limitation in opening of the mouth, stiff and fibrotic bands formed under mucosa, were the most common complications of OSF. Ranganathan (2004) in his study conducted on healthy Indian subjects showed average amount mouth opening in men was 47.5mm and in women 44.5 mm.(3) The amount of mouth opening in OSF patients depend on severity of the lesions. The more is the severity of the lesion, the less is the opening of mouth and based on this fact, severity of lesions are divided into three (stage I,II, and III) stages. In the studies of Kumar (2007) 75% men and 80% women were in stage II, the limitations of amount of their mouth opening was in the range of 21-30mm. (6) In present study, 50% of subjects were in stage II and 40% in stage III that had severe limitation of mouth opening below 20 mm.

The recent findings confirm that the treatment issue of patients with OSF is delayed in Chabahar, because of poor knowledge of most of the subjects about its negative impact on health, even in advanced stages of disease, they never attend for treatment, but in the study of Kumar 75% of patients who were in stage II consulted the doctor for treatment at early stage of disease (6). Early treatment can prevent lesion development. In our study most OSF patients used areca nut products as a mouth freshener and cleaning material. In other studies, this material has been referred as an exciter. (6) In present study, the most common area involvement was buccal mucosa. In a similar study conducted in Vietnam, the most common area involved include the buccal mucosa(27.9%) and tongue and lip(26%). Considering that most OSF patients in the current study, were very young, it can be concluded, consumption of areca nut products at an early age is very common in Chabahar. In other studies, also it has been noted that initiation age of areca nut product

consumption declined far more than that of the past and the occurrence age of OSF has also been reduced to the same ratio(4). In OSF disease, collagen metabolism is affected in early stages of disease and collagen fibers are deposited within the sub-mucosal tissue, and then the disease progresses, the replaced dense collagen fibers cause severe stiffness of mucosa. In this stage, tissues lose their elasticity properties, and can result in severe limitation of mouth opening in patients. Finally, mucosal tissues involved in atrophy prone to change to pre-cancerous condition. The risk of oral cancer in OSF lesions is equivalent to 30% (6).It should be mentioned that the possibility of malignant change in young people with OSF is very high, so it is necessary to reduce the incidence of oral cancer in young community, and also upgrading their awareness of hazards in areca nut containing products such as pan and Gutka

Suggestions:

In the present study the prevalence of OSF was higher in the 10-30 years old age group. Pan and Gutka chewing was higher in men, and also, the incidence ratio of OSF in men was more than in women. Pan was the most consumed substance, but the prevalence of OSF was more in Gutka chewers. Dose, frequency, and amount of Pan and Gutka consumed, had direct correlation with the OSF occurrence. Due to, this being a precancerous lesion it appears it is necessary to increase public awareness to the hazards of chewing areca nut products in this region, and an immediate need for planning an appropriate program is highly recommended.

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