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Research Article

Clinicopathological study of oral submucosal fibrosis androle of steroid, benzoic acid and salicylic acid alone or in combination therapy

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ABSTRACT

Background: Oral submucosal fibrosis is a potentially malignant disease. This study aims to compare the efficacy of corticosteroid, benzoic acid, salicylic acid alone or in combination therapy for the treatment of oral submucous fibrosis and to analyse the histopathology of biopsied samples from all patients.
Methods: This study was conducted at Sardar Patel medical College from 2014 to 2015. Corticosteroids locally and in combination of oral administration. Group II was treated with 4% salicylic acid alone and in combination of 4% benzoic acid. The last group III was treated with both the drug used in Group I and II. All the collected biopsy specimen was stained by haematoxilin and eosin stain. All collected data was tabulated and stastically analyzed by using SPSS software.
Results: The common presenting symptoms were intolerance to spicy food. A mild to moderate improvement was observed in symptomatology and physical findings in majority of cases of Group I A. The magnitude of the improvement was, however, found to be more in patients of Group IB. A moderate to marked improvement was observed in patients of Group II. The magnitude of improvement was better in II B to II A Group. The improvement in symptomatology and physical findings was found to be much more marked in patients of Group III treated with combination therapy.
Conclusions: Oral submucosal fibrosis is a premalignant condition. Early recognition and treatment is necessary. Therapy with keratolytic agents along with local infiltration of corticosteroids helps in improvement of the condition.

Keywords: Oral submucosal fibrosis, Keratolytic agent, Steroid, Biopsy, Bikaner

INTRODUCTION

Oral submucous fibrosis, first described in the early1950s, is a potentially malignant disease predominantly seen in people of Asian descent. The submucous fibrosis is an insidious, non-fatal, chronic progressive disorder of unknown etiology affecting any part of the oral cavity and sometime pharynx, although occasionally preceded by and/or associated with vesicle formation almost associated with a juxta epithelial inflammatory reaction followed by fibroblastic changes of lamina propria, with epithelial atrophy leading to stiffness of oral mucosa resulting in trismus with resultant difficulty in eating. Etiopathogenesis of submucous fibrosis is yet an enigma. Several factors vis., racial, environmental, genetic, poor dental hygiene, malnutrition, addiction to betel nuts, betels, tobacco with or without lime, hot spicy food, mechanical or chemical trauma and localized collagen disease have been attributed to cause the submucous fibrosis. Although the

disease was described in 1950s, its pathogenesis and more importantly the mechanisms of malignant transformation have not been clear up to date. However, all of the above mentioned predisposing factors possibly would lead to either increased production or decreased degradation of the collagen.[1] The common distressing symptoms are burning sensation in mouth, inability to protrude the tongue fully and gradually progressive trismus of varying degree forces the patient to restrict his diet to liquid and pasty edibles only. Apart from this, inability to whistle, to blow, to suck and even speech disturbances may occur. Cox and Aziz in 1997 mentioned that oral submucous fibrosis is a progressive inability to open the mouth is the major complaint, because of accumulation of inelastic fibrous tissue in the juxtaepithelial region of the oral mucosa, along concomitant muscle degeneration.[2] According to Paissat in 1981, the buccal mucosa is the most commonly involved site, but may also involve the other parts of the oral cavity including pharynx.[3]

No really effective treatment is available in this malady, however, treatment with oral steroids intralesional hydrocortisone injection in combination with oral corticosteroids injections of firbrolysin, vitamin supplementation have been tried for this.[4-9] The effective treatment practiced now a days at most of the centers is a systemic and local corticosteroid therapy. Since a large cross section of the population in this area is addicted to betel nuts, betel with tobacco or consumption of tobacco mixed with lime and a good number of patients have been observed to attend out-patient department of otolaryngology department. It was thought worthwhile to study the clinico-pathological features of this disease and to evaluate the efficacy of different therapeutic regimes in this disease process specially the use of keratolytic agents such as acid salicylic and/or benzoic acid. In the modern medical literature the reports on submucous fibrosis were first published in Indian literature by Joshi who in some of his patients noted a peculiar blanching and sclerosis of palate and pillars of the fauces and called it 'submucous fibrosis'.[10]

METHODS

The present Study was conducted on 30 patients of oral submucous fibrosis diagnosed clinically and histopathologically, attending out-patient department of otolaryngology of Sardar Patel Medical College and Associated group of Hospitals, Bikaner, Rajasthan, India.

Table 1: Different therapeutic procedures.

Groups	No. of patients	Sub groups	Drugs used in therapy
I	10	A- 5 Pts.	Local injection of 10mg hydrocortisone weekly Local injection of 10mg hydrocortisone weekly
		B- 5 Pts.	And tablets dexamethasone orally 2mg daily for first month, 1mg daily for second month and 0.5mg daily for third month.
II	10	A- 5 Pts.	4% Salicylic acid solution for local application every fifth day.
		B- 5 Pts.	4% Salicylic acid with 4% Benzoic acid sol. for local application every fifth day.
III	10	-	Local injection of 10 mg hydrocortisone weekly and 4% Salicylic acid with 4% Benzoic acid sol. for local application every fifth day.

Informed consent was taken from enrolled patients attenders. A detailed interrogation, complete clinical examination and routine investigations were carried out. These cases were divided into three broad groups Viz., I, II and III for evaluation of results of different therapeutic procedures adopted in each of the table given.

All aseptic precautions will be observed during the procedure. The biopsy tissue preserved in buffered 10% neutral formalin solution for 24 hours to fixation. The paraffin micro sections of 5 thicknesses cut and stained with following staining's. Haematoxilin and eosin, phosphotungustic periodic acid and schiff reaction, van gieson's staining, toluline blue, masson's trichrone staining. All the collected data was tabulated and stastically analyzed by using SPSS software.

RESULTS

This The present study was conducted on 30 patients of oral submucous fibrosis diagnosed clinically and histopathologically, attending out-patient Department of otorhinolaryngology of Sardar Patel Medical College and Associated Group of Hospitals, Bikaner, Rajasthan, India. All the cases were divided in to three broad groups. Group I was treated with corticosteroids locally and in combination of oral administration. Group II was treated with 4% salicylic acid alone and in combination of 4% benzoic acid. The last group III was treated with both the drug used in group I and II. Majority of the patients belongs to second, third and fourth decade. Females were more affected. Though betel nuts addiction was found in almost all the cases yet other addictions pan, spices, tobacco chewing and smoking were also found in most of

the cases. The common presenting symptoms were intolerance to spicy food, difficulty in opening the mouth, difficulty in chewing, burning sensations in oral cavity and pain in throat. Cheeks was found to be involved in almost all the cases, however, palate, retro molar region, anterior tonsillar pillars, uvula, floor of mouth and tonsils were also involved. The main lesions at these sites were presence of fibrous bands, change in the color of the mucosa and ulcerations. Moderate anaemia was seen in most of the cases.

Table 2: Physical finding in 30 cases of submucous fibrosis.

	Cheeks	Floor of mouth	Retro molar region	Palate	Ant. Tonsillar pillar	Uvula	Tonsils
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
White color of mucosa	27 (90%)	-	24 (80%)	24 (80%)	24 (80%)	-	-
Pinkish white color of mucosa	3 (10%)	6 (20%)	6 (20%)	6 (20%)	6 (20%)	24 (80%)	6 (20%)
Pink color of mucosa	-	24 (80%)	-	-	-	6 (20%)	24(80%)
Fibrous band	27 (90%)	6 (20%)	24 (80%)	24 (80%)	15(50%)	9 (30%)	-
Ulceration	10 (33%)	-	6 (20%)	6 (20%)	3 (10%)	-	-
Distortion of shape	-	-	-	-	-	9 (30%)	-
Buried tonsils	-	-	-	-	-	-	3 (10%)

The subepithelial connective tissue showed an increased amount of collagen in all the cases with an increase in neutral mucopolysaccharides and fibrinoid degeneration in majority of the cases. A mild to moderate improvement was observed in symptomatology and physical findings in majority of cases of group I A. The magnitude of the improvement was, however, found to be more in patients of group IB. A moderate to marked improvement was observed in patients of group II. The magnitude of improvement was better in II B to II A group. The improvement in symptomatology and physical findings was found to be much more marked in patients of group III treated with combination therapy.

Table 3: Epithelial changes in biopsies taken from 30 cases of oral submucous fibrosis.

Change in epithelium	Total no. of patients	Percentage
Atrophy	2	6.66
Hypertrophy	27	90
Keratosis	15	50
Parakeratosis	30	100
Dysplasia	1	3.33
Basal cell degeneration in basement membrane	2	6.66
Atrophy of rete pegs	21	70

Table 4: Different staining with results in 30 cases of oral submucous fibrosis.

Stain	Results	No. of patient	Parcentage
H and E	Marked hyalinisation, hypocellular, eosinophillic homogenous	30	100
P.T.A.H	Positive	24	80
	Negative	6	20
V.G	Highly positive	6	20
	Positive	24	80
P.A.S	Highly positive	2	6.66
	Positive	27	90
	Weakly positive	1	3.33
T.B	Positive	3	10
	Negative	27	90
M.T.S	Also shows curled up, at places broken red stained thick fibers seen.	30	100

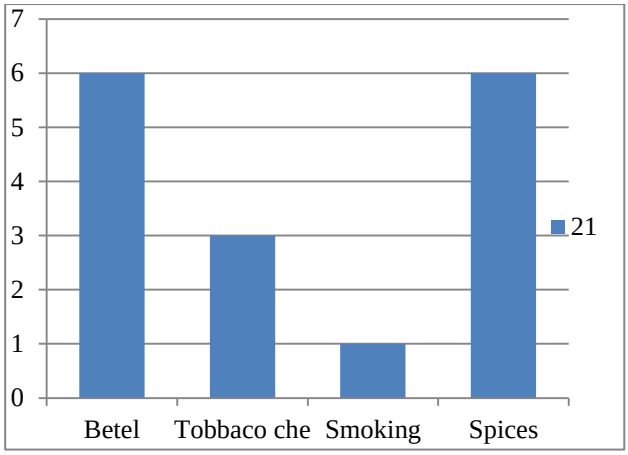

Figure 1: Addiction distribution.

DISCUSSION

Oral submucous fibrosis is a chronic, progressive and irreversible disease of unknown aetiology. It affects oral and oropharyngeal mucosa. The earliest description of the disease was given by Schwartz, who coined the term atrophica idiopathic mucosa oris to describe an oral fibrosing disease.[11] Joshi subsequently termed the condition as oral submucous fibrosis.[10] The present study has been carried out in 30 cases of submucous fibrosis that attended the outpatient department of otorhinolaryngology, PBM and associated group of hospitals, Bikaner, Rajasthan, India, with an aim to evaluate the efficacy of different therapeutic procedures.

Majority of patients (83%) in the present study belonged to second, third and fourth decade of life with predominance of second and third decade. This is an agreement with age incidence observed by Desa, Rao and Raju, Rao have observed the female sex predominance in their studies.[4,6,7] In the present study also the female sex predominance was observed. The present study revealed that the Hindus were (80%) affected more than Muslims in submucous fibrosis. Similar observations were made by Wahi et al.[12] Various addictions vis. betel nut (supari), tobacco (chewing, smoking), chilies and spices have been attributed to be the causative agents. In the present study 70% of the cases revealed addiction to chewing of betel nuts which is in agreement the findings of Su, Sharan.[5,13] Other addiction e.g. pan (20%), spices (20%), tobacco chewing (10%) and smoking (3.33%) was observes in the present study which is in the agreement of the finding of Desa.[6] In almost all of the patients in the present study, intolerance to spicy food was chief presenting symptom (90%), which was however, followed by difficulty opening mouth (80%), difficulty in chewing (70%), burning sensation in the oral cavity (60%), and pain in the throat (60%). Progressive stiffness of cheeks, inability to blow, nasal voice and whiteness of palate were also observed in few cases. All other workers on this subject agree with the symptomatology of the present study.[5,6,8,10,12]

Cheek was found to be involved in almost all the patients in the present study having fibrous band in 90%, while mucosa in 90% and ulceration in 30% of the patients. The next common site found to be involved in descending order of frequency were palate, retro molar region, anterior tonsilar pillar, uvula, floor of the mouth and tonsils. These observations are in the agreement to the observation made by Joshi and Paissat DK.[3,10] Anemia of varying grade has been found to occur in submucous fibrosis.[2,6,7] In the present study also 23 out of 30 cases revealed a mild to moderate degree of anemia. The histological study of the biopsy taken from the site of the lesion of all the cases in the present study revealed Para keratosis (100%), hypertrophy (90%), atrophy of rete pegs (70%), and keratosis (50%), basal cell degeneration, dysplasia and atrophy of the epithelium were observed in the few of the cases. These findings have also been observed by several workers.[10,13] The differential connective tissue stain employed in the present study show increased amount of collagen in all the cases with increases in neutral mucopolysaccharides and fibrinoid degeneration in majority of the cases. The PTAH positive staining demonstrating fibrinoid degeneration 24 out of the 30 cases in the present study lends support to the view hold by Sirsat and Khaniolkar.[13] The most serious complications is the development of carcinoma. Sirsat and Khanolkar found only 6 cases of leukoplakia and 4 cases of carcinoma in their series of 85.[14] In the present study no evidence of leukoplakia was found in any 30 patients.

No really effective treatment is available in this malady, however, treatment with oral steroids, intralesional hydrocortisone in combination with oral corticosteroids; injections of fibrinolysis, vitamin supplementation have been tried for this. Effective treatment practiced now a day at most of the centers is a systemic and local corticosteroids therapy.[4-9]

In the present series a mild to moderate improvement was observed in symptomatology and physical finding in majority of the cases of group IA treated with intralesional injection of 10 mg hydrocortisone every week. The colour of the mucosa of cheeks, anterior tonsillar pillars, uvula and retro molar regions where the lesions were located turned pink. The magnitude of the improvement was, however, found to be more when intralesional injection of hydrocortisone every fifth day was supplemented with oral administration of cortisone. The role of corticosteroids as anti-inflammatory and immunosuppressive agent is well established, these may halt further fibrosis and increase in vascular tone giving rise to pink colouration of the mucosa and afford relief in symptomatology and physical finding of the patient. Benzoic acid and hydroxy benzoic acid (salicylic acid) are employed locally remove horny larger of the skin in epidermophytosis and similar conditions (Krantz and Carr).[15] keratosis and Para keratosis of mucous membrane being a commonest change in submucous fibrosis, it was thought worth, while to try it as a local

treatment alone and in combination with local intralesional injection of 10 mg hydrocortisone every fifth day.

In patients of group II A, treated with 4% salicylic acid locally every fifth day, after three months of treatment showed marked improvement in intolerance to spices (all cases), burning sensations in oral cavity (2 out of 3 cases). Rest of other symptoms showed moderate improvement only. Almost all physical findings in this group showed only moderate improvement. Colour of the mucosa at various places in oral cavity showed marked improvement. The combination of 4% salicylic acid and 4% benzoic acid employed in the treatment in patient of group II B, revealed a slight increased magnitude of improvement as compared to the patients of group II A in symptomatology of physical findings.

The improvement in symptomatology and physical findings was found to be much more marked in patients of group III treated with combination therapy of local application salicylic acid and benzoic acid along with local injection of hydrocortisone. The exact mechanism of action of acid salicylic and benzoic in combination affording relief to the patient is not known. Probably these agents by their keratolytic action on the hyperkeratosis and parakeratotic mucosa present in submucous fibrosis gradually diminish the unequal pressure being exerted on the exposed nerve endings giving rise to varied type of sensations. The combination with local infiltration of hydrocortisone may further improve the condition by relieving oedema, inflammatory response and increased vascularity.

CONCLUSION

Our study concluded that therapy with keratolytic agents along with local infiltration of corticosteroids helps in improvement of the condition and further progression of the lesion to fibrosis. It may, however, be added that whatever amount of fibrosis that has occurred in these lesions will not be reversed.

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REFERENCES

1. Tilakratnen WF, Klinikowski MF, Saku T, PetersTJ, Warnakulasuriya S. Oral submucous fibrosis: Review on aetiology and pathogenesis Oral oncology. 2006;42(6):561-8.
2. Aziz SR. Oral submucous fibrosis: an unusual disease. J N J Dent Assoc. 2007;68:17-9.
3. Paissat DK. Oral submucous fibrosis.int j oral surg. 1981;(10)3:310-2.
4. Rao R, Raju V, Ram P. A preliminary report on the treatment of submucous fibrosis of oral cavity with cortisone. Indian J. otolaryng. 1954;6:81.
5. Su IP. Idiopathic scleroderma. A.N.A. Arch. otolaryng. 1954;59:330.
6. Desa JV. Submucous fibrosis of the palate and cheek. Ann. otol. 1957;66:1143.
7. Rao ABN. Idiopathic palatal fibrosis. Er. J. Surg. 1962;50:23.
8. Pindborg JJ, Sirsat MS. Oral Surg. 1966;27:764.
9. Rowell NR. Submucous fibrosis of mouth. Er. J. Derm. 1967;79:64.
10. Joshi SC. Submucous fibrosis of palate and pillars. Indian J. otol. 1953;4:1-10.
11. Sirsat SM, Khaenolkar VR. Submucous fibrosis of palate and pillars of fauces. Schwarts J. atrophia idiopathica "tropion" mucosae oris. Demonstrated at the XI international dental congress london. Ind. J. Med. Sci.1962;16:189.
12. Wahi PN, Kapur VL, Luthra UK, Srivastave MC. Bull. wld. Hith. org. 1966;35:793.
13. Sharan J. Histopathological observation on cases of submucous fibrosis of oral cavity. Ind. J. path. and Bact.1959;2:150.
14. Sirsat SM, Khanolkar VR. Submucous fibrosis of the palate and pillars of the cancer. Indian J. Med. Sci.1962;16:189.
15. Krantz JC, Carr CJ. Pharmacologic principles of medical practice. VI Ed. The Williams and Wilkins compony scientific book agency, Calcutta; 1967.

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