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RESEARCH ARTICLE

VITACIN C METABOLISM IN ACTIVE SMOKERS. DO THEY NEED VITAMIN C SUPPLEMENTS ?.

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Abstract

Smoking is a established cardiovascular disease risk factor. Oxygen derived free radicals play a crucial role in causing endothelial dysfunction. Endothelial dysfunction in turn has been proposed to play a pathogenic role in the initiation of vascular diseases. Vitamin c is an important physiological antioxidant. Vitamin c has also been shown to regenerate other antioxidants within the body. By limiting the damaging effects of free radicals through its antioxidant activity it might help prevent or delay the development of certain diseases including cardiovascular diseases. This study was aimed to evaluate vitamin C metabolism in chronic smokers from central Bihar, India. 50 male cigarette smokers and 50 male non-smokers were enrolled. It was found that mean serum vitamin C level were significantly lowered and mean urinary vitamin C excretion were significantly higher in smokers as compared to non-smokers. Serum vitamin C level and urinary excretion of vitamin C showed a inverse strong correlation in smokers (r=- -0.9335) but interestingly this correlation was very poor in non-smokers(r=-0.2201). .So smoking causes serious risk of hypovitaminosis which may lead to serious diseases including cardiovascular disease. For active smokers vitamin C supplementation should be seriously considered, if cessation of smoking is not possible.

INTRODUCTION

Cigarette smoking is the most common type of tobacco use . By 2030, if current trends continue, smoking will kill more than 9 million people annually [1].Smoking is considered as a major risk factor for many diseases including cardiovascular disease.[2]

There is a dose response relationship between the number of cigarettes smoked and cardiovascular morbidity and mortality [3]. The mechanism by which cigarette smoking causes atherosclerosis remains obscure.

Blood of cigarette smokers routinely displays decreased antioxidant capacity and increased oxidized lipids compared to non-smokers [4]. Oxidative pathway appears to be one important mechanism for modifying LDL, because a wide variety of structurally unrelated antioxidants inhibit atherosclerosis in animal models of hypercholesterolemia [5]. Evidence suggests that oxidatively modified LDL contribute to the pathogenesis of atherosclerosis [6].

Cigarette smoke contains approximately 10^{17} oxidant molecules per puff [1] that can cause damage to lipids, proteins, DNA, carbohydrates, and other bio-molecules [7] . It is becoming increasingly evident that a pro-oxidant / antioxidant imbalance largely contributes to atherosclerosis processes [8]. It has been postulated that many of the adverse effect of smoking may result from oxidative damage to critical biological substances[9]. Previous reports have demonstrated abnormal endothelial function in chronic smokers [10]. Endothelial dysfunction in turn has been proposed to play a pathogenic role in the initiation of vascular disease [11]. Although smoking induced endothelial

dysfunction is very likely multifactorial, more recent clinical and experimental observations strongly point to a potential role of oxygen derived free radicals in mediating this phenomenon [6].

In vivo, antioxidant nutrients, including vitamin C play crucial roles in defending against oxidant damage [7]. Vitamin C protects against oxidation of isolated LDL by different types of oxidative stress, including metal ion dependent and independent processes [12].

Cigarette smoking is associated with decreased serum vitamin C concentration [7] and this association was seen despite correction for factors which independently affected serum vitamin C levels such as age, gender, race, and BMI [13].

Present study is undertaken to evaluate serum vitamin C as indicator of antioxidant level in smokers and non smokers. Changes in serum concentration of vitamin C in chronic smokers might be due to changes in urinary excretion of vitamin C . But no study to date has confirmed it. It is interesting to study the effects of smoking on serum concentration of vitamin C and urinary excretion of vitamin C together and to get some clue to decreased serum concentration of vitamin C among them.

MATERIAL AND METHOD

The study was conducted on 50 healthy male cigarette smokers in age group of 25-45 years and it was compared with 50 healthy age, diet and Body mass index (BMI) matched non smokers. Controls and cases were selected from a tertiary care hospital in Bihar after obtaining informed consent and this study was approved by the ethical committee.

Inclusion criteria:

1 Male subjects aged between 20-50 years.

2 Smokers - Persons smoking 5 Cigarettes or more per day continuously for 2 year were considered as smokers.

3 The smokers were divided into three groups. Mild smokers (Group a) = 5-10 cigarettes per day. Moderate smokers (Group b) = 11-15 cigarettes per day. Heavy smokers (Group c) = >15 cigarettes per day.

Exclusion criteria:

1. Subjects with history of medical disorders such as diabetes, hypertension, hepatic, renal and cardiac disorders.
2. Ex smokers, alcoholics, obese (BMI >30).
3. Subjects on medications such as vitamin supplementation and herbal medications.

A detailed physical examination of the subjects of both groups was done. After 12 hrs overnight fasting, venous blood samples were drawn and subjected to laboratory investigations including blood glucose, blood urea ,serum alkaline phosphatase, haemogram and serum vitamin C. Serum vitamin C concentrations were measured by the ascorbate oxidase method [14] . Just before taking the blood sample, the subjects were instructed to collect about 15-20 ml urine in a dry beaker .It was used for the estimation of urinary vitamin C. For the estimation of urinary vitamin enzymatic C, a method given by Harris and Ray [15] ,was used .

Table 1

Showing clinical characteristics in non-smokers and smokers.

Parameters	Smokers(n=35)	Non-smoker(n= 35)
Age(yrs)	33.60± 5.80	33.52±4.58
Body weight(Kg)	57.80±6.10	56.78±5.78
Height(cm)	165±10.20	165±9.99
BMI(Kg/m2	22.56±3.20	22.52±3.71

All parameters were not significantly different between groups.

Table 2

Showing lipid profile and urinary excretion of vitamin C in smokers in comparison to non-smokers

Tests	Smokers	Non -smokers	p value
Serum Vit. C (mg/ml)	0.80±0.04	1.22±0.06	0.032*

Urinary Vit. C(mg/ml)	1.68±0.09	1.00±0.08	0.000*

*P value <0.05 is considered as statistically significant

Table 3

Showing serum vitamin C and urinary excretion of vitamin C in relation to no. of cigarettes smoked per day.

tests	***5-10 Cigarettes/day (n=20) (a)***	***11-15 Cigarettes/day (n=18) (b)***	***P value (a)-(b)***	**>15 cigarettes/ Day(n=20) *(n=12)* ©**	***P value (a)-(c)***
Serum Vit. C (mg/ml)	0.870±0.06	0.81±0.07	***0.083***	0.72±0.08	***0.052***
Urinary Vit. C(mg/ml)	1.42±0.07	1.68±0.04	***0.064***	2.02±0.06	***0.005****

*P value <0.05 is considered as statistically significant.

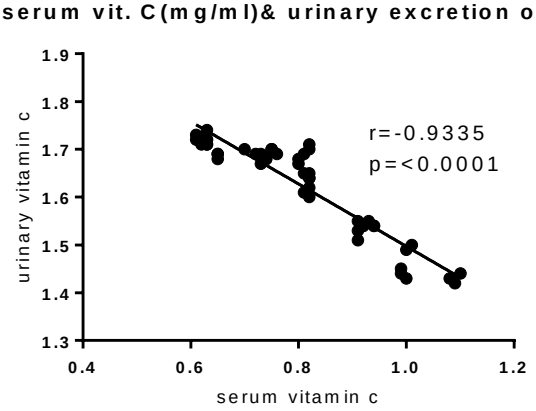

Figure 1

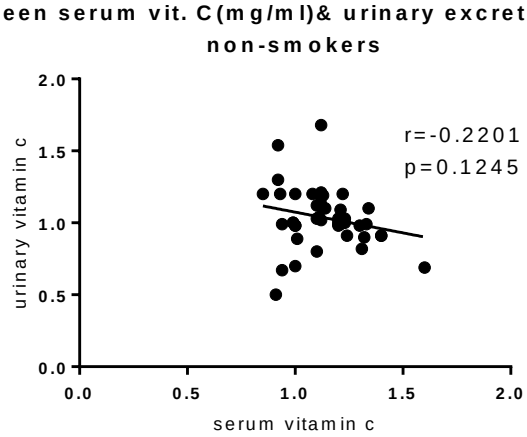

Figure 2

DISCUSSION

In the study, the two groups of subjects (smokers and non-smokers) were of Comparable sex, age, BMI and diet. They were non-diabetic, non-alcoholic, normotensive Subjects.

It was observed that mean serum vitamin C level is significantly lower in smokers as compared to non smokers. The mean serum vitamin C level was lower in smokers who smoked higher numbers of cigarettes than those who smoked lesser number of cigarettes. These findings are in accordance with the study of Schectman *et al*.[13]

Rosemary L S et al[16] has reported that mean serum concentration of vitamin C of smokers was 33% lower than that of nonsmokers. They have also reported that Vitamin C supplement users had significantly higher mean serum concentrations of vitamin C than did nonusers of vitamin C supplements.

The mean value of urinary excretion of vitamin C was significantly higher in smokers than non smokers. The mean value of urinary excretion of vitamin C was higher in smokers who smoked higher numbers of cigarettes than those who smoked lesser number of cigarettes/day.

Sulochana G and Arunagiri R have reported that smoking acutely increases urinary excretion of vitamin C, [17] also suggesting an accelerated metabolism in smokers.The two group of subjects were comparable regarding the variable known to affect vit. C status. There was inverse strong inverse correlation(Figure 1) between serum level of vitamin C and urinary excretion of vitamin C in smokers. Rosemary L S et al[16] has also reported that smoking increases turnover of vitamin C. Thus it seems reasonable to speculate that the difference in fasting serum vitamin C levels we observed between the two groups were secondary to cigarette smoking and lower plasma vitamin C level in smokers could be caused by increased turn over of vitamin C in smokers.

The biological mechanism linking smoking and atherogenesis, the process leading to cardiovascular diseases, is complex and not fully understood. The current opinion is that atherosclerosis is an immune/ inflammatory response of the intima to endothelial injury [18,19] It is also well known that the injury is mainly initiated by lipid accumulation.[19,20]. Native plasma lipids, in particular native LDLs, can freely enter the intima and are taken up by vascular cells via LDL receptor-mediated endocytosis. Nevertheless, they do not primarily initiate an inflammatory response, they are not phagocytosed by monocytes, and they do not initiate atherosclerotic alterations [20,21]. Oxidation or other modifications of LDL, however, substantially alter its role: oxidized or modified lipids are chemotactic for monocytes, induce migration, initiate inflammatory responses, alter the endothelium, induce differentiation of monocytes into macrophages, and are avidly taken up by macrophages via scavengerreceptors [20,22,23].

Modified LDL is recognized by scavenger receptors distinct from the 'classical' LDL receptors present on all mammalian cells 30. Scavenger receptors bind and internalize modified low-density lipoprotein (LDL). Because the expression of scavenger receptors is not down-regulated by cholesterol, macrophages expressing scavenger receptors can internalize substantial quantities of cholesteryl ester from oxidized LDL leading to foam cell formation.

In cigarette smokers, low density lipoprotein (LDL) is more prone to oxidation due to higher level of ROS and reactive nitrogen species [24]. Oxidatively modified LDL limits the bioactivity of endothelium-derived NO; and, in turn, the loss of NO bioactivity is associated with increased inflammatory cell entry into the arterial wall [25]. Antioxidant vitamin C improves endothelial dysfunction in chronic smokers. Antioxidant mechanism of vitamin C include an inhibition of smoke- induced leukocyte adhesion to vascular endothelium, and protection of LDL against atherogenic modification [9].

Wei wei et al [7] using NHANES III data reported that serum vitamin C was inversely associated with serum cotinine even after diet adjustment, this indicates that declines in serum level of vitamin C in smokers is a metabolic effect of smoking.

The lowered serum vitamin C levels in smokers could be due to either impaired vitamin C absorption or increased turnover. On the basis of studies measuring urinary vitamin C excretion in conjunction with the administration of known vitamin C intakes, Pelletier suggested the presence of impaired bioavailability but normal turnover of vitamin C in smokers [26,27]. On the other hand, Kallner, et al, [28] measured vitamin C kinetics using radio-labeled ascorbic acid and demonstrated increased turnover in smokers but only small differences in absorption when compared to non-smokers. Our study is consistent with this experimental study. So smokers not taking nutritional supplements, may be at substantial risk.

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