COMPARISON BETWEEN TWO DIFFERENT TREATMENT MODALITY FOR THE MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS

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ABSTRACT

Oral submucous fibrosis (OSMF) is a potentially malignant disorder that primarily affects any part of the oral cavity and sometimes the pharynx. The disease is chronic, insidious, and progressive in nature. This generalized condition of the mouth eventually becomes a debilitating disease with mucosal rigidity causing discomfort, burning, and limitation of opening of the mouth. People with OSMF carry a high risk for development of oral cancer. We divided 100 patients of confirmed OSMF case into two groups, containing 50 patients each. In group 1 Patients were administered orally tablet colchicine 0.5 mg twice daily. Hyaluronidase 1,500 IU was mixed in 1 ml of lignocaine. 0.5 ml of this solution was injected intralesionally in each buccal mucosa once a week. In group 2-Patients were administered intralesional injection of Hyaluronidase 1,500 IU as in group 1 and 0.5 ml of injection Hydrocortisone acetate 25 mg/ In buccal mucosa once a week alternatively. Patients in both the groups were asked to discontinue all betel nut chewing habits during the entire study period.

INTRODUCTION

Oral submucous fibrosis (OSF) is a chronic disease that produces scars, tissue fibrosis, and precancerous lesions. It frequently occurs in the buccal mucosa [1,2]. Pathological characteristics include chronic inflammation, excessive collagen deposition in the connective tissue below the oral mucosal epithelium, local inflammation in the lamina propria or deep connective tissues, and degenerative changes in the muscles. OSF patients experience a severe burning sensation in the mouth after ingesting spicy foods. Other symptoms of OSF include dry mouth, pain, taste disorders, restricted tongue sensation in below the oral cavity, xerostomia, a burning sensation and limited ability to open the mouth [14,15]. These effects interfere with the daily life of the patient and may lead to complications.

Chewing betel nut and tobacco together substantially increases the incidence of OSF [7]. Other studies confirmed that drinking alcohol and chewing betel nut have an additive effect on OSF induction [8,9].

Chewing betel nut is the main cause of OSF [10–11]. The histopathology of OSF comprises various epithelial alterations, rete-peg shapes, and subepithelial deposition of dense bands of collagen fibers. At different OSF stages, epithelial alterations vary from atrophy with hypoplasia to hyperplasia and/or dysplasia [12,13].

The most common initial symptoms of OSF are ulceration, xerostomia, a burning sensation and limited ability to open the mouth [14,15]. These effects interfere with the daily life of the patient and may lead to complications.

MATERIAL AND METHOD

This study was conducted in Career post graduate institute of Dental Sciences and hospital, Lucknow (UP) India between 2018 and 2020. The patients for the study were selected from those who visited in Oral & Maxillofacial Pathology department. An informed consent was taken from the patients before including them in the study. A detailed case history of
the patient with emphasis on their habits (chewing betel nut, pan masala, etc.) and a thorough clinical examination was recorded on a standard proforma. A clinical diagnosis of OSF was made based on the World Health Organization (WHO) criteria. Baseline liver function tests, serum urea, and creatinine were done for these patients to rule out any existing hepatic pathology and the tests were repeated once every month during the study period and one month following cessation of treatment. The diagnosis was confirmed histopathologically by a punch biopsy of the lesion. Hematoxylin and Eosin and van Gieson stains were used to analyze the staining intensity of the inflammatory infiltrate and the density of collagen fibrils, respectively, in the pre and post treatment biopsy specimens. 50 patients (40 males & 10 females) in the age group of 20 years to 50 years, thus diagnosed as having OSF, were included in the study and were divided randomly into two groups for the purpose of treatment. Group 1-Patients were administered orally tablet colchicine (Tablet Zycolin), 5 mg twice daily. Hyaluronidase 1,500 IU was mixed in 1 ml of lignocaine. 0.5 ml of this solution was injected intralesionally in buccal mucosa once a week. Group 2-Patients were administered intralesional injection of Hyaluronidase 1,500 IU as in group 1 and 0.5 ml of injection Hydrocortisone acetate 25 mg/ml in each buccal mucosa once a week alternatively. Patients in both the groups were asked to discontinue all betel nut chewing habits during the entire study period. Treatment done for 16 weeks. Post-treatment punch biopsy was taken one week after the cessation of treatment for histopathological evaluation. During the subsequent visits the patient's response to the treatment procedures was recorded with emphasis on specific symptoms like burning sensation, trismus, and intolerance to hot and spicy foods. Clinical examination of the oral mucosa, site of lesion, margins, extension, color and surface texture and presence of fibrotic bands was recorded. The interincisal opening of the mouth was recorded during each visit [Figures 1&2]. Pre and post treatment histopathological specimens were compared for the inflammatory cells and fibrous tissue [Figure 3a,3b 4a&4b]. Student's t-test and analysis of variance (ANOVA) were used to compare pre and post treatment results. P<0.05 was considered as significant.

Fig 1 Mouth opening before treatment belonging to group 1

Fig 2 Clinical improvement in mouth opening after 12 weeks in same patient

Fig 3a Photomicrograph of tissue section taken before treatment showing atrophic epithelium, relatively avascular hyalinized collagen with abundant inflammatory infiltrate (low-power view: H and E ×40)

Fig 3b Photomicrograph of the same tissue specimen stained with van Gieson's showing dense avascular hyalinzed collagen (low-power view: ×40)

Fig 4a Photomicrograph of tissue section taken after treatment showing reduced density of collagen and inflammatory infiltrate (low-power view: H and E ×40)
OSMF leads to difficulty in mouth opening progressively. In our study of 50 patients, the peak incidence of OSMF, we observed was in age group of 20-50 years of age which was similar to that of Ghom et al and Bhuvana et al respectively.[19,20]

In our study the ratio of male female is 4:1. It is evident from the various studies that the peak incidence of OSMF is seen in the age group of 20-30 years. This could be because of local differences in the use of the various predisposing factors. The youngest patient in our study was of 20 years of age and oldest was 50 years of age. The common aetiological agents was found to be Areca nut, which was taken plain or with additional ingredients like chunna, kattha, peppermint or in some other form like paan masala, gutkha, or betel quid.

The patients in group 1 showed an early reduction in the burning sensation. There was also a significant improvement in the mouth opening and in the movement of the tongue (clinical grade 5). The histopathological findings also showed a marked reduction in the inflammatory cell infiltrate and density of collagen fibrils. The mechanism by which colchicine improved the clinical status of OSMF patients in our study was difficult to ascertain since the drug was used in combination with Hyaluronidase.

Also since this was the rare study where cochin had been used in the treatment of OSF, we could not compare our results. However, we attributed them to the effect of cochin which is both an anti-fibrotic and anti-inflammatory agent. Like IFN-γ, colchicine also reduces collagen synthesis, down regulates fibroblast proliferation and upregulates anti-fibrotic cytokine and collagenase synthesis in the basal layer of the epithelium and lamina propria.[21]

Colchicin has been reported to be beneficial in the treatment of diseases associated with fibrosis in animals and human beings.[22]

The short and long term administration of colchicin therapy in moderate dosages is surprisingly well tolerated. None of our patients reported any local or systemic adverse reactions during treatment and also after the cessation of drug intake. The most common toxic side effect reported reflect the drug's action on rapidly proliferating gastrointestinal tract epithelial cells and include nausea, vomiting, diarrhea, and abdominal pain.

These symptoms are especially frequent at dosage levels 2-3 mg/day although they are rapidly and completely reversible. [23] It is possible that the dosage we used in our study, i.e. 0.5 mg colchicin administered orally twice a day, is an acceptable dosage, because at this dosage the patients achieved significant therapeutic results with no adverse reaction.[24] Large amounts of the drug and its metabolites enter the liver and then the bile and, hence, should not be administered to patients with hepatic disease.[25]

CONCLUSION

Patients should avoid the predisposing etiology factors and improvement in dietary habits along with orodental hygiene. We can get markedly good results in OSMF patients, importantly in mouth opening which is the major problem of OSMF patients. Restricted mouth opening leads to decrease in food intake, leads to weight loss, anemia. This baseline study
gives scope for further studies with the systemic use of colchicin alone in the treatment of OSMF.

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**References**


