Alterations in plasma lipid profile patterns in leukoplakia and oral submucous fibrosis - a pilot study

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ABSTRACT

Introduction: Oral submucous fibrosis and leukoplakia are highly prevalent in India Lipids are the chief cell membrane components which are essential for various biological functions like cell growth and division of normal as well as malignant tissues. Lipids can be helpful for studying the variation in the cholesterol levels for diagnosing and treating the diseases.

Aim: The present study evaluated the plasma lipid profiles in patients with Oral submucous fibrosis and leukoplakia and controls**.**

Methodology: 21 patients were selected for the study out of which 7 had OSMF 7 had oral leukoplakia and 7 were included in control group. Patients with cardiovascular diseases, uncontrolled diabetes, acute hepatitis, thyroid dysfunction, and any drug history were excluded from the study. 5ml blood sample was taken and the serum was tested for triglycride levels(TG) , total cholesterol (TC), LDL, HDL, LDL VLDL level were analyzed using triglycerides were analyzed by auto-analyzer used for the analysis of the results is a fully automated biochemistry analyzer.

Results: In this study TC, HDL, LDL level analysis showed lower levels in oral leukoplakia and OSMF patients than that of the controls.

Conclusion: The alterations in the plasma lipid profile patterns were considerable and recommend a still in-depth study with larger sample size in this aspect for early diagnosis and management of oral leukoplakia to prevent malignant transformation.

Keywords: Lipids, Cholesterol, Triglycerides, Leukoplakia, Oral submucous fibrosis.

INTRODUCTION

Lipids are the chief cell membrane components which are essential for various biological functions like cell growth and division of normal as well as malignant tissues. Lipids can be helpful for studying the variation in the cholesterol levels for diagnosing and treating the diseases.[1,2] Changes in circulatory levels cholesterol has been associated in the etiology of colorectal as well as breast cancer.[2,3]

Using tobacco is an important etiologic factor which aids in the development of oral precancerous lesions / conditions and head and neck cancer.[4] The carcinogens present in tobacco stimulate free radicals and reactive oxygen species (ROS) generation, which further cause increase in the rate of oxidation / peroxidation of polyunsaturated fatty acids. This peroxidation will further release peroxide radicals. This affects essential components of the cell membrane and can be involved in tumorigenesis.[5] Lipid peroxidation, will increase the consumption of lipids which includes total cholesterol, triglycerides and lipoproteins for generation of new membrane. Cells carry out these requirements either via circulation, by the production through the metabolism or from the degradation of major lipoprotein fractions like VLDL, LDL or HDL. Reports have shown that antioxidant vitamins have protective effects against lipid peroxidation.[6,7]

Hence the present study was aimed to evaluate the plasma lipid profile including: (i) total cholesterol(TC) (ii) LDL cholesterol (LDLC), (iii) HDL cholesterol (HDLC), (iv) VLDL cholesterol (VLDLC) and (v) triglycerides(TG) patients with oral submucous fibrosis OSMF , leukoplakia and healthy controls.

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METHODOLOGY

A study was conducted in the Department of Oral Medicine and Radiology of I.T.S.-C.D.S.R., Dental College, Muradnagar. A total of 21 patients were taken from those visiting the department in the months of May – June, 2014. Patients were selected after taking a thorough history and on the basis of clinical examination by a trained oral medicine and radiology faculty. Patients with cardiovascular diseases, uncontrolled diabetes, acute hepatitis, thyroid dysfunction, and any drug history were excluded from the study.

Ethical clearance obtained from the institutional ethical committee. Patients were then divided into 3

groups, Three groups were leukoplakia, OSMF and healthy controls each group had 7 patients. Patients were informed prior to the study and a written consent form was obtained. All 7 patients with leukoplakia underwent biopsy however only 5 patients with OSMF underwent biopsy. Patients with OSMF are classified on the basis of Khanna et al. After confirmed biopsy report patients were recalled again empty stomach in the morning and 5ml of blood was collected from each patient and was allowed to clot. The serum was separated by centrifugation. Auto-analyzer was used for the analysis of the results. It is a fully automated biochemistry analyzer. After that the lipid profile assay of the specific parameters like HDL, LDL, VLDL, Total cholesterol, Triglycerides were made.

RESULTS

Patients age group ranged from 19- 50 years. Habit of tobacco consumption in one or the other form (smoking/chewing/snuff) was present in all the cases. Out of 21 patients 20 patients were male and one patient with OSMF was female. In the leukplakia group out of 7 patients 5 had moderate dysplasia and 2 patients had mild dysplasia. In OSMF group out of 5 patients who underwent biopsy 1 had moderately advanced and 4 had Early OSMF. Other 2 patients had grade III OSMF according to Khanna et al classification.

Table – 1: Mean of TG, TC, HDL, LD in all the patients of leukoplakia, OSMF, and healthy controls

	LEUKOPLAKIA (mean)	OSMF (mean)	CONTROL (mean)
TG	126.14	134.85	143.14
TC	114.42	128.57	157.85
HDL	22.85	33.71	42
LDL	35.14	50.14	82.42
VLDL	17.28	26.71	31

Table - 2: Histopathological stages of dyspalsia[12]

Stages of dysplasia	Features
Squamous hyperplasia	This may be in the spinous layer (acanthosis) and/or in the basal/parabasal cell layers (basal cell hyperplasia); the architecture shows regular stratification without cellular atypia
Mild dysplasia	The architectural disturbance is limited to the lower third of the epithelium accompanied by cytological atypia
Moderate dysplasia	The architectural disturbance extends into the middle third of the epithelium; consideration of the degree of cytological atypia may require upgrading
Severe dysplasia	The architectural disturbance involves more than two thirds of the epithelium; architectural disturbance into the middle third of the epithelium with sufficient cytologic atypia is upgraded from moderate to severe dysplasia
Carcinoma in situ	Full thickness or almost full thickness architectural disturbance in the viable cell layers accompanied by pronounced cytological atypia

DISCUSSION

Oral submucous fibrosis (OSMF) is a chronic disease of the oral cavity, characterized by an epithelial and subepithelial inflammatory reaction followed by fibroelastic changes in the submucosa.[8] Oral submucous fibrosis has high occurrence in India. Most of the OSMF cases in this study were in their second and third decades with a male predominance. All the cases of OSMF consumed areca nut in some form. OSMF is considered a disease of multi factorial etiology and various theories have been proposed.[9] Excessive use of areca nut may cause fibrosis due to increased synthesis of collagen and induce the production of free radicals and reactive oxygen species, which are responsible for high rate of oxidation/peroxidation of polyunsaturated fatty acids which affect essential constituents of cell membrane and might be involved in tumorigenesis.[10] Leukoplakia is the most common premalignant or potentially malignant lesion of the oral mucosa.[11] Leukoplakia is at present defined as ‘‘A white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer”.[12]

On histopathological basis, difference can be seen in dysplastic and non-dysplastic leukoplakia. Dysplasia can be assessed on the basis of architectural disturbance with cytological atypia. In 2005 WHO classified dysplasia in 5 stages. (Table 2).[12] It is supposed that tobacco carcinogens can stimulate production of free radicals as well as reactive oxygen species, which are accountable for the increased rate of oxidation/ peroxidation of polyunsaturated fatty acids. Release of peroxide radicals is promoted by this peroxidation which leads to increased consumption of lipids.[5]

This affects important components of the cell membrane and might be involved in carcinogenesis / tumorigenesis.[13] Animal studies have shown that nicotine, which is a tobacco carcinogen, affects the activity of enzymes responsible for lipid metabolism.[14]

Newly forming and fast proliferating malignant cells need many basic components such as lipids well above the normal physiological limits leading to diminished lipid stores.[15,16] Lipid peroxidation can also develop lipid peroxidation product,

malondialdehyde, which cross-links with deoxyribonucleic acid (DNA) on the same as well as opposite strands via adenine and cytosine. This can contribute to carcinogenecity and mutagenecity in mammalian cells. [17]

The inverse relation was observed between the total cholesterol and disease stage and mortality in various malignancies.[15] In 1999 Rywik SL et al had shown a relatively high risk of cancer mortality with a significant lower total cholesterol and HDL. Lower level of TC was recommended due to increased consumption by tumor cells.[16]

Lower level was observed in plasma HDL in Oral leukoplakia and OSMF than controls were present in the study. This finding is in accordance with earlier reports, that low HDL levels is an additional predictor of cancer. Patel et al also reported that low levels of HDL may be a consequence of disease that is mediated by utilization of cholesterol for membrane biogenesis.[18] Jacqueline et al observed a lower HDL in widespread disease than with localized tumors.[17]

The range of LDL in oral leukoplakia and OSMF patients was respectively lower than the controls. Patel et al did not observe low levels of LDL in head and neck malignancies.[18]

Rose et al reported 66% higher mortality rate due to cancer in the group of cancer patients with lowest plasma cholesterol than in the highest plasma cholesterol.[19] The low plasma lipid status of the patient may be a positive indicator for initial changes occurring in neoplastic cells.

Neufeld et al have reported passive smoking as a significant risk factor for decreased HDLC.[20] In this study TC, HDL, LDL level analysis showed lower levels in oral leukoplakia and OSMF patients than that of the controls. Less difference was present in triglycerides and VLDL levels was observed in leukoplakia and OSMF patients than the control group. Our results have been in accordance to the previous studies that have been conducted before.[21,22,23] There was much more decrease in all the parameters in leukoplakia as compared to OSMF that can be due to the fact that most of the patients suffering from leukoplakia showed more dysplastic changes as compared to the OSMF patients who mostly showed early changes.[24,25] As it was a pilot study small sample size was taken. Tissue level lipid analysis should be done in further studies tissue to determine uptake of lipid by the altered tissue and comparision with oral cancer is also suggested for further studies

In conclusion TC, HDL, LDL level analysis showed lower levels in oral leukoplakia and OSMF patients than that of the controls. Less difference was present in triglycerides and VLDL levels was observed in leukoplakia and OSMF patients than the control group. Study with larger sample size should be done in this aspect for early diagnosis and management of oral leukoplakia and OSMF.

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