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Oral Leukoplakia and its Management

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Abstract: ***Oral leukoplakia (OL) is a premalignant lesion described as "a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion". This article aims to discuss the various treatment managements available for it.***

Keywords: leukoplakia, oral, management, premalignant lesions, surgery, malignant

1. Introduction

Oral leukoplakia (OL) is a premalignant lesion described as "a predominant white lesion of the oral mucosa which cannot be defined as any other known lesion" [(1)]. According to Warnakulasuriya et al. [(2)], the new concept of Oral leukoplakia shall acknowledge white lesions with questionable risk of being an OL, being excluded any other pathologies or known disorders which do not present potential malignant risk such as candidiasis, lupus erythematosus, lichen planus, hairy leukoplakia, frictional keratosis, nicotinic stomatitis, and leukoedema[(3,4)].Oral leukoplakiasetiopathogenesis encompasses two broad categories, as follows: Oral leukoplakia of unknown etiology or idiophatic and Oral leukoplakia associated with tobacco use [(3)]

Leukoplakia is most common premalignant, potentially malignant or precancerous lesion of the oral mucosa. The word leukoplakia is derived from two words, leuko meaning white and plakia meaning patch. Leukoplakia is usually found in between fourth to seventh decade of life, but has been found to occur in initial decades of life also. Males have been found to be more affected than females. According to Petti[(5)] et al (2003), oral pre-malignant diseases affect males at least three times as often as females. Clinically leukoplakia exhibits varying features.[(6,7)] The surface can be smooth or wrinkled, sometimes smooth surfaced lesions may be traversed by small cracks or fissures .The lesions may be white, whitish yellow or gray. The surface may be homogenous, ulcerated, or speckled. The homogenous varieties are uniformly flat and thin having shallow cracks of surface keratin giving an appearance likened to cracked mud. The non-homogenous varieties, like nodular and verrucous have irregular surfaces.

Surgical treatment of oral leukoplakia standard treatments for OL range from careful consideration to complete resection.[(8,9)] However, OL presenting low to moderate malignant risk may be either completely removed. Surgical treatment for OL may prevent the development of oral squamous cell carcinoma, provided by assuring that the resection margins are adequately thick and free of epithelial abnormalities [(9,10)] However, it has been shown that surgical intervention does not appear to prevent OL from developing recurrence [(9,10)].Malignant transformation of these lesions is independent of drug or laser therapy [(10)].

2. Incidence and Prevalence

In the year 1992, Gupta et al. found a wide range of leukoplakia prevalence in various populations. In India, leukoplakia was found in 0.2% and 4.9% of the population present over 15 years of age[(11)]. Bánóczy (1983) found that the adult population prevalence varied between 0.6% and 3.6%.[(12)] Downer and Petti found an annual oral cancer incidence rate attributable to leukoplakia between 6.2 and 29.1 cases per 100,000 people.[(13)]

Martorell-Calatayud et al. found the prevalence of OL ranges from 0.4% to 0.7% of the population.[(15)] Feller and Lemmer estimated the prevalence of OL ranged from 0.5% to 3.46%, and also found the malignant transformation of OL from 0.7% to 2.9%.[(14)]

Brouns et al. found the prevalence of OL is approximately 2% with an annual malignant transformation of approximately 1%.[(16)]

3. Management of Oral Leukoplakia

Surgical Treatment still remains one of the most common treatment methods in OL and should be the method of choice in OL with histologically diagnosed epithelial dysplasia. [(17)]

Surgical treatment includes conventional surgery, electrocoagulation, cryosurgery, and laser surgery (excision or evaporation). [(19)]

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Laser:
Carbondioxide laser has been recommended to treat benign oral lesions as well as premalignant lesions such as OL (26, 27, 28). The treatment of OL using CO2 laser can be best obtained by ablation or vaporization of the lesion. Ablation being done at defocused mode (achieved by moving the laser away from the tissue and beyond its focal length), reduces the power and depth of penetration of the laser beam (200-400 lm per pass), limiting the destruction to the epithelium and hence resulting in lesser pain, swelling and

even scarring with better regain of elastic property of the tissue (29).

Non-Surgical Treatment of Oral Leukoplakia

1. Carotenoids

Carotenoids belong to a group of highly hydrophobic molecules with little or no solubility in water. [20,21]

1.a. Beta-Carotene

Beta-carotene is a vitamin A precursor.[18,20] This carotenoid is commonly found in dark green, orange or yellowish vegetables, such as spinach, carrots, sweet potato, mango, papaya, and oranges. [21]

The use of beta-carotene has been recommended for the prevention of potential malignant lesions, such as OL and cancer, possibly oral cancer. The potential benefits and protective effects against cancer are possibly related to its antioxidant action. [20]

This function is accomplished through a ligation be- tween beta-carotene and oxygen, which is an unstable re- active molecule, thus diminishing the damaging effects of free radicals. [21]

It has been shown that beta-carotene has a better therapeutic clinical response in preventing oral leukoplakia lesions in smokers than in nonsmokers.

A known side effect of excessive beta-carotene consumption is a change in skin colour, which becomes very yellowish, called carotenoderma, which disappears in a few weeks after the reduction of consumption. [20]

Some studies report that clinical resolution of oral leukoplakia ranges from 4% to 54%, with dosages regimes from 20 to 90mg/day of beta-carotene in time periods from 3 to 12 months. [18,20]

1.b. Lycopene

Lycopene is a fat-soluble red pigment found in some fruit and vegetables. [18] The greatest known source of lycopene is tomatoes. [21]

Some authors tried to estimate the relation between nutrient intake and prevalence of oral leukoplakia. They observed that tomato consumption, the main source of lycopene, has the most protective effect on oral leukoplakia among all dietary factors. [21]Lycopene is better absorbed in oil resin capsules and in tomato juice than in the form of raw tomatoes. [21]

A study evaluated lycopene in oral leukoplakia for a three months period, with dosages regimes from 4mg/day and 8mg/day and patients had clinical resolution 25 and 55%, respectively. [18]

2. Retinoic Acid (Vitamin A)

The current definition of retinoid includes all the natural and synthetic compounds with an activity similar to that of Vitamin A. Vitamin A exists in the human body as various interconvertible compounds, notably retinal (essential for vision) and retinol, which is the most potent analogue and the main form of storage and transportation [22,23]

3. Bleomycin

Bleomycin, a cytotoxic antibiotic, was first used for the treatment of neoplasms of the penis and scrotum, but has also been employed for squamous cell carcinoma of the head and neck region, oesophagus, and skin [24]. The most commonly adverse effects are mucocutaneous reactions, which include stomatitis, alopecia, pruritic erythema, and vesiculation of the skin [22]. Eight patients with OL were treated by the daily application of a 0.5% (w/v) solution of bleomycin sulphate in dimethyl sulphoxide (DMSO). After 12 to 15 applications, the white patch peeled off and the resultant raw surface was epithelialized over the following 14 days. Repeated biopsies showed a significant reduction of dysplasia and keratinisation [22]. The use of topical 1% bleomycin in DMSO was evaluated for the treatment of dysplastic OL. Bleomycin was applied once daily for 14 consecutive days to lesions of the oral mucosa in 19 patients. It was well tolerated with minor mucosal reactions. Immediate posttreatment biopsies showed that 75% of patients had resolution of dysplasia. 94% of the patients attained at least partial clinical resolution. After a mean follow-up period of 3.4 years, 31.6% of patients had no clinically visible lesions. In 2 patients (11%), malignant transformation occurred[25].

4. Conclusion

Cessation of smoking should be highly recommended to prevent further complication of the lesion. It is understood that various treatment modalitiesare available for the management of oral leukoplakia ,but in cases of dysplastic changes surgical management remains to be the primary choice and regular follow up is required even if there is complete clinical resolution of the lesion.

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