USE OF AMOROLFINE IN CANDIDA- ASSOCIATED DENTURE STOMATITIS

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Abstract

Denture stomatitis (DS) is an inflammatory lesion, in which there is redness of the oral mucosa underneath a removable denture. Although Candida albicans is a component of normal microbial flora, local and systemic factors can cause opportunistic infections. Poorly fitting or unhygienic dentures leads to the presence of yeasts attached to it., and cause inflammation. Treatment procedures include correction of ill-fitting dentures, plaque control, and topical and systemic antifungal therapy. Nystatin and Amphoteresin B are used topically as suspension. Since candidiasis is highly resistant to antifungal agents, systemic usage of ketoconazole, fluconazole or itraconazole are necessary. But the systemic use of these drugs can cause side effects like liver toxicity, drug interactions etc. Lucio; Lorengo etal had conducted a study of the efficacy of amorolfine antifungal varnish, by local application, and found that it suppresses the nystatin resistant Candida associated denture stomatitis.

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Introduction

Denture sore mouth [Denture Stomatitis (D.S.)] is an inflammation of the denture bearing area with or without cracking and inflammation of the oral commissures. Though D.S. can be trauma induced, most of them are candida related. Candida fungi are opportunistic pathogens commonly found in the oral cavity of asymptomatic individuals. In health and in a normal local environment, the host defence system prevents overt infection[1]. Local and systemic factors can cause transformation of this commensal pathogenic organism. The most frequent cause of opportunistic infection by Candida is poorly fitting or uncleaned dentures which leads to presence of yeasts attached to it.

Risk factors associated with oral candidiasis and D.S are wearing complete (in contrast to partial) dentures, wearing a maxillary (in contrast to a mandibular) removable denture, inadequate denture hygiene, nocturnal denture wear, poor denture quality, diabetes mellitus, antibiotic therapy, immune deficiencies, Vitamin A, folate and iron deficiencies,

impaired salivary gland function, Xerogenic medication, tobacco use, decreased salivary secretion rate and gender.

Discussion

Based on the clinical appearance and natural history of the infection, Lehnar has classified oral candidiasis as follows [2]

- **I. Acute**
  - **(a) Acute pseudomembraneous candidiasis(thrush)**
  - **(b) Acute-atrophic Candidiasis-Antibiotic sore-mouth .**
- **II Chronic**
  - **(a) Chronic-atrophic Candidiasis**
    - **(1) Denture-Stomatitis (Denture-sore mouth)**
    - **(2) Angular chelitis**
    - **(3) Medianrhomboid glossitis**
  - **(b) Chronic-hyperplastic candidiasis**

Newton has classified Denture- sore mouth as [3]

- **(1) A localized simple inflammation or pin point hyperemia**
- **(2) A more diffuse erythema involving a part or the entire denture covered mucosa and**
- **(3) A granular type (papillary hyperplasia)commonly involving the central hard palate and alveolar ridges**

Unclean and poor hygiene are the major predisposing factors. The tissue surface of the dentures usually shows micro pits and microporosities, that harbour microorganisms, that are difficult to remove mechanically or by chemical cleaning. Soft liners in dentures provide a porous surface and opportunity for additional mechanical locking of plaque and yeast, to the appliance. Denture sore mouth is rarely found under the mandibular denture.

Epinoza, Rojan etal had found that individuals who wore complete dentures, day and night had more D.S, than those who wore them only when awake.[1] They explained that it may be because when the dentures are worn in this fashion, the beneficial effect from the saliva[4] are not present. Salivary components and the cleaning action of tongue are a part of the host defense

balance. The isolation of oral tissues under a denture, especially a large area under a complete maxillary denture, that seals and forms its own microenvironment represents a local alteration that disturbs the normal balance. Schulman, Revera etal in their study showed that the more surface area covered by the denture the greater the likelihood of D.S.[1]

Clinical features

The mucosa beneath the denture become red, swollen, smooth or granular and painful. Multiple pin point foci of hyperemia, frequently occur. A burning sensation is common. The redness of the mucosa is sharply outlined and restricted to the tissue actually in contact with the denture.[5]

Diagnosis

The diagnosis of the candida associated denture stomatitis is confirmed by the finding of mycelia or pseudohyphae in a direct smear or the isolation of candia species in high numbers from the lesions.[3]

Preventive measures and Treatment

Since the cause of the denture stomatitis are different, several treatment procedures are to be followed, like correction of ill –fitting dentures, plaque control and topical or systemic antifungal therapy.

Rough areas on the tissue surface of the denture should be smoothened. About 1mm of the internal surface, being penetrated by the organisms, may be removed and relined with a soft tissue conditioner. A new denture should be given only when the mucosa has healed properly.

The denture must be cleaned thoroughly and left out of the mouth and kept in hypochlorite or chlorhexidine solution at night.

For the treatment of candida associated denture stomatitis, a topical and/ or systemic approach can be used. Polyene agents(eg. nystatin, amphoteresin B) and azole antifungals (eg. Miconazole, ketoconazole, fluconazole, itraconazole) are the drugs most commonly used.[6] Budtz Jorgensen and Bertran had reported significant therapeutic effects on denture stomatitis by antifungal therapy.[5]

Nystatin tablets 500,000 units were allowed to dissolve in the mouth three times a day for 14 days. Bergendal and Isacsson reported similar results by treating D.S with nystatin powder, placed on the fitting surface of the denture , three times a day for 14 days.[5] Nystatin is

formulated for oral use as suspension or pastille.

Amphoteresin B is available as an oral suspension, for the management of the oral candidiasis. Since the absorption of the polyne agents nystatin and amphoteresin by gastrointestinal tract is poor, multiple daily doses are necessary to adequately expose the yeast to the drug.[7]

A miconazole varnish or gel can be topically administrated in denture related stomatitis . A once daily application of the miconazole varnish or a thrice daily application of the miconazole gel for 15 days is sufficient.[8]

Because the biofilm formation in candidiasis is highly resistant to antifungal agents, systemic ketoconazole, fluconazole or itraconazole can be used. Since ketoconazole is absorbed by GIT, systemic therapy by oral route is possible. Since acidic environment is required for proper absorption, patients must not take antacids, or H_2 blocking agents. Ketoconazole administration for more than 2 weeks can cause idiosyncratic liver toxicity. So it should not be used as an initial therapy for the routine oral candidiasis. Ketoconazole has been implicated in drug interactions., with macrolide antibiotics (e.g.erythromycin), and the antihistamine astemizole, all of which may produce potentially life threatening cardiac arrhythmias.

Fluconazole is well absorbed systemically and an acidic environment is not required. Liver toxicity is rare. But resistance to drugs seems to develop in some instance. Drug interaction include a potentiation of the effect of phenytoin, warfarin compounds (anticoagulants) and oral hypoglycemic agents.

Itraconazole has an efficiency equivalent to that of fluconazole, but drug interactions are possible with astemizole, triazolam, midazolam and cisapride.[9]

Lucio Milillo, Lorengo etal in 2005 had conducted a study of the efficacy of amorolfine antifungal varnish in Candida related denture stomatitis. They had done this to avoid the use of systemic antifungal agents in nystatin resistant cases. Amorolfine varnish is a medicine used in the topical treatment of onychomycosis caused by dermatophytes, yeasts and moulds. The varnish contain 5% w/v amorolfine (as hydrochloride) as active ingredient in an ethanol base. The active substance Amorolfine, belongs to the morpholine derivatives class of antifungal substances. Its antifungal and fungistatic effect is based on an alteration of the fungal cell

membrane, targeted primarily on sterol biosynthesis. The ergosterol content is reduced, and at the same time unusual, sterically nonplanar sterols accumulate. The ingrediants of locetar 5% varnish are, amorolfine chloride, copolymer of methacrylic acid, triacetin, butyl acetate, ethyl acetate and ethyl alcohol.[8] Triacetin or glyceryl tri acetate is a cosmetic biocide, plasticizer and solvent used in cosmetic formulation. It is a commonly used carrier for flavours and fragrances. Triacetin is a safe human food ingredient according to the food and drug administration(FDA) and appears not to have any potentially dangerous effects. Butyl acetate is a colourless and volatile liquid, used as an industrial solvent in the production of essences, lacquers, photographic films and finger nail varnish. It is characterized by low systemic toxicity, but possible symptoms include mucosal irritation, headache, mental confusion, nausea, vomiting, and cough. Ethyl acetate is an inflammable solvent(soluble in water and oil) irritating to the eyes, respiratory tract and skins. It has been associated with an increased rate of lymphatic leukemia, in rubber workers, who are heavily exposed.

Amorolfine has a broad antifungal spectrum in vitro. It is effective against

Dermatophytes:
Tricophyton,Microsporum, Epidermophyton

Yeast : Candida, Malassezia or Pityrosporum, Cryptococcus.

Moulds: Alternaria, Hendersonula, scapulariopsis, Scytalidium, Aspergillus.

Dermatiacea : Cladosporium, Fonsaceae, Wangiella.

Dimorphic fungi : Coccidioides, Histoplasma, Sporothrix

With the exception of Actinomyces, bacteria are not sensitive to Amorolfine

Contraindications

The varnish must not be reused by patients who have shown hypersensitivity to any ingredient of the product. No experience exists with pregnancy and nursing. Therefore the use of the varnish should be avoided during pregnancy and lactation.

Side effects such as itching and complications such as allergic contact dermatitis, had been reported.

The amorolfine varnish was used by Lucio Milillo, Lorenzo etal in the following manner. It was applied to the fitting surface of denture, once or twice a week for 6 months. Before varnish was

applied, the surface of the prosthesis was carefully cleaned with gauze soaked with ethyl acetate solvent to remove any trace of varnish from the preceding application . After the treatment, all patients were subjected to examination of the palatal mucosa and quantitative culture of candida from the palatal mucosa and denture fitting surface. The results showed that it was able to suppress the nystatin – resistant denture related stomatitis by using amorolfine varnish.

Surgical elimination of deep crypt formation in the type III denture stomatitis usually is a pre requisite for the effective mucosal hygiene. This could preferably be achieved with cryo surgery.

Summary and Conclusion

Denture stomatitis, an inflammatory lesion found in many people is due to trauma or candida related by the use of unhygienic denture. Though Candida albicans is a component of normal oral microflora, local and systemic factors can transform this to a pathogen. Management of D.S depends on accurate diagnosis, identification and elimination of predisposing factors and often use of antifungal agents. Topical application of nystatin, amphoteresin, miconazole etc: are effective in many cases. Because the biofilm formation in candidiasis is highly resistant to antifungal agents, systemic ketoconazole, fluconazole, or itraconazole can be used. But these can cause drug interactions. To avoid the use of systemic antifungal agents, amorolfine varnish (which is used in the treatment of onichomycosis) was tried in nystatin resistant candia related denture stomatitis . Amorolfine in a varnish vehicle applied biweekly to the denture base, for 6 months was proved to be effective.

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