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A Study of Salivary and Serum Lactate Dehydrogenase Levels in Tobacco Users and Potentially Malignant Disorders

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Abstract
Aim: *To measure and compare the LDH levels in serum and saliva in tobacco users and potentially malignant disorders.*
Materials And Methods: *Thirty subjects were recruited for this study and divided into three groups, 10 subjects with tobacco habits, 10 subjects with potentially malignant disorders and 10 healthy controls. Venous blood and unstimulated whole saliva measuring 1 ml was collected from each of these were evaluated for LDH levels using the standard kit method. The data obtained were subjected to statistical analysis using the spss software version 17.*
Results: *LDH activity increased in serum as well as saliva in tobacco users and potentially malignant disorders in comparison to normal control.*
Conclusion: *Salivary LDH estimation can prove to be a valuable substitute to serum LDH as a biochemical marker, as it is a simple, non invasive and tool for diagnosis and monitoring of oral precancer and cancer.*
Keywords: *Lactate dehydrogenase, tobacco, potentially malignant disorders, serum, saliva.*

Introduction

Cancer is one of the leading causes of adult deaths worldwide. Oral cancer is a serious problem in many countries. It accounts for significant mortality and is also responsible for extensive disfigurement, loss of function, behavioral changes, financial and sociologic hardship. In India the incidence of oral cancer is about three to seven times more common as compared to developed countries[1].

The development of oral cancer is a multistep process, arising from pre-existing potentially malignant disorders[2].

Recently, the role of tumor markers in management of head and neck cancer has received increasing attention. Tumor markers in serum, tissue and other body fluids during neoplastic process are of clinical value in the management of patients with various body cancers. Among all the body fluids, blood has been the media of choice for the study of the biochemical markers by the medical community but it does have some inherent disadvantages. Collecting blood for investigation is an invasive procedure and has a potential risk of disease transmission through needle stick injuries. Despite the absence of

charisma, however, a growing number of researchers are finding that saliva provides an easily available, non-invasive diagnostic medium for rapidly widening range of disease and clinical situations[3]. Lactate dehydrogenase activityis mainly due to genomic changes during malignant transformation. Increased LDH levels are due to increased mitotic index and more lactic acid productionby tumor cells due to breakdown of glycoprotein. Value of LDH elevates in OSCC and potentially malignant disorders; this finding can be used for benefit of the patient in predicting prognosis[1].

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.

The salivary LDH levels have been rarely studied in oral cancer. tobacco users and potentially malignant disorders. The present study is aimed to evaluate the salivary LDH tobacco users potentially malignant disorders and among the control individuals and to correlate the LDH levels in these selected cases using the relatively noninvasive saliva as the diagnostic tool[2].

LDH isoenzymes originally in tissues, to obtain a reference record, as well as in routine analysis of fluids, in order to make meaningful com parisons and to enhance diagnostic specificity. Our contribution in this field has been the development of a method forthe quantitative determination of LDH isoenzymes as well as its application for the detection of biochemical abnormalities and to aid the diagnosis of disease[5].

Materials and Methods

Source of Data:

Patients were selected from those attending the outpatient department (opd) of vinayaka mission sankarachariyar dental college and patients attending the clinics in the institute and divided into three groups as follows:

Study Groups

- Group I: normal healthy controls with no tobacco habits: 10 individuals
- Group II:subjects with tobacco habit with no clinical alteration of oral mucosa: 10 individuals
- Group III: clinically diagnosed and histopathologically confirmed cases of tobacco users with pmd. :10 individual

Total sample size: 30 individuals

Inclusion Criteria

Patients with the age range of 30-60 yrs

- Group I: Healthy controls with no tobacco habits
- Group II: Subjects with tobacco habit with no clinical alteration of mucosa duration of more than 5 years.
- Group III Clinically diagnosed and histopathologically confirmed cases of tobacco users with pmd.

Exclusion Criteria

- Patients treated for cancers (surgery,chemotherapy, radiotherapy)
- Systemic diseases known to increase ser-um LDH levels such as MI, liver diseases, renal disease, and muscle dystrophy
- Immuno compromised patients.
- Individuals with other mucosal lesions[2]
- Institutional Ethical Clearance was obtained prior to begin the study. Written informed consent of the patient was obtained and case history was recorded.

Sample Collection

Five milliliters of blood was drawn from the peripheral veins (Brachial or Anticubital Vein) under aseptic conditions. Collected blood sample was kept in test tubes at room, 5 ml of unstimulated whole saliva was aseptically collected by the spit method in a wide mouthed container. Care Will Be Taken To See That The Volunteers Did Not Consume Food Or Chew Gum At Least One Hour Before And Smoke Three Hours Before The Saliva Collection Procedure. Following, the collected sample was centrifuged at 2500 rpm for 15 minutes and the samples will be diluted in 1:1 ratio with saline,

then it was assayed using the standard kit and measured sphectrophotometrically at 340 nm . Since saliva supernatant was used which can be treated like serum the same kit was used to process both the samples. Incisional biopsy of the potentially malignant disorder cases was performed and clinical diagnosis of the cases was confirmed by histopathological examination[4].

Aims and Objectives

- To measure and compare serum and salivary LDH levels in tobacco users and patients with potentially malignant disorders carcinoma.
- To correlate LDH levels among healthy individuals, tobacco users and potentially malignant disorders.
- To evaluate whether salivary analysis of LDH can substitute serum LDH analysis.
- To evaluate if these levels can be used as biomarker in the progression into potentially malignant disorders.

Results

The data obtained was analyzed using the SPSS software 18 for windows. Appropriate univariate and bivariate analysis were carried out using the Student 't' test for the continuous variable. The comparisons of mean LDH levels between three groups were done using ANOVA.

A total of 30 patients (10 control subjects,10 tobacco users,10 potentially malignant disorders) with a mean age ranging from 30 to 60 were included in this study.

Figure 2 shows increased levels of Serum LDH in tobacco users and potentially malignant disorders as compared to healthy controls.

Figure 3 shows increased levels of salivary LDH in tobacco users and potentially malignant disorders as compared to healthy controls.

Figure 4shows increased levels of salivary and Serum LDH in TOBACCO USERS and PMD as compared to healthy controls.

Comparision of Both Serum and Saliva Level

- The increase in LDH levels was consistent in saliva and serum of CONTROL GROUP.
- The increase in LDH levels was less in SERUM as compared to SALIVA in group II (TOBACCO USERS) patients.
- The increase in LDH levels was less in saliva as compared to serum in group III (PMD) patients.

Figure1 Shows mean LDH values

		N	Mean	SD	t	p
Control	Serum	10	422.20	92.53	0.051	0.960
	Saliva	10	426.70	216.51		
Tobacco	Serum	10	495.60	123.49	2.40	0.040*
	Saliva	10	677.90	235.87		
PMD	Serum	10	3,516.80	1,297.30	2.51	0.033*
	Saliva	10	2,470.60	938.20		

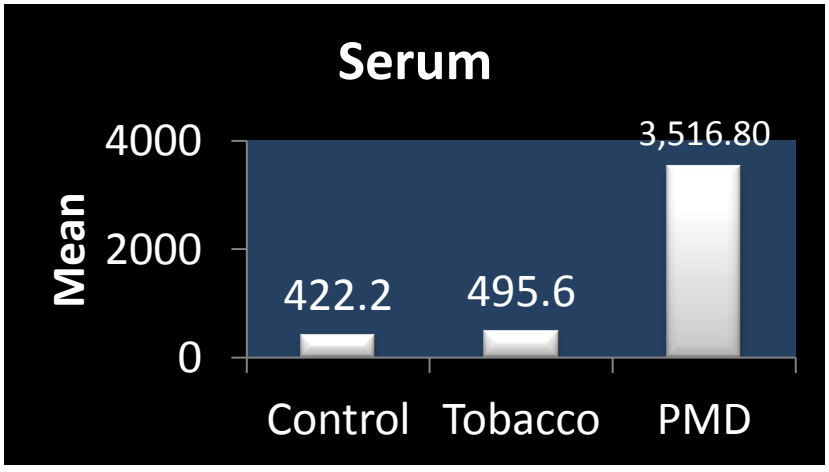

Figure 2 : Serum level in PMD is elevated in this graph compared to tobacco users and control

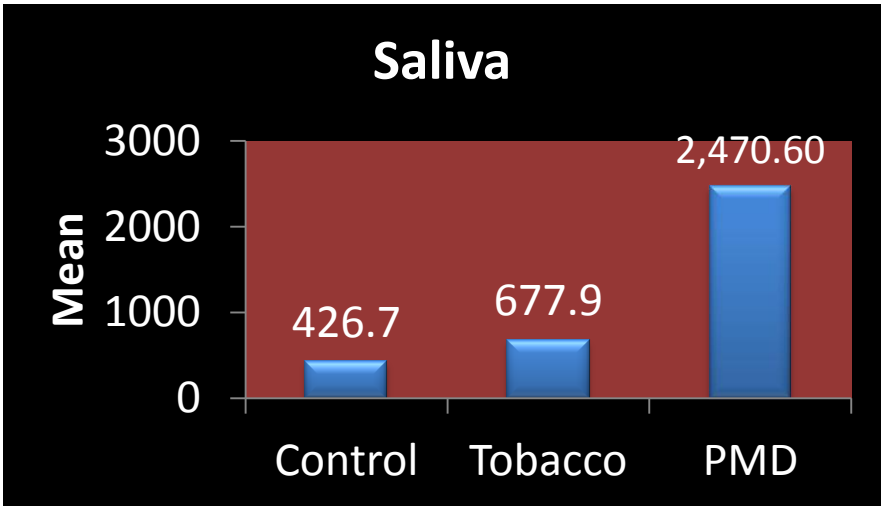

Figure 3 : Salivary level in PMD is elevated in this graph compared to tobacco users and control

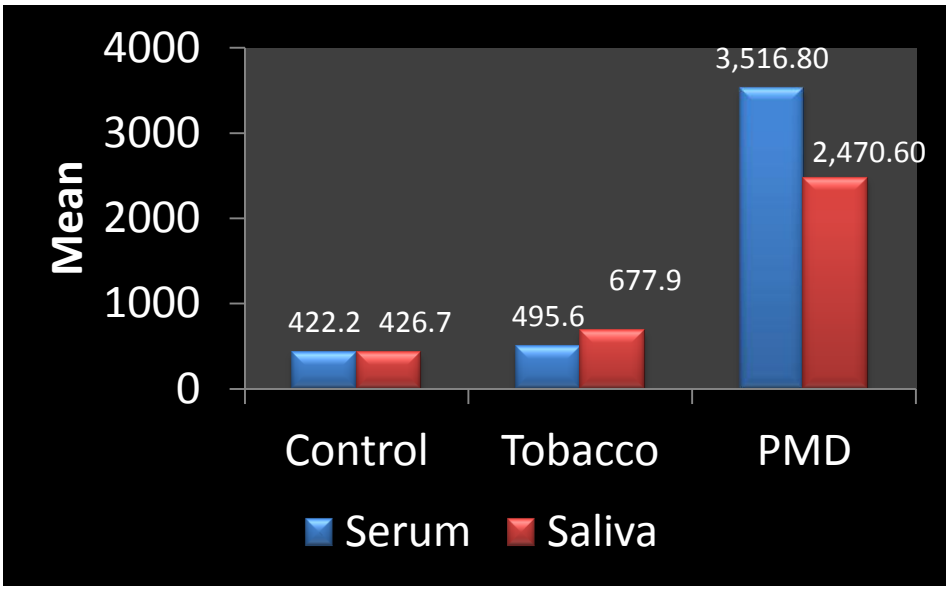

Figure 4 shows increased levels of salivary and Serum LDH in TOBACCO USERS and PMD as compared to healthy controls.

Discussion

The use of biomarkers as a diagnostic tool during dental examinations could be helpful in early diagnosis of oral cancer. In recent years, total LDH and LDH isoenzyme activity has been used for screening oral potentially malignant disorders like OSMF, leukoplakia , lichen planus [6].

Lactate dehydrogenase (LDH) is an intracellular enzyme that catalyzes the reaction of lactate production via pyruvate reduction during anerobic glycolysis. Its extracellular presence is always related to cell necrosis and tissue breakdown. Serum LDH nonspecifically increases in many pathological conditions such as myocardial infarction, megaloblastic anemias, liver and renal diseases. LDH concentration in saliva could be a specific indicator for oral lesions that affect the integrity of the oral mucosa[7].

Previous study has reported that the LDH isoenzyme profile of the oral epithelium was found to be similar to that of the whole saliva and the study concluded that the major source for whole saliva LDH is nonglandular. It has been shown that saliva as a diagnostic fluid meets the demand for an inexpensive, noninvasive, and accessible diagnostic methodology for oral cancer detection[7].

Cigarrate smoke consists of many chemicals, including nicotine, tar with its many carcinogen-nesis, and gaseous compounds including carbon monoxide (CO). CO was shown to accumulated in

the human body with repeated smoking. Chronic exposure to low level of CO results in tissue hypoxia. Increased carboxyheamoglobin and decreased oxyhemoglobin has resulted in respiratory acidosis and electrolyte imbalance[8,12]. Due to this imbalance, it act as the diagnostic tool in evaluation of LDH for the detection of oral cancer.

Saliva may provide a cost‑effective and practical approach for the screening of large populations. Salivary "tools" are those focused on measuring changes of specific salivary macromolecules such as proteins or nucleic acids (as fatty acids are rather scarce in saliva), that is, examining genomic or proteomic targets like enzymes, cytokines, growth factors, metalloproteinases, endothelin, telomerase, cytokeratines, mRNA's, DNA aberrations, etc. Clinical significance of salivary biomarkers in various malignancies is studied by several investigators[15].

Serum ldh a key lung cancer (nsclc), crc, and ewing's sarcoma of the bone. As previously explained, ldh and lactate biomarker in many types of cancer as baseline ldh levels become elevated following tissue injury or during disease, and high serum ldh levels are frequently found in human malignancies, including non-small cell production are involved

In tumor initiation, invasive potential, metastasis, and recurrence[11].

Santanu Kar Mahapatra et al ..,studied on Smoking induced oxidative stress in serum and neutrophil in that they concluded LDH activity was generally higher in serum rather than blood cell in both smoker and non-smoker and it was increased with short term smoking habit in both serum and neutrophil of our studied subjects[9].M. Dhivyalakshmi et al did a study on Expression of Salivary Biomarkers – Alkaline Phosphatase & Lactate dehydrogenase in Oral Leukoplakia and concluded that Salivary Alkaline phosphatase and Lactate dehydrogenase are equally sensitive markers for the early detection of oral carcinoma[14].

Conclusion

This study shows significant difference in salivary LDH level between healthy controls and tobacco users subjects and also healthy controls and potentially malignant disorders subjects. So estimation of salivary LDH level could be a reliable marker to diagnose potentially malignant disorders and also to monitor the tobacco users. Salivary testing, a noninvasive alternative to serum testing, can be an effective modality for diagnosis and prognosis predicting of oral cancer as well as for monitoring the patient's post therapy status.

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