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Induced Biochemical Changes and Associated Complications In Smokers

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Abstract: *Worldwide more than 3 million people currently die each year from smoking. Smoking of tobacco is practised worldwide & common in the developing countries like India. The study is designed to determine the lipid peroxidation and antioxidant status along with serum calcium level in smokers (cigarette/bidi) with reference to the normal healthy non-smokers. 50 smokers(Cigarette/Bidi) of mean age 35± 5 years were enrolled for the study & were compared to 50 normal healthy non-smokers of the same age. Blood samples were obtained by puncture of antecubital vein and the following tests were performed i.e. P-MDA, Serum-SOD andS-Calcium. Increased plasma lipid per oxidation (P<0.05) was observed in cigarette / Bidi smokers. Also a significant hike (P<0.05) in serum SOD & serum Calcium were observed in smokers when compared to normal/healthy control subjects. The increased level of lipid per oxidation products in smokers reflects that there is increased cell wall damage that may further leads to several complications such as COPD, Stroke and the variety of lung and other cancers. It was also found that cigarette / bidi smoke alters the antioxidants status as well as minerals imbalance in smokers and increases atherogenecity.*

Keywords: *antioxidant, Bidi,cigarette,lipid peroxidation, smoking*.

I. Introduction

Smoking is an escalating health problem especially in a developing country like India[1]. Smoking is a well-recognised risk factor in the pathogenesis of pulmonary emphysema[2], coronary artery disease and aortic aneurysms[3].

Smokers are at greater risk for respiratory disorders, cancer, peptic ulcers, cardiovascular diseases, gastroesophageal reflux disease, bone matrix loss, hepatotoxicity[4, 5, 6] and pancreatitis[7]. In population where smoking has been common for several decades, about 90-95% of lung cancers, 80-85% of chronic bronchitis and emphysema and 20-25% deaths from heart disease and stroke are attributable to tobacco. For the developed world as a whole, about 40-45% of all cancer deaths among men are caused by smoking[8]. Smokers are generally reported to have almost doubled age-adjusted death rates[9].

Much recent concern has been risen about the possible health effects of involuntary health exposure of non-smoker to other people's tobacco smoke i.e. passive smoking. Passive smoking is reported to cause exacerbation of asthma and angina and chronic effects like increased risk of lung cancer, respiratory tract infection and atherosclerosis[10].

Cigarette smoke contains over 4700 different chemicals, 400 of which are proven carcinogens it also contains various oxidants such as oxygen free radicals and volatile aldehydes which are probably the major cause of damage to bio molecules[11].

In normal lung there are 50-70 inflammatory cells per alveolus; more than 80% are alveolar macrophages and less than 1% neutrophils[12]. In cigarette / bidi smokers the number of alveolar macrophages increases by at least 2-4 times and neutrophils by 10 times[13]. In vitro studies have shown that alveolar leucocytes and macrophages from cigarette / bidi smokers spontaneously release highly increased amounts of oxidants such as O_2^- and H_2O_2 compared with non-smokers[14, 15]. Passive cigarette smoking has also been associated with increased peripheral blood leucocytes count which shows enhanced release of oxidants[16].

Oxidants whether inhaled or generated from leucocytes, can inactivate the major antiprotease in the airways- alpha$_1$-Proteinase inhibitor (α_1PI) by oxidation of its active site[17, 18]. This diminishes the binding of α_1PI to elastase, hence reducing its inactivation and allowing it to bind to and destroy elastin leading to emphysema[19].

The WHO has been defined pulmonary emphysema as the combination of permanent dilatation of air spaces distal to the terminal bronchioles and the destruction of the walls of dilated air spaces[20].

Smoking induces three major adverse effects on liver: direct or indirect toxic effects[21], immunological effects[22] and oncogenic effects[23].Smoking yields chemical substances with cytotoxic potential which increases necroinflammation and fibrosis.

Minerals are involved as catalyst in most cellular enzyme catalyzed reactions and assume a major role in metabolism.

The present study was planned to understand induced biochemical changes influencing oxidant/antioxidant balance as well as mineral alterations in smokers (cigarette / bidi).

II. Material And Methods

50 Smokers aged between 18-75 years residing in Bhopal, India taking local diet were recruited in the study. 50 healthy non-smokers matched for age and dietary habitswere enrolled for the comparative assessment. Smokers were included if they had a history of smoking 7 or more cigarette/bidi per day. No participants had a history of hypertension, DM or any other systemic diseasepredisposing them to endothelial dysfunction. Further exclusion criteria were, current use of any transquillizers, drugs and anaesthetics. All the participants gave written informed consent.

Overnight fasting blood samples from human volunteers were taken by venipunture and were used immediately for analysis.

II.I Estimation of Serum Antioxidant Enzyme and Serum Mineral Content

The S-SOD was determined by Mishra H.P. and Fridovich I. (1972) method and S-Calcium by OCPC (O-cresolpthaleinComplexone) method.

II.II Estimation of Lipid Peroxidation

P-MDA was determined by thiobarbituric acid assay by Jean C.D. et al (1983).

III. Statistical Analysis

All variables are shown as the mean ± S.D. The data between control and test groups was compared using unpaired student's t-test. The level of significance used was $p<0.005$.

IV. Results

Table 1 shows stress markerenzymes (P-MDA and S-SOD) in plasma and serum of cigarette/bidi smokers and control groups. Cigarette / bidi smoking significantly ($p<0.001$) altered stress marker enzyme when compared with the control group. Enhanced activities of the minerals viz. S-Calcium ($p<0.001$) was observed in cigarette/bidi smokers when compared with the control group (Table 3). Table 4 shows stress marker enzymes and minerals in cigarette and bidi smokers. And the difference of all parameters viz. P-MDA, S-SOD, S-Calcium and S-Iron was found to be statistically ($p>0.05$) insignificant.

V. Tables

Table 1 Stress marker enzymes (P-MDA and S-SOD) in smokers and control group.

PARAMETER	CONTROLS	SMOKERS
P-MDA(nm/ml)	3.64±0.35	5.39±0.32
S-SOD(U/mg Protein/ml)	6.75±0.56	9.95±0.23

Table 2 Minerals (S-Calcium) in smokers and control group.

PARAMETER	CONTROLS	SMOKERS
S-Calcium (mg/dl)	7.80±0.30	9.62±0.36

Table 3 Stress marker enzymes and Minerals in Cigarette and Bidi Smokers.

S.No.	**GROUP**	**P-MDA (nm/ml)**	**S-SOD (U/mg Protein/ml)**	**S-CALCIUM (mg/dl)**
1	CIGARETTE SMOKERS	5.36±0.16	9.56±0.23	9.60±0.29
2	BIDI SMOKERS	5.43±0.41	9.53±0.23	9.64±0.42

VI. Discussion

Tobacco smoking has been identified as the single most important preventable cause of death for past three decades but unfortunately continues to be a common practise irrespective of all statutory warnings.

Cigarette smoking is known to cause free-radical generation in lungs. Cigarette smoke contains large amounts of proxidants that can directly initiate the process of lipid peroxidation as well as deplete the body of

nutrient antioxidant. Additionally, smoking elevates plasma and low density lipoproteins levels of peroxidation and favours low density lipoprotein oxidation in vivo. Free radical mediated lipid peroxidation has been associated with the pathogenesis of many diseases and clinical conditions.

The increased level of MDA demonstrated by us is an evidence of intensification of lipid peroxidation processes in smokers which may cause chronic stress for endothelial cells[24]. On the other hand it can also reorientate enzymatic systems of the arachidonic acid cascade towards intensified TXA_2 synthesis[25]. This increased lipid peroxidation in smokers are consistent with that reported by several authors.[26, 27, 28, 29, 30]

Our study found a significant increase in S-SOD level in smokers when compared with the control group. The present findings are in accordance with the study of Toth K M et al[31], I Rahman, W MacNEE[32], P. Padmavati et al [32], B Yokus et al[33], Abdurrahimet al[34]. Increased S-SOD enzyme activity may reflect the damaging effects of Reactive Oxygen Species which are involved in the development of degenerative diseases. It was also found that the circulating RBC's from cigarette/bidi smokers contains increased levels S-SOD and are more capable of protecting the endothelial cells from the effects of H_2O_2 than cells from non-smokers.

Ample evidence exists to suggest that smoking influences S-Calcium level, the significantly higher levels of S-Calcium obtained may be due to the toxic effects produced by smoking which causes a decrease in intestinal calcium absorption. Furthermore, there are substances in smoke such as cadmium that decreases calcium absorption. S-Calcium may be an independent risk factor for Myocardial Infarction in middle aged men followed for 18 years [35]. Smokers are susceptible to coronary artery disease [36]. It has been reported that the severity of coronary atherosclerosis is closely related to coronary artery calcification, which itself may correlate with s-calcium concentration. The present findings are in accordance with P.Padmavatiet al[37], R Jorde et al [38], Landin-Wilhelsen et al [39].

Our study found increased P-MDA, S-SOD and S-Calcium in Bidi smokers as compared to Cigarette smokers. Bidi's has been reported to produce higher levels of carbon monoxide, nicotine and tar than cigarettes[40].Bidi's produce approximately three times the amount of carbon monoxide and nicotine and five times the amount of tar than cigarettes.These substances may produce a greater amount of free radicals which causes more deleterious effect on lipid peroxidation resulting in an increased P- MDA and S-Calcium level and a decreased concentration of S-SOD activity due to utilization of the antioxidant in scavenging of the free radicals generated.

VII. Conclusion

In summary the findings from the present study have both clinical as well as public health implications. Cigarette / Bidi smoke with its heterogeneous composition of two phases- the gas and particulate, the resultant membrane - Cigarette / Bidi smoke interactions appear to be complex and the exact mechanism by which smoking enhances its effect remains uncertain. However the precise mechanism(s) of interactions of tobacco consumption products absorbed into the circulation with lipids, lipoproteins and other biomolecules and the consequences are of great importance which needs further in-depth study. It is also clear from the present study that smoking is an under estimated risk factor for respiratory, cardiac and liver diseases. In this respect also further well-designed studies are needed to clarify this issue.

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