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Altered Levels of Ceruloplasmin, Glutathione, Beta-Carotene in the Serum of Chronic Cigarette Smokers In Comparison With Non-Smokers

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ABSTRACT

Antioxidants areaccepted as some of the best tumour markers and hence there is a requirementand need to co-relate the levels of these biomarkers with the habits which are implicated in carcinogenesis. The objective of this study is to evaluatethe effect of smoking on various antioxidant level required for normal functioning and assess the deleterious effects of smoking on the normal metabolism function of body. Serum levels of ceruloplasmin, glutathione and b-carotene were estimated in200 age-matched subjects in 3rd and 5th decade of life. These subjects were grouped intotwo groups of, one control group comprising of healthy individuals without habits and the other case group comprising ofindividuals who were chronic smokers. The levels of ceruloplasmin and glutathione were found to be significantly decreased in case group whereas b-carotene level was significantly elevated when compared to control group. Ceruloplasmin and glutathione issignificantly decreased in case group while b-carotene significantly elevated indicatingthe severity of effects of smoking on normal tissue as well as body's attempt to thwart off the deleterious effect of this habit from effecting normal homeostasis and function.

keywords: Ceruloplasmin; Glutathione; B-Carotene; Antioxidants; Tumour Markers; Smoking

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INTRODUCTION

A very intimate relationship exists between oxidative challenge caused due to excessive smoking and oxidative stress leading to carcinogenesis. Oxidative challenge due to chronic smoking of cigarettes results due to the generation of free radicals under the effect of chemical carcinogenesis.

Tobacco use leads most commonly to diseases affecting the heart and lungs, with smoking being a major risk factor for heart attacks, strokes, chronic obstructive pulmonary disease, emphysema, and cancer (particularly lung cancer, cancers of the larynx and mouth, and pancreatic cancer). Smoke contains several carcinogenic pyrolytic products that bind to DNA and cause many genetic mutations. Smoke contains several carcinogenic pyrolytic products that bind to DNA and cause genetic mutations. Particularly potent carcinogens are polynuclear aromatic hydrocarbons (benzopyrene,acrolein,crotonaldehyde) and Nitrosamines, which are toxicated to mutagenicepoxides which are electrophilicalkylating agents.

One significant characteristic of free radical reactivity is lipid peroxidation which results in deleterious effects on cell leading to their damage. Many chemical carcinogens are shown to b metabolically converted to free radicals which is facilitated by lipid peroxidation [1]. To combat these oxidative challenges our body has evolved quite a lot of anti-oxidant systems and one of the most efficient being the ceruloplasmin.

Glutathione is a ubiquitous thiol containing tripeptide which is important defense against free radicals and hydroperoxides. Glutathione has important function such as storage and transport of cysteine, maintaining the reducing state of proteins and thiols, and protecting the cells from toxic compounds such as reactive oxygen species, drugs or heavy metal ions [2].

Beta-carotene is one of the most efficient substances known for quenching the excitation energy of singlet oxygen and for trapping certain organic free radicals [3, 4]. The properties of beta carotene on enhancing gap junctional communication and inhibitory lipid peroxidation in chemically induced neoplastic transformation and as a chain breaking anti-oxidant in the lipid phase by neutralizing peroxy radicals have obvious implications for controlling cancer growth [5].

In the present study, the concentration of ceruloplasmin, glutathione and b-carotene in serum samples from patients with chronic smoking were observed to gauge the possible use of the anti-oxidants in assessing the amount of oxidative damage caused by the deleterious habit as well as help in charting better treatment plan in managing lesions caused in association with this habit.

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MATERIAL AND METHODS

The material for the present study comprised a total of 200 subjects reported to various hospitals in and around Mangalore. These entire individual were age-matched in range of 3rd and 5th decade of life. These subjects were grouped into two groups:

Group 1 (Control Group)→ 100 healthy subjects in control group without any habit and oral lesions.
Group 2 (CaseGroup)→ 100 patients who were chronic smokers without any other habit and oral lesions.

Inclusion criteria:

1. Smokers with frequency of more than 15 cigarettes per day and duration of 10 or more years
2. Patients are males in age group in range of 3rd and 5th decade of life.
3. Patients with absolutely no other habits other than smoking.
4. Patients who are otherwise healthy with no evidence of oral or systemic diseases.

Exclusion criteria:

1. Patients who have any other habits other than smoking.
2. Patients who have any evidence of oral or systemic diseases.
3. Patients with metabolic disorders either congenital or acquired.

5ml of venous blood was drawn and was centrifuged, serum separated and transferred into vaccutainers for transport to laboratory for analysis.

Estimation of serum ceruloplasmin was done usingDiamine Oxidase Method. Serum glutathione level estimation was done using DTNB Method [5,5-Dithio Bis-2-Nitro Benzoide]. Estimation of serum b-carotene was done using Atomic Absorption Spectrophotometry.

RESULTS AND OBSERVATIONS

In the present study, descriptive statistics of ceruloplasmin, glutathione and b-carotenewas done for both the groups and this includes mean and standard deviation. Also the results were analyzed using Mann-Whitney 'U' test for ceruloplasmin, glutathione as well as Students Unpaired testfor b-carotene and assessed for significance.

Table 1: Descriptive Statistics of Serum Ceruloplasmin(*mg/Dl)*in Case and Control Group

Case	Control	Z	p
Mean + SD	Mean + SD		
0.1525+0.05	38.8+12.37	28.74	<.001 vhs

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Table 2: Descriptive Statistics of Serum Glutathione(*mg/Dl)*in Case and Control Group

Case	Control	Z	p
Mean + SD	Mean + SD		
0.8824+0.1583	36.61+ 14.43	14.85	<.001 vhs

Table 3: Descriptive Statistics of Serum B-Carotene(*µg/Dl)* in Case and Control Group

Case	Control	t	p
Mean + SD	Mean + SD		
15.96+0.735	8.502+0.751	70.973	<.001 vhs

In the present study, when inter-group comparison was done for serum ceruloplasmin levels between control (Group 1) and case (Group 2) using Mann-Whitney 'U' test for significance, it was found to be very highly significant with decreased serum ceruloplasmin level in Group 2 (p=<0.001). Likewise when inter-group comparison was done for serum glutathione levels between control (Group 1) and case (Group 2) using Mann-Whitney 'U' test for significance, it was found to be very highly significant with decreased serum glutathione level in Group 2 (p=<0.001). Also when inter-group comparison was done for serum b-carotene levels between control (Group 1) and case (Group 2) using Students Unpaired test for significance, it was found to bevery highly significant with increased serum b-carotene level in Group 2 (p=<0.001). Adecrease was seen in the mean serum ceruloplasmin value in Group 2 (mean=0.1525) on comparison with Group 1 (mean=38.8). Likewise adecrease was also seen in the mean serum glutathione value in Group 2 (mean=0.8824) on comparison with Group 1 (mean=36.61). Anincrease was seen in the mean serum b-carotene value in Group 2 (mean=15.96) on comparison with Group 1 (mean=8.502).

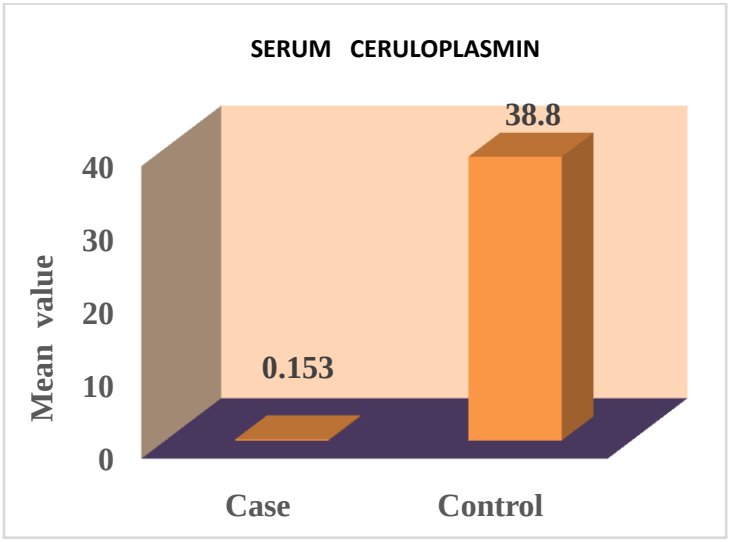

Diagram 1: Comparison of Mean Serum Ceruloplasmin*(Mg/Dl)* among Control and Case Groups

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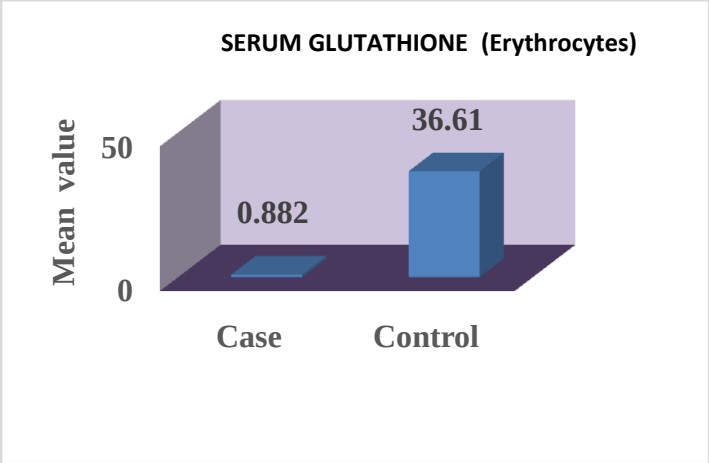

Diagram 2: Comparison of Mean Serum Glutathione*(Mg/Dl)* among Control and Case Groups

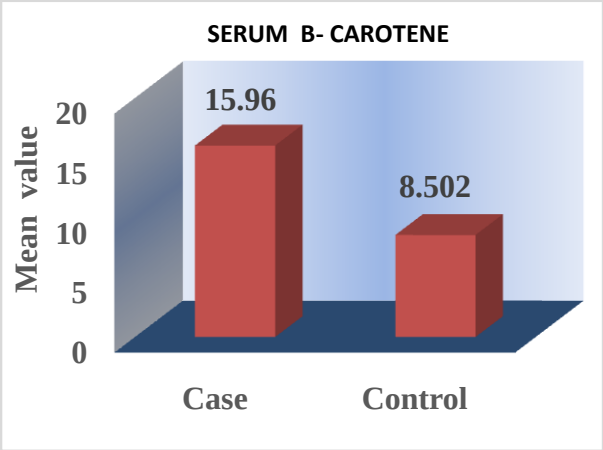

Diagram 3: Comparison of Mean Serum B-Carotene*(µg/Dl)* Among Control and Case Groups

DISCUSSION

Chronic smoking leads to oxidative challenge and results in formation of oxidative stress leading to formation of many deleterious substances including free radicals. It is very clear that free radicals play an essential part in carcinogenesis by damaging the cellular material and in transforming the normal cells to malignant cells. To destroy these free radicals and to reduce the reactive oxygen intermediates, the body synthesizes antioxidants in the form of ceruloplasmin, glutathione and b-carotene.

Ceruloplasmin is a potent free radical inhibitor both in tissue homogenates and in simple lipid emulsions- an antioxidant. The protein is one of the acute phase reactants whose concentration in plasma rises after tissue injury. Most acute phase proteins can be thought of as protecting the organism as a whole from the possible ill-effects of local damage. One of the ill-effects could be the release of free-radical oxidation products. Thus the organism responds by raising the antioxidant efficiency of plasma [6].

Since free radical and superoxide production increases in case of oxidative challenge, there is excessive sequestration of ceruloplasmin as the body tries to ward off any potential damage being caused due to excessive smoking. As a result of this serum ceruloplasmin level decreases in chronic smoking.

Glutathione and other antioxidants have been shown to protect against mutagenesis and also delay in apoptosis stimulated by various signals. Efflux of glutathione from the cell stimulates apoptosis providing antioxidants extracellularly, and possibly stimulates phagocytic cells to engulf the apoptotic cells. These mechanisms play a vital role in prevention of mutagenesis in patients [7].It is the also major intracellular antioxidant [8], detoxifies many carcinogens through Phase II conjugation, and maintains immune function by regulating mitogenic response and lymphocytic proliferation [9,10].

For the same reason as with ceruloplasmin even the level of serum glutathione decreases in cases of excessive oxidative stress such as chronic smoking. Beta carotene is an essential precursor of vitamin A or retinol. It is an excellent antioxidant and radical trapping agent, especially for peroxyl and hydroxyl radicals, which have been implicatedin the genesis of a number of cancers [11]. Role of beta-carotene, a well- known carotenoid, as a cancer protective agent has been acceptedand an apparent primary mechanism of effect as an antioxidant has been established[12].The free radical scavenging nature of beta-carotene and its immediate involvement in trapping singlet oxygen providing an overall increased reducing environment in the tissues entails its anticancer potential.

Since smoke from cigarettes contain a wide variety of carcinogens and mutagens, the absorption and expression of b-carotene increases in chronic smokers. Decrease in serum ceruloplasmin concentration correlates with increase in free radical and superoxide production due to increased oxidative challenge resulting from chronic smoking. The results of the present study strongly suggest the deleterious effects of smokingin oxidative stress and subsequently in carcinogenesis.

Serum glutathione has been shown to be a powerful antioxidant of free radicals and superoxide ions and its level directly correlates to the amount of oxidative stress caused as a result of excessive chronic smoking. In present study there is a highly significant decrease in its level in chronic smokers indicating the deleterious effects of smoking on the cellular metabolism of the body. Serum b-carotene levels are increased in chronic smokers in the present study indicating the body's effort to counter the deleterious effects of smoking and thereby establishing the toxic effects of smoking on various body compartments.

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