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ORAL SUBMUCOUS FIBROSIS – A LITERARY REVIEW ACCORDING TO MODERN SCIENCES AND AYURVEDA.

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ABSTRACT

Oral submucous fibrosis is a precancerous disease of oral mucosa predominantly found in India and few other Asian countries as a result of chewing areca nut and its byproducts. It is characterized by juxta epithelial inflammatory reaction and progressive fibrosis of submucosal tissues of oral cavity and sometimes pharynx. Symptoms include burning sensation, ulcerations, xerostomia, vesicle formation, fibrosis, difficulty in opening mouth and malignancy of oral cavity in some cases which greatly affects patient's quality of life. Arecoline found in betel nut increases the formation of collagen which leads to fibrosis. Deficiencies of micronutrients also play important role in development of the disease. Acharya Sushruta has described similar symptoms in Sarvasar Mukharoga which means diseases of oral cavity. Treatment for this disease is stoppage of chewing habits, avoiding irritants, nutritional supplements, oral hygiene and steroids. This article gives a brief modern and Ayurvedic review of etiopathogenesis, clinical features, treatment, preventive measures of Oral Submucous Fibrosis.

KEYWORDS: areca nut, collagen deposition, hypoxia, trismus, fibrosis, sarvasar mukharoga.

INTRODUCTION

Oral submucous fibrosis is a chronic insidious process which is characterized by juxtaepithelial deposition of fibrous tissue, formation of scars and development of cancerous lesions in oral cavity and pharynx.[1,2] The mucosa of oral cavity constantly undergoes changes in temperatures, exposures to various irritants and microorganisms. The epithelium

and connective tissues of oral cavity exhibit acute and chronic reactions in response to those exposures. Amongst these comes oral submucous fibrosis. There is deposition of dense collagen in connective tissue. Chewing of betel nut is considered main culprit in this disease.

History

The symptoms of oral submucous fibrosis were first described by Acharya Sushrut in ancient Indian manuscripts. Sushrut has described the symptoms like difficulty in opening of mouth in Nidan sthan of Sushrut Samhita under the diseases of Mukha. Other Acharyas also described these symptoms in diseases of oral cavity in later period of Ayurved literature. In 1952, Schwartz observed symptoms of oral submucous fibrosis in 5 females living in Kenya and described it as 'atrophica idiopathic mucosae oris'. In 1953, Joshi from Bombay redesignated the condition as 'submucous fibrosis'.[3,4]

Epidemiology

Although this disease is almost exclusively seen in Indian population, its prevalence is noted in few Asian countries like Taiwan, Pakistan, Bangladesh, Shri Lanka, Nepal and Thailand; also, in migrated population in South Africa, South America.[5,6,7] Prevalence of this disease in India and other Asian countries is a reflection of food, culture and religious habits. The disease is more prevalent in age group of 20 to 40 years.[8,9] Predominantly found in women.

Definition

There are various definitions given by scientists, but most widely accepted definition is by Pindborg JJ and Sirsat SM. It states – "Oral submucous fibrosis is an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta epithelial inflammatory reaction, followed by a fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness.[10,11]

SYMPTOMS AND CLASSIFICATION

Most common initial symptoms are ulceration, xerostomia, burning sensation, intolerance to chillies and spicy food. These symptoms later progress to inability to open mouth, difficulty in protruding tongue out, inability to whistle, restrictions in chewing food, nasal intonation of voice, thinning and stiffening of lips, formation of malignant lesions in oral cavity.[12,13,14]

In Aurveda, no Acharya has specifically described the disease oral submucous fibrosis as one disease, but symptoms are found scattered in description of diseases of mouth i.e. Mukharoga. In Nidan Sthan of Sushrut Samhita, Uttar sthan of Ashtang Sangrah, Madhav Nidan, Bhav Prakash, Yog Ratnakar and in Sharang Samhita, Sarvasar Mukharoga are described. Sarvasar Mukharoga means the disease which occupies all oral cavity and parts in it like, tongue, lips, palate, buccal mucosa, posterior pharyngeal wall. The symptoms which better corelate with oral submucous fibrosis are as follows, Difficulty in opening mouth (vivrunoti ch kruchhena – Vataja Sarvasar), Pain (toda – Vataja Saravasar), burning sensation (mukhadaha, usha – Pittaja Sarvasar).[15]

Over the time many classifications are given by scientists during their studies. But a few classifications help in clinical practice are noted here.[16]

1)Based on clinical findings by Pindborg JJ.

Stage I – Stomatitis, erythematous mucosa, vesicles, ulcers, petechiae.

Stage II – Fibrosis in healing vesicles and ulcers, blanching, palpable bands, mottled marble like appearance.

Stage III – Sequelae of Oral Submucous Fibrosis; leukoplakia, speech and hearing deficit.

2)Based on mouth opening (interincisal distance) by Lai DR.

Group 1- >35 mm

Group 2- between 30 and 35 mm

Group 3- between 20 to 30 mm

Group 4- <20 mm

ETIOPATHOGENESIS

Etiology[17,18,19]

1)Local factors

Areca nut: chewed alone, with dried tobacco and lime, in form of Paan (betel quid) containing areca nuts with catechu with lime wrapped in betel leaf.

Dietary habits of regular eating chillies and spicey food.

2)Systemic factors

Nutritional deficiencies of vitamin B12, vitamin A, antioxidants, zinc.

Autoimmunity

Genetic predisposition

Major factor is chewing of areca nut and its byproducts.

Pathogenesis

Ayurveda describes the etiopathogenesis of Mukha roga as follows.

Not maintaining the oral hygiene by brushing of teeth, gargles, dhumpana, panchkarma leads to prakopa of kapha dominant tridoshas. These prakupit doshas find a place in oral cavity and give rise to various diseases.[20]

Pathogenesis according to modern sciences[21,22,23]

Main pathology in Oral Submucous Fibrosis is over deposition of collagen in the connective tissues of various areas in oral cavity. Chronic chewing of areca nut leads to this pathogenesis. Studies show that areca nut contains alkaloids like arecoline, arecaidine, guvacine, guvacoline and flavonoids like tannins and catechins. The main culprit is Arecoline.

Arecoline stimulates and proliferates the fibroblasts. Which results into increased synthesis of collagen. Also, tannin inhibits collagenase which reduces the degradation of collagen. So combined effect results into increased synthesis and decreased degradation of collagen. Hence the over deposition of collagen.

Arecoline increases the oxidative stress which activates various transcription factors leading to stimulation of fibroblasts and endothelial cells resulting in fibroblasts proliferation and increased collagen formation.

Copper present in areca nut increases activity of lysyl oxidase enzyme. It stimulates and proliferates fibroblasts again resulting into increased synthesis of collagen.

This increased synthesis of collagen results in accumulate in extra cellular matrix. The repeated cell injury due to local irritants increases oxidative stress and it alters normal morphology of keratinocytes. These keratinocytes lead to fibrosis.

Oral submucous fibrosis patients develop nutrition deficiencies. Intolerance of food, burning sensations, pain and difficulty in opening mouth (due to trismus) lead to reduced oral intake and it further worsens submucous fibrosis due to poor nutrition. Patients land up in vicious cycle of this nutritional deficiency.

Due to extensive fibrosis, there is reduction in vascularity. This gives hypoxia. This results into atrophy, ulcer formation and malignant transformation (due to alterations in cells cycle). About 1.5 to 15% of the cases develop malignancy.

Diagnosis[24,25]

1)Diagnosis is mainly based on clinical examination. Early stage patients present with stomatitis and vesicle formation. Moderate stage shows marble like appearance and palpable fibrous bands. Severe patients present with stage of leukoplakia, severe trismus and erythroplakia. A detailed history taking is required about food habits and other chronic chewing habits.

2)Biopsy – solid or liquid biopsy of affected mucosa is studied to confirm presence of disease.

3)Biomarkers- oral submucous fibrosis tissues, serum and saliva are studied for biomarkers.

4)Staining- using H and E stain (Hematoxyllin and Eosin stain).

TREATMENT

Prevention of disease seems better option. Patients with addiction of areca nut and habit of eating spicy food should be recognized early and encouraged to stop the addiction. Also maintaining good oral hygiene is important in such patients.

Ayurveda has described poor oral hygiene as one of the causes of mouth diseases. Hence mukhadhawana (mouth wash) is given as general treatment line in all types of sarvasar mukharogas. Local applications (pratisarana) and gargle solutions (kawala-gandusha) are useful in relieving the difficulty in mouth opening. The movements of mouth done during kawal-gandusha can act as exercises and help in relieving trismus. Local application will also act on tight fibrous bands and help relieve fibrosis.

1)Mukhadhawana yogas (mouthwash)[26]

kwatha (decoctions) made with trifala, patha, mrudwika, jaati, pallava is to be mixed with madhu (honey) and used for mouthwash.

Kwatha made with fresh leaves of patola, nimba, jamra, aamra, malati is to be used for mouth wash.

2)Pratisaran yogas (local applications)[27]

darvi swarasa rasanjana mixed with madhu and gairika is to be applied locally.

3)Kawala/gandusha yogas (mouth gargles)[28]

Nishadi taila – sidhha taila with kwatha and kalka made of haridra, nimba patra, yashtimadhu, neel utpala.

All these formulations described help maintaining good oral hygiene and giving physical exercise to mouth. Hence can be used to prevent further development of Oral Submucous Fibrosis in early detected cases.

According to modern sciences, no definite standardized treatment protocol is available. But following treatments are practiced widely.[29,30]

1)Restricting the chewing habits of areca nut, paan, tobacco, etc. Avoiding spicey food and chillies like irritants.

2)local steroids: steroids suppress inflammatory response by their anti-inflammatory properties. Also prevent fibrosis by decreasing fibroblast proliferation and collagen deposition.

Topical applications of steroids like triamsinolone gel form is widely popular.

Local (inralesional) injections of inj. Dexamethasone 4mg combined with inj. Hyaluronidase 1500 IU, chymotrypsin 5000 IU and 2% lignocaine.

3)Nutritional supplements: antioxidants, vitamin B12, zinc, lycopene, vitamin A, iron are given.

4)Physical exercises to promote forceful mouth opening.

5)Surgical: simple release of fibrosis with LASER and skin grafting is done for severe Oral Submucous Fibrosis patients.

CONCLUSION

Oral submucous fibrosis is prevalent in Asian countries. Caused mainly by chronic chewing habits of areca nut and its byproducts. Symptoms of disease are intolerance to spicey food, burning sensation, pain, difficulty in chewing, opening mouth, blowing whistle and sometimes malignancy formation. Clinical features include vesicles, ulcerations, palpable fibrous bands in affected area and trismus. Arecoline present in areca nut leads to excessive deposition of collagen in mucosa of oral cavity. Diagnosis is made clinically and can be confirmed by biopsies, biomarkers and stains histologically. Treatment is mainly restricting chewing habits, good oral hygiene, steroid applications, nutritional supplements and sometime surgical release of fibrous bands. But as there is no standard treatment protocol

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