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Original Article

Comparison of curcumin with intralesional steroid injections in Oral Submucous Fibrosis – A randomized, open-label interventional study

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ABSTRACT

Introduction: Oral Submucous Fibrosis (OSMF) is precancerous condition caused by areca nut chewing characterized by restricted mouth opening, burning sensation and stiffness & blanching of oral mucosa. Complete regression of the condition had not been achieved in all cases with any of the present treatment regimens. Curcumin is (diferuloylmethane), a yellow pigment in curry powder, exhibits anti-oxidant, anti-inflammatory, and pro-apoptotic activities. Hence an interventional study was undertaken to establish the efficacy of curcumin in OSMF patients.

Settings & design: A randomized open label, interventional study was conducted in forty patients with clinically and histologically proven Oral Submucous Fibrosis.

Materials & methods: Forty patients with clinically and histologically proven Oral Submucous Fibrosis were selected for the study and were randomly divided into 2 groups. The first group was treated with weekly intralesional injection of 4 mg Dexamethasone & 1500 I.U Hyaluronidase and the second group by oral administration of two Curcumin tablets (Turmix 300 mg) per day for 3 months each. Improvement of burning sensation, interincisal distance and tongue protrusion was evaluated on a weekly basis.

Results: Burning sensation improved in both the groups from early to late stages. Complete resolution of burning sensation was noted with turmix. The mean increase in interincisal distance was 3.13 mm and 1.25 mm respectively in groups 1 &2. The interincisal distance improved in both the groups, with significant results at the end of first month. Tongue protrusion showed greater recovery at the end of 1st month in group 1 when compared with group 2.

Conclusion: Turmix is beneficial and effective in reducing burning sensation in early OSMF patients.

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Key message

In the earlier studies, Curcumin had not been compared with intralesional steroid therapy in OSMF patients. This study encourages the use of curcumin as it effectively reduced burning sensation and also improved the mouth opening.

1. Introduction

Pindborg has defined Oral Submucous Fibrosis (OSMF) as "an insidious chronic disease affecting any part of the oral cavity and occasionally extending to the pharynx and esophagus, although, occasionally preceded by and/or associated vesicle formation. It is always associated with juxta-epithelial 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".[1] The prevalence in India had increased in the recent years to 6.42% with a higher predominance in the southern parts of the subcontinent.[2] OSMF is seen commonly in males between 20 and 40 yrs age. The common sites involved are labial mucosa, buccal mucosa, retromolar pads, soft palate and floor of the mouth. Fibrotic changes of the pharynx, esophagus and paratubal muscles of eustachian tubes had been reported.[2] Early features of OSMF include burning sensation, hypersalivation/xerostomia and mucosal blanching with marble like appearance. The mucosa later becomes leathery and inelastic with palpable fibrous bands resulting in restricted mouth opening. Eventually, OSMF leads to restriction of tongue movements, difficulty in swallowing, speech & hearing defects and defective gustatory sensation.[3]

The etiopathogenesis of OSMF is complex and incompletely understood. Oral Submucous Fibrosis is a potentially malignant disorder attributed to areca nut (betel nut) chewing. The other proposed etiological factors include excessive chilly consumption, vitamin B and iron deficiency, autoimmunity, genetic and environmental factors.[2–5] Areca nut consists of alkaloids like arecoline, arecaidine, guvacine and guvacoline apart from flavanoids, tannins, catechin and copper. The alkaloids stimulate the fibroblasts to produce more collagen, while its structure is stabilized by catechin and tannins. The increased crosslinkage of collagen results from upregulation of the copper dependent enzyme lysyl oxidase.[4,5] Documented evidence favors areca nut as the main etiological agent owing to cytotoxic, apoptotic and proliferative effects. The cytotoxic effects, in addition to the release of free radical induced mutations by areca nut, induces genotypic & phenotypic alterations, a key point in the pathogenesis of OSMF.[6] Apart from areca nut, commercial products like gutkha, mawa and pan masala have been shown to cause OSMF rapidly due to larger amounts of areca nut in these processed products and/or the synergistic action of nicotine over arecoline.[6–8] The ideal goals of therapy of this potentially malignant disorder include not only amelioration of the symptoms (burning sensation, restriction of mouth opening), but also stop further disease progression and malignant transformation. Complete regression of this mucosal condition had not been achieved in any of the case studies reported till date, despite the number of drugs or interventions tried, hence an attempt at finding a permanent cure is still going on.[6,9,10]

Plants have been widely used as medicinal cure since ancient times among which Turmeric had always occupied an important place.[11] Turmeric (the common name for *Curcuma longa*) is an Indian spice derived from the rhizomes of the plant and is used in Ayurvedic medicine to treat inflammatory conditions. The primary active constituent of turmeric 'Curcumin' (diferuloylmethane), had been identified in 1910 by Lampe, Milobedzka.[12] Curcumin is a pleiotropic molecule that targets molecular mediators of inflammation. It had been widely used in inflammatory bowel disease, pancreatitis, rheumatoid arthritis, etc. with good results. The medicinal activity had been attributed to various pharmacological activities, including antioxidant, antimicrobial, pro-apoptotic and anti-inflammatory effects.[12,13] Zhang SS et al have demonstrated antifibrotic activity of curcumin on human myofibroblasts and suggested that it may be of use in the treatment of OSMF.[13]

It may hence be hypothesized that the anti-inflammatory, antioxidant and antifibrotic properties of curcumin acting simultaneously, may interfere with the progression of OSMF at multiple stages in the pathogenesis of this complex disease. These invaluable properties of a commonly available, well tolerated, house hold ingredient with a non invasive route of administration prompted us to undertake this study. Intralesional steroid therapy in the management had been well documented and accepted for its beneficial effects.[9,10,14] However, Thakur N et al report that management of OSMF by various surgical and intralesional injections results in scarring and fibrosis in the long term.[6]

Hence, the current study was undertaken to assess the efficacy of curcumin in OSMF by comparing it with the most accepted therapy viz. intralesional steroid injections.

2. Materials and method

2.1. *Study design*

A randomized open label, interventional study was conducted in forty patients with clinically and histologically proven Oral Submucous Fibrosis.

2.2. *Subjects*

Forty OSMF patients attending dept. of Oral Medicine & Radiology, Career Dental College, over a period of 8 months, were included in the final study as shown in Fig. 1. Institutional ethical clearance for the study was obtained. Informed consent was taken from all the study participants. Diagnosis and clinical staging of OSMF was based Khanna & Andrade classification.[15]

2.3. *Inclusion & exclusion criteria*

Patients within the age group of 20–40 years, with a histological diagnosis of OSMF were included in the study. Patients