STUDY ON THYROID STATUS AND OXIDANTS IN SMOKERS AND ALCOHOLICS

Praveen Kumar J[1], Deepa M[2], Julius A[3], Nadiger H.A[4]

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ABSTRACT: OBJECTIVES: Cigarette smoking and alcohol consumption has multiple effects on the thyroid gland. Ingestion of alcohol produces striking of metabolic imbalance in the liver, it leads to formation of reactive oxygen species, cigarette smoke is known to stimulate the alveolar macrophages to release excessive amount of free radicals which causes pathogenicity. Our study was designed to assess the thyroid status in smoking & alcoholism, also oxidant and antioxidant status in smokers and alcoholics. **MATERIALS & METHODS:** The study was conducted in50 smokers & alcoholics, they smoke 10-15 cigarettes per day and all are having history of alcohol intake from past 10-15years, as well as 25 healthy non-smoker volunteers served as controls. All the subjects are attended to O.P.D and admitted in medicine department P.E.S. Medical College & Hospital, Kuppam, A.P. The study was done by assessing thyroid profile (FreeT3,FreeT4,TSH) by ELISA method and oxidative stress parameters protein carbonylation, reduced glutathione were studied in RBC by colorimetric method. **RESULTS:** There is slightly elevated levels of TSH compared with controls (p=0.005). Free T3 levels slightly lowered compared with controls (p=0.001). Free T4 levels are normal in range for smokers and alcoholics. Reduced glutathione levels are decreased slightly compared with controls (P=0.076). Protein carbonylation is increased compared with controls (P=0.001). **CONCLUSIONS:** The above findings suggest that there is fall in thyroid action due to alcoholic liver damage, Antioxidants levels are decreased and oxidant levels are increased due to oxidative damage.

KEY WORDS: oxidants, antioxidants, alcoholic liver disease, cigarette smoking, alcoholism, thyroid status

INTRODUCTION: The health consequences of cigarette smoking and of other tobacco products are well known. They are important cause of increased mortality and morbidity in developed countries and the prevalence is increasing in the developing world as well. Cigarette smoking has multiple effects on hormone secretion in normal adults. These effects are mainly mediated by the pharmacological action of nicotine and also by toxins such as thiocyanate, 2, 3 hydroxy pyridine. Smoking affects pituitary, thyroid, adrenal and ovarian function (1).

The effect of tobacco smoke on thyroid function one related to higher levels of thyroxin binding globulin among smokers compared to non smokers and other related to higher levels of throtoxins in tobacco smoke in heavy smokers compared to light and moderate smokers(2)

Alcoholic liver disease is associated with abnormalities in circulating levels of thyroid hormone. Daily ethanol consumption decreases the levels of Free T3 & Free T4 in morning but not in the afternoon, the evidence that thyroid function commonly diminished in alcoholism, the correlation between Free T3 and liver function tests, suggests that changes in Free T3 reflects the severity of underlying liver diseases (3).

Thyroid dysfunction is known factor in alcoholism, where Free T3 & Free T4 levels are lower compare to normal and decreased hormone levels may be a result of heavy alcohol consumption (or) a trait marker of alcoholism(4).

Oxidative stress resulting from increased free radical production and or decreased antioxidant defense, the toxic substances generated during the metabolism of alcohol in the liver may contribute to the development of alcohol liver disease. Glutathione plays a major role in cellular protection against oxidative damage in patients suffering from liver diseases either due to nonalcoholic or excessive alcohol intake showed depletion of reduced glutathione levels, several factors contribute to the fall in glutathione level in alcoholic and non alcoholic liver diseases (5).

The reduced glutathione content of liver decreased with increasing concentration of ethanol exposure. These may be due to enhancement in the production of oxygen reactive species and or due to reduction in the level of endogenous antioxidants (6). The microsomal Cytochrome P450 system and xanthine oxidase pathway may be responsible for the generation of ethanol induced oxygen radicals, so the consequences of radical formation include the peroxidation of lipids, carbonylation of proteins and hydroxylation of nucleotides (7). Cigarette smoking contain 10^{15} oxidant molecules per puff, the oxidants in cigarette smoke causes injury to the lung by a number of mechanisms including the depletion of glutathione and other antioxidants(8).

Oxidized glutathione associated with excessive protein carbonylation accumulation in lungs of older smokers with long term smoking histories even in the absence of lung disease (9).

MATERIALS AND METHODS: The study conducted over a period of six months. The study was done by assessing thyroid profile [Free T3, Free T4, TSH] by ELISA methods and oxidative stress parameters, protein carbonylation and reduced glutathione by colorimetric method.

The study was conducted in 50 smokers and alcoholics, they smoke 10-15 cigarettes per day and all are having history of alcohol intake for past 10-15 years, suffering from alcoholic liver disease and all the subjects are attended to O.P.D and admitted in medicine department in P.E.S. medical college & hospital. As well as 25 health non smokers volunteers served as controls. The same procedure of sample collection and estimation of FreeT3, FreeT4, TSH, reduced glutathione, protein carbonylation is adopted for control subjects. The blood samples were collected after 12 hours of fasting for estimation of FreeT3, FreeT4 & TSH levels. Samples are collected in plain test tubes for thyroid profile and heparin bottles for the estimation of reduced glutathione and protein carbonylation estimation.

RESULTS: The study was carried out on 50 alcoholic liver disease patients, all are smokers compared with 25 controls (non alcoholic and non smokers). The results are statistically evaluated by standard statistical methods including Mean, Standard deviation (SD), and 'P' value. The mean values and standard deviation have been calculated and compared between patients and controls.

Sl.No	Parameter	Mean	S.D
01	FreeT3	1.77	0.58
02	FreeT4	1.52	0.67
03	TSH	5.53	3.29
04	Red. Glutathione	2.22	0.67
05	Pro. carbonylation	2.44	0.80

Table 1. Shows the status of mean and standard deviation of Free T3, Free T4, TSH, Reduced glutathione and protein carbonylation in smokers and alcoholics.

Sl.No	Parameter	Mean	S.D
01	FreeT3	2.76	0.65
02	FreeT4	1.54	0.63
03	TSH	3.90	0.88
04	Red.Glutathione	2.51	0.72
05	Pro.carbonylation	1.74	0.55

Table 2. Shows the status of mean and standard deviation of FreeT3, FreeT4, TSH, Reduced glutathione and protein carbonylation in control subjects.

Sl.No	Parameter	Patients		Controls		'P' value
		Mean	S.D	Mean	S.D	
01	FreeT3	1.77	0.58	2.76	0.65	0.001
02	FreeT4	1.52	0.67	1.54	0.63	0.460
03	TSH	5.53	3.29	3.90	0.88	0.005
04	Red. Glutathione	2.22	0.67	2.51	0.72	0.076
05	Pro. carbonylation	2.44	0.80	1.74	0.55	0.001

Table 3. Shows the Mean, Standard deviation and P values of all the investigations of the study done in smokers, alcoholics and controls.

Significant Findings: Among the smokers and alcoholics the mean value of Free T3 is found to be 1.77.pg/ml which significantly lower when compared to controls mean value 2.76.pg/ml.

Among the smokers and alcoholics the mean value of Free T4 is found to 1.52ng/dl. Which is closer to the mean value of controls group i,e. 1.54.ng/dl.

Among the smokers and alcoholics the mean value of TSH is found to be 5.53.mIu/l which is significantly higher than the mean value of 3.90mIu/l of the control group.

The mean value of reduced glutathione is found to be lower than the mean value of control group.

The mean value of protein carbonylation is found to be 2.44nmol/l which is significantly higher than the mean value of 1.74nmol/l of the control group.

DISCUSSION: The present study was conducted to find out whether, the thyroid status is normal or increased or decreased in smokers and alcoholics. Alcoholism and smoking is associated with changes in biochemical functions of various organ systems. Chronic daily ethanol consumption leads to 1) Chronically increased adrenal glucocorticoid activity 2) Decreased plasma testosterone 3) Decreased forebrain pro-opiomelanocortin gene expression. All of which are consistent with reported changes during abuse and alcoholism, each of these systems interact with Hypothalamo-pituitary- thyroid regulation.

Tobacco smoke contains several toxins such as thiocynate, 2,3 hydroxy pyridine, nicotine etc, several mechanisms by which smoking affects thyroid hormone levels are, thiocynate has been to be a potential goitrogen, thiocynate which has a half life of more than 6 days. It inhibits iodide transport and organification as well as increasing the efflux of iodide from the gland. Thiocynate also inhibit deiodinase activity there by lowering Free T3 levels which is physiologically active (10).

In the presence of iodine deficiency thiocynate can cause goiter, on the other hand 2,3 hydroxy pyridine inhibits thyroxin deiodination by limiting iodothyronine deiodinase activity this effect may slightly, but temporarily elevate serum thyroxin levels as a result of its deiodinase altering activity prior to decrease the levels(11).

Smoking and alcohol consumption are associated with a number of changes in cell functions and the oxidant and antioxidant system. The oxidative stress from cigarette smoking is substantial; cigarette smoke is known to stimulate the alveolar macrophages to release excessive amounts of free radicals which cause pathogenicity. Free radicals inhaled with smoke and the increased levels of oxygen derivatives generated in the lungs of smokers enter the circulation and modulate the antioxidant enzyme activities (12).

Based on the number of cigarette smoked per day the amount of exogenous reactive oxygen species (ROS) from cigarette smoke was similar for all current smokers regardless of their age. The reaction of ROS with protein results in the formation of carbonyl groups of amino acid residues. So oxidative stress overwhelming the antioxidant defense of the lung may lead to injury through a variety of mechanisms including lipid peroxidation of endothelial cell membrane, total proteins carbonyls are reportedly increased (13).

In alcohol metabolism and detoxifying metabolism liver plays the major role, liver is sensitized by induction of Cytochrome P 450 especially Cytochrome P II E for catabolism of alcohol in the process of detoxification and the metabolism of Cytochrome P 450 ROS is produced more, which are responsible for the damage of cellular proteins and membrane. Inadequate clearances of ROS are produced disproportionately higher than the antioxidants (14). Inadequate removal of ROS may cause cell damage by attacking membrane lipids, proteins and inactivating enzymes thus mediating several forms of tissue damage (15).

The present study was conducted to test the thyroid status and oxidants/antioxidant status in smokers and alcoholics, thyroid dysfunction is a probable association with alcoholism and smoking, Free T3 levels are decreased, Free T4 levels are normal and TSH levels are raised may be a result of chronic alcoholism and trait marker of alcohol consumption and smoking.

FreeT4 is the primary secretory product of the normal thyroid gland. FT4 undergoes peripheral deiodination of the outer ring at 5'position to yield FT3. This deiodination occurs in a number of tissues but primarily in the liver (16). Due to alcoholic liver damage conversion of FT4 to FT3 is decreased, and by automatic feedback stimulation TSH levels are raised.

In smokers and alcoholics the oxidant/antioxidant levels are altered, reduced glutathione a major intracellular non-enzymatic antioxidant was reduced in alcoholics and smokers (17).

There are significant increasing protein carbonyls in smokers and alcoholics compared to normal subjects. Alcoholism and smoking seen to have still greater degree of oxidative stress, which may be due to compounding effect of smoking. The present study suggests that, with increasing oxidative stress, there is corresponding decrease in antioxidant defense system.

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AUTHORS:

1. Praveen Kumar J.
2. Deepa M.
3. Julius A.
4. Nadiger H.A.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Biochemistry, PES Institute of Medical Sciences and research.
2. Assistant Professor, Department of Biochemistry, PES Institute of Medical Sciences and research.
3. Professor and HOD, Department of Biochemistry, Sri Balaji Dental College, Chennai.
4. Professor and HOD, Department of Biochemistry, PES Institute of Medical Sciences and research.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Praveen Kumar J,
No. 308, E-Block, Staff Quarters,
PESIMSR Campus,
Kuppam, Chittor – 517425, A.P.
Email- jpraveen007@yahoo.com

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