Establishing a new staging system for oral submucous fibrosis and correlation of the proposed staging system to traditional histopathological grading: A clinico-histopathological study

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Abstract  Background & objectives: Oral submucous fibrosis (OSF) is a potentially malignant disorder of the oral cavity leading to reduction in mouth opening. Mouth opening assessment is used as one of the methods to assess the severity of the disease. In this study the normal maximum mouth-opening capacity of an individual is considered in assessing the reduction in mouth opening. This study was done to establish a new clinical staging pattern in OSF and to evaluate the relationship between the proposed staging system and traditional histopathological grading system of OSF.

Materials and methods: The study included 50 clinically diagnosed OSF patients. Normal mouth opening was established by measuring three-finger index (TFI). Existing maximum mouth opening was established by measuring the interincisal distance. Presence of palpable vertical bands was recorded. Histopathological grading was done according to Pindborg and Sirsat. Percentage of reduction in mouth opening (PRMO) was calculated and the mean of PRMO in different clinical and histopathological stages was analysed by fisherman’s extract test. A new staging pattern for OSF was proposed from the data.

Results: PRMO was assessed at different clinical stages. A range between 16% and 47% was obtained, and statistically the p value of <0.001 was very highly significant. Similarly, a range between 17% and 45.6% was obtained when PRMO was assessed at different histopathological grading; again the statistical value was very highly significant with a p value of < 0.001.

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1. Introduction

Oral submucous fibrosis (OSF) is a persistent condition that affects the oral cavity and sometimes affects the pharynx. Infrequently the disease starts as a vesicle formation, but it is always affiliated with juxtaepithelial inflammation and fibrotic changes in the connective tissue leading to rigid oral mucosa causing inability to eat (Pindborg and Sirsat, 1966). OSF occurs as a result of habitually chewing the areca nut in various forms. Recently most of the subjects with OSF are in the young age group (Wollina et al., 2015). Around 600 million people chew areca nut worldwide. However it is very commonly used by south Asian populations. Approximately 2.5 million people worldwide suffer from OSF (Mehrotra et al., 2013).

The initial stage of the disease is usually characterized by atrophic and blanching oral mucosal epithelium. Vesicles and erosive lesions may also develop in some patients. As the disease advances, fibrotic band formation leads to characteristic erosive lesions may also develop in some patients. As the disease advances, fibrotic band formation leads to characteristic erosive lesions (Haider et al., 2000). It is observed that the band formation initiates posteriorly and progresses anteriorly, which leads to a progressive decline in the mouth opening ability of a person with disease progression. After the disease reaches the fibrosis stage, there will not be complete resolution even if the subject stops the habit completely (VanWyk, 1997). The disease is considered a premalignant condition with a malignant potential of about 7.6% having a prevalence of about 0.2–0.5% (Bansal et al., 2013; Arakeri et al., 2014).

Assessment of mouth opening ability is used as one of the procedures to appraise the disease severity. Many of the OSF staging systems do not consider the limit of normal mouth opening in a person when assessing reduction in mouth opening. The normal level of mouth opening fluctuates from population to population and from person to person (Chima and Obiechina, 1995; Agrawal et al., 2015). Hence a mere measurement of reduced mouth opening without assessing normal mouth opening may not be appropriate for staging OSF. The normal maximum mouth opening capacity of an individual has been considered in this study to assess the reduction in mouth opening.

2. Materials and methods

2.1. Ethical clearance

The University ethical committee approved the study, and the ethical clearance was obtained. All of the participants were informed that participation was voluntary; they had all been given the choice to discontinue at any step of the study. The complete procedure was described to all of the subjects in detail, and informed consent was obtained from each of them.

2.2. Sample selection

The present study was performed in the Oral Medicine and Radiology department. A total of 50 patients between the ages of 20 and 50 years old who had been clinically diagnosed with OSF were included in this study.

2.3. Eligibility criteria

Those patients with a history of deleterious areca nut chewing reported to the department with such clinical features as a burning sensation, blanching, presence of vertical fibrous bands involving the oral cavity, and reduced mouth opening. Both male and female gender groups in the age range of 20–50 years were selected. Patients with complex medical conditions, traumatic injuries to maxillofacial structures, and who were not willing to be biopsied were excluded from the study.

2.4. Personal data recording

Patient data including name, age, gender, occupation, and race were recorded. A detailed report regarding the deleterious habit of chewing areca nut in any form and the frequency and duration of its usage were obtained from the patients. It was then followed by proper clinical examination.

2.5. Clinical evaluation

All of the subjects were assessed for the presence of blanching, rigidity of oral mucosa, palpable vertical bands, and interincisal mouth opening. The measurement was done by using a calibrated Vernier caliper and recorded in millimetres by measuring the maximum mouth opening (MMO) from the ‘mesioincisal edge of the upper left central incisor tooth to the mesioincisal edge of the lower left central incisor tooth’ (Fig. 1). Clinical staging was done as ‘stage I, which has only faucial bands, stage II having faucial and buccal bands, and stage III consisting of faucial, buccal, and labial bands,’ according to Haider et al. (2000).

2.6. Assessment of normal mouth opening

The patients’ normal mouth opening was established by measuring the three finger (index, middle, and ring fingers) width. The measurements were done at distal interphalangeal folds using a calibrated Vernier caliper and recorded in millimetres (Fig. 2).
2.7. Assessment of percentage of reduction in mouth opening

The percentage of reduction in mouth opening (PRMO) was calculated by subtracting the maximum mouth opening (MMO) from the three finger width (TFI) in millimetres.

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PRMO = \frac{TFI - MMO \times 100}{TFI}
\]

2.8. Biopsy procedure

All of the patients were subjected to incisional biopsy, and the histologic gradings were obtained according to the criteria proposed by Pindborg and Sirsat (1966).

2.9. Statistical analysis

All 50 samples were clinically staged from stage I to stage III, and the mean of PRMO was calculated in each stage and correlated using Fisher’s exact test. All 50 samples were grouped into four groups histologically, according to the Pindborg and Sirsat staging system, and the mean value of PRMO was calculated in each group (Pindborg and Sirsat, 1966). The mean values of the four groups were compared from stage I to stage IV using Fisher’s exact test. Thus a new staging pattern was proposed for OSF from the obtained data.

3. Results

3.1. Age- and gender-wise assessment in study group (Table 1)

The age range in the study group was from 20 to 50 years old with a mean age of 28.94 years. The maximum number of patients (70%) were in the 20- to 30-year-old age group. There were 11 subjects (22%) in the 30- to 40-year-old range and 4 subjects (8%) in the above-40-years-old range. Among the total of 50 patients; 47 were males and 3 were females.

3.2. Assessment of PRMO in different clinical stages (Table 2)

PRMO was assessed in different clinical stages. The mean of PRMO was found to be 16% in clinical stage I, 35.60% in stage II, and 47.56% in stage III. The F value was 8.105 when analyzed with Fisher’s exact test by ANOVA software showing very high significance with a p value of <0.001.

3.3. Assessment of PRMO in different histopathological grading of OSF (Table 3)

PRMO was assessed in different histopathological grades. The mean of PRMO was found to be 17% in grade I, 25.91% in grade II, 43.21% in grade III, and 45.6% in grade IV. The F value was 7.342 when analyzed with Fisher’s exact test by ANOVA software with very high significance with a p value of <0.001.

3.4. Proposed staging system and its correlation to histopathological grading (Tables 4 and 5)

In the proposed three-stage staging system, the PRMO in stage I was <30%, in stage II was 30–45%, and in stage III was >45% (Table 4). These values were then correlated with the histopathological grading by the chi-square test. The chi-square value of 11.585 obtained a p value of <0.021, suggesting a good significance (Table 5).

4. Discussion

OSF is a chronic progressive disease of the oral cavity characterized by atrophic epithelium and fibrotic band formation.
leading to restricted mouth opening. The disease has remarkable morbidity caused by limitation of mouth opening and mortality because it can transform into squamous cell carcinoma. The severity of disease morbidity is assessed by evaluating the maximum mouth opening measurement of an individual. Various authors have proposed different staging patterns to assess OSF progression. These staging proposals were mostly based on distribution and location of fibrous bands in the oral cavity (Haider et al., 2000; Bhagvan More et al., 2012). Another staging proposal was based on mouth opening measurements in OSF patients (Haider et al., 2000; Bhagvan More et al., 2012; Passi et al., 2017), however many of the OSF staging systems do not consider the normal mouth opening limit of a person when assessing reduction in mouth opening. In this study we have considered the normal maximum mouth opening capacity of an individual in assessing the reduction in mouth opening.

The present study was performed on 50 subjects between the ages of 20 and 50 years old with the mean age of 28.94 years old. Of the subjects, 70% were in the 20- to 30-year-old age group. It is alarming to see that OSF is now being seen at such an early age. This observation has been documented in many studies done around the world (Paissat, 1981; Haider et al., 2000). This could be because of the easy accessibility of areca products in youngsters. Among the 50 subjects, 47 (94%) patients were males, which suggests that there is a strong male predilection for OSF in the present study group. This result is in accordance with the study conducted by Yang et al. (2018) and Dayal et al. (1996). The reports of sex distribution in OSF are varied; Pindborg and Sirsat (1966) showed equal sex distribution, whereas Pindborg et al. (1980) reported female predominance (F:M = 8:3). The incidence in gender ratio varies from study to study probably because of varying habits in various populations. Females in the villages consume local pan, and males mainly use processed betel nut with local pan. This may be the main reason for male predominance in OSF in the current research.

| Clinical staging | N  | Mean | Standard deviation | Minimum | Maximum |
|------------------|----|------|--------------------|---------|---------|
| I                | 2  | 16.00| 1.414              | 15      | 17      |
| II               | 30 | 35.60| 14.675             | 7       | 63      |
| III              | 18 | 47.56| 9.703              | 29      | 73      |

*p Value was significant at p < 0.001.

| Histopathological grades | N  | Mean | Standard deviation | Minimum | Maximum |
|--------------------------|----|------|--------------------|---------|---------|
| I                        | 1  | 17.00|                    | 17      | 17      |
| II                       | 11 | 25.91| 13.277             | 7       | 48      |
| III                      | 33 | 43.21| 12.489             | 20      | 73      |
| IV                       | 5  | 45.60| 12.681             | 30      | 63      |

*p Value was very highly significant at p < 0.001.

| Proposed staging | Percentage of reduction in mouth opening | Frequency | Percent |
|------------------|------------------------------------------|-----------|---------|
| I                | <30                                      | 15        | 30.0    |
| II               | 30-45                                    | 16        | 32.0    |
| III              | >45                                      | 19        | 38.0    |
| Total            |                                          | 50        | 100.0   |

| PRMO in percentage | Total |
|--------------------|-------|
| <30%               | 12    |
| 30–45%             |       |
| >45%               |       |

| Histopathological grading | Count | <30%  | 30–45% | >45%  |
|---------------------------|-------|-------|--------|-------|
| I & II                    | 8     | 53.3% | 18.8%  | 5.3%  |
|                           |       | 24.0% |        |       |
| III                       | 6     | 40.0% | 75.0%  | 78.9% |
|                           |       |       |        | 66.0% |
| IV                        | 1     | 6.7%  | 6.3%   | 15.8% |
|                           |       |       |        | 10.0% |
| Total                     | 15    | 100.0%| 100.0% | 100.0%|

*p Value was highly significant at p < 0.021.
The various clinical and functional stagings were done earlier without considering the normal maximum mouth-opening limit of an individual (Haider et al., 2000; Bhagvan More et al., 2012; Patil and Maheshwari, 2014; Jani and Dudhia, 2016; Passi et al., 2017). The TFI is an established method to estimate a normal maximum mouth-opening limit in an individual and was used by different authors (Chima and Obiechina, 1995; Zawawi et al., 2003; Agrawal et al., 2015). The study conducted in a south Indian population demonstrated that the subjects were able to vertically align their right and left three fingers between the upper and lower central incisors up to the first distal interphalangeal folds. It suggests that the width of three fingers can be used as a “tool” to distinguish normal from restricted mouth opening. Hence the TFI measurement is the normal range in our population when estimating reduction by Agrawal et al. (2015).

In our study we measured the maximum interincisal distance and the TFI by using a Vernier caliper. Later, the severity of disease was calculated by assessing PRMO. Although PRMO was assessed at different clinical stages as suggested by Haider et al. (2000), we obtained a range between 16% and 47%, and statistically the p value of < 0.001 was highly significant (see Table 2). Similarly, a range between 17% and 45.6% was obtained when PRMO was assessed at different histopathological gradings as suggested by Pindborg and Sirsat (1966). Again, the statistical value was highly significant with a p value of < 0.001 (see Table 3). In the proposed three-stage staging system in which PRMO in stage I was < 30%, in stage II was 30–45%, and in stage III was > 45%, the results are correlated with the histopathological grading by Pearson’s chi-square test in which the chi-square value of 11.585 was obtained with a significant p value of < 0.021 (see Table 5).

With the above findings we believe that the following clinical staging pattern can be adapted.

Stage I < 30%
Stage II 30–45%
Stage III > 45%

Many authors (Narayan et al., 2014; Modak et al., 2015; Abidullah et al., 2018; Kattappagari et al., 2018) have attempted to correlate clinicohistopathological features with the older staging system without considering the amount of normal mouth opening; none of those studies showed significant correlations. This strongly indicates the need of the proposed staging system to be implemented in staging OSF.

5. Conclusion

With the data obtained from this study, the following clinical staging pattern can be adapted. Stage I of PRMO is < 30%, Stage II between 30–45%, and stage III is > 45%. Hence it may be appropriate to assess the disease severity and stage by assessing the degree of disability (i.e., mouth opening reduction considering the individual’s normal mouth opening ability). The determination of PRMO may be a useful tool in this direction. Hence we encourage more studies on this topic with larger sample sizes in the future so that each clinical and histopathological stage is represented by adequate numbers.

Conflict of interest

This is to certify that there is no conflict of interest in this research.

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