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RESEARCH ARTICLE

ORAL SUBMUCOUS FIBROSIS: A REVIEW.

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Abstract

Introduction:-

Oral submucous fibrosis (OSMF) is a chronic, premalignant condition of the oral mucosa. It has been reported in the Indian literature since the time of Sushruta as 'Vidari'. But was first described by Schwartz 1952.[1] In 1956, Paymaster identified its pre-cancerous nature. Pindborg and his associates in 1966 defined the condition as Oral Submucous Fibrosis is "an insidious chronic disease affecting any part of the oral cavity and sometimes pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxtaepithelial inflammatory reaction followed by fibroelastic changes in the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and difficulty in eating."[2]This condition has also been described and named as idiopathicscleroderma ofmouth(Su1954),idiopathicpalatal fibrosis(Rao1962)[3]andsclerosingstomatitis(Behl1962).[3]It is stronglyassociatedwithbetelnutandgutkhachewing, andcharacterizedby:Generalized submucosalfibrosis of the oral soft tissue, resultinginmarkedrigidityandprogressiveinabilitytoopen themouthandrestrictedmovementsoftongue, reductioninthevasculaturewhichappearsasoralmucosal pallor, atrophyofthesurfaceepithelium,dysphagia,whichmayoccurinseverecases. It has highest malignant transformation potential of 4 to 13% worldwide, whereas it is 7.6% in Indian population.However,theratevariesfrom0.2to2.3%inmales and1.2to4.57%infemalesinIndiancommunities.[3,4,5]The most commonly involved site is buccal mucosa, followed by palate, retromolar region, faucial pillars and pharynx. The overall prevalence rate in India is about 0.2-0.5% and prevalence by gender varying from 0.2% to 2.3% in males and 1.2% to 4.57% in females. The age range of the patients with OSF is wide ranging between 20 years and 40 years of age. Ingestion of chilies, genetic susceptibility, nutritional deficiencies, altered salivary constituents, autoimmunity and collagen disorders also considered to be involved in the pathogenesis of this condition.[6]

Classifications:-

Several classifications based on clinical, histological and combined feature have been put forth by several researchers in different year.

Classification Based On Clinical Features[7]:-

JV Desa (1957) divided OSMF into three stages as follows:
Stage 1:- Stomatitis and vesiculation

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Stage 2:- Fibrosis.
Stage 3:- As its sequelae.

Pindborg JJ (1989) divided OSMF into three stage:-

Stage 1:- Stomatitis includes erythematous mucosa, vesicles, mucosal ulcers, melanotic mucosal pigmentation andmucosalpetechiae.
Stage 2:- Fibrosis occurs in healing vesicles and ulcers,which is the hallmark of this stage.
Stage 3:-Sequelae of OSMF are as follows: Leukoplakia is found in more than 25% of individuals with OSMF. Speech and hearing deficit may occur because of
involvement of tongue and the Eustachian tube.

SkKathaiia et al (1992) have given different scoresassigned to the patients on the basis of mouth openingbetween upper and lower central incisors as follows:

Score 0:- Mouth opening is 41 mm or more.
Score 1:- Mouth opening is 37 to 40 mm.
Score 2:- Mouth opening is 33 to 36 mm.
Score 3:- Mouth opening is 29 to 32 mm.
Score 4:- Mouth opening is 25 to 28 mm.
Score 5:- Mouth opening is 21 to 24 mm.
Score 6:- Mouth opening is 17 to 20 mm.
Score 7:- Mouth opening is 13 to 16 mm.
Score 8:- Mouth opening is 09 to 12 mm.
Score 9:- Mouth opening is 05 to 08 mm
Score 10:- Mouth opening is 0 to 04 mm

Ranganathan K et al (2001) divided OSMF based on mouth opening as follows:-
Group I: Only symptoms, with no demonstrable restriction of mouth opening.
Group II: Limited mouth opening 20 mm and above.
Group III*:* Mouth opening less than 20 mm.
Group IV*:* OSMF advanced with limited mouth opening.Precancerous or cancerous changes seen throughout the mucosa.

Nagesh and Bailoor (1993) based on diagnosis :-
Stage I early OSMF*:* Mild blanching, no restriction in mouth opening (normal distance between central incisor tips: Males 35 to 45 mm, females 30 to 42 mm), no restriction tongue protrusion.

Stage II moderate OSMF*:* Moderate to severe blanching, mouth opening reduced by 33%, cheek flexibility also demonstrably reduced, burning sensation also in absence of stimuli, palpable bands felt. Lymphadenopathy either unilateral or bilateral and demonstrable anemia on hematological examination.

Stage III severe OSMF*:* Burning sensation is very severe patient unable to do day-to-day work, more than 66% reduction in the mouth opening, cheek flexibility and tongue protrusion. Tongue may appear fixed. Ulcerative lesions may appear on the cheek, thick palpable bands and lymphadenopathy bilaterally evident.

Wahi P N et al (1996) classified osmf based on clinical severity and extent of involvement into three groups :
Group 1: No symptoms referable to buccal mucosa, focal pallor/whitish discolouration of mucosa.
Group 2: Symptoms of soreness of mucosa increased sensitivity to chilli, lesions diffuse, white, extensive, indurated involving one or anatomical sites.
Group 3: Trismus, stretching at angles of mouth and altered pronunciation.Firm mucosal bands. Surface might me fissured or ulcerated.

Kiran Kumar et al (2007) categorized three clinical stages:-
of OSMF on the basis of mouth opening as follows:
Stage I: Mouth opening >45 mm

Stage II: Restricted mouth opening 20 to 44 mm
Stage III: Mouth opening <20 mm

Chandramam More et al (2011):-
Clinical staging:-
Stage 1 (SI): Stomatitis and/or blanching of oral mucosa.
Stage 2 (S2): Presence of palpable fibrous bands in buccal
inucosa and/or oropharynx, with /without stomatitis.
Stage 3 (S3): Presence of palpable fibrous bands in buccal mucosa and/or oropharyiix, and in any other parts of oral cavity, with/without stomatitis.
Stage 4 (S4) as follows:

A.Any one of the above stage along with other potentially malignant disorders, e.g. oral leukoplakia, oral erythroplakia, etc.
B.Any one of the above stage along with oral carcinoma. Functional staging:
o Ml: Interincisal mouth opening up to or greater than 35mm.
o M2: Interincisal mouth opening between 25 and 35mm.
o M3: Interincisal mouth opening between 15 and 25mm.
o M4: Interincisal mouth opening less than IS mm.

Classifications Based on Histopathological Features of OSMF[7]:-
Kiran Kumar et al (2007) proposed histological grading asfollows:'
Grade 1: Loose, thick and thin fibers
Grade II: Loose or thick fibers with partial hyalinization.
Grade III: Complete hyalinization

Classification based on clinical and Histopathological Features:-[7]
Khanna JN and Andrade NN (1995) developed a group classification system for the surgical management of OSMF.
Group I:-
Very early cases: Common symptom is burning sensation in the mouth, acute ulceration and recurrent stomatitis and not associated with mouth opening limitation.

Histology:-
Fine fibrillar collagen network interspersed with marked edema, blood vessels dilated and congested, large aggregate of plump young fibroblasts present with abundant cytoplasm, inflammatory cells mainly consist of polymorphonuclear leukocytes with few eosinophils. The epithelium is normal.

Group II:-
Early cases—Buccal mucosa appears mottled and marble like, widespread sheets of fibrosis palpable, interincisal distance of 26 to 35 mm.

Histology:-
Juxta-epithelial hyalinizalion present, collagen present as thickened but separate bundles, blood vessels dilated and congested, young fibroblasts seen in moderate number, inflammatory cells mainly consist of polymorphonuclear leukocytes with few eosinophils and occasional plasma cells, flattening or shortening of epithelial rete-pegs evident with varying degree of
keratinization.

Group III:-
Moderately advanced cases—Trismus, interincisal distance of 15 to 25 mm, buccal mucosa appeal's pale firmly attached to underlying tissues, atrophy of vermilion border, vertical fibrous bands palpable at the soft palate, pterygomandibular raphe and anterior faucial pillars.

Histology:-
Juxta-epithelial hyalinization present, thickened collagen bundles, residual edema, constricted blood vessels, mature fibroblasts with scanty cytoplasm and spindle-shaped nuclei, inflammatory exudates which consists of lymphocytes and plasma cells, epithelium markedly atrophic with loss of rete pegs, muscle fibers seen with thickened and dense collagen fibers.

Group IVA:-
Advanced cases—severe trismus, interincisal distance of less than 15 mm, thickened faucial pillars, shrunken uvula, restricted tongue movement, presence of circular band around entire lip and mouth.

Group IVB:-
Advanced cases—presence of hyperkeratotic leukoplakia and/or squamous cell carcinoma.

Histology:-
Collagen hyalinized smooth sheet, extensive fibrosis, obliterated the mucosal blood vessels, eliminated melanocytes, absent fibroblasts within the hyalinized zones, total loss of epithelial rete pegs, presence of mild to moderate atypia and extensive degeneration of muscle fibers.

Aetiology& Pathophysiology:-
The pathogenesis of the disease is not well established, but the cause of OSMF is believed to be multifactorial. Caniff et al in 1986and Pindborg in 1968described disease asa form of hypersensitivity to capsaicin, anirritant in chilies, but this was not totallysubstantiated in experimental work. Anumber of factors may trigger the diseaseprocess by causing a juxtaepithelialinflammatory reaction in the oral mucosa. Factors include are areca nut chewing, ingestion of chilies, genetic and immunologic processes, nutritional deficiencies and other factors.[8,9,10]

Areca Nut (Betel Nut) Chewing:-
The exact mechanism is not clear yet. But the arecoline and flavonoid, components of areca nut when exposed to buccal mucosal fibroblast results in the accumulation of collagen. Reduced collagenase activity and increased cross‑linking of the fibers results in decreased degradation of collagen. This evidence implies that OSMF may be considered a collagen‑metabolic disorder resulting from exposure to areca nut.[8]

Nutritional Deficiencies:-
Iron deficiency anemia, vitamin B complex deficiency and malnutrition are promoting factors that derange the repair of the inflamed oral mucosa, leading to defective healing and resultant scarring (Aziz, 1997)**.** The resultant atrophic oral mucosa is more susceptible to the effects of chilies and betel nuts. Mucosal changes similar to those in vitamin B and iron deficiency are seen in oral sub mucosal fibrosis.[8,11]

Chillies:-
The role of chillies ingestion in the pathogenesis of OSMF is controversial. Sirsat in 1960 done a study demonstrated that the capsaicin in chilies stimulates widespread palatal fibrosis in rats, while another study failed to duplicate the results that are done by Hamner, in 1974. According to Pillai in 1992 the incidence of OSMF is lower in Mexico and South America than in India, despite the higher dietary intake of chilies.26 A hypersensitivity reaction to chilies is believed to contribute to OSMF (Aziz, 1997).[8,11]

Genetic and Immunologic Processes:-
A genetic component is assumed to be involved in OSF Patients with increased frequency of HLA-A10, HLA-B7, and HLA-DR3 (Aziz, 1997)**.**[11]According to Canniff in 1985 an immunologic process is believed to play a role in the pathogenesis of OSMF. The increase in CD4 and cells with HLA-DR in OSF tissues suggests that lymphocytes are activated and that the number of Langerhans cells is increased. The presence of these immunocompetent cells and the with increased of CD4 to CD8 in OSF tissues suggest a ongoing cellular immune response results in imbalance of immunoregulation and an alteration in local tissue architecture. These reactions may be the result either of direct stimulation from exogenous antigens, such as areca alkaloids, or of changes in tissue antigenicity that leads to an autoimmune response. Haque in 2000 demonstrated increased levels of proinflammatory cytokines and reduced antifibrotic interferon gamma (IFN-gamma) in patients with OSMF, which may be central to the pathogenesis of OSMF.[8]

Clinical features:
The disease can be classified clinically into two phases: An eruptive phase and the fibrosis induction phase. These two phases appear in a cyclic manner. Initially, most patients present with a burning sensation followed by vesicles formation, ulceration, Xerostomia and is later followed by fibrosis of the oral mucosa, which leads to rigidity of the lips, tongue, and palate, and trismus.[12,13] useful clinical sign is pain on palpation in the sites where submucosal fibrotic bands are developing and trismusnis caused mostly by fibrosis in the dense tissue around the pterygomandibularraphae. In advanced stages the patients may experience referred pain to ear,dysphagia due to fibrosis involving nasopharynx or oesophagus and even ,deafness due to fibrosis of Eustachian tube.[12]

Management:-
The management of an OSMF patient depends on the degree of clinical involvement. It comprises of: discontinuation of areca-nut related habit, nutritional support and antioxidants , physiotherapy ,immunomodulatory drugs(steroids) for local/systemic application, intra-lesional injections of steroids, hyaluronidase, human placental extracts etc, either singly or in combination for early/milder form of disease and surgical measures for advanced cases with post-operative nutritional support and anti-oxidants alongwith active physiotherapy to prevent contracture at the surgical site and recurrence. It is very essential to follow these patients closely in order to prevent recurrence and to detect any developing malignancy at its earliest so as to manage this untoward and most common eventuality.[14]

Conclusion:-
OSMF is a disease with a high degree of incidence. It also carries a significant morbidity rate from oral cancer. As no effective medical and surgical treatment is available for this condition. It is desirable OSMF is diagnosed at early stages. Cessation of the areca nut chewing & other factors should be advised. Intervention studies and public health awareness programme linked with OSMF condition & habits may prove the best way to control disease process at the community level.

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