

Original Research Article

Evaluation Of The Relationship Of Various Patterns Of Quid Usage In Patients With Oral Submucous Fibrosis And Leukoplakia In Central India Population: A Cross Sectional Study.

ABSTRACT

BACKGROUND- Oral habits can cause severe oral potentially malignant disorders. There is a need to deeply analyse the role of betel nut in the causation of these disorders. Patients must be educated in order to prevent them from grabbing these conditions as inspection leads to prevention.

AIM - The aim of our study was to study and analyse the different patterns of quid usage among the participants with oral submucous fibrosis and leukoplakia in Central India population.

PATIENTS & METHODS - The study was performed on 90 patients amongst which 45 patients were clinically diagnosed of oral submucous fibrosis & the other 45 patients were diagnosed of leukoplakia. The cases were then subjected to a detailed questionnaire which aimed to extract information regarding the various types of quid usage habits, their frequency and duration. The data was recorded and statistical analysis was done.

RESULTS - The study included 90 subjects – 86 males & 4 females. Out of 6 types of quid habits it is found that type IV (processed areca nut), Type VI (combined quid usage) quid caused OSMF stage II, Stage III & homogenous leukoplakia respectively. There is a strong association between duration and frequency of habit in causation of OSMF & leukoplakia.

CONCLUSION- The present study showed increased prevalence of OSMF & leukoplakia with type IV & VI quid usage among the population of Central India.

Keywords- osmf ; betel quid; leukoplakia; areca nut; betel leaf

Abbreviations- OSMF – oral submucous fibrosis

INTRODUCTION

The term “betel quid” is often used with insufficient attention given to its varied contents and practices in different parts of the world.¹ A betel quid (synonymous with pan or paan) generally contains betel leaf, areca nut and slaked lime & may contain tobacco. Many betel quid products in the different parts of the world are not actually chewed; rather they are placed in the mouth or applied to the the oral cavity and remain in contact with oral mucosa¹.

Chewing pan releases carcinogenic nitrosamines from the areca nut that can cause pre-neoplastic changes. Betel nut induced lichenoid lesions mainly on buccal mucosa at quid retained sites.

In chronic chewers, a condition called betel chewers mucosa is often found where quid is placed. Betel nut chewing is implicated in oral submucous fibrosis and its use along with tobacco can cause leukoplakia, both of which are potentially malignant in the oral cavity. Oral cancer often arises from such precancerous changes.

Oral submucous fibrosis (OSF) is a chronic, insidious oral mucosal condition that occurs predominantly among Indians and occasionally in other Asians especially Taiwanese and sporadically in Europeans. It was first described by Pindborg and Sirsat . It is regarded as a pre-cancerous condition.²

The hallmark of the disease is submucosal fibrosis that affects the oral cavity and progressively involves the pharynx and the upper oesophagus. It is characterized by juxta-epithelial inflammatory reaction followed by chronic change in the fibro-elasticity of the lamina propria and is associated with epithelial atrophy. This causes burning sensation in the oral cavity, along with blanching, and stiffening of oral mucosa and oropharynx, resulting in inadequate and restricted mouth opening which in turn causes limited food consumption, difficulty in maintaining oral health and hygiene, and impairs the ability to speak.²

The presence of palpable fibrous bands is an important diagnostic criterion for OSF. The fibrous bands occur especially in the buccal mucosa, retromolar areas, and around the rima oris. If the tongue is affected, it gets devoid of papillae and becomes smooth. Its mobility, especially the protrusion, is impaired. The opening of the mouth is restricted. Some investigators adhered to the earlier signs and symptoms such as pain, history of vesicles and ulcers, and blanching of the mucosa for diagnosis of OSMF.²

Leukoplakia is the one of the most common premalignant or potentially malignant lesion affecting the oral mucosa. In cases when a biopsy is taken, the term leukoplakia should be replaced by the diagnosis which is obtained histologically. The percentage of annual malignant transformation varies in different parts of the world, probably as a result of differences in tobacco and dietary habits. Although epithelial dysplasia is an important predictive factor of malignant transformation, it should be analysed that not all dysplastic lesions will become malignant. On the other hand non-dysplastic lesions may become malignant as well. In some parts of the world, the tongue and the floor of the mouth can be considered as high-risk sites in regard to malignant transformation of leukoplakia, while this does not have to be the case in other parts of the world.³

Thus, public health measures to quit betel quid use are recommended as a prophylactic measure to control disabling conditions such as oral submucous fibrosis and oral cancer.

In the present study, the different patterns of quid usage among the participants with oral submucous fibrosis and oral leukoplakia were studied and evaluated in the people of Central India so as to prevent the premalignant conditions from getting turned into advanced malignancy.

MATERIAL & METHODS

The present study was carried in the Department of Oral Medicine & Radiology of our institution wherein 45 cases of OSMF & 45 cases of leukoplakia between the age range of

20-70 years were selected among the patients attending the out patient department of our institute. OSMF was diagnosed as per the clinical criteria set by Haider et al and leukoplakia was diagnosed as per the classification given by Axell & Pindborg et al in 1983 based on the clinical type. A detailed case history was taken and a habit based questionnaire was formed in which each patients were enquired about their betel quid chewing habits, type of quid, frequency and duration and all the data was recorded in a prepared proforma. The data obtained after the detailed examination was tabulated and statistically analyzed.

Chart 1. Haider et al’s classification of OSMF

Stage I	Faucial bands only
Stage II	Faucial and buccal bands
Stage III	Faucial, buccal, and labial bands

Classification of Leukoplakia according to Axell & Pindborg et al in 1983 based on the clinical type.

- Homogeneous
- Non Homogeneous

RESULTS-

The data obtained was completely analysed, a detailed statistical analysis was done, the results were obtained and the following observations were made and summarized in Tables 1–6.

TYPE OF QUID

A total of 45 subjects were distributed according to the type of quid in Leukoplakia group. (Table 1)

A total of 45 subjects with homogenous leukoplakia were distributed according to the type of quid. In Type I group, a total of 4 subjects (8.89%) who chewed betel leaf and areca nut were found to have homogenous leukoplakia . **(Table 1)**

In Type II group, a total of 5 subjects (11.11%) who chewed betel leaf, areca nut, slaked lime were found to have homogenous leukoplakia.

In Type III group, a total of 5 subjects (11.11%) who chewed betel leaf, areca nut and slaked lime and tobacco were found to have homogenous leukoplakia.

In Type IV group, a total of 8 subjects (17.78%) who chewed processed areca nut were found to have homogenous leukoplakia.

In Type V group, a total of 12 subjects (26.67%) who chewed processed areca nut and processed tobacco were found to be with homogenous leukoplakia.

In Type VI group, a total of 11 subjects (24.44%) who chew combined quid usage were found. Out of them, a total of 10 subjects (22.22%) were found to be with homogenous leukoplakia and 1 subject (2.22%) was found to be with non-homogenous leukoplakia.

TYPE OF QUID	NAME OF QUID	NO PATIENTS	HOMOGENOUS	NO OF PATIENTS OF NON HOMOGENOUS LEUKOPLAKIA
TYPE I	BETEL LEAF AND ARECA NUT	4(8.89%)	4(8.89%)	
TYPE II	BETEL LEAF, ARECA NUT AND SLACKED LIME AND TOBACCO	5(11.11%)	5(11.11%)	
TYPE III	BETEL LEAF , ARECA NUT AND SLACKED LIME & TOBACCO	5(11.11%)	5(11.11%)	
TYPE IV	PROCESSED ARECA NUT	8(17.78%)	8(17.78%)	
TYPE V	PROCESSED ARECA NUT AND PROCESSED TOBACCO	12(26.67%)	12(26.67%)	
TYPE VI	COMBINED QUID USAGE	10(22.22%)	10(22.22%)	1(2.22%)

Table 1: Distribution Of Patients According To Type Of Quid In Leukoplakia

A total of 45 subjects were distributed according to the type of quid in OSMF group. (Table 2)

In Type I group, a total of 2 subjects (4.44%) who chew betel leaf and areca nut were found to have stage 1 of OSMF.

In Type II group, a total of 5 subjects (11.11%) who chew betel leaf, areca nut, slaked lime and acked were found to have stage 1 of OSMF.

In Type III group, a total of 8 subjects (17.78%) who chew betel leaf F, Areca nut and slaked lime were found to have stage 1 of OSMF.

In type IV group, a total of 11 subjects (24.44%) who chew processed areca nut were found to have stage 2 of OSMF.

In type V group, a total of 6 subjects (13.33%) who chew processed areca nut and processed tobacco were found having stage 3 of OSMF.

In type VI group, a total of 13 subjects (28.89%) who chew combined quid usage were found having stage 3 of OSMF.

Table 2: Distribution Of Patients According To Type Of Quid In Osmf Group

TYPE OF QUID	NAME OF QUID	NO PATIENTS	Stage
TYPE I	BETEL LEAF AND ARECA NUT	2(4.44%)	Stage I
TYPE II	BETEL LEAF, ARECA NUT AND SLACKED LIME and ACKED	5(11.11%)	Stage I
TYPE III	BETEL LEAF F, ARECA NUT AND SLACKED LIME	8(17.78%)	Stage I
TYPE IV	PROCESSED ARECA NUT	11(24.44%)	Stage II
TYPE V	PROCESSED ARECA NUT AND PROCESSED TOBACCO	6(13.33%)	Stage III
TYPE VI	COMBINED QUID USAGE	13(28.89%)	Stage III

DURATION OF HABIT

A total of 45 subjects were distributed according to the duration of habit in Leukoplakia. (Table 3)

A total of 45 subjects with homogenous leukoplakia were distributed according to the duration of their habit. It was found that

In Type I group with 1 subject, only 1 subject (2.22%) was found having the habit duration of 1 year.

In Type II group with 2 subjects, 1 subject (2.22%) was found having the habit duration between 1-5 years, and 1 subject (2.22%) with habit duration between 5-10 years.

In Type III group with 7 subjects, 1 subject (2.22%) was having the habit duration of 1 year, 4 subjects (8.89%) with habit duration between 1-5 years and 2 subjects (4.44%) with habit duration between 5-10 years were found.

In type IV group with 11 subjects, 3 subjects (6.67%) with habit duration between 1-5 years, 7 subjects (15.56%) with habit duration between 5-10 years and only 1 subject (2.22%) was found with habit duration of >10 years.

In Type V group with 7 subjects, 2 subjects (4.44%) with 1-5 years of habit duration, 4 subjects (8.89%) with habit duration of 5-10 years and 1 subject (2.22%) with >10 years of habit duration were found.

In Type VI group with 17 subjects, 1 subject (2.22%) with 1 year of habit duration, 4 subject (8.89%) with 1-5 years of habit duration, 8 subjects (17.78%) with 5-10 years of habit duration and 4 subject (8.89%) with >10years of habit duration were found.

The Chi Square test was applied and the value was found to be 21.96. P value was also calculated and it was found to be 0.10 which states that there is no statistical significance.

TYPE OF QUID	1 year	1-5 years	5-10 year	>10 years
TYPE I	1(2.22%)	0(0%)	0(0%)	0(0%)
TYPE II	0(0%)	1(2.22%)	1(2.22%)	0(0%)
TYPE III	1(2.22%)	4(8.89%)	2(4.44%)	0(0%)
TYPE IV	0(0%)	3(6.67%)	7(15.56%)	1(2.22%)
TYPE V	0(0%)	2(4.44%)	4(8.89%)	1(2.22%)
TYPE VI	1(2.22%)	4(8.89%)	8(17.78%)	4(8.89%)
χ^2 -value	21.96,p=0.10,Not Significant			

Table 3- Distribution Of Patients According To Duration Of Habit In Leukoplakia

A total of 45 subjects were distributed according to the duration of habit in OSMF. (Table 4)

In Type I group, only 2 subjects (4.44%) were found to have duration of habit of OSMF >10years.

In Type II group, out of 5 subjects, 2 subjects (4.44%) were found to have duration of habit of OSMF between 1-5 years and 3 subjects (6.67%) were found to have duration of habit of OSMF between 5-10 years.

In Type III group, out of 8 subjects, 1 subject (2.22%) was found to have duration of habit of OSMF between 1-5 years, 5 subjects (11.11%) were found to have duration of habit of OSMF between 5-10 years and 2 subjects (4.44%) were found to have duration of habit of OSMF >10 years.

In Type IV group, out of 11 subjects, 2 subjects (4.44%) were found to have duration of habit of OSMF between 1-5 years, 8 subjects (17.78 %) were found to have duration of habit of OSMF between 5-10 years and 1 subject (2.22%) was found to have duration of habit of OSMF >10 years.

In Type V group, out of 6 subjects, 4 subjects (8.89%) were found to have duration of habit of OSMF between 1-5 years and 2 subjects (4.44%) were found to have duration of habit of OSMF between 5-10 years.

In Type VI group, out of 13 subjects, 5 subjects (11.11%) were found to have duration of habit of OSMF between 5-10 years and 8 subjects (17.78%) were found to have duration of habit of OSMF >10 years.

It was also found that there were no patients who had the duration of habit of 1 year in the occurrence of OSMF.

The Chi square test was applied and the value was found to 26.87. The p value was calculated and was found to be 0.0027 which was found to be statistically significant.

Type of Quid	1 year	1-5 years	5-10 year	>10 years
TYPE I	0(0%)	0(0%)	0(0%)	2(4.44%)
TYPE II	0(0%)	2(4.44%)	3(6.67%)	0(0%)
TYPE III	0(0%)	1(2.22%)	5(11.11%)	2(4.44%)
TYPE IV	0(0%)	2(4.44%)	8(17.78%)	1(2.22%)
TYPE V	0(0%)	4(8.89%)	2(4.44%)	0(0%)
TYPE VI	0(0%)	0(0%)	5(11.11%)	8(17.78%)
χ^2 -value	26.87,p=0.0027,Significant			

Table 4: Distribution Of Patients According To Duration Of Habit In Osmf

FREQUENCY OF QUID

For Leukoplakia (Table 5)

A total of 45 subjects were distributed according to the frequency of habit in leukoplakia group. In Type I group, 1 subject (2.22%) was found to consume the quid 1-5 times per day.

In Type II group, 2 subjects (4.44 %) were found to consume the quid 1-5 times per day.

In Type III group, in a total of 7 subjects, 1 subject (2.22%) was found to consume the quid 1-5 times per day, 5 subjects (11.11%) were found to consume the quid 8-10 times per day and 1 subject (2.22%) was found to consume the quid 10-12 times per day.

In Type IV group, out of 11 subjects, 2 subjects (4.44%) were found to consume the quid 5-8 times per day, 8 subjects (17.78%) were found to consume the quid 8-10 times per day and 1 subject (2.22%) was found to consume the quid 10-12 times per day.

In Type V group, out of 7 subjects, 4 subjects (8.89%) were found to consume the quid 8-10 times per day and 3 subjects (6.67%) were found to consume the quid 10-12 times per day.

In Type VI group, out of 17 subjects, 1 subject (2.22%) were found to consume the quid 1-5 times per day, 4 subjects (8.89%) were found to consume the quid 5-8 times per day, 9 subjects (20%) were found to consume the quid 8-10 times per day and 3 subjects (6.67%) were found to consume the quid 10-12 times per day.

The Chi square test was applied and the value was found to be 33.58. P value was calculated and the value was found to be 0.0039 which showed statistical significance.

TYPE OF QUID	1-5 times/day	5-8 times/day	8-10 times/day	10-12 times/day
TYPE I	1(2.22%)	0(0%)	0(0%)	0(0%)
TYPE II	2(4.44%)	0(0%)	0(0%)	0(0%)
TYPE III	1(2.22%)	0(0%)	5(11.11%)	1(2.22%)
TYPE IV	0(0%)	2(4.44%)	8(17.78%)	1(2.22%)
TYPE V	0(0%)	0(0%)	4(8.89%)	3(6.67%)
TYPE VI	1(2.22%)	4(8.89%)	9(20%)	3(6.67%)
χ^2 -value	33.58,p=0.0039,Significant			

Table 5: Distribution Of Patients According To Frequency Of Habit In Leukoplakia Group

For OSMF (Table 6)

A total of 55 subjects were distributed according to the frequency of habit in OSMF group. In Type I group, 2 subjects (4.44%) were found to consume the quid 10-12 times per day.

In Type II group, out of 5 subjects, 2 subjects (4.44 %) were found to consume the quid 5-8 times per day and 3 subjects (6.67%) were found to consume the quid 8-10 times per day.

In Type III group, out of 8 subjects, 5 subjects (11.11%) were found to consume the quid 1-5 times per day, 1 subject (2.22%) consumed he quid 5-8 times per day and 2 subjects (4.44%) consumed the quid 8-10 times per day.

In Type IV group, out of 21 subjects, 2 subjects (4.44%) consumed the quid 1-5 times per day, 11 subjects (24.44%) consumed the quid 5-8 times per day and 8 subjects (17.78%) consumed the quid 8-10 times per day.

In Type V group, out of 6 subjects, 2 subjects (4.44%) were found to consume the quid 5-8 times per day and 4 subjects (8.89%) were found to consume the quid 8-10 times per day.

In Type VI group, out of 13 subjects, 8 subjects (17.78%) were found to consume the quid 5-8 times per day and 5 subjects (11.11%) were found to consume the quid 8-10 times per day.

It was found that only 2 subjects (4.44%) of Type I group consumed the quid 10-12 times per day.

The Chi square test was applied and the value was found to be 79.03. The p value was calculated and was found to be 0.0001 which **signifies** statistical significance.

TYPE OF QUID	1-5 times/day	5-8 times/day	8-10 times/day	10-12 times/day
TYPE I	0(0%)	0(0%)	0(0%)	2(4.44%)
TYPE II	0(0%)	2(4.44%)	3(6.67%)	0(0%)
TYPE III	5(11.11%)	1(2.22%)	2(4.44%)	0(0%)
TYPE IV	2(4.44%)	11(24.44%)	8(17.78%)	0(0%)
TYPE V	0(0%)	2(4.44%)	4(8.89%)	0(0%)
TYPE VI	0(0%)	8(17.78%)	5(11.11%)	0(0%)
χ^2-value	79.03,p=0.0001,Significant			

Table 6: Distribution Of Patients According To Frequency Of Habit In Osmf Group

Statistical analysis was done by using descriptive and inferential statistics using chi square test and software used in the analysis was SPSS 24.0 version and GraphPad Prism 7.0 version and $p < 0.05$ is considered as level of significance.

DISCUSSION

Areca nuts are chewed with betel leaf for their effects as a mild central nervous system stimulant.^{4,5} The effect is thought due to one of its content known as arecoline that leads to alertness, increased stamina, a sense of well-being and euphoria. It is known to stimulate salivation and thus aiding in digestion. According to traditional Ayurvedic medicine, chewing areca nut is a good remedy for deworming and along with betel leaf it prevents halitosis.²¹ Along with these beneficial effects of areca nut one of its most harmful effects on the human body in general and oral cavity in particular is the development of a potentially malignant disorder called Oral Submucous Fibrosis (OSF).⁴

Oral submucous fibrosis (OSF) is a chronic, insidious oral mucosal condition that occurs predominantly among Indians and occasionally in other Asians especially Taiwanese and sporadically in Europeans. It was first described by Pindborg and Sirsat.⁹ It is regarded as a pre-cancerous condition.⁸ The hallmark of the disease is submucosal fibrosis that affects the oral cavity and progressively involves the pharynx and the upper esophagus. It is characterized by juxta-epithelial inflammatory reaction followed by chronic change in the fibro-elasticity of the lamina propria and is associated with epithelial atrophy. This leads to burning sensation in the oral cavity, blanching, and stiffening of oral mucosa and oropharynx, resulting in restricted mouth opening which in turn causes limited food consumption, difficulty in maintaining oral health, and impairs the ability to speak.^{7,10} The presence of palpable fibrous bands is a diagnostic criterion for OSF. The fibrous bands occur especially

in the buccal mucosa, retromolar areas, and around the rima oris. When the tongue is affected, it is devoid of papillae and becomes smooth. Its mobility, especially the protrusion, is impaired. The opening of the mouth is restricted. Some investigators adhered to the earlier signs and symptoms such as pain, history of vesicles and ulcers, and blanching of the mucosa for diagnosis of OSMF.¹¹ Due to this characteristic clinical appearance there are very few conditions that need to be differentiated from it such as scleroderma, anemia and lichen sclerosis.

The present study was conducted on 90 patients in the Central India population and showed a strong association between duration and frequency of habit in the causation of OSF and leukoplakia. Moreover, it was found that out of the 6 types of quid habits, type IV (Processed Areca Nut) and type VI (combined quid usage) were more responsible in causing Stage II and Stage III OSF along with homogeneous leukoplakia. Among the cases, included in our study, the number of patients with homogenous leukoplakia who chewed type I quid were 8.89%, type II were 11.11%, type III were 11.11%, type IV were 17.78%, type V were 26.67% and type VI were 22.22%. Patients with OSF who chewed type I quid were 4.44%, type II were 11.11%, type III were 17.78%, type IV were 24.44%, type V were 13.33%, and type VI were 28.89%. This was similar to the observation of Goel et al¹³ where around 40% of patients chewed pan masala, 30% chewed betel nut, and remaining 30% chewed betel quid. In a study done by Ahmad et al¹², around 55% patients chewed gutkha only and 16% of fibrosed cases were addicted to pan chewing habit. This study showed an increased prevalence of the type IV (processed areca nut) and type VI (combined quid usage) quids attributing to the addictive effect associated with the usage of various forms of tobacco. This implies an increase prevalence of oral potentially malignant disorders due to consumption of processed form of tobacco.

Association Between Type Of Quid , Duration Of Habit, Frequency of habit and clinical staging of OSF Patients.

In the present study it was observed that out of 45 subjects with OSF, 24.44% of patients who chewed type IV quid (processed areca nut) were found to have stage II of OSF. While 28.89% who chewed type VI (combined quid usage) quid were found to have stage III OSF. When studied about the duration of habit in OSF patients, it was seen that in Type IV group, out of 11 subjects, 2 subjects (4.44%) were found to have duration of habit of OSMF between 1-5 years, 8 subjects (17.78%) were found to have duration of habit of OSMF between 5-10 years and 1 subject (2.22%) was found to have duration of habit of OSMF >10 years. While in Type VI group, out of 13 subjects, 5 subjects (11.11%) were found to have duration of habit of OSMF between 5-10 years and 8 subjects (17.78%) were found to have duration of habit of OSMF >10 years. It was also found that there were no patients who had the duration of habit of 1 year in the occurrence of OSMF. The Chi square test was applied and the value was found to be 26.87. The p value was calculated and was found to be 0.0027 which was found to be statistically significant. Frequency of habit was also evaluated and it was found that in Type IV group, out of 21 subjects, 2 subjects (4.44%) consumed the quid 1-5 times per day, 11 subjects (24.44%) consumed the quid 5-8 times per day and 8 subjects (17.78%)

consumed the quid 8-10 times per day. While in Type VI group, out of 13 subjects, 8 subjects (17.78%) were found to consume the quid 5-8 times per day and 5 subjects (11.11%) were found to consume the quid 8-10 times per day. The Chi square test was applied and the value was found to be 79.03. Hence, p value was calculated and was found to be 0.0001 which **signifies** statistical significance. This denotes a strong association between duration of habit, type of quid and frequency of habit in causation of OSF and it was observed that type IV and type VI quid chewing patients were more prone to have OSF stage II & stage III when chewed with a frequency of 5-8 times per day.

Association Between Type Of Quid , Duration Of Habit, Frequency of habit and clinical staging of Leukoplakia Patients.

The association between type of quid in the causation of leukoplakia was also studied and it was found that out of 45 subjects, 8 patients (17.78%) who had homogeneous leukoplakia chewed type IV quid while 12 patients (26.67%) chewed type V quid (processed areca nut and processed tobacco), while 10 patients (combined quid usage) chewed type VI quid. It was found that only 1 patient (2.22%) who chewed type VI quid had non-homogeneous type of leukoplakia. This showed a prevalence of homogenous type of leukoplakia associated with chewing type IV, V and type VI quid. Duration of habit in the causation of leukoplakia did not show statistically significant differences with a p value of 0.10 which was insignificant. While statistically significant association was found between frequency of quid habit and occurrence of leukoplakia. It was found out that a frequency of 8-10 times /day was more prevalent in the causation of homogeneous leukoplakia in type IV and type VI quid chewing groups. Chi square test was applied and the value was found to be 33.58 with a p value of 0.0039 which was statistically significant implying a strong association between frequency and the type of quid in causation of leukoplakia.

The fact that processed areca nut is so prevalent in causing OSF & leukoplakia is that it is made up of alkaloid and flavonoid components namely arecoline, arecaidine, guvacine, and guvacoline. Arecoline being is the most potent agent plays a major role in the pathogenesis of OSF by causing an abnormal increase in collagen production. The flavonoid components like tannins and catechins have also been found to have some direct influence on collagen metabolism.^{12,14}

Basic mechanisms involved in the pathogenesis of OSF can be divided into four steps:

1. Occurrence of the chronic inflammation at the site of betel quid placement
2. Increased collagen synthesis
3. Collagen cross-linking
4. Decreased collagen degradation

- Occurrence of the chronic inflammation at the site of betel quid placement:

Placement of the betel quid in the vestibule for varying duration and frequency is the most common habit. Due to the continuous contact between the betel quid and the oral mucosa, the

alkaloids and the flavonoids from the quid are absorbed and undergoes metabolism. These constituents along with their metabolites then serve as a constant source of irritation to the oral mucosa. Along with this chemical irritation, the mechanical irritation of the oral mucosa also occurs due to the presence of the coarse fibres in the betel quid. This causes micro trauma resulting from this continues friction of coarse fibers of areca nut which facilitates the diffusion of betel quid alkaloids and flavonoids into the subepithelial connective tissue, resulting in juxtaepithelial inflammatory cell infiltration.¹⁴ Due to the persistent habit of areca nut chewing, chronic inflammation occurs in at the site. Inflammation is characterized by the presence of activated T cells, macrophages, etc.¹⁴

In the above study, association between the clinical staging, duration, frequency and type of quid was found to be highly significant in OSF and leukoplakia patients. The above study also shows that the subjects who chewed type IV and type VI quid developed OSF and leukoplakia earlier and those who chewed type IV and type VI quid with a greater frequency developed more severe clinical stages of OSF and homogeneous leukoplakia. This is similar to the observations done by Pandya et al. where maximum subjects who had histopathological grade III OSF took tobacco products for 8–10 years or with a frequency of 7–10 times per day.¹⁵ Kumar et al. also suggested that the patients who used pan masala with a greater frequency/day developed OSF with a shorter duration of the habit.¹⁶

CONCLUSION

Areca nut plays a major role in causation of OSF and leukoplakia. Mainly the alkaloid and flavonoid content of the areca nut plays a very important role in the major events that occur in pathogenesis of OSF as they enhance the collagen production, strengthen the cross-linking and reduce their degradation by various discussed molecular pathways. It is a progressive process and hence relieving the patient's symptoms to improve the life quality forms the basis of its management. Its potential to turn into malignancy is also of concern. It is well said that 'Prevention is better than cure' and it holds true in case of the management of this irreversible disease. Thus cessation of the areca nut chewing habit forms the mainstay for the therapy.

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