ROLE OF PAN CHEWING IN ORAL SUBMUCOUS FIBROSIS - OUR EXPERIENCE

Anoop M1, Sukhchain Singh Bullar2, Shobit Gupta3, Himanshu Kumar Gupta4, Sumit Gupta5, Yusra Lataaf5

1Associate Professor, Department of ENT, Affiliated to B. R. Ambedkar University, Agra, Uttar Pradesh.
2Professor, Department of ENT, Affiliated to B. R. Ambedkar University, Agra, Uttar Pradesh.
3Assistant Professor, Department of ENT, Affiliated to B. R. Ambedkar University, Agra, Uttar Pradesh.
4Assistant Professor, Department of ENT, Affiliated to B. R. Ambedkar University, Agra, Uttar Pradesh.
5Senior Resident, Department of ENT, Affiliated to B. R. Ambedkar University, Agra, Uttar Pradesh.
6Senior Resident, Department of ENT, Affiliated to B. R. Ambedkar University, Agra, Uttar Pradesh.

ABSTRACT

BACKGROUND
Pan chewing causes Oral Sub-Mucous Fibrosis (OSMF) which is one of the major premalignant conditions of the oral cavity. It is seen mainly in South East Asia, Europe and North America. Malignant transformation to squamous cell carcinoma accounts for 2-3%. This risk is enhanced by the usage of pan and various tobacco products.

MATERIALS AND METHODS
We took up the present study in FH Medical College Etmadpur, Agra, from June 2017 to June 2018. 100 patients between the age group 21 years to 60 years where included in the study; who were attending outpatient department of ENT.

RESULTS
Most of them were having pan chewing as a habit. Pan chewing, tobacco chewing, and tobacco smoking were present in 16 patients. 78 patients were men. Most of the patients belonged to 30 to 39 age group. Conservative OPD treatment combined with surgical treatment gave good outcome in the treatment process.

CONCLUSION
We conclude that pan chewing and its various products has got strong association in the development of OSMF. Tobacco usage adds to the magnitude of the problem. Early diagnosis and treatment are important to prevent carcinomatous transformation.

KEYWORDS
OSMF, Pan, Carcinoma, Tobacco, Fibrosis, Trismus.


BACKGROUND
Pan chewing has gained popularity among world population due to social acceptancy, religious faiths, perceived health benefits and addiction.1 There is regional variations in the type of pan preparations used. Varied patterns of pan chewing have lead a specific site in the oral cavity to be involved.2 References to pan appear in ancient Sanskrit literature as early as 1st century BC. The practice of pan chewing after meals, had become common in 75 AD to 300 AD. Sushruta, a renowned Indian physician, in his book Mouth and Throat Diseases mentioned a condition “vidari” that has the features of OSMF.3

The major ingredients of traditional pan or commercial gutka are arecanut, betel leaf, lime, catechu, spices and various sweeteners.3

Usage of pan has been found as the single-most etiological factor, considered to be in the development of OSMF.4 OSMF was described first in India by Joshi in 1953. It is widely seen in India, Pakistan, Sri Lanka, Nepal. This is mainly due to pan chewing and tobacco smoking. OSMF is a chronic illness which affect any part of oral cavity or pharynx. Occasionally associated with vesicle formation and is always associated with a juxta epithelial inflammatory reaction followed by progressive hyalinization of the lamina propria. There is atrophy of epithelia later on; leading to stiffness of oral mucosa causing trismus and inability to eat.5

OSMF graded into 3 stages. Stage 1 involves faucial bands only. In stage 2 there is involvement of faucial and buccal bands. Stage 3 involves faucial, buccal and labial bands.6,7 OSMF can cause significant morbidity and mortality. The mortality rate is increased when OSMF transforms to squamous cell carcinoma. The combined usage of pan and tobacco has led to a sharp increase in the frequency of OSMF.7

Cell-mediated immune reaction to pan plays a major role in the development of OSMF. It also reflects an autoimmune process in the oropharynx or a localized collagen disorder.8

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Corresponding Author:
Dr. Anoop M, Associate Professor,
Department of ENT,
F. H. Medical College, Etmadpur,
Agra- 283204, Uttar Pradesh.
E-mail: dranooppavittom@gmail.com
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In advanced cases, trismus is the classical sequelae. Trismus cause problems in speech, oral hygiene, mastication and swallowing. A cross-sectional study in Karachi which included 325 patients, showed a strong association among labial bands in the fauces and buccal bands.

In some cases, fibrosis affects the soft palate and uvula whereas gingiva is relatively spared. Blockage of Eustachian tube causes hearing impairment and oesophageal fibrosis causes swallowing difficulty.

Western UP, in India which comprises Agra and Firozabad districts; has got dense population of low socio-economic people. They are having strong habit of pan chewing irrespective of age, sex and religious backgrounds. So we took up the present study in FH Medical College, Agra; to know the various pattern of pan chewing and its subsequent course to OSMF and Carcinoma oral cavity in this local population.

**MATERIALS AND METHODS**

We took up this clinical study in FH Medical College Etmadpur, Agra during the period between June 2017 to June 2018. It included 100 adult patients between the age of 21 years to 60 years. Extremes of age were avoided due to health reasons. Patients were having a diagnosis of OSMF with trismus. Detailed history about pan chewing and pattern of tobacco usage was elicited from each patient. They were regularly followed up. Various treatment modalities like conservative treatment, submucosal injection of triamcinolone and hyaluronidase and surgical treatment were given to patients after assessing each patient. They were followed up regularly for 6 months after treatment.

**Inclusion Criteria**

1. Adult patients between 21 years to 60 years.
2. Regular pan chewing for 2 years or more.
3. No systemic illness like diabetes mellitus, hypertension, bronchial asthma.
4. Dentulous patients.

**Exclusion Criteria**

1. Patients below 21 years and above 60 years.
2. Irregular pan chewing habit or less than 2 years of pan chewing.
3. Systemic illness diabetes mellitus, hypertension, bronchial asthma.
4. Edentulous patients.

**RESULTS**

Findings

In this study of 100 patents 54 patents were having pan chewing as a habit. 33 were having tobacco chewing as habit and 13 were having tobacco smoking as habit. 78% patients were men. This is attributed to various life styles and living conditions of male gender.

32% patients were improved by conservative treatment like vitamin E, alpha lipoic acid, lycopene drugs.

As shown in table 5, the number of patients with OSMF increased as the duration of exposure to pan increased.

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>31-40</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>41-50</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>51-60</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>60&gt; above</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table 1. Age Wise Distribution**

<table>
<thead>
<tr>
<th>Sex</th>
<th>No. of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table 2. Sex Wise Distribution**

<table>
<thead>
<tr>
<th>Habit</th>
<th>No. of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan chewing</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>Tobacco chewing</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Tobacco smoking</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>All the 3 habits</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

**Table 3. Type of Habits in OSMF**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative medicines</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Injection triamcinolone &amp; Injection hyaluronidase</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>Surgical treatment</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

**Table 4. Type of Treatment Given in OSMF**

<table>
<thead>
<tr>
<th>No. of Years</th>
<th>No. of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 years</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>2-3 Years</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>3-4 Years</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>4-5 Years</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>More than 5</td>
<td>41</td>
<td>41</td>
</tr>
</tbody>
</table>

**Table 5. Duration of Exposure to Pan**
DISCUSSION

On an average 700 million persons are pan chewing with a hot spot throughout South Asia. This makes pan the fourth most consumed drug after nicotine, ethanol and caffeine. OSMF subjects are mainly younger and have brief history of pan chewing compared to chewers not having OSMF.

OSMF does not revert back to normal after cessation of pan chewing and remains permanent. In 2005, the OSMF prevalence among visitors at a Dental college in Manipal, India was estimated as 2% with a preference for male sex and age group ranging from 40-60 years. In a study conducted in Allahabad, India 239 OSMF patients were studied, 46% of them were in 3rd decade of life. The most common affected site was buccal mucosa (20.8%) followed by palate (17.7%). Trismus was noticed in 37.2% of patients. 25.9% suffered from burning sensations, 22.5% noticed to have excessive salivation and 14.2% suffered from recurrent oral ulcerations.

Grading of OSMF in relation to pan chewing demonstrated a dependence from years of habits and frequency of pan chewing. Most of the patients with stage 1 OSMF were habituated for at least 3-5 years, whereas most of the patients with stage 3 OSMF had consumed pan and tobacco products for 8-10 years. Trismus was noticed often in stage 2 & stage 3 OSMF, but a clear correlation between severity of trismus and OSMF staging was missing.

Extracellular matrix of submucous tissue layer is the major seat for changes in OSMF. Fibrosis is associated with both quantitative as well as qualitative alterations of collagen deposition with in the subepithelial layer of oral mucosa. This is mainly due to marked deficiencies of collagen and fibronectin phagocytosis by fibroblasts caused by pan alkaloids (arecoline, arecaidine).

Arecoline—the main component of pan—can induce various growth factors in OSMF fibroblasts in vitro, like insulin-like growth factor-1 and keratinocyte growth factor -1. Arecoline activates another key chemical in the regulation of fibrosis - the hypoxia-inducible factor-1 alpha in a dose dependent manner.

Most of the studies show an increase in the incidence of OSMF when pan and tobacco consumption are combined. A relative risk of 489 has been reported for OSMF in consumption of pan & tobacco compared with non-users.

The consumers of mixed products are often younger. OSMF develops faster in the combined users (after 2.7 years) than in pan chewers alone (after 8.6 years). Cancerous transformation took an early course.

Recently, the expression sequence of genes in OSMF mucosa and normal oral mucosa have been studied extensively. In one study, 14,500 genes were analysed gene chip arrays. This study demonstrated 716 genes were upregulated and 149 genes were down regulated in OSMF. There were distinct genes pertaining to immune response, inflammatory response and TGF-B induced epithelial mesenchymal transition.
Involved genes are TGF-B2, SMAD-3, matrix metalloproteinase MMP1, MMP2 and MMP9. There was no TGF signaling induced in fibroblasts. It can be considered that direct effects on epithelial cells with TGF-B activation can suppress anti fibrogenic cytokines including bone morphogenetic protein-7 and stimulated fibroblast activity. Both OSMF and oral squamous cell carcinoma development are complex there is no single factor responsible for the them. The major treatment options are anti-inflammatory, oxygen radical- scavenging and antibioretic medicines. Mostly combined drug therapy is given, but controlled clinical trials are completely lacking. In some patients, depending on severity of disease physical therapy and/surgery is added to drug therapy. In early inflammatory stage of OSMF corticosteroids are of use, as suggested by various invitro studies. OSMF has been treated with hyaluronidase, chymotrypsin, collagenase, triamcinolone, pentoxifylline, nylidrin hydrochloride, iron, lycopene, but the level of evidence for any of these therapies is low as of today. A study for 6 weeks with 1mg Triamcinolone and 1, 500U Hyaluronidase twice weekly improved trismus and other clinical parameters associated with fibrosis. In addition, auto fluorescence of the affected mucosa normalised for collagen and NAD spectra. In case of advanced cases of OSMF to relieve trismus, various surgical techniques are used. It includes simple release of fibrosis and skin grafting, bilateral tongue flaps, nasolabial flaps, island palatal mucoperiosteal flap, bilateral radial forearm free flap, coronoidectomy and temporal muscle myotomy.

CONCLUSION
In this present study, we found that chewing of Pan and various other tobacco products have a strong association in the development of Oral Sub Mucous Fibrosis (OSMF). Tobacco usage adds to the magnitude of OSMF. In our study, there is linear relation with rising incidence of OSMF and duration of exposure to pan. This is strongly suggestive of pan as a major risk factor in the development OSMF.

Prevention is better than cure in the case of OSMF. Early diagnosis and treatment are very useful to the patient. Chance of development of squamous cell carcinoma is the main concern. Various conservative treatments along with surgical treatment gives favourable results in the case of OSMF. New drugs and treatment modalities are in the research process. Health education of public regarding the side effects of pan chewing and tobacco usage could curtail the development of OSMF.

REFERENCES


