Effect of Active and Passive Smoking on Heavy Metals Toxic and Antioxidant Trace Elements

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***Abstract*—Smoking is not only associated with decreased concentrations of several antioxidant vitamins and trace elements but also increased morbidity and mortality risk of diseases. Those due to heavy metal, other toxic and antioxidant trace elements in tobacco smoke are not sufficiently emphasized. Tobacco smoking influences the concentrations of several elements in some organs. We sought to determine the relationship between the known effects of some trace elements and other biochemically important elements (cadium (Cd), chromium (Cr), copper (Cu), mercury (Hg), lead (Pb), selenium (Se) and zinc (Zn)) which are linked with smoking. Cigarette smoking may be a substantial source of intake of these hazardous elements not only to the smokers but also, through passive smoking, to nonsmokers. Studies were carried out on 150 smokers (50 industrial cigarette smokers, 50 passive smokers and 50 local tobacco smokers) compared with 50 nonsmoking controls. Levels of whole blood Pb and Cd were significantly higher in smokers than in controls. Whereas Cr, Se, and Zn levels were significantly lower among smokers than controls. No significant differences of Hg and Cu were found between both groups. For dietary intake assessment, smokers consumed significantly less energy from carbohydrate, fat compared to controls, while energy derived from protein did not differ between groups. Moreover, smokers consumed less dietary fiber and vitamins compared with controls. Increasing whole blood toxic trace elements in healthy smokers may be explained by low antioxidant trace elements and vitamins that lead to develop oxidative stress and diseases and increased turnover or breakdown of vitamins and micronutrients. Therefore public health should not only aim for smoking cessation, but also concern about diet in terms of vitamin and trace element content.**

***Index Terms*—smoking; heavy metal; toxic and antioxidant trace elements**

I. Introduction

The scientific literature has evidence on the harmful health effects of chemical compounds and gasses emitted in tobacco smoke. Cigarette is also well known to generate large numbers of oxidants. There are now many studies linking cigarette smoking to increase morbidity and mortality from cardiovascular diseases, various forms of cancer and chronic obstructive pulmonary disease. Smoking delivers heavy metals (the term is used sensu lato to include some lighter metals and metalloids [1] to the lung [2], particularly the more volatile metals such as cadmium and mercury that partition preferentially into the smoke phase on combustion [3]-[5]. Some of these readily pass into the bloodstream and may accumulate in specific organs [6]. Indeed smoking has long been considered a major source of several heavy metals in blood and various organs [2], and Cd in particular is regarded as one of the "strong carcinogen" in tobacco smoke [7] with Cd, nicle (Ni) and arsenic (As) currently classified "carcinogenic to humans" by the International Agency for Research on Cancer (IARC) among 87 mainly organic carcinogens.

The study has been paid to presence of heavy metal toxic and antioxidant trace elements in tobacco smoke and their possible effects on biochemical process in the human body. Inhales through smoking, heavy metals have a long biological half-life. Chronic adverse effects on human health may, therefore, in later years results from prolonged intake of such toxic elements, some of which are powerful carcinogens. Tobacco is also great contributor on the total level of Cd and Pb concentration in blood. Usually smokers absorb a greater amount of Cd compared to the other ways of absorption through human body.

Smoking of one cigarette, containing 1-2 μg of Cd, results in the inhalation of about 1-2 μg Cd [8]. Cd can cause oxidative DNA damage by various oxygen species, increasing lipid peroxidation, induction of oxidative stress and inhibition of enzymes responsible from DNA repair [9], [10]. Moreover Cd is including testicular damage, hypertension, atherosclerosis, osteporisis and

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cancer [11], [12]. Pb can cause several unwanted effects such as anemia, a rise in blood pressure, kidney damage, disruption the biosynthesis of hemoglobin miscarriages and subtle abortions, disruption of nervous systems, brain damage, declined fertility of men through sperm damage [13]. Average concentration of Pb in filter-tipped cigarettes is 2.4 μg/g, about 6% passing into mainstream smoke [14].Concentrations of chromium (Cr) in urine are influenced by smoking habits. It must be borne in mind that the biological effects of Cr depend on its valency; in the trivalent form Cr is an essential element [15], in the hexavalent form it is carcinogenic. Smoking does not affect the Hg levels in urine, hair, blood, kidney cortex, liver and lung. No significant differences due to smoking were found in Cu concentrations in the kidney cortex [16]. Smoking also does not influence the Zn level in most human tissues and biological fluids. Mean Zn and albumin levels in plasma in smoking women, 24 and 48 hours after delivery, were lower than in control non-smoking mother [17]. Analyses of Se levels in serum tend to show slightly lower concentrations in smokers than in non-smokers [18].

This research was undertaken to investigate the toxic metals (Cd, Pb, Hg) and antioxidant trace elements (Cr, Cu, Se, Zn) in healthy Thai smokers compared with nonsmokers.

II. Materials and Methods

The subjects in this study consisted of participants 100 male smokers from a military unit in Bangkok, and 50 male passive smokers from a village in Phitsanulok who participated in the study, were investigated. 50 male non-smokers from the same unit were selected as controls. Information on age, socio-economic status, lifestyle patterns such as consumption of alcohol, smoking and medicines, including past and present illnesses, were obtained by questionnaires. The number of cigarettes smoked per day and the duration of cigarette smoking were multiplied together and expressed as 'cigarette-years'. About 20 ml of venous blood was taken from each subject in the morning, after an overnight fast. EDTA blood from both groups were formed to determine not only the hematological variables but also kept at 4 ℃ in order to measure the amounts of heavy metals and antioxidant trace elements.

Determination of Pb, Cd, Hg, Cr, Cu, Se and Zn

About 8, 20 and 40 μg/dl standard Pb solution was prepared for the determination of Pb amount. About 4.8 and 8.6 μg/l standard Cd solution was prepared for the determination of Cd amount. About 2.5 and 5.0 μg/l standard Cr solution was prepared for the determination of Cr amount. About 75 and 150 μg/l standard Se solution was prepared for the determination of Se amount. About 50, 100 and 150 μg/dl standard Cu and Zn solution was prepared for the determination of Cu and Zn amount.

For Pb: Control
IQC Lyphochek-Whole Blood Control, Bio-rad levels1, 2 and 3 Lot 73180 (Level I- 73181,II- 73182'III - 73183)
EQC - WSLH proficiency testing of CDC
- Department of Medical Science, Ministry of Public Health
- Faculty of Medical Technology, Mahidol University
For Cd: Control
IQC Seronorm™ Trace Element Whole Blood L1 lot 1003191 Seronorm™ Trace Element Whole Blood L2 lot 1103192
EQC - Department of Medical Science, Ministry of Public Health
- Faculty of Medical Technology, Mahidol University
For Hg: Control
IQC Seronorm™ Trace Element Whole Blood L1 lot 1003119 Seronorm™ Trace Element Whole Blood L2 lot 1103129
EQC Interlaboratory comparisons, Faculty of Medical Technology, Mahidol University

For Se: Control
IQC Seronorm™ Trace Element Serum L1 lot 0903106
For Cr: Control
IQC Seronorm™ Trace Element Serum L1 lot 0903106
For Cu and Zn: Control
IQC Seronorm™ Trace Element Serum L1 lot 0903106

Then graphite furnance atomic absorption spectrometry was used for Pb, Cd, Cr and Se measurements. Flame atomic absorption spectrometry was used for Cu and Zn measurements. For Hg measurement was used Mercury analyzer.

Table I. Descriptive Data and Characteristics of the Study Sample in Relation to Smoking Status

Parameter	Smokers n (%)	Nonsmokers n (%)	P-value
Age (years)			
18-30	15/150	16/50 (32.0)	NS
31-40	(33.3)	13/50 (26.0)	NS
41-50	30/150	11/50 (22.0)	NS
51-60	(20.0)	10/50 (20.0)	NS
>60	30/150	0/50 (0.0)	
	(20.0)		
	20/150		
	(13.3)		
	20/150		
	(13.3)		
Education			
Primary	18/150	1/50 (2.0)	0.008
High	(12.0)	5/50 (10.0)	0.006
Vocational	72/150	14/50 (28.0)	0.018
Under/postgraduate	(48.0)	30/50 (60.0)	0.032
	10/150		
	(6.7)		
	50/150		
	(33.3)		
Marital status			
Single	54 (36.0)	13/50 (26.0)	NS
Married	90 (60.0)	38/50 (70.0)	NS
Widow	5 (3.3)	1/50 (2.0)	NS
Divorced	1 (0.7)	1/50 (2.0)	NS
Alcohol drinking			
Not drink	42/150	22/50 (44.0)	0.045
Drink	(28.0)	23/50 (46.0)	0.018
Give up	100/150	5/50 (10.0)	0.042
	(66.7)		
	8/150 (5.3)		

III. Results

Table I and Fig. 1 show the characteristics of the participants (smokers and nonsmokers) and the distribution of smokers according to the quantity of cigarette smoked.

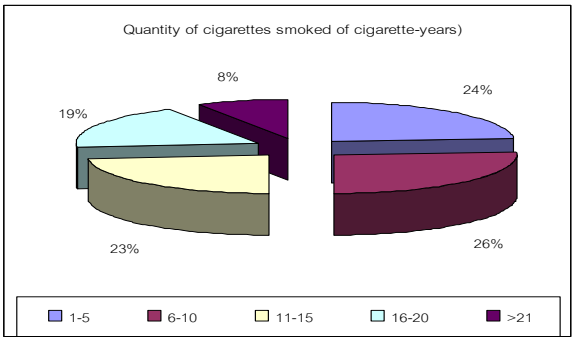

Figure 1. Distribution of smokers according to the quantity of cigarettes smoked for the whole period of smoking (units in number of cigarette per day multiplied by duration of smoking years).

The results showed the toxic heavy metals Cd, Pb, Hg and antioxidant trace elements Cr, Cu, Se and Zn in smokers and nonsmokers. Levels of whole blood Pb and Cd were significantly higher in smokers than in controls. Among smokers, the highest concentration level of Cd was found in the industrial cigarette smokers group and the lowest level found in the self local smokers group. The highest concentration level of Pb was found in the self local smokers group. Whereas Cr, Se, and Zn levels were significantly lower among smokers than controls. No significant differences of mercury (Hg) and Cupper (Cu) were found between both groups (Table II). Heavy metal toxic elements and antioxidant trace elements abnormalities in smokers and nonsmokers were shown in Table. Of smokers 4.03% had high blood lead levels compared with 0% of nonsmokers using a whole blood lead concentration more than 15 µg/dl as the cut-off point. However 40% of controls had a Hg levels above the cut-off point of 5 µg/l compared with 11.49% of smokers. On the other hand, % of antioxidant trace elements deficiency (Se<70 µg/dl, Cr<0.12 µg/dl, Cu<75 µg/dl and Zn<75 µg/dl) were found more frequently in smokers 10.74%, 0.67%, 26.85% and 31.54% respectively than compared with 0%, 0%, 18% and 4% respectively in controls. Regarding to hypertension 3 out of 149 (2.01%) of smokers and none of controls had systolic blood pressure above the cut-off point of ≥160 mmHg. 16 out of 149 (10.73%) of smokers and 3 out of 50 (6%) of controls diastolic blood pressure above the cut-off point of ≥95 mmHg (Table III).

Table II. Median, range and 95% Confidence Interval (CI) of Heavy Metals and Antioxidant Trace Elements in Smokers and Nonsmokers

parameter	Industrial smokers (N=50)		Passive smokers (N=50)		Self local smokers (N=50)		Total smokers (N=150)		Controls (N=50)		P-value
	Median (Range)	95% CI	Median (Range)	95% CI	Median (Range)	95% CI	Median (Range)	95% CI	Median (Range)	95% CI	
Cd (µg/l)	0.93abc (0.29-2.24)	0.88-0.98	0.76 (0.37-3.26)	0.72-0.80	0.71 (0.33-1.68)	0.67-0.81	0.8 (0.37-3.26)	0.77-0.91	0.7 (0.44-1.02)	0.67-0.74	0.012 *
Pb (µg/dl)	4.0 bc (2.0-7.0)	3.8-4.2	4.0 de (2.0-7.0)	2.0-7.0	7.0f (2.0-29.0)	5.0-9.0	5.5 (2.0-29.0)	3.8-4.2	3.0 (2.7-3.4)	2.7-3.4	0.000 **
Hg (µg/l)	2.6bc (0.1-8.8)	2.47-2.73	2.5de (1.0-17.7)	1.0-17.7	3.7 (1.9-11.20)	3.26-4.20	3.5 (0.1-17.7)	3.06-4.02	4.1 (1.8-29.9)	2.8-5.6	0.153
Cr (µg/dl)	0.34c (0.16-1.44)	0.32-0.36	0.38 e (0.1-5.47)	0.1-5.47	0.41f (0.13-0.82)	0.36-0.47	0.38 (0.1-5.47)	0.33-0.42	0.71 (0.15-2.53)	0.56-0.86	0.000 **
Cu (µg/dl)	80b 954-112)	76-84	78de (51-117)	51-117	83 (54-155)	80.5-91.0	81 (51-155)	77.5-84.5	85 (65-118)	81.72-88.56	0.245
Se (µg/dl)	81ac (61-180)	76.95-85.05	88 (62-201)	62-126	85f (76.6-94.1)	76.6-94.1	83 (61-201)	78.9-87.1	95 (69-132)	91.8-98.8	0.000 **
Zn (µg/dl)	73abc (48-98)	63.35-76.65	81de (47-121)	47-109	94 (90.3-96.7)	90.3-96.7	82 (47-121)	77.9-86.10	93 (67-109)	89.51-95.28	0.000 **

a = significant between industrial smokers and passive smokers b= significant between industrial smokers and local tobacco smokers
c= significant between industrial smokers and controls d= significant between passive smokers and local tobacco smokers
e= significant between passive smokers and controls f= significant between local tobacco smokers and controls
*= significant between total smokers and controls

Table III. Heavy Metal Toxic Elements and Antioxidant Trace Elements Deficiency in Smokers and Nonsmokers

Parameter	Smokers						Total		Controls	
	Industrial smokers		Passive smokers		Self local smokers					
	N	%	N	%	N	%	N	%	N	%
Hyper toxic elements										
Cd>5 µg/l	0/50	0	0/50	0	0/49	0	0/149	0	0/50	0
Pb>15 µg/dl	0/50	0	0/50	0	6/49	12.24	6/149	4.03	0/50	0
Hg>5 µg/l	3/50	6	7/50	14	7/49	14.28	17/149	11.49	20/50	40
Antioxidant trace elements deficiency										
Se<70 µg/dl	4/50	8	4/50	8	8/49	16.33	16/149	10.74	0/50	0
Cr<0.12 µg/dl	0/50	0	1/50	2	0/49	0	1/149	0.67	0/50	0
Cu<75 µg/dl	15/50	30	20/50	40	5/49	10.2	40/149	26.85	9/50	18
Zn<75 µg/dl	30/50	60	16/50	32	1/49	2.04	47/149	31.54	2/50	4
Hypertension										
SBP≥160 mmHg	0/50	0	2/50	4	1/49	2.04	3/149	2.01	0/50	0
DBP≥95 mmHg	0/50	0	6/50	12	10/49	20.41	16/149	10.73	3/50	6

SBP = **systolic blood pressure** DBP = diastolic blood pressure

IV. Discussion

According to the Table II Pb amount was significant at the rate of 5.5±0.28 μg/dl in smoker and 3.0±0.15 μg/dl in the control group ($p<0.01$). In addition all groups (industrial, passive, local tobacco) had Pb levels significantly higher than control group. Similar result of Cd was significantly higher in smokers (0.8±0.04 μg/dl) than in controls (0.7±0.03 μg/dl). These results were similar with the findings of Qu *et al*., (1993) [19] in the study in China that blood Pb amount in nonsmokers is 92.3 μg/l, Cd amount is 0.94 μg/l and Pb amount of smokers is 123.4 μg/l and Cd amount is 2.61ug/l. Guo and Jaing [20] concluded in a research in China that blood Pb amount is higher in men compared to women and nonsmokers. Cigarette consumption depress the activity of the enzyme 5-aminolevulinic acid dehydratase (the most sensitive indicator of the Pb burden to the body) in erythrocyte from 117.5 activity units in nonsmokers to 88.8 in smokers of less than 20 cigarettes/day, to 74.1 in heavy smokers of more than 20 cigarettes/day [21]. This was confirmed by other authors [22]. Passive smoking plays an important role in exposure of children to Pb. Parental smoking but no other environmental or dietary factors, was found to be related to the blood Pb level in children 30 μg/l on average in children of nonsmoking parents, 37 μg/l if only the father smoked, and 47 μg/l if the mother, or both parents, smoked [23]. Even if children live near a Pb smoker parental smoking had a significantly stronger influence on blood Pb levels (35 μg/l in children with nonsmoking parents, 38 μg/l if only the father smoked, and 43 μg/l if the mother, or both parents, smoked, and 46 μg/l if mother more than 15 cigarettes/day [24].

A large proportion of the Cd contained in the cigarette passes into the smoke. Since Cd concentration in the ash is practically constant (about 16 % of the present in the un-smoked cigarette and a further 15% is retained by the filter), the greater part (nearly 70 %) passes into the smoke [25]. Most of the Cd passes into side stream smoke, thus posing a risk to passive smokers. Cd results of the present study show 0.93 μg/l Cd almost in industrial smokers 0.8 μg/l in passive smoker, 0.71ug/l in local tobacco smokers and 0.7 μg/l in control group. The difference between the smokers 0.8 μg/l and 0.7 μg/l nonsmokers were significant at the role of $p< 0.05$ %. In all studies, blood Cd concentrations were found to rise with increasing smoking [26], [27]. Possible relationships between smoking, Cd tissue level, hypertension, and cardiovascular diseases have been reported [28], [29]. Smoking has an unclear or no influence on Cd urinary levels.

In unsmoked cigarettes, the Hg content is, on average 30 ± 10 ng/cigarettes. Upon burning, one cigarette release 14 – 34 ng of Hg into the smoke [30]. In this study there was no significant difference of Hg levels between smokers and nonsmoker.

Concentration of Cr in the smokers group (0.38 ± 0.019 μg/dl) were considerably low compared to the concentration obtained from control group (0.71 ± 0.035 μg/dl).

Concentrations of Se in the smokers group (83 ± 4.1 μg/dl) were significant lower than control group (95 ± 3.2 μg/dl).

Several mechanisms may explain and increased risk of atherosclerosis with Pb or Cd. Experimental studies show that both metals contribute the oxidative stress by catalyzing the formation of reactive oxygen species [31], [32], increasing lipid peroxidation [33], [34], and depleting glutathione and protein-bound sulfhydryl groups [31]. These may be decreased the antioxidant vitamin and trace elements such as Zn, Se. Pb and Cd may all so stimulate the production of inflammatory cytokines [35] and may induce endothelial damage by down regulating nitric oxide production [32]-[36]. Both metals have also included atherosclerosis in some model in vivo [37]. In addition to Cd, several agents in tobacco are considered to contribute to cardiovascular disease, including carbon monoxide, nitrogen oxides, hydrogen cyanide, tar, Zn and carbon disulfide. However, it is well established that smoking is more strongly associated with peripheral arterial disease (PAD) than atherosclerosis in other arteries therefore; the effect of Cd on other cardiovascular outcomes is of great interest. Our analyses were based on single blood measurement of Pb and Cd imperfect biomarker of chronic exposure. Environmental exposures, however, are likely to be less changeable than occupational exposures, and single blood levels are frequently used biomarkers in population studies [38], [39]. Furthermore, Pb and Cd in blood are biomarkers of internal dose that integrate all routes of exposure [39]. Although our findings need confirmation in prospective studies and support from mechanistic studies at low levels of exposure and low antioxidant trace elements, we conclude that blood Pb and Cd at levels well below current safety standards, and low levels of antioxidant trace elements, Se and Zn. Furthermore, the increasing of oxidative stress and decreasing of antioxidant were associated with an increase prevalence of PAD in a representative sample of Thai adults. In addition, Pb and Cd exposure explained a substantial part of the effect of smoking on PAD.

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