A Study of Salivary Lactate Dehydrogenase (LDH) Levels in Oral Cancer and Oral Submucosal Fibrosis Patients amoung the Normal Individulas

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Abstract:

Oral cancer is the commonest cause of death in Indian population. It araises from premalignant lesion. The most common premalignant lesions are Oral Leukoplakia and Oral Submucosal Fibrosis. Early diagnosis and appropriate treatment will prevent progression of disease condition from premalignant level to malignant level.
A simple biochemical parameter that helps to diagnose the disease in early stage is lactate dehydrogenase enzyme. LDH is present in almost all the cells of our body. According to Warburg hypothesis due to hyperplasia the LDH level will be increased due to increased level of anaerobic glycolysis.

INTRODUCTION:

Cancer is the second most common disease in India responsible for maximum mortality rate with about 0.3 million deaths per year. The Oral Cancer is an important global concern accounting for an estimated 2,75,000 cases and 1,28,000 death annually (1). The main reason is attributed for the usage of tobacco yet 1.93% is not releated tobacco and genetics constitutes 5-10% (2). Potentially malignant lesions of oral cavity are relatively common occurring in about 2.5% of the population (3), with a malignant transformation rate in various studies and locations that range from 0.6 to 20% (2). Potentially malignant lesions are usually asymptomatic and they are diagnosed by dentist during routine dental examination.

Oral Submucosal Fibrosis is an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx (4).Occasionally it is preceded by and/or associated with vesicle formation (5) and is always associated with juxta-epithilial inflammatory reaction followed by progressive hyalinization of lamina propria (6). The later subeoithilial and submucosal myofibrosis leads to stiffness of the oral mucosa and deeper tissues with progressive limitation in the opening of the mouth and prostrusion of the tongue, thus causing difficulty in eating, swallowing and phonation (7). Epithelial atropy is marked in advanced stages of the disease.

Apparent divergencies in these characteristics between groups of patients in different studies raised the question whether OSMF should be considered as one, or more than one disease. The evidence that it will predispose to cancer is not yet absolutely conclusive. The OSMF is an precancerous condition or premalignant condition-a generalized pathological state of the oral mucosa associated with a significantly increased risk of cancer (8) according to world health organization (WHO) which accords well with the characteristics of OSMF.

The enzyme Lactate Dehydrogenase (LDH) is an ubiquitous enzyme that was discovered in early periods of enzymology. This enzyme catalyzes the reaction of lactate production via pyruvate reduction during anaerobic glycolysis. This enzyme is mostly all body tissues but mainly concentrated in heart, liver, red blood cells, kidneys, muscles, brains and lungs. The salivary LDH isoenzymes profile is similar to that of LDH isoenzymes present in the oral epithelium, which indicates that the major source of LDH is the oral epithelium probably, which is derived from the surface exfoliated cells.

Consequently, LDH concentration in saliva as an expression of cellular necrosis can be considered to be a specific indicator for lesions affecting the integrity of the oral mucosa (9). The studies on the analysis of the salivary LDH either total or isoenzymes in oral cancer or oral submucosal fibrosis patients have not been carried out extensively. The salivary LDH levels have been rarely studied in oral cancer and oral submucosal fibrosis people. The present study is aimed to evaluate the salivary LDH levels in OC, OSMF among the control individuals and to correlate the LDH levels in these selected cases using the relatively noninvasive saliva as the diagnostic tool.

MATERIALS AND METHODS:

Source of data:

Patients were selected from those attending the Out Patient Department (OPD) of Saveetha Dental College and patients attending the clinics in the institute and divided into three groups as follows:

Study Groups:

- Group I: Normal healthy individuals: 20 individuals
- Group II: Patients with OSMF: 20 individuals
- Group III: Patients with Oral Cancer: 20 individuals

Total Sample Size: 60individuals

Inclusion Criteria:
1.   Patients with the age groups of thirty to fifty years.
2.   Patients with Oral Submucosal Fibrosis (OSMF).
3.   Patients with Oral Cancer (OC).

Exclusion Criteria:
1. Immuno Compromised patients.
2. Infectious   diseased   individuals   like Tuberculosis,Syphylis etc.
3. Endocrine disorder patients.
4. Coronary artery disease.

Saliva Collection:
Informed written consent was obtained from the patients prior saliva collection. 5 ml of unstimulated whole saliva was aseptically collected in a wide mouthed container. Following the collected, saliva was centrifuged at 2500 rpm for 15 minutes and then it was analysed by ERBA CHEM 5 semi auto analyser.

RESULTS:

The values obtained were statistically analysed using Chi-Square test, One way ANOVA and Tukey's HSD post hoc test. To compare proportions between groups, to compare the mean values between groups and for the multiple comparisons.
Mean salivary LDH level in HC ,OSMF and OC groups were 126.7 ± 58.2 IU/L, 612.2 ± 328.9 IU/L and 515.7 ± 257.8 IU/L respectively. The mean salivary LDH level in male subjects in HC, OSMF and OC groups were 134.6 ± 55.6 IU/L, 398.6 ± 166.9 IU/L and 580.6 ± 286.1 IU/L respectively. The mean salivary LDH level of female subjects un the coreesponding groups were 54.5 ± 20.5 IU/L, 727.2 ± 341.2 IU/L and 418.4 ± 183.6 IU/L respectively. The salivary LDH levels were significantly higher *(p=0.01)* in females when compared to male subjects in OSMF but in HC and OC the LDH levels are higher in females when compared to males. There was a highly statistically significant difference (p=0.001) when the mean saliva LDH levels of group HC was compared to group OSMF. On comparison of the mean salivary LDH levels of group OSMF to group OC there was no significant difference because I have selected the OC patients who were in chemotherapy. When mean salivary LDH levels of group HC were compared to group OC and OSMF there was a very high significant difference.

Mean LDH level
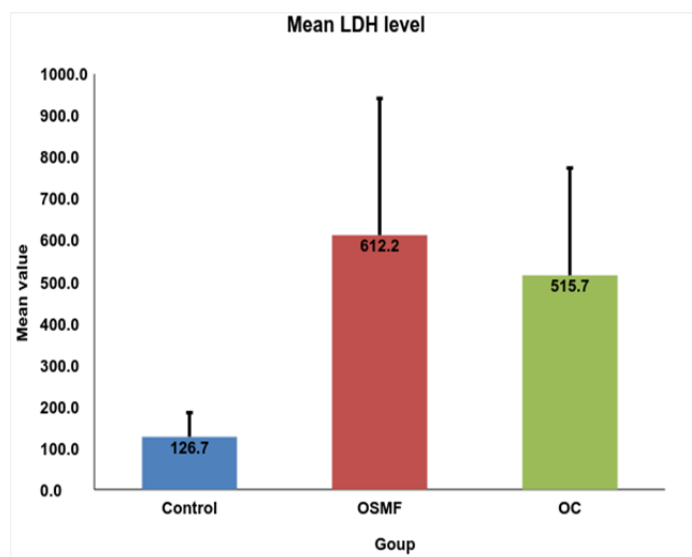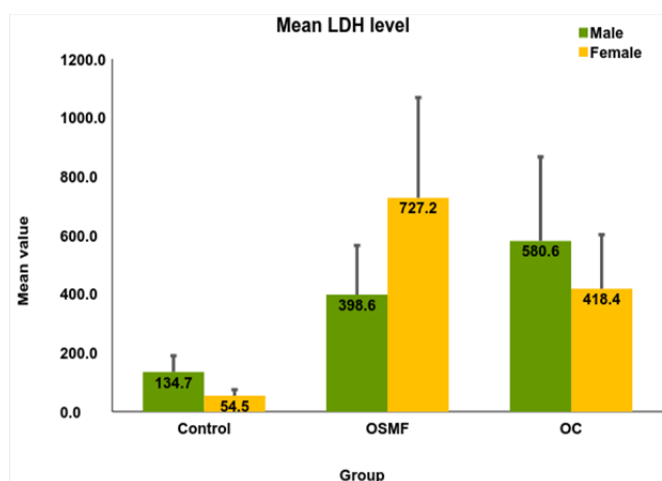
DISCUSSION:

Oral submucous fibrosis is a chronic insidious and a disabling condition. Patients with OSMF have an assertive habit history betel nut chewing, and a clear dose dependant relation is observed for both frequency and duration of chewing betel nut. The popularity and commercial availability of tobacco and betel nut products etc has been associated with a sharp increase in the frequency of OSMF (10).
The direct contact and continuous irritation from the various components of the betel nut and tobacco products to the oral tissues produces a hypersensitivity reaction in the oral mucosa , thus initiating the disease. The period between initiation of chewing habit and the development of clinical symptoms of OSMF varies tremendously ranging from a few months to several decades, depending on the type and duration of the betel nut chewing habit (11). Soluble irritants as alkaloids present in betel nut and tobacco etc act as initiating factors causing juxta-epithelial inflammatory reaction thus leading t burning sensation , vesiculation and ulceration of the oral mucosa, which renders a phase for difficulty in consumption of the normal diet leading to poor nutrition (12).
An atrophic epithelium makes the oral mucosa vulnerable to the soluble irritants.
Further lack of iron in tissues causes improper vascular channel formation decreasing in vascularity. This leads to derangement in the inflammatory-reparative response of the lamina propria resulting in defective healing and scarification. Thus, the cumulative effect of these initiating and promoting factors leads to further fibrosis, which is a hallmark of OSMF (13).
Lactate dehydrogenase has been described as an ubiquitous enzyme that plays a very important role in the diagnosis of the pathologic process (14). Studies on serum, tissue and urine LDH levels in detection of various disorders have been conducted in the recent past (15,16,17). Saliva testing, has been promoted as a noninvasive alternative to serum testing in diagnosis and prognosis of oral cancer that may be an effective modality for diagnosis and for prognosis prediction of oral cancer (18). This study evaluated the LDH level in saliva of OC, OSMF patients and HC. In our

study, male subjects had relatively higher salivary LDH levels when compared to female subjects. This pattern is normally observed in serum but has not been highlighted in saliva (19).

In our study, salivary LDH levels were higher in OSMF patients because I selected the oral cancer patients who are in the chemotherapy treatment. Studies have reported elevated tissues, salivary and serum LDH levels in different types of malignancies (15). The salivary LDH levels were significantly higher in oral cancer patients (16). An immunohistochemical evaluation of LDH in various types of malignant cells showed the irrespective of the malignancy, the levels were higher than that of normal cells (20). In a study involving five salivary parameters, elevated salivary LDH levels were observed in tongue cancer patients when compared to health controls (21).

The salivary LDH has been considered as reliable molecular marker for oral cancer in some studies (22). In our study there is a significant difference in the salivary LDH between HC and OSMF and among HC and OC subjects. The recent studies have revealed that the salivary LDH levels significantly vary after smoking (22,23).

CONCLUSION:

My study shoes significant difference in salivary LDH level between healthy controls and OSMF subjects and also healthy controls and oral cancer subjects. So estimation of salivary LDH level could be a reliable marker to diagnose OSMF (premalignant condition) and Oral Cancer. It is a good non-invasive and cost effective investigation. So, this is helpful to diagnose the disease in early stages itself.

REFERENCES:

1. ALiu L, Kumar SK, Sedghizadeh PP, JayakarAN, Shuler, authors. Oral squamous cell carcinoma incident by subsite among diverse racial and ethnic populations in California. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;105:470-80.
2. Prassan Kumar Rao J.,Potentially malignant lesion – oral leukoplakia, Globally Advanced Research Journal of Medicine Sciences.,2012; 1(11):286-291.
3. McCullough MJ, Prasad G, Farah CS.,Oral mucosal malignancy and patentially malignant lesions: an update on the epidemiology, risk factors, diagnosis and management,Aust Dent J., 2010 Jun, 55 Suppl 1:61-65.doi:10.1111/j,1834-7819.2010.01200.x.
4. Lemmer J, Singh B. Formation of vesicles in oral cavity submucous fibrosis. Acta path. Microbial. Scand., 1967, 70: 161-173.
5. Pinborg JJ, Singh B. Formation of vesicles in oral submucous fibrosis. Acta path. Microbial scand., 1967, 70: 161-173.
6. Sirsat SM, Pindborg JJ. Subepithelial changes in oral submucous fibrosis. Acta path. Scand., 1967, 70: 161-173.
7. Wahi PN et al. Submucous fibrosis of the oral cavity: histomorphological studies. Br. J. cancer, 1966,20: 676-687.
8. World Health Organisation (WHO). Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. Community dent. Oral epidemiol., 1980, 8: 1-26.
9. Lingen MW, Kalmar JR, Karrison T, Speight PM. Critical evaluation of diagnostic aids for the detection of oral cancer. Oral Oncol2008;44:10-22.
10. Aulack Ajit, Rosin Miriam P, Zhang Lewei, Sumanth KN. Oral submucous fibrosis, a clinically benign but potentially malignant disease: Report of 3 cases and review of the literature. JCDA 2008; 74:735-40.
11. De Rossi Scott S, Raghavendra Sree. Anemia. OOOE 2003; 95:131-41.
12. Rajendran R, Vijayakumar T. An alternative pathogenic pathway for oral submucous fibrosis. Medical hypothesis 1989; 30:35-37.
13. Lavina Taneja, Bagewadi Anjana, Keluskar Vaishali. Hemoglobin levels in patients with oral submucous fibrosis. JIAOMR 2007; 19:329-33.
14. Nagler RM, Lischinsky S, Diamond E, Klein I, Reznick AZ. New insights into salivary lactate dehydrogenase of human subjects. J Lab Clin Med 2001;137:363-9.
15. Schneider RJ, Seibert K, Passe S, Little C, Gee T, Lee BJ, et al. Prognostic significance of serum lactate dehydrogenase in malignant lymphoma. Cancer 1980; 46:149-53.
16. Shpitzer T, Bahar G, Feinmesser R, Nagler RM. A comprehensive salivary analysis for oral cancer diagnosis. J Cancer Res Clin Oncol 2007;133:613-7.
17. Kehrer G,Blech M, Kallerhoff M, BretschneiderHJ. Urinary LDH release for evaluation of postschemic renal function. J Mol Med 1989;67:477-85.
18. Nagler RM. Saliva as a tool for oral cancer diagnosis and prognosis. Oral Oncol 2009;45:1006-10.
19. Henry JB. Clinical diagnosis and management by laboratory methods. 1st ed. Philadelphia: WB Saunders and Company; 1979.
20. Pan L, Xu J, Isaacson PG. Cellular H- and M-type lactate dehydrogenase (LDH) isoenzyme and tumour diagnosis- an immunohistochemical assessment. J Pathol 1991;163:53-60.
21. Shpitzer T, Hamzany y, Bahar G, Feinmesser R, Savulescu D, Borovoi I, et al. Salivary analysis of oral cancer biomarkers. Br J cancer 2009;101:1194-8.
22. Markopoulos AK, Michailidou EZ, Tzimagiorgis G. Salivary markes for oral cancer detection. Open Dent J 2010;4:172-8.