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Pain Management in Oral Sub-Mucosal Fibrosis (OSMF) with Alternanthera sessilis *(Matsyaakshi)*: An Adjuvant Therapy

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Abstract

Oral cavity is a major entrance for bodily entities. It has a high risk of getting infections, irritations, etc. Oral Sub-mucosal Fibrosis (OSMF) is an Oral sub-mucous fibrosis is a chronic debilitating disease of the oral cavity characterized by inflammation and progressive fibrosis of the sub-mucosal tissues. This is called a disease of Indians. Because, it is most predominantly found in Indians and Indians living abroad. Exact etiology is unknown. The pathogenesis of the disease is not well established, believed to be multifactorial. No definite cure and management is available for OSMF. Only symptomatic relieving measures should be done. Use of topical anesthetics and analgesics alters the taste perception thus, impairs digestion and subsequent processes.

Matsyaakshi is a drug with traditional values, available in all the seasons, throughout the India. It is rich in anti-oxidant beta-carotene, Vitamin C and other essential chemicals. It is a traditional drug of choice for controlling the pain in oral cavity. This controls the pain in oral cavity rather than altering the taste perception and thus, does not interfere with the digestion.

Keywords: OSMF (Oral Submucosal Fibrosis); Matsyaakshi; Anaesthesia.

Introdution

Oral cavity is a major entrance for bodily entities. It has a high risk of getting infections, irritations, etc.

Oral cavity mucosa and saliva plays a vital role in controlling utmost possible irritations and infections of the oral cavity and further bodily systems. Thus, maintains the integrity of oral mucosa and underlying structures.

Oral Submucosal Fibrosis (OSMF)

Oral submucous fibrosis is a chronic debilitating disease of the oral cavity characterized by inflammation and progressive fibrosis of the submucosal tissues.[1]

This is called a disease of Indians. Because, it is most predominantly found in Indians and Indians living abroad. In 1952, Schwartz coined the term *atrophica idiopathica mucosa oris*. He discovered in 5 Indian women from Kenya.[2] Subsequently in 1953, Joshi coined the termed *oral submucous fibrosis (OSMF)*.[3]

The condition is well recognized for its malignant potential (40% incidence).[4]

Some of the clinical features of OSMF resembles with the signs & symptoms of *Talukacchapa or Vidaari* explained in the context of *Taalugata & Kanthagata Roaga* respectively by *Sushruta*.[5]

Aetiology & Pathogenesis

Exact etiology is unknown. But, following factors have been mentioned as suppose to be relevant with OSMF –

1. Hereditary Predisposition: Found in Indians and Indians living abroad. Thus, a genetic factors is suspected.

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2. Prolonged Local Irritation

- *Betel nut:* Acts by mechanical and chemical irritation
  - √ *Mechanical:* Nut is hard and its sharp jagged edges cut into mucosa. It causes superficial ulceration, which heals by fibrosis.
  - √ *Chemical:* Arecolins – alkaloid present in areca catechu nut. It is a local irritant and also acts on nerve endings in oral mucosa – Neutrophic changes.
  - √ Flavanoid, catechin, and tannin in betel nuts cause collagen fibers to cross-link, making them less susceptible to collagenase degradation.
- *Betel Nut Lime:* It contains arecolins, lime and tannic acid. It causes local irritation, damage to mucosa, vesiculation and ulceration.
- *Paan: Paan* with various combinations like betel lime, tobacco, *Maava*, *Gutaka*, camphor, etc. Chewing areca quid may also activate NF-kappaB expression, thereby stimulating collagen fibroblasts and leading to further fibrosis in persons with oral submucous fibrosis.
- *Tobacco (Desa 1957):* Tobacco alone or in various forms like *Manipuri* Tobacco (famous in northern part of India), *Kapuri* Tobacco has highly irritant qualities to oral mucosa, thus predispose to OSMF.
- *Chillies (Desa 1957):* Allergic reaction to chillies is an important factor. Capsicin – an active ingredient from capsicum has been shown to be an irritant.

3. Deficiency Diseases

- Vitamin B Complex (Roy 1952)
- Vitamin A (Krishnamoorthy 1970)

4. Defective Iron Metabolism

- Hiranandini (1970) reported achlorhydria in OSMF
- Microcytic hypochromic anaemia with increase serum Fe has been reported by Millard (1966)

5. Localized Collagen Disease (Rao 1960)

6. Reaction to Bacterial Infection

- Streptococcal toxin (Mukherjee and Biswas) – Rise in mucopolysaccharides and mucoprotein – represents reactants in active stage of disease. Rise in ASO titer suggests association of streptococci as a contributing factor.
- Growth of Klebsiella Rhinoscleromatis was reported in OSMF (Sengupta 1952), suspected may be a factor.

7. Auto-Immune Basis

Incidence

- OSMF is rare in the US and is found only in the immigrant members of the South Asian population who chew betel nuts.
- Occasional cases reported in Europeans.
- Worldwide, estimates of OSMF indicate that 2.5 million people are affected, with most cases concentrated on the Indian subcontinent, especially southern India.
- The rate varies from 0.2 – 2.3% in males and 1.2 – 4.57% in females in Indian communities. OSMF is widely prevalent in all age groups and across all socioeconomic strata in India.

Pathology

The pathogenesis of the disease is not well established, but the cause of OSMF is believed to be multifactorial. A number of factors trigger the disease process by causing a juxtaepithelial inflammatory reaction in the oral mucosa.

Histopathologically, there are connective tissue and epithelial changes. In the connective tissue, there is progressive accumulation of fluid, constriction of blood vessels, hyalinization of collagen and fibrosis. The epithelium shows progressive atrophy,

Table 1: Showing Various Clinical Stages of OSMF

Sl.	STAGE	SYMPTOMS	SIGNS
01	Stage of stomatitis & Vesiculation	➢ Burning sensation ➢ Inability to eat spicy food ➢ Increase / Decrease salivation	➢ Vesicles, ulceration ➢ Granulating spots on cheek, palate, pillars
02	Stage of fibrosis	➢ Difficulty in opening mouth ➢ Difficulty in protruding tongue ➢ Difficulty in blowing out cheeks, whistling ➢ Nasal twang of speech – Rhinolalia aperta (Decrease palatal movements)	➢ Vesicles on soft palate, anterior pillar, buccal mucosa, mucosa of lips ➢ Vesicles are painful & when rupture leave superficial ulcers ➢ Culture of fluid from vesicles is sterile
03	Stage of sequelae & complication	➢ This stage is similar to stage of fibrosis ➢ Oral mucosa loses its natural suppleness	➢ Oral mucosa – whitish blanched or mottled ➢ Soft palate – Whitish. Decrease mobility. ➢ Fibrous bands originates from Pterygomandibular ➢ raphe to anterior faucial pillar ➢ Trismus is seen due to contraction of fibrous tissue underneath the mucosa ➢ Faucial pillars – Thick, short & hard. Tonsils pressed ➢ between fibrosed pillars ➢ Progressive narrowing

hyperkeratosis and parakeratosis.

Pathologically, it is divided into very early, early, moderate and advanced and advanced cases.

Clinical Features

OSMF is insidious in onset. It has 3 clinical stages:

1. Stage of stomatitis and vesiculation
2. Stage of fibrosis
3. Stage of sequelae and complication

Clinical Grading of OSMF

- *Grade I:* Only blanching of oral mucosa without symptoms
- *Grade II:* Burning sensation, dryness of mouth, vesicles, ulcers
- *Grade III:* In addition to Gr. II, restriction of mouth opening
- *Grade IV:* In addition to Gr. III, palpable fibrotic bands all over the mouth without involvement of tongue
- *Grade V:* Grade IV and involvement of tongue
- *Grade VI:* OSMF with histologically proves oral cancer

Investigations

- Complete Hemogram – Decrease Hb, Increase Eosinophils
- ESR is raised in 50% of individuals
- Serum proteins – Decrease albumin, increase Y – globulins
- Electromyography – EMG of temporalis, buccinators, etc.
- Exfoliative cytology – Morphological characteristics are examined

Modern Management

Conservative Management

- Discourage from chewing betel nut and tobacco
- Avoid spicy food and restrict chilies treat periodontal and periapical diseases and maintain oral hygiene
- Multi-vitamin (Vitamin A and B complex)
- Iron supplements Systemic corticosteroid therapy
- Use of topical analgesics and anaesthetics to control the pain and burning sensation symptomatically
- Topical application of Triamcinolone acetomide 0.1% with neomycin
- Betnosol 0.5 mg tablet dissolve in water and use for gargle

Submucosal Injections

- Fibrinolysin
- Gold
- Vitamin A and D
- Corticosteroids
- Steroids –
  - √ Cortisone 20 mg / 100 mg daily for a total 1500 – 2500mg can be given orally/parenterally
  - √ Hydrocortisone with lignocaine is most effective in early/moderate advanced cases
- Hyalase – Hyaluronic acid decreases fibrinogenesis
  - √ 1500 i.e. of Hyalase + 1 ml of 2% lignox – Twice weekly for 3 weeks
  - √ 1500 i.u. of Hyalase + 4 ml of Dexamethasone – Twice weekly for 7 weeks.
- Placental extract & dexamethasone – Temporary improvement
- POTABA – Potassium Amino Benzioc Acid – It decreases collagen formation and intern decreases fibrosis.

Surgical Treatment

Indications

- Severe trismus
- Dysplastic / neoplastic changes

Surgical Techniques

- Excision of fibrotic bands with split thickness skin grafting
- Excision of fibrotic bands with split thickness skin grafting with bilateral temporalis myotomy or coronoidectomy
- Excision of fibrotic bands with reconstruction Prognosis
- No definite cure and management is available for OSMF. Only symptomatic relieving measures should be done.
- Biopsy is to confirm the diagnosis and early identification of dysplasia.
- Cases with dysplasia to be managed along with the line of management as CA in situ.
- Non-dysplastic / mildly dysplastic cases must be kept under long term observation with necessary preventive measures.

Classical Approach

The explanation of oral submucosal fibrosis doesn't exactly correlate with the any of the disease explained in classics. Some of the clinical features of *Taalukacchapa* explained by *Sushruta* and *Vaagabhata* in the context of *Taalugataroga.*

कूर्मोत्सन्नो अवेदनोशीघ्रजन्मारक्तज्ञेयः
कच्छपः श्लेष्मजा स्यात् ।
सु.नि.16/43

कच्छपः कच्छपाकारश्चिरवृध्दिः कफादरूक् ।।
अ.हृ.21/39

• According to *Sushruta* – The vitiated *Kapha Dosha* causes painless, slowly progressive elevation like that of back of tortoise.[5]

• According to *Vaagabhata* – The vitiated *Kapha Dosha* causes a swelling in *Taalu* resembling the back of tortoise which will be slowly progressive, painless and which will not undergo *Paaka.*[6]

• As per *Zakir Hussain* and *Sasi Kumaran Nair* – OSMF is correlated with *Vidaari* of Kanthagata Roga.

सदाहतोदं श्वयथुं सरक्तमन्तर्गले पूतिविशीर्णमांसम् ।
पित्तेन विद्याद् वदने विदारीं पार्श्वेविशेषात् स तु येन शेते ॥
सु.नि.16/62

Vitiated *Pitta* causes burning sensation and pricking sensation in either side of *Gala.* It will be associated with reddish foul smelling lacerated fleshy swellings. Such type of swellings develops in persons who are morehabituated to sleep in particular lateral side.[7]

- Critical Analysis On *Sushruta* – OSMF is a condition with severe pain, burning sensation, trismus in the oral cavity & with no swelling. But, Sushruta has mentioned the features like painless swelling resembling the back of tortoise, that to any one side towards which the person is habituated to sleep.
- Critical Analysis On *Vaagabhata* – Apaaka is additional feature given by *Vaagabhata.* But in OSMF, *Paaka* is markedly found in first two stages of disease.
- Critical Analysis On *Zakir Hussain* & *Sasi Kumaran Nair* – OSMF is a condition which slowly progresses in the buccal cavity mucosa evenly. It does not have any relation with the habit of the person sleeping in that particular side. In OSMF no reddish foul smelling lacerated fleshy swellings are found.

Hence, by considering all above points, we can conclude that, OSMF as a whole disease is not mentioned under one heading like *Taalukacchapa, Vidaari,* etc. But, the clinical features of OSMF might be explained in the context of various diseases.

Matsyaakshi (*Alternanthera sessilis*)

Botanical name: Alternanthera sessilis (Linn.)

Family: Amaranthaceae

Sanskrit synonyms: Matsyaksi, Matsyagandhaa, Matsyaadini, Minaakshi, Bahli, Gandali, Gartkalambukaa, Vaahlikaa, Matsyaakshika

Properties

- Rasa: Tikta, Kashaya, Madhura
- Guna: Guru, Snigdha
- Veerya: Sheeta
- Vipaka: Madhura

Distribution

Throughout India in moist places, growing wild and often cultivated. Occurs in diverse ecological niches from ponds to dry roadsides. Available throughout the year in wet places and during summer, it is absent from dry places.

Plant Description

A profusely branched prostrate herb, grows spreading over ground; leaves simple, opposite, fleshy, lanceolate, linear-oblong, acute, sometimes obtuse, glabrous, shortly petiolate; flowers small, white, in axillary clusters; fruits compressed obcordate urticles, seeds sub-orbicular and small.

Medicinal Properties

Plant pacifies vitiated kapha and pitta, burning sensation, diarrhea, skin disease, dyspepsia, hemorrhoids, liver and spleen diseases and fever.

Useful Part

Whole plant.

Chemical Contents

Young shoots contain protein 5% and iron 16.7 mg/100 g. Leaves also contain a good amount of alpha- and beta-tocopherols. The plant gave stigmasterol, betasitosterol, a saturated aliphatic hydrocarbon and aliphatic ester.

It is rich in anti-oxidant b-carotene and Vitamin C.

Sitosterol, campesterol, a-spinasterol, Oleanolic acid, rhamnoside, 24-methylene cycloartenol, cycloeucalenol, lupeol, 5-astigmasta-7-enol and its palmitate.

Phytochemical studies yielded B-carotene, ricinoleic acid, myristic, palmitic, stearic, oleic and linoleic acids, a-spiraterol, uronic acid, and B-sitosterol.

Study of phenolic and flavonoid content revealed: total crude phenolic content, 1.529; total phenolic acid, 1.404; and flavonoids, 0.370 (values in mg/g dry wt.).

Toxicology

No adverse effect has been reported on the use of this plant as medicine or food.

Indications

The herb is used as a galactagogue, cholagogue, abortifacient and febrifuge. The leaves are used like spinach, and in soups. Applied externally on acne and pimples.

Dosage

Whole plant— 2–6 g powder. (API Vol. II.)

Parts Utilized

Entire plant; use fresh.

May be collected the whole year round.

Properties

Slightly tart tasting, cooling, antiphlogistic, analgesic, antidermatosis, antiseptic.

Considered febrifugal, galactagogue, abortifacient.

Uses

Edibility

- Some places, leaves and young shoots eaten as vegetables
- In Ceylon, largely eaten as vegetable
- In Africa, used for relishes, sauces and soups
- Considered a famine plant

Folkloric

- Poultice of pounded fresh material to sprains, burns & eczema
- Carbuncle, erysipelas
- Used as a wash for eyes
- In other countries, used for treating acne vulgaris, dyspepsia, liver problems
- Decoction used for nausea, vomiting, diarrhea, dysentery, cough, bronchitis and diabetes
- In West Tropical Africa, used as poultice for boils
- In Sri Lanka, used for cystitis, gonorrhea, snake bite. Also, used by mothers to increase flow of milk
- In Ghana, salted decoction used for hemetemesis
- In India, used for gastrointestinal problems; also as cholagogue, abortifacient, febrifuge & even used for snake bites
- In Nigeria, for headaches and vertigo
- In Taiwan, for hepatitis, bronchitis, asthma

Others

Used for animal feed supplement. In many places of the world, the leaves of *Alternanthera sessilis* are eaten as a cooked vegetable or raw as a salad.

Research Studies

- *Antimicrobial/Wound Healing Activities:* Study on extract of leaves showed significant results in different parameters of wound healing. The presence of sterols was also confirmed.
- *Hepatoprotective:* A study on the hepatoprotective effects of Taiwanese herb Alternanthera sessilis on liver damage induced by various hepatotoxins showed hepatoprotective effects with a reduction of elevation of SGOT and SGPT .
- *Ionone Derivatives/Antimicrobial:* Chloroform extract of dried leaves yielded a mixture of diasteromers of a new ionone derivative with low activities against Pseudomonas aeruginosa and Trichophyton mentagrophytes.
- *Antioxidant:* (1) Study showed ethanol extract to have 70% free radical scavenging activity. (2) Study concludes Alternanthera sessilis showed potent radical-scavenging activity and metal ion chelating activity.
- *Antidiabetic:* Study of aqueous extract of aerial parts showed significant dosedependent antidiabetic activity with lowering of blood glucose concentration, glycosylated hemoglobin, LDL, total cholesterol.
- *Antibacterial:* The antibacterial effect of leaves and internodal-segments derived calli of A. sessilis was evaluated against Proteus vulgaris, Strep pyogenes, B subtilis and Salmonella typhi. the ethanolic extracts of leaves and leavesderived calli were more effective against the selected bacterial than other solvents. Plants extracts showed antibacterial activity against Gram negative P.aeruginosa and Gram positive Staph epidermis.
- *Hematinic Activity:* Study showed that *Lupo* (A. sessilis) has hematinic activity particularly in iron deficiency anemia. Results suggest AS is a potential drug for augmentation of hemoglobin and serum ferritin in iron deficiency anemia.
- *Antipyretic Activity:* Study showed the ethanol extract of aerial parts of Alternanthera sessilis has dosedependent antipyretic activity.
- *Antibacterial / Antifungal:* Plants extracts showed antibacterial activity against Gram negative P. aeruginosa and Gram positive Staph epidermis. Plant also showed antifungal activity against yeasts S. cerevisiae and Candida albicans.
- Immunomodulatory effect is studied *in vitro*

Folklore Practice

People who perform the courageous and astonishing acts performed as street players in rural area use this plant. Brittle stones and bricks are chewed causally like soft cake. They do such activities after chewing leaves of Matsyaakshi. It makes the oral cavity painless.

This concept was taken into consideration and used in OSMF, where patient experiences severe pain and burning sensation even for taking regular food.

Discussion

The OSMF is a disease of unknown origin and with poorly understood histopathology. The clinical features of OSMF includes burning sensation in oral cavity, trismus, sensitivity to sour, bitter, salty, etc irritants, restricted angle of oral cavity, etc. debilitates the patients general health and physical condition.

The cases in which tongue is also involved

will hamper the appreciation of food and its taste. Lack of proper appreciation leads to hypostimulation of superior and inferior nuclei which controls the submandibular, sublingual and parotid glands intern hampers the digestion.

Matsyaakshi is rich in b-carotene, Vitamin C, and Iron. It has several properties like cooling, analgesic, antidermatosis and antiseptic. It is immune-modulator, antimicrobial, antifungal, analgesic, antipyretic, antioxidant, hematinic & hepatoprotective.

As a folklore practice, this drug can be used to relieve the pain (trismus) and burning sensation in OSMF. But, its pain relieving action is still obscure.

Matsyaakshi is widely available in India as a weed. It is used as a food and medicine which is in practice since long time with no known side effects.

Conclusion

- Utility of Matsyaakshi in OSMF to control pain as an adjuvant therapy.
- This drug might help to improve taste perception, subsequently the digestion of patient improves, also may help in improving general well being of the patient.
- This drug is immune-modulator and rich source of micronutrients, antioxidants, iron Vitamin A and Vitamin C, hence may improve health of oral mucosa.
- This is drug is proven as antimicrobial and antifungal. Thus, cleans up the oral cavity and reduces the irritation of mucosa due to stasis of saliva, which contributes in continuation of pathophysiology of OSMF.

Suggestions & Scope for Furtue Studies

- Detail clinical study is required on large sample to conclude its effect in OSMF
- The additive effect of the drug can be studied on various parameters like body weight, physical well being of the patient.

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