ORIGINAL RESEARCH

Evaluation of serum Copper levels as marker of disease activity in oral submucous fibrosis patients in known population.

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ABSTRACT:
Background: Trace elements are involved in vital biochemical reactions of the body. Redox reactions and free radical formation reactions are few of them which helps in maintaining cellular homeostasis. The aim of this study was to the evaluatethe serum levels of Copper (Cu) in oral submucous fibrosis (OSMF) patients. **Materials and Methods:** Sera of OSMF (n = 30) patients and that of healthy controls (n=30) were analyzed for the estimation of Cu using atomic absorption spectrophotometry. Comparison of mean values between the two groups was carried out using Student's t-test using appropriate level of significance and degrees of freedom. **Results:** Sera levels of Cu were found to be increased in OSMF patients as compared to that of healthy controls. **Conclusion:** It could be concluded that altered sera levels of Cu element in combination with clinical evaluation can be a helpful method in the early detection and management in OSMF patients.
Key words: Copper, oral squamous cell carcinoma, oral submucous fibrosis, Trace elements.

INTRODUCTION

Oral cancer is one of the deadly diseases found in head and neck region of the human being. Usually oral cancer lesions are preceded by the formation of premalignant lesions and/or conditions. Oral submucous fibrosis (OSMF) is an chronic, insidious and debilitating, high-risk, precancerous condition affecting patients, especially, of South-East Asian origin. The exact etiology of OSMF is poorly understood but is believed to be closely related to the habit of chewing areca nut.[1] Furthermore, OSMF patients are strongly associated with a risk of developing frank oral squamous cell carcinomas (OSCCs) with a malignant transformation rate of 7.6% over a period of 17 years. The prevalence of oral precancerous lesions and/or conditions is much higher than that of oral cancer, and these lesions provide useful clinical markers for oral cancer.[1] Timely recognition of oral cancers and precancers improves the quality of life of the affected patients. At present, the diagnosis of oral precancerous lesions and conditions and oral cancer is done by histopathology. Therefore, there is a need for the development of susceptible, precise, and quicker tests for the early diagnosis of the primary tumor and its recurrence or malignant conversion in premalignant states. Hence, detection of trace elements which can forecast disease succession becomes an absolute necessity for the better management of such patients. Serum levels of trace elements are significantly altered in the head and neck cancers, lung and breast carcinomas, and they also have an imperative role in carcinogenesis.[2]

Cytological studies have confirmed the important role of copper (Cu) in the pathogenesis of OSMF showing intense staining in smears of OSMF patients as compared to smears from the non chewers. Thus, it

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can prove an efficient marker of early diagnosis of malignant transformation.[3,4] In the assessment for several trace elements, the concentrations in serum are often used as an index. The importance of these trace elements in cancer was reported to be of significance first by Schwartz M[5] which opened the door for almost a new diagnostic and therapeutic endeavor in many areas of medicine and particularly, in the areas of oncology. Immunological and biochemical alterations in the serum of such patients can help not only in the early diagnosis and treatment but also in assessing the prognosis, as well as the disease progression, and response to treatment.[6]

MATERIALS AND METHODS

A detailed oral examination of the patients was carried out using diagnostic instruments (mouth mirror and probe), and findings were recorded. A clinical diagnosis of OSMF was made based on the clinical appearance of the lesion, and a detailed case history was taken. Biopsy was taken from the site of the lesion. Biopsy tissue was processed and stained, and the diagnosis was histopathologically confirmed. Then, sera samples of patients afflicted with OSMF as also of the healthy controls were collected, processed, and analyzed for the estimation of Cu using atomic absorption spectrophotometry (AAS).

The study sample comprised sixty participants that was divided into two groups as:

Group A: Patients with histopathologically diagnosed OSMF, n = 30

Group B: Healthy controls, n = 30

The selection of the patients for the study was done after obtaining their written consent. Ethical clearance was obtained from the Institutional Ethics Committee.

Procedure

After the patients were clinically and histopathologically diagnosed to have OSMF, 2 ml of intravenous blood was drawn under aseptic precautions. The blood was allowed to clot and centrifuged at 1000 rpm for 15 min to separate serum. Serum was subjected to digestion using concentrated nitric acid and perchloric acid. For the determination of serum Cu, the sample was diluted with an equal volume of deionized water. Estimation of serum Cu levels was done using AAS (Perkin Elmer, Shelton, CT 06484, USA Analyst 200/4000 spectrometer).

Independent sample's t-test was used to compare the mean values between the two groups. Comparison of mean values between different groups was done using the Student's t-test using appropriate level of significance and degree of freedom.

RESULTS

As per [Table 1], in Group A, the mean serum levels in OSMF significantly increased as compared to healthy control with habit or without habit.

Group	n	Minimum value (µg/dl)	Maximum value (µg/dl)	Mean ± SD (µg/dl)
A	30	128	144	136.8 5.499
B	30	98	115	108.3 5.080
P<0.0001, Significant				

Table 1: Serum Copper levels in various patients.

DISCUSSION

Oral cancer is one of the leading causes of death in the Indian subcontinent. Similarly, the existence of precancerous lesions and conditions such as OSMF and leukoplakia is also very high due to various adverse oral habits.[1] Recently, much attention is being provided toward the detection of trace elements in oral cancer and the various precancerous lesions and conditions due to the encouraging results of the studies on head and neck carcinoma, lymphomas, lung and breast carcinomas.[7] Many studies have reported that these trace elements play an inhibitory role in cancers. Trace elements play, directly or indirectly, an important role in various physiological metabolic processes in the humans.

OSMF is a well-recognized, potentially malignant condition of the oral cavity. Controlling the devastating, widespread consequences of OSMF requires interventions in at-risk persons ideally before the disease becomes invasive. Detection of the premalignancies and preventing them from malignant transformation seem to be the best available tool in the fight against oral cancer. Very few studies have been conducted to find out the role of different trace elements in oral precancer and cancer.

In our study, the serum copper level was significantly (P < 0.0001) higher among the OSMF cases than controls. It was similar to the study by Balpande et al.[8] and Shetty et al.[9]

Increased serum copper in OSMF can be correlated to copper present in areca nut increases the collagen

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production in oral fibroblasts by upregulating lysyl oxidase leading to crosslinking of collagen and elastin Trivedy et al.[9] has also reported on the copper-induced mutagenesis through the p53 aberrations in OSMF, which may be critical in the progression of the potentially malignant lesions to squamous cell carcinoma.[10]

CONCLUSION

Determination of sera levels of Cu is simple as well as an inexpensive procedure and can be used as an adjunct screening tool for determining risk in patients with potentially malignant OSMF.

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