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นิพนธ์ต้นฉบับ
ORIGINAL ARTICLE

ระดับแคดเมียมในเลือดกับการสูบบุหรี่ในผู้ที่ไม่ได้ทำงานสัมผัสกับแคดเมียม
Blood Cadmium and Cigarette Smoking in Non-occupationally Exposed People

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บทคัดย่อ

แคดเมียมเป็นสารอันตรายชนิดหนึ่งที่ตรวจพบในบุหรี่ วัตถุประสงค์ของการศึกษานี้คือ เพื่อหาความสัมพันธ์ของระดับแคดเมียมในเลือดกับการสูบบุหรี่และปัจจัยอื่นๆ ค่าเฉลี่ยเรขาคณิตของระดับแคดเมียมในเลือด ในผู้ชายที่ไม่ได้ทำงานสัมผัสกับโลหะ จำนวน 229 คน ที่อาศัยอยู่ในเขตกรุงเทพและปริมณฑล อายุเฉลี่ย 43.9 ปี (ช่วงอายุ 35-54 ปี) ที่ตรวจวัดโดยใช้เครื่อง graphite furnance atomic absorption spectrometer เท่ากับ 1.14 ไมโครกรัม/ลิตร พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างระดับแคดเมียมในเลือดกับอายุและการสูบบุหรี่ แต่ไม่พบความสัมพันธ์กับการดื่มแอลกอฮอล์และดัชนีความหนาของร่างกาย พบว่ากลุ่มคนที่สูบบุหรี่มีระดับแคดเมียมในเลือด (1.40 ไมโครกรัม/ลิตร) สูงกว่ากลุ่มที่ไม่สูบบุหรี่ (0.95 ไมโครกรัม/ลิตร, $p<0.01$), กลุ่มที่ไม่สูบบุหรี่แต่ได้รับควันบุหรี่จากคนใกล้ชิด (1.03 ไมโครกรัม/ลิตร, $p<0.05$), และกลุ่มคนที่เคยสูบบุหรี่ (1.10 ไมโครกรัม/ลิตร, $p<0.05$) นอกจากนี้ ยังพบว่าแคดเมียมในเลือดมีระดับสูงขึ้นเมื่อปริมาณการสูบบุหรี่ในปริมาณต่อวันเพิ่มขึ้น แต่ไม่พบความสัมพันธ์กับระยะเวลาที่สูบบุหรี่ การศึกษาครั้งนี้แสดงให้เห็นว่าการสูบบุหรี่มีผลให้ระดับแคดเมียมในเลือดสูงขึ้น

คำหัส: แคดเมียมในเลือด • การสูบบุหรี่

Introduction

Cadmium (Cd) is one of the most important heavy metals when the adverse health effects of cigarette smoking are considered. Each cigarette contained 1-2 μg of cadmium.[1-2] The analysis of the Cd content in 26 brands of cigarette found that the amount of Cd inhaled from one cigarette (containing about 1.7 μg of Cd) smoking was approximately 0.14 to 0.19 μg, corresponding to about 10% of the total Cd content in the cigarette.[3] Long-term exposure to Cd that originated from tobacco smoke can cause the development of chronic diseases since Cd is known to accumulate in the human body over a lifetime and the biological half-life of Cd is estimated to be about 10-20 years.[4,5] With regard to the toxicity of chronic exposure to Cd, the kidney is the target organ and the lung, liver, bone and reproductive organ may also be affected. Moreover, Cd is a lung carcinogen in occupationally exposed populations according to the International Agency for Research on Cancer (group I).[6]

Blood Cd level is extensively used as biomarker of occupational and environmental exposures.[4,5] In most studies, blood Cd

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Blood Cadmium and Cigarette Smoking in Non-occupationally Exposed People

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Abstract

Cadmium (Cd) is one of the harmful chemicals in the cigarette. The aim of this study was to determine blood cadmium (Cd) in relation to cigarette smoking and other variables. The blood cadmium concentrations of 229 non-occupationally exposed male, inhabitants of Bangkok and metropolitan area (mean age 43.9 years; range 35-54), were measured by graphite furnace atomic absorption spectrometer. Geometric mean of this subjects was 1.14 μg/L. Blood Cd levels were statistically associated with age and smoking status but had no relation to alcohol consumption and body mass index. Current smokers had significantly higher blood Cd (1.40 μg/L) than nonsmokers (0.95 μg/L, $p<0.01$), passive smokers (1.03 μg/L, $p<0.05$) and former smokers (1.10 μg/L, $p<0.05$). In addition, blood Cd levels were statistically correlated with the number of daily cigarette smoking, but found to have no correlation with years of smoking. It is clearly demonstrated that cigarette smoking has a more pronounced and significant effect on blood Cd levels.

Key words: blood cadmium • smoking habit

concentrations were found to rise with increasing cigarette smoking.[7,8] Omo et al. reported that blood cadmium levels were 2 folds increased in smokers when compared to non-smokers, with median values of 1.1 μg/L and 0.5 μg/L, respectively.[9] Another report from Canada found that the unusually high blood Cd levels of current cigarette smokers were 10-20 times higher than nonsmokers.[10] Assessment of Cd released from cigarette smoke in Japan from 7 Japanese brands showed that one cigarette contained about 1 μg of Cd and about 50 ng of which were released to the mainstream and 250 ng to the sidestream by smoking.[11] For smokers, an analysis of smoking history exhibited significant correlations between the number of daily cigarettes smoked, years of smoking and the blood Cd concentration.[12] The influences of body mass index (BMI), hematocrit, age, dietary habits, and alcohol consumption appeared to relate with Cd level, according to previous results multiple regression analysis.[13,14] Moreover, many experimental animal and human studies showed that chronic exposure to Cd could increase systolic and/or diastolic blood pressure.[15,16]

To our knowledge, there are no data available concerning the blood Cd concentration and smoking cigarette in Thai men. This study attempted to evaluate blood Cd concentration in relation to cigarette smoking in non-occupationally exposed male subjects, including other possible factors that might affect Cd level.

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Materials and Methods

The study was carried out in 240 male blood donors from Pramongkulklao College of Medicine, who were non-occupationally exposed to Cd and lived in Bangkok and metropolitan area. During the study period, 11 subjects were excluded on the basis of probably occupational Cd exposure. Their mean age was 43.9 (SD 6.2) years, range 35-54 years. Data about age, smoking habit, alcohol consumption, occupation and medical history of the subjects were collected by the medical staff. Exclusion criterior were age under 20 or over 60 year, occupational exposure to Cd, and current disease, e.g. liver, kidney, haematological, cardiovascular or metabolic diseases.

Individuals having an occupation associated with exposure to Cd for more than 1 year were classified as occupationally exposed to the metal. The occupations considered to be associated with exposure to Cd such as Cd plating, ceramics pottery, copper-cadmium alloy, battery production, glass making, pigment production, soldering, plastic production, zinc mining and smelting, and welding (Cd alloy and plated).[1,5,6]

Questions on smoking status were included in the questionnaire. Individuals who had not smoked within the last 3 years were designed as nonsmokers. Former smokers were individuals who had stopped smoking more than 1 month but less than 3 years ago, and current smokers were present smokers. Alcohol consumption used the categories: current drinker were classified as drinking daily/ most day or more than 6 drinks once or twice a week (a drink being a single measure of spirits, a glass of wine or small beer). Nondrinkers were defined as those had not drinked within the last 3 years. Former drinkers were individuals who had stopped drinking at least 1 month but less than 3 years ago, and individuals who had drunk once or twice a month or less were designed as occasional drinkers.

Samples of venous blood (3 mL) were collected from the cubital vein using heparinized test tubes that contained no detected amounts of heavy metals. The concentration of Cd in whole blood was determined by using graphite furnace atomic absorption spectrometer (Spectra AA 30, Varian Techtron, Victoria, Australia), equipped with a Zeeman background correction system at wave-length 228.8 nm . Blood samples were diluted 10 folds in a 0.05% diammonium hydrogen phosphate solution containing 0.1% Triton X-100 (Merck, Darmstadt, Germany). Ten µL were injected into the graphite furnace. Calibribation was performed by standard addition method. Other analytical conditions and procedures were as previous described.[17] The detection limit was 0.1 µg/L.

Within-run precision was assessed by 10 assays of Cd levels in two blood samples (mean values 0.6 and 2.3 µg/L). The coefficients of variation were 9.65 and 7.42%, respectively. Between-run precision by the same concentrations of blood Cd samples presented the coefficients of variation were 8.95 and 5.79%, respectively. In addition, two external reference control samples (Seronorm Trace Elements, Whole Blood No. 404107, No. 404108, Nycomed Pharma, Oslo) were analyzed for Cd. Results from the analysis for Cd were 0.75 and 6.56 µg/L (reference values 0.7, range 0.67-0.76 µg/L, and 6.40, range 6.30-7.90 µg/L).

Blood Cd values with a skewed distribution were log transformed (log 10) to achieve normal distribution; geometric mean (GM) and 95% confidence interval (95%CI) were reported. Other data such as age, BMI, and blood pressure were expressed as mean ± SD and range (minimum and maximium value). Analysis of variance (ANOVA) was applied to the effects of some variables on blood Cd levels.

Results

The geometric mean (GM) and geometric standard deviation (GSD) of blood Cd concentration from this study (reported in Table 1) was 1.14±0.96 μg/L. The highest value observed was 4.26 μg/L, which was from a 52-year-old smoker. Mean BMI, systolic and diastolic blood pressure were within normal ranges.[18] For smoking habit categories, it was found that 39.7% were current smokers, 25.8% former smokers, 22.3% nonsmokers and 12.2% passive smokers. Alcohol consumption of subjects were presented approximately 47.2% for current drinkers, 23.1% for former drinkers, 15.7% for nondrinkers and 14% for occasional drinkers.

Table 1 General characteristic of the subjects. (N=229)

Characteristics	Mean ± SD (range)*
Age, years	43.9±6.2 (35-54)
Body mass index, kg/m^2	24.2±3.7 (16.8-37.2)
Systolic blood pressure, mmHg	126.4±20.0 (104-150)
Diastolic blood pressure, mmHg	80.7±13.3 (52-130)
Blood cadmium**, μg/L	1.14±0.96 (0.15-4.26)
Smoking habit	%
- Non-smoker	22.3
- Passive smoker	12.2
- Former smoker	25.8
- Current smoker	39.7
Alcohol consumption	%
- Non-drinker	15.7
- Former drinker	23.1
- Occasional drinker	14.0
- Current drinker	47.2

* Range was minimium and maximium value from each measured parameter.
** Geometric mean

The GM of blood Cd concentrations were classified by age, BMI, alcohol consumption and smoking habit (data presented in Table 2). There were positive correlation between blood Cd and age. The influence of age on blood Cd was more pronounced in the older group (50-55 years) than the younger group (35-40 years) (1.52 μg/L vs 0.87 μg/L, $p<0.01$). Blood Cd concentrations were not associated with BMI and alcohol consumption characteristics of participants. Furthermore, the results showed that the GM of Cd level in current smokers was statistically higher (1.40 μg/L) than in nonsmokers (0.95 μg/L, $p<0.01$), passive smokers and former smokers (1.03 μg/L and 1.10 μg/L, respectively, $p<0.05$). The mean Cd level in passive smokers was closed to that of former smokers.

Table 2 Geometric mean of blood cadmium in relation to age, BMI, alcohol consumption and smoking habit

Number	Blood	Cadmium, μg/L	95%CI
Age, years			
- 35-40	84	0.87	0.78-0.98
- 41-45	40	1.13 [**a]	0.99-1.41
- 46-50	59	1.37 [**a]	1.14-1.65
- 50-55	46	1.52 [*a]	1.31-1.76
Body mass index, kg/m^2			
- < 20	37	1.13	0.89-1.44
- 20-25	142	1.14	1.00-1.28
- > 25	50	1.10	0.73-1.50
Alcohol consumption			
- Nondrinker	36	1.02	0.79-1.41
- Former drinker	53	0.99	0.85-1.15
- Occasional drinker	32	1.32	1.04-1.68
- Current drinker	108	1.17	1.05-1.33
Smoking habit			
- Nonsmoker	51	0.95 [*b]	0.81-1.09
- Passive smoker	28	1.03 [**b]	0.87-1.22
- Former smoker	59	1.10 [**b]	0.97-1.28
- Current smoker	91	1.40	1.17-1.67

[a] significantly different from group of aged 35-40 years

[b] significantly different from current smoker

[*] $p<0.01$, [**] $p<0.05$

Among current smokers, we also found blood Cd concentration increased with the number of cigarette smoking daily but no relationship with the length of time of smoking (Table 3). Men with smoking, 16-20 cigarettes/day had significantly higher blood Cd level than that of 1-5 cigarettes/day, 6-10 cigarettes/day and 11-15 cigarettes/day, respectively (1.03 μg/L, 1.29 μg/L and 1.17 μg/L, respectively).

Table 3 Blood cadmium in relation to cigarette exposure

	Number	Blood Cadmium, μg/L	95%CI
Number of cigarette/day			
- 1-5	18	1.03*a	0.48-2.17
- 6-10	35	1.29**a	1.02-1.62
- 11-15	15	1.17**a	0.62-2.23
- 16-20	23	2.11	1.60-2.79
Length of time of cigarette smoking, years			
- 1-10	19	1.77	1.23-2.53
- 11-20	28	1.22	0.92-1.62
- 21-30	29	1.39	0.95-2.03
- > 30	15	1.52	0.59-2.44

[a] significantly different from the group of smoking 16-20 cigarette/day

* $p< 0.01$, ** $p<0.05$

Conclusion and Discussion

Critical evaluation of studies on blood Cd in general populations emphasis on the quality of analytical method. In our study we took care of pre-analytical and analytical factors which might interfere with blood Cd measurement, e.g. by using Cd free materials for blood sample collection and analysis. Furthermore, our results of blood cadmium analytical method showed that the procedures were simple and accurate, as well as the detection limit and precision were satisfactory.

In this study, all subjects had blood Cd concentrations lower than 5 μg/L, the recommended value by World Health Organization.[5] The GM of blood Cd in our studied men subjects (1.14 μg/L) was in the range of the values reported for the general population of Sweden (range 0.05-6.8 μg/L)[19], Italy (range 0.1-3.4 μg/L)[9] and Taiwan (range 0.13-3.35 μg/L).[20] Higher exposure has been reported in England and Japan.[21,22] Another study in Thailand by Zhang, et al. showed that the GM for blood Cd of 52 non-smoking adult women was 0.41 μg/L[23] which was lower than our value of male subjects. It might be the effect of cigarette smoking as known in previous issue.[8-10]

Several factors can influence blood Cd concentration such as smoking cigarette, diet, age, sex, occupation, area of residence and medication.[24] We ensured that no participant had been exposed to Cd through his job or affected by renal, cardiovascular, respiratory diseases as well as requiring pharmacological treatment. In our subjects, blood Cd slightly increased with age. GM showed that the blood Cd levels increased from 0.87 μg/L for younger individuals to 1.52 μg/L for the oldest individuals. A similar increase has been previous reported.[9,25] since Cd is a highly accumulative metal and preferentially concentrated in the kidney and liver. We observed that high Cd level in the older subjects had no correlation with cigarette smoking. It might be the effect of the lesser smoking in some older individual subjects.

Cigarette is considered as a burden factor for human health. Inhalation of cigarette smoke is the largest source of Cd exposure for general population.[4] Cd levels in blood for normal population are between 0.1-1.0 μg/L for nonsmokers and 1.0-4.0 μg/L for smokers.[8] Our studied subjects seemed to have the blood Cd levels (0.95 μg/L for nonsmokers and 1.40 μg/L for current smokers) similar to the study in Morocco (0.9±0.6 μg/L for nonsmokers and 1.3±0.9 μg/L for smokers)[26], but might have slighty higher than the study of Omo et al.[9] This study also found that blood Cd levels were significantly higher in current smokers than in nonsmokers, passive smokers and former smokers. Two major reasons, for higher blood Cd level in smokers than nonsmokers were the relatively high Cd content in cigarette (range of 0.5-2.0 μg/g) and the higher pulmonary absorption rate (25 to 50%) of inhaled Cd than the gastrointestinal absorption rate (1 to 10%).[1,3-5]

The blood Cd of our current smokers was 1.47 times higher than that of nonsmokers which was less than the report of Rey et al. (5.5 times in smokers compared with nonsmokers).[27] The increases might be depended mostly on current consumption, brands of cigarette and possibly on a lesser extent, the cumulative amount of cadmium. According to the study of Shaham et al.[28], exposure to cigarette smoked via passive smoking could increase blood Cd level by an average of 0.01 μg% but from our result, blood Cd level in nonsmoker was close to that of passive smokers. In addition, we also found that blood Cd level in current smokers was increased with the number of cigarettes smoked per day but was not associated with the length of time of cigarette smoking. The results were silmilar to the study of Staessen et al.[29]

Other variables that were reported to have effect on the blood Cd levels like alcohol consumption and BMI were not seen in our study, similar to the previous reports.[26,30]

In conclusion, our results indicated that two factors involving in the elevation of blood Cd concentration in non-occupationally exposed subjects were age and smoking cigarette. Cd measurement was necessary and useful for evaluation of individual internal Cd dose. The blood Cd concentrations observed in the present study were fairly low. However, prohibition of smoking at the workplace and public area will help eliminate another source of exposure to Cd.

References

1. Newman-Taylor AJ. Cadmium. In: Rom WN, ed. Environmental occupational exposures. Boston: Little Brown; 1992:767-72.
2. Kipling M, Waterhouse J. Cadmium and lead in the smoke of a filter cigarettes. Sci Total Environ 1993;128:21-35.
3. Elinder CG, Kjellstrom T, Lind B, Linnman L, Piscator M, Sundstedt K. Cadmium exposure from smoking cigarettes: variations with time and country where purchased. Environ Res 1983;32:220-7.
4. Goyer RA. Toxic effects of metals. In: Klassen CD, ed. Casarette and Doull's toxicology: the basic science of poison. 5th ed. New York: McGrew Hill, 1995:634-736.
5. WHO. International Programme on Chemical safety. Environmental Health Criteria 134. Cadmium. Geneva: World Health Organization, 1992.
6. International Agency for Research on Cancer (IARC). Cadmium and cadmium compounds. In: Berillium, cadmium, mercury and exposure in the glass manufacturing industry. IARC

monographs on the evaluation of carcinogenic risks to humans, vol. 58. Lyon: International Agency for Research on Cancer, 1993:119-237.
7. Friberg L, Vahter M. Assessment of exposure to lead and cadmium through biological monitoring: results of a UNEP/WHO global study. Environ Res 1983;30:95-128.
8. Jarup L, Berglund M, Elinder CG, Nordberg G, Vahter M. Health effects of cadmium exposure: a review of the literature and a risk estimate. Scand J Work Environ Health 1998;24(suppl 1):1-52.
9. Omo MD, Muzi G, Piccinini R, Gambelunghe A, Morucci P, Fiordi T, et al. Blood cadmium concentrations in the general population of Umbria, Central Italy. Sci Total Environ 1999;226:57-64.
10. Benedetti JL, Dewailly E, Turcotte F, Lefebvre M. Unusually high blood cadmium associated with cigarette smoking among three subgroups of the general population, Quebec, Canada. Sci Total Environ 1994;152:161-7.
11. Suna S, Asakawa F, Jitsunari F, Manabe Y, Gotou A, Fukunaga I, et al. Assessment of cadmium and lead released from cigarette smoke. Nippon Eiseigaku Zasshi 1991;46:1014-24.
12. El-Agha O, Gokmen IG. Smoking habits and cadmium intake in Tukey. Biol Trace Elem Res 2002;88:31-43.
13. Menditto A, Chiodo F, Patriarca M, Morisi G, Menotti A, Spagnolo A. Blood cadmium levels in nonexposed male subjects living in the Rome area: relationship to selected cardiovascular risk factors. Microchem J 1998;59:173-9.
14. Staessen JA, Buchet JP, Ginucchio G, Lauwerys RR, Lijnen P, Roles H, et al. Public health implications of environmental exposure to cadmium and lead: an overview of epidemiological studies in Belgium. J Cardiovascular Risk 1996;3:26-41.
15. Perry HM, Erlanger MW. Metal-induced hypertension following chronic feeding of low doses of cadmium and mercury. J Lab Clin Med 1974;83:541-7.
16. Luoma PV, Nayha S, Pyy L, Hassi J. Association of blood cadmium to the area of residence and hypertensive disease in Arctic Finland. Sci Total Environ 1995;161:571-5.
17. Subramanian KS, Meranger JC. Rapid electrothermal atomic absorption spectrometric method for cadmium and lead in human whole blood. Clin Chem 1981;27:1866-71.
18. WHO-ISH. World Health Organization-International Society of Hypertension guidelines for the management of hypertension. J Hypertension 1999;17:151-83.
19. Baecklund M, Pedersen NL, Bjorkman L, Vahter M. Variation in blood concentrations of cadmium and lead in the elderly. Environ Res 1999;80:222-30.
20. Chen YC, Pu YS, Lin RS,Yang CY, Lai MK, Liu SH, et al. Blood and urine cadmium levels in relation to demographic and life style in middle-aged and elderly men. Bull Environ Contam Toxicol 2001;66:287-94.
21. Pocock SJ, Delves HT, Ashby D, Sharper AG, Clayton BE. Blood cadmium concentrations in the general population of British middle-aged men. Hum Toxicol 1988;7:95-103.

22. Watanabe T, Koizumi A, Fuijita H, Kumai M, Ikeda M. Cadmium levels in nonpolluted areas in Japan with special references to aging and smoking. Environ Res 1983;31:472-83.
23. Zhang ZW, Shimbo S, Watanabe T, Srianujata S, Banjong O, Chitchumroonchokchai C, et al. Non-occupational lead and cadmium exposure of adult women in Bangkok, Thailand. Sci Total Environ 1999;226:65-74.
24. Herber RFM, Christensen JM, Sabbioni E. Critical evaluation and review of cadmium concentrations in blood for use in occupational health according to the TRACY protocol. Int Occup Environ Health 1997;69:372-8.
25. Alessio L, Apostoli P, Forni A, Toffoletto F. Biological monitoring of cadmium exposure-an Italian experience. Scand J Work Environ Health 1993;19:27-33.
26. Khassouani CE, Soulaymani R, Mauras Y, Allain P. Blood cadmium concentration in the population of the Rabat area, Morocco. Clin Chim Acta 2000;302:155-60.
27. Rey M, Turcotte F, Lapointe, Dewaily E. High blood cadmium levels are not associated with consumption of traditional food among the Inuit of Nunavik. J Toxicol Environ Health 1997;51:5-14.
28. Shaham J, Meltzer A, Ashkenazi R, Ribak J. Biological monitoring of exposure to cadmium, a human carcinogen, as a result of active and passive smoking. J Occup Environ Med 1996;38:1220-8.
29. Staessen J, Yeoman WB, Fletcher AE, Markowe HL, Marmott MG, Rose G, et al. Blood cadmium in London civil servants. Int J Epidemiol 1990;19:362-6.
30. Grasmick C, Huel G, Moreau T, Sarmni H. The combined effects of tobacco and alcohol consumption on the levels of lead and cadmium in blood. Sci Total Environ 1985;41:207-17.