

Original Article

Role of Copper in the Pathogenesis of Oral Submucous Fibrosis: A Comparative Study

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ABSTRACT:

Background: Oral submucous fibrosis (OSMF) is a chronic debilitating disease and a premalignant condition of the oral cavity. Copper content of areca nut was found to be more than the content in nuts in snacks consumed by the population. Hence; we planned the present study to assess the mucosal copper levels in OSMF patients. Hence; we planned the present study to assess the mucosal copper levels in OSMF patients. **Materials & methods:** We planned the present study for assessing mucosal copper levels in OSMF patients. We included a total of 20 OSMF patients and 20 normal controls were included in the present study. Estimation of the copper content was achieved by the colourimetric method. We analyzed all the results by using SPSS software. **Results:** Mean mucosal copper levels among OSMF patients were found to be significantly higher in comparison to the normal controls. **Conclusion:** In the pathogenesis of oral submucous fibrosis, copper does play a significant role.

Key words: Copper, Oral submucous fibrosis.

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INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic debilitating disease and a premalignant condition of the oral cavity.¹⁻³ Of late, a renewed interest in the role of copper as a mediator of fibrosis in OSMF has been postulated. Trivedy et al. have carried out a series of studies on the estimation of copper in areca nut, in sera and tissue of OSMF patients. Copper content of areca nut was found to be more than the content in nuts in snacks consumed by the population. When whole saliva from volunteers chewing pan parag (a proprietary form of areca with additives) was analyzed copper concentrations were found to be high, indicating release, and absorption of copper.⁴⁻⁷ Hence; we planned the present study to assess the mucosal copper levels in OSMF patients.

MATERIALS & METHODS

We planned the present study in the department of oral medicine and radiology of the medical institute and included assessment of mucosal copper levels in OSMF patients. We included a total of 20 OSMF patients and 20 normal controls were included in the present study. Exclusion Criteria for the present study included:

- Patients with history of previous treatment for OSMF,
- Patients with history of any systemic diseases such as diabetes, hypertension, anemia, jaundice, liver or

kidney disorders or any other were excluded from the study.

- Patients with history of any known drug allergy

Ethical approval was taken from institutional ethical committee and written consent was obtained after explaining in detail the entire research protocol. We took an incisional biopsy was taken of representative part of oral mucosa of patients. For the copper estimation a dilution in the ratio of 1:1 of the solution was used. Estimation of the copper content was achieved by the colourimetric method. The absorbance of these samples was compared to that of the standard solution provided in the kits at 578 nm in a digital photometer. We analyzed all the results by using SPSS software. Chi-square test was used to compare the mean scores among the study groups. P-value of less than 0.05 was taken as significant.

RESULTS

We conducted the present study in the department of oral medicine and radiology and included assessment of mucosal copper levels in 20 OSMF patients and 20 controls. Mean mucosal copper levels in the OSMF patients was 2.85 µg/gm, while among normal controls, mean mucosal copper levels were found to be 4.71 µg/gm. Mean mucosal copper levels among OSMF patients were found to be significantly higher in comparison to the normal controls.

Table 1: Comparison of mucosal copper concentration ($\mu\text{g}/\text{gm}$) observed in 20 Normal Control (NC) and 20 patients of OSMF.

GROUPS	NO. OF SPECIMENS	MUCOSAL COPPER LEVELS		P- value
		MEAN	S.D	
NC	20	2.85	0.66	0.03*
OSMF	20	4.71	0.61	

NC: Normal control

*: Significant

DISCUSSION

In the present clinical study, we observed that a significant difference exists in the mean mucosal copper levels in OSMF patients and normal control. Srilekha et al evaluated the level of copper, zinc and copper zinc ratio in serum of patients containing OSMF and to evaluate whether copper and zinc could be used as prognostic indicators in the development of OSMF. 60 age and sex matched individuals of OSMF and healthy controls were taken for this study. Under aseptic precautions 5 ml of venous blood was collected and serum copper and zinc level were estimated by spectrophotometric method. From the results, they concluded that that copper and zinc deficiency develop in OSMF. Copper and zinc level have important causative role in OSMF. Serum copper and zinc level are sensitive, but not specific, whereas serum copper zinc ratio is the most reliable indicator in assessing progression of malignancy. Though the trace elements are required in minimum quantity, their amount is necessary for the functioning of the body. This study indicates that the Copper / zinc ratio can be used as a reliable bio marker for the detection of Oral Cancer.⁸ Shetty et al evaluated the levels of copper, zinc and iron in saliva of patients with oral leukoplakia, oral submucous fibrosis and oral squamous cell carcinoma. There was a highly significant increase in the level of salivary copper in oral submucous fibrosis patients when compared to controls ($P = 0.001$). Salivary copper levels were also elevated in oral leukoplakia and oral cancer patients ($P = 0.01$). There was a significant decrease in the salivary zinc levels in all three study groups when compared to controls ($P = 0.001$). A highly significant reduction in salivary iron levels was noticed oral submucous fibrosis group. The copper to zinc ratio significantly increased in all the study groups when compared to controls. Results suggest that salivary copper zinc and iron could be used as biomarkers for oral precancer and cancer.⁹ Singh et al estimated tissue copper level in OSMF patients with habit of areca nut chewing and to correlate any change in tissue copper level with histopathological grading of OSMF. A hospital based case-control study was done on 30 subjects visiting out-patient department (OPD) of Kothiwal Dental College Moradabad, of which 15 were clinically diagnosed OSMF cases with habit of areca nut chewing and 15 were taken as controls with no habit of areca nut chewing. Tissue copper levels were measured by Atomic Absorption Spectrophotometer (AAS). The study showed highly significant difference in mean tissue copper level ($P < 0.001$) in patients with OSMF and controls, with patients exhibiting higher tissue copper level (6.43 ± 1.11) in contrast to control who presented low tissue

copper level (4.35 ± 0.91), also a highly significant correlation ($P < 0.001$) was seen between increase in tissue copper level and histopathological staging of OSMF. The present study confirms the hypothesis that copper level in increased in areca nut chewers presenting OSMF. Moreover, copper level increased with increased in histopathological grade of OSMF.¹⁰

Dey et al evaluated the salivary Cu and Zn levels in OSMF patients. They evaluated a total of 60 patients and divided them into two groups; Group A consisted of 30 patients that were histologically diagnosed with OSMF. Group B consisted of patients that were control and didn't have any oral lesion. Salivary Cu and Zn levels were estimated. All the results were analyzed by SPSS software. Chi square test were used for the assessment of level of significance. Mean salivary Cu levels in OSMF and normal control patients were 0.087 and 0.055 respectively. Mean salivary Zn levels in both OSMF and normal control patients were 0.102. Significant alterations were observed while comparing the mean salivary Cu levels in the two study groups while comparing the mean salivary Zn levels, no significant alterations was seen. Salivary markers can be used for predicting the prognosis and diagnosis of the disease.¹¹

CONCLUSION

In the pathogenesis of OSMF, Copper does plays a definite role. However; we recommend future research.

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