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Depressive, hypertensive and dyslipidemic effects of exposure of Nickel along Cigarette smoking

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Abstract: In human body cigarette smoking disturb the metal homeostasis that has a vital part in maintaining the health and growth. The objective of the current work is to evaluate the link of toxic element such as nickel (Ni) through cigarette smoking with commencement of physiologic (hypertension and dyslipidemia) and psychiatric illness (depression) in adolescent age. Hundred smokers and hundred non-smoker males, with 19-23 years of age, having body mass index (BMI) $\leq$ 25kg/m^2 were participated in this study. Serum levels of cholesterol, tryptophan (TRP), Ni, and mean systolic and diastolic blood pressure (BP) were analyzed with conventional techniques. Statistic was done by SPSS software using Paired sample *t-test*. Serum quantities of cholesterol and Ni were greater while tryptophan was smaller in smoker than non-smokers. On the other hand, average BP was elevated in smokers than normal subjects. It is concluded that high contact to toxic metals like Ni via cigarette smoking possibly be associated with high risk of psychiatric and physiologic illnesses.

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INTRODUCTION

Discrepancy of various trace elements may be involved in the pathology of number of diseases[1]. Smoking, however, is a vital basis of exposure to toxic elements such as nickel (Ni), lead (Pb) and cadmium (Cd) that have been projected as contributing agents of cigarette smoke-induced hypertension[2,3], cardiovascular (CVD)[4] as well as depression[5].

In general, high rate of cigarette smoking was observed in peoples with depression. Studies suggested that tryptophan (TRP), an essential amino acid is the precursor of serotonin. The plasma levels of TRP become decreased in depressed peoples[6]. Though, the relationship between tobacco smoking and depression seems to be bidirectional. Conversely, there is proof suggesting cigarette smoking increases the risk of depression[7]. Tobacco and tobacco smoke contain over 8,400 chemical constituents[8,9]. The compounds present in tobacco smoke is Pb, which has been allied with depression[10], and Ni[11], which has neurotoxic properties.

Hypertension and CVD are major community health concern. The occurrence of hypertension and CVD increases with age[12]. Yet people < 25 years old have hypertension and CVD troubles because of deficiency of exercise, fatty meals, smoking, caffeine and ethanol intake[13]. Inherited consequence may also be a factor[14]. An observational study revealed that severe symptoms (sturdy wish to smoke) occurred in young people within days after the early initiation of smoking[15].

Cigarettes contain 1-3 µg of Ni and an individual can inhale 3-13 µg of Ni for every set of cigarettes smoked[16]. It is a very important trace constituent, if too little or surplus amount of Ni is taken up it could be a result of toxicity symptoms[17]. As Ni is ubiquitous and is crucial for the physiology of several organisms, concentrations in some areas from both anthropogenic release and naturally varying levels may be toxic to living organisms[9].

Studies on animals and human both have confirmed that Ni and various Ni compounds are involved in progression of cancer[19]. Ni might engage in oxidative response such as lipid peroxidation (LP). Extensive studies have confirmed that increase LP was observed in various organs such as liver, lung, bone marrow, serum and kidney[20]. LP might be a contributing factor in Ni-elicited oxidative stress[21].

In the light of above mentioned literature, the aim of the current piece of work is to find the link of noxious metal experience *mainly Ni* via cigarette smoking with physiologic (CVD, hypertension) and psychiatric (depression) troubles.

MATERIALS AND METHODS

Subjects

One hundred smokers and one hundred non-smokers males (from 19 to 23 years) were selected for the present study, which are resident of various areas of Karachi (North Karachi, Gulshan-e-Iqbal, Gulshan-e-hadeed, Nepa Chorangi, Nazimabad), Pakistan. Subjects those engaged in this study were having normal body mass index (BMI)$\geq$ 25kg/m^2 (Table 1). The study protocol and procedures were approved by institutional ethics committee; all participants gave informed consent for their participation.

Study design

Thirty minutes before starting physical/health check up, participant advised to withdraw from smoking. Individual tallness and total body weight were calculated with complete garments and shoes, and 1.0 kilogram was deducted to get the total weight. The net weight/square of height in meter shown as body mass index (BMI).

Blood pressure (BP) was calculated subsequent to latent on chair for 5min or greater by sphygmomanometer with a right size cuff with arm set at the cardiac level. The mean of BP was calculated by the method illustrated by Noborisaka et al[3] for the expediency of the statistical analysis.

Sample collection and biochemical estimation

Serum was extracted from blood samples and ice-covered at –35°C until the estimation of Ni, TRP and cholesterol.

Estimation of TRP

Serum TRP concentration was analyzed by High performance liquid chromatography (HPLC-EC) as documented previously[22]

Estimation of Ni

Serum Ni was quantified by Flam atomic absorption spectrophotometry (FAAS) as reported previously.[23]

Estimation of Cholesterol

Serum cholesterol was determined by method of Arnold and Cheryl[24].

Statistical analysis

Paired sample *t-test* was used for the statistical analysis of serum levels of Ni, tryptophan, cholesterol and mean BP. *P* value of < 0.05 was considered as significant.

RESULTS

Paired sample *t-test* was used for statistical analysis of average BP, cholesterol, TRP and Ni in smokers and control individuals. The mean values of BP ($t_{df,99}$=10.344), Ni ($t_{df,99}$=36.52) and cholesterol ($t_{df,99}$=14.943) were significantly (P<0.05) greater, while concentration of TRP ($t_{df,99}$=20.178) was significantly (P<0.05) smaller in smokers than control individual.

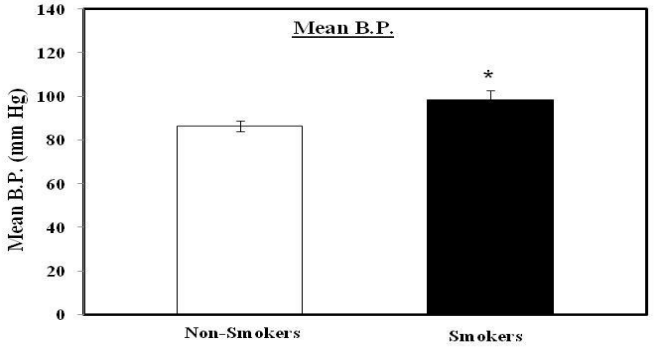

Figure 1: The mean BP of smokers and non-smokers subjects. Values are mean+ S.D.

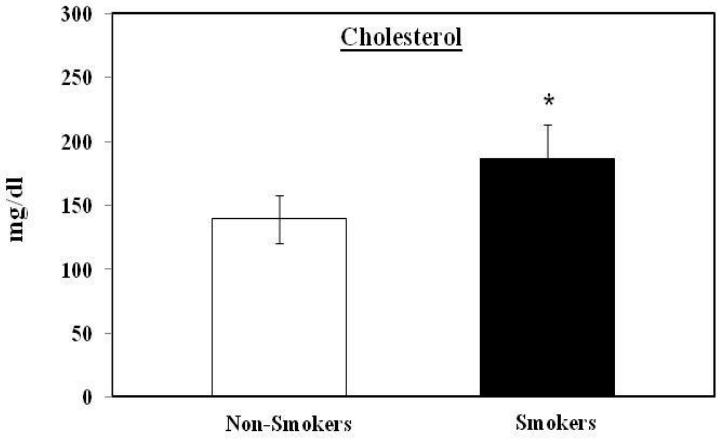

Figure 2: The serum levels of cholesterol of smokers and non-smokers subjects. Values are mean+ S.D.

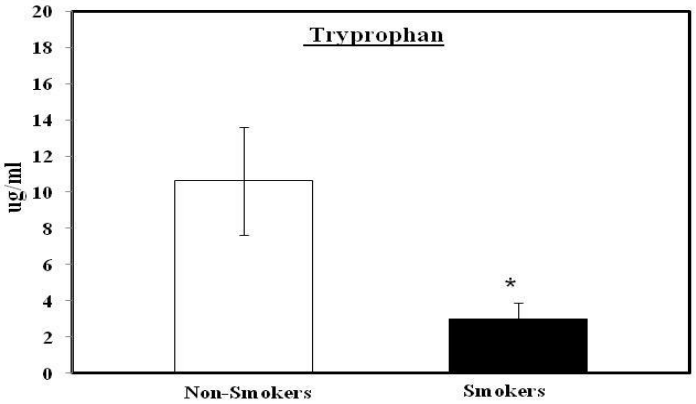

Figure 3: The serum levels of Tryptophan (TRP) of smokers and non-smokers subjects. Values are mean+ S.D.

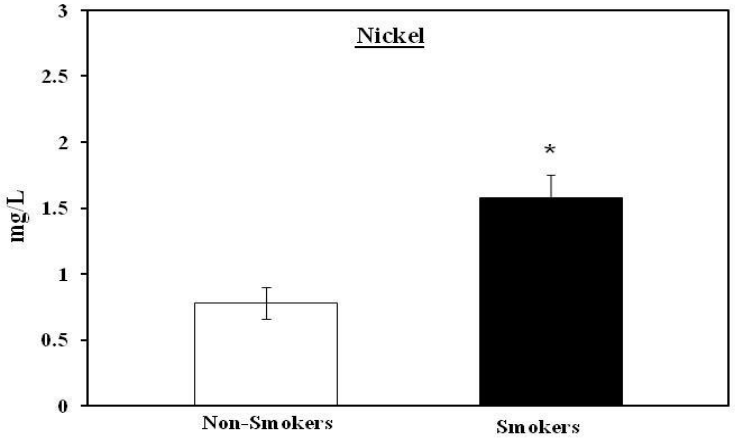

Figure 4: The serum levels of Nickel (Ni) of smokers and non-smokers subjects. Values are mean+ S.D.

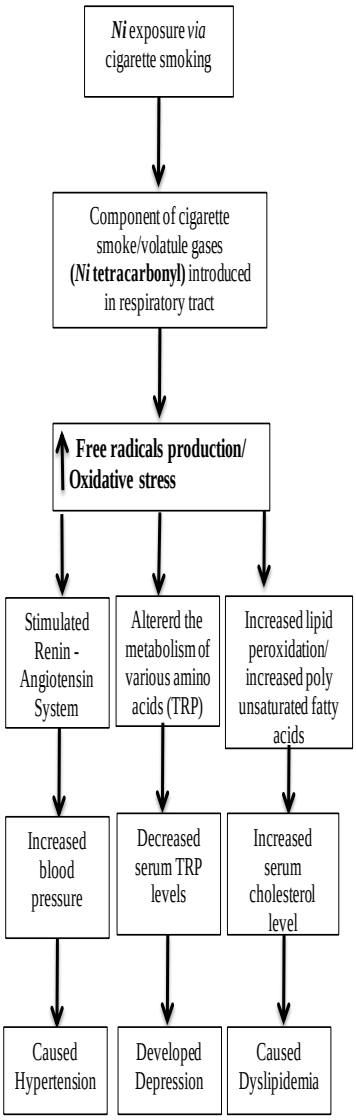

Figure 5: Mechanisms for *Ni* exposure via cigarette smoking-mediated hypertension, depression and dyslipidemia.

DISCUSSION

In smokers, serum levels of cholesterol (fig. 2) and Ni (fig. 4) were elevated while TRP (fig. 3) levels were decreased. At the same way, mean BP (fig. 1) was also greater (indicates hypertension) in smokers. Significance of the present work is that, we pivoted on to seek likely association of Ni to depression (decreased serum TRP level), hypertension (increased BP) and CVD (increased cholesterol level).

Immunotoxicity, neurotoxicity, genotoxicity, hepatotoxicity and nephrotoxicity are the harmful effects which could be linked to Ni[25]. It has harmful effect on reproduction because it is an endocrine distorter[25, 26] both *in vitro* and in experimental animals[27].

Studies show that cigarette smoke produced by Ni tetra carbonyl could instigate hooked on respiratory airways of smokers[25]. Previous studies[25] are in conformity with those revealed in present work (fig. 4) wherever serum levels of Ni were markedly increased in test than control.

Hypertension categorically step ups the aggravating of cardiac function costs in CVD. BP is elevated by cigarette addiction is mostly ascribed to invigoration of the rennin-angiotensin system (RAS) by nicotine[28]. Conversely, smoker gravitated to illustrate an elevated BP at ambulatory monitoring[29]. The present data is in accord (fig. 1) with past report[28]. Hence, BP would be elevated by regular smoking most likely using stimulation of RAS[30], although it may be frequently veiled and provoked the development of CVD.

Hyperlipidemia may be caused by smoking, which may be increased the levels of triglycerides, cholesterol and decreased the levels of high density lipoprotein that could be a cause of CVD [3, 28]. Serum cholesterol levels were markedly increased in the present study (fig. 2) with cigarette smoking as described previously[28].

Oxidative stress (OS) caused by smoking is a probable mechanism although it is not examined in the present study could be plays a crucial role in all related disease conditions. Tobacco smoke contains a variety of oxidants[31] like Ni [32]and smokers a lot paraded elevation of free radicals in the blood[33] and in the urine[34]. Oxidative damage by LP is occurred due to reduce glutathione and antioxidant levels[35]. As a result, increased OS is not connected with greater serum concentration of cholesterol, while the higher BP with concomitant increase of serum cholesterol possibly a symbol of high OS in the smokers.

Extensive studies[36] have exhibited that cigarette addiction is allied with decrease in serum TRP levels as revealed on our present study (fig. 3). An essential amino acid TRP is the originator of neurotransmitter serotonin[36]. The practical dearth in serotonin has been apprehensive in the pathophysiology of major depression[37].

OS is the most pathogenic channel that can elucidate in various problems. Except other elements find in cigarette neurotoxic element such as Ni is involved in the increase production of free

radicals and cause OS. In the body Ni is not completely destroyed, but it becomes altered chemically. The metabolism of Ni is most duly noticed in beam of its binding to form ligand and its go all over the body[38]. Research has shown that manganese (Mn) levels in the liver become increased with elevated levels of Ni that might affect on the existence of other elements. The metabolism of carbohydrates and amino acid are affected by Mn[25], likewise Ni. It is suggested that Ni via its oxidant activity may involve in reduce levels of TRP in smokers (fig. 3).

CONCLUSION

Current epidemiological and experimental studies depicted Ni as a causative agent of various illnesses. The result point out that Ni is the character which is involved in the modification of physiological and biochemical processes (fig. 5). While there are variety of ways existing for use of Ni, the present work recommend that termination of cigarette smoking may implicate in diminishing the use of Ni as well causative agents those are allied with physiologic and psychiatric illnesses.

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