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Examining of Thallium in Cigarette Smokers

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Abstract Smoking is one of the sources of thallium which is considered as a toxic heavy metal. The aim of this study was to determine urinary thallium levels and related variables in smokers, compared to a control group. The study was conducted on 56 participants who had smoked continuously during the year before they were referred to Kashan Smoking Cessation Clinic. Fifty-three nonsmokers who were family members or friends of the smokers were selected as the control group. Urinary thallium was measured in both groups (n = 109) using atomic absorption spectrophotometry. The mean value (with SD) for urinary thallium in the smokers (10.16 ± 1.82 μg/L) was significantly higher than in the control group (2.39 ± 0.63 μg/L). There was a significant relationship between smoking duration and urinary thallium levels (P = 0.003). In a subgroup of smokers who was addicted to opium and opium residues (n = 9), the mean level of thallium (37.5 ± 13.09 μg/L) was significantly higher than in the other smokers (4.93 ± 4.45; P = 0.001). Multiple regression analysis showed opioid abuse, insomnia, and chronic obstructive pulmonary disease (COPD), together were strong predictors of urinary thallium levels in smokers. There was no significant difference in thallium level in hookah smokers (P = 0.299) or in those with COPD compared to other smokers (P = 0.375). Urinary thallium levels of smokers with clinical signs of depression, sleep disorders, memory loss, and sweating were higher than those of smokers without these signs. Since thallium, as other toxic metals is accumulated in the body, and cigarette smoking also involves carcinogenic exposures and health hazards for passively exposed people, the need for cigarette control policies is emphasized.

Keywords Thallium · Smoking · Urinary level · Poisoning

Introduction

There are 15.1 billion smokers in the world, and 8% of this abuse is related to developing countries based on World

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Health Organization (WHO) statistics. WHO reported the prevalence of cigarette consumption in Iran to be 18.5% among adult men and 0.2% among women in 2010. Furthermore, they estimated that these figures would reach 19% among men and 10% among women in 2025. Nine percent of the total population in Iran was anticipated to be smokers in 2025 [1, 2]. WHO also estimated that smoking (cigarette and smoke) is currently responsible for death of 6 million people worldwide; this rate includes 600,000 people who are also estimated to die from the effects of second-hand smoke. And a third of all cancer deaths are associated with smoking [3, 4]. Tobacco contains more than 4000 different toxic substances, including tobacco-specific nitrosamines, carcinogens, heavy metals, and polyaromatic hydrocarbons. Among the toxic metals are cadmium, thallium, and lead, which can give rise to heart disease, as well as renal and respiratory problems, hair loss and dermatology, and obesity in females upon long-term exposure [3–12]. The occurrence of thallium in the lithosphere is 100 ppm. Thallium can be considered as one of the most toxic metals [13]. In the past, thallium compounds have been used as rat poisons and insecticides, but today, they have been banned due to their toxicity and harmful effects on humans. This metal is now used as radioisotope forms for medical purposes, i.e., to visualize scintigraphically the circulation in the heart and to trace melanoma worsening [14, 15]. The most frequent reasons for thallium intoxication are unintentional or deliberate use in industrial settings. The amount estimated to cause thallium poisoning is 8 mg/kg body weight, and an amount of 10–15 mg/kg is considered to be life-threatening. Thallium in such doses may lead to death after few days—due to kidney failure, serious symptoms from the nervous system, and heart disorders. Although the mechanisms of thallium toxicity are essentially unknown, two proposed mechanisms can be mentioned: First, thallium like lead and mercury is strongly bond to sulfhydryl groups on proteins, thereby disrupting the functions of the kidneys and heart and the nervous and digestive systems. Secondly, thallium can replace potassium in human body because of its similarity with potassium ions, and thus, thallium can be accumulated intracellularly where it hits and disrupts vital proteins and enzymes [15–17]. Gastroenteritis, polyneuropathy, and hair loss are described as main symptoms of thallium poisoning, but other symptoms may arise depending on exposure dose and duration [18]. Any amount of thallium is abnormal in the human body [13]; according to Ćurković et al. [19], the normality cut-off point concentration of thallium in normal population is considered to be less than 5 μg/L. Thallium compounds are considered to have teratogenic properties, even in relatively low doses [20–22]. Also, various drug abuses, especially heroin and opium abuse, can involve thallium exposure with neurologic, gastrointestinal, and skin symptoms [23–25]. The Agency of Toxic Substances and Disease Registry in a report on toxicological profile of thallium has shown that smoking is one of the thallium sources and they suspect that the amount of thallium in smokers is significantly increased as compared to nonsmokers [26]. According to their report, thallium can be detected in the urine for 2 months after exposure [26].

The present study was precipitated by concerns related to the widespread use of cigarettes together with the presumed thallium exposure resulting from cigarette smoking.

Materials and Methods

This was a case-control study. This research was carried out in accordance with the Declaration of Helsinki, and informed consent was taken from all subjects. Fifty-six smokers who were referred to Kashan Smoking Cessation Outpatient Clinic, with an age range of 23–77 years, were consecutively enrolled in the study. And 53 nonsmokers, who were relatives or friends of the smokers and comparable to the smokers in terms of demographic variables (age, sex, and socioeconomic terms), were selected. The smokers had a smoking history of at least 1 year and had smoked continuously during the last year. The control group included people who had no history of smoking. People with thallium exposure in their occupational history such as battery makers, soldiers, or painters were excluded in order to control factors affecting thallium level.

Samples and demographic information were collected within 4 months. Given that thallium is slowly removed from body and the maximum amount is excreted in the urine and lesser amount is excreted in the stool [26], urine samples were considered as good indices of thallium exposure.

Urine samples were collected from both groups and were stored at − 20 °C until analysis. Analyses of all samples were conducted by using atomic absorption spectrometry (Perkin Elmer Model 3030 with HGA 400 Programmer) in the toxicology laboratory [27]. An aliquot (0.5 ml) of the urine was put in a test tube and 0.5 ml of sulfuric acid 1% and 0.5 cc of nitric acid 0.2%, and 10 ml of Triton X-100 were added. After centrifugation, 25 μL of the highly transparent supernatant was injected into the graphite tube. Standard, blank, and control samples were prepared in a similar way. Thermal program was selected in atomic absorption spectrometry as follows: 130 °C was used for drying, 300 °C for organic compounds for incinerate, and 800 °C for inorganic compounds. Atomization was performed at 1700 °C [28, 29]. Detection limit was assessed to be 0.2 μg/L; precision (3.65%) and accuracy (97.4%) were determined by analyses and repeated measurements of thallium standard control samples (SERONORM urine trace element level 2, lot 1011645) [30]. Intra-day and day-to-day tests were carried out in order to verify accuracy and repeatability of the system.

All patients were given information on the study and agreed to participate on a consent form before inclusion. The

study was approved by the committee for ethics at the Kashan University of Medical Sciences (KAUMS.REC.20).

Statistical Analysis

Statistical analysis of data was performed by using the 17 SPSS software. Quantitative data were analyzed using *t* test on data with normal distribution and equality of variances in both groups. Nonparametric Mann-Whitney *U* test was used in the absence of parametric statistical preconditions. Qualitative data were analyzed using chi-square test, and relationship between variables was analyzed using Pearson or Spearman correlation. A *P* value less than 0.05 was considered throughout the study as the indication of significant difference (significance level) between groups. Multiple regression analysis was used to explore strong predictors of urinary thallium levels.

Results

Demographic Data

At start, 120 subjects were recruited to the two groups: 60 patients constituted the smoker group and 60 patients constituted the control group. A total of 109 subjects signed the consent form and thus remained included: 56 smokers and 53 controls. The mean age and SD of the smoker group was 44.98 ± 15.62 years (range 23–77 years) and that of the control group 42 ± 18.30 years (range 18–89 years). Cigarette consumption of the smoking group during the year was in average (number per day) 21.48 ± 8.15 cigarettes (range 8–40 cigarettes). Also, in the smoking group, 36 patients (64.3%) had a history of family consumption, 29 patients (51.8%) were cigarette consumers of an Iranian brand (Bahman, Boston, Zika), 20 patients (35.7%) consumed hookah, 11 patients (19.64%) were with COPD, and 9 patients (16%) consumed opium and opium residues in addition to smoking.

Clinical Symptoms

Thirty-four patients of the smoking group had neurological symptoms (60.7%), 5 patients had skin symptoms (8.9%), and 4 patients had gastrointestinal symptoms (7.1%), and the others were asymptomatic.

With regard to neurological symptoms among the smokers, the frequency of aggressiveness was 57% ($n = 56$), and weakness and jerking movements was observed in 50 and 49%, respectively, and tremor (45%), paresthesia (45%), fatigue (43%), headache (42%), insomnia (41%), memory deficits (38%), blurred vision (34%), depression (29%), emotional liability (27%), vertigo (25%), tinnitus (20%), ataxia (13%), delirium-psychosis-coma (13%), choreoathetosis (9%), and seizures (6%) were also observed, particularly in the subgroup with combined abuse of cigarettes and narcotics.

With regard to dermatological symptoms, scalp hair loss was observed in 38%, and sweating (29%), dry skin (27%), body hair loss (16%), rashes (11%), Mees' lines (5%), palmar erythema (3%), and acne (2%) were also reported.

Gastrointestinal symptoms included constipation (32%), abdominal pain (25%), nausea (16%), vomiting (7%), and diarrhea (4%).

Thallium levels in smokers ($N = 56$) with symptoms of memory deficits ($t = 3.06$, $P = 0.004$), insomnia ($t = 2.01$, $P = 0.049$), depression ($t = 3.34$, $P = 0.002$), and sweating ($t = 2.08$, $P = 0.042$) were higher than in those who did not have these symptoms (Table 1).

Quantity Level of Urinary Thallium

Among all samples, the mean (SEM and range) of urinary thallium in smokers, 10.16 μg/L (1.82 μg/L, 0–61.54 μg/L), was significantly higher than in the controls, 2.39 μg/L (0.63 μg/L, 0–23.8 μg/L) ($P = 0.001$, $Z = 6.63$). There was a correlation between duration of smoking and thallium level ($r = 0.36$, $P = 0.003$). Comparison of 22 ultra-light cigarette consumers (Esse, Winston, Kent) and 34 light cigarette consumers (Bahman, Boston, Zika, magna, Montana) that were

Table 1 Comparison of thallium level in smokers regarding clinical symptoms

Clinical symptom[a]	Positive *N*, mean (SE)	Negative *N*, mean (SE)	*P*
Neurological			
Aggression	32, 11.93 (2.8)	24, 7.8 (2.03)	0.23
Weakness	28, 11.01 (2.8)	28, 9.31 (2.4)	0.64
Tremor	25, 9.58 (2.81)	31, 10.63 (2.44)	0.77
Paresthesia	25, 8.99 (1.99)	31, 11.1 (2.90)	0.55
Fatigue	24, 8.66 (2.75)	32, 11.29 (2.46)	0.47
Headache	23, 7.01 (1.95)	33, 12.36 (2.74)	0.11
Insomnia	24, 14.30 (3.50)	32, 7.06 (1.68)	0.049*
Memory deficits	21, 4.6 (0.98)	35, 13.5 (2.72)	0.004**
Blurred vision	19, 11.91 (2.95)	37, 9.27 (2.32)	0.48
Depression	16, 4.08 (0.69)	40, 12.59 (2.44)	0.002**
Gastrointestinal			
Constipation	18, 8.07 (2.45)	38, 11.15 (2.43)	0.37
Dermal			
Scalp hair loss	21, 11.88 (3.44)	35, 9.13 (2.09)	0.49
Sweating	16, 5.68 (1.8)	40, 11.95 (2.41)	0.042*

[a] Small samples were omitted

* $p < 0.05$; ** $p < 0.01$

classified based on cigarette tar showed that smokers consuming ultra-light cigarette (tar found = <8 mg/cigarette) had lower thallium (mean rank = 19.59) than those consuming light cigarettes (tar found > 8 mg / cigarette, mean rank = 34.26) ($P = 0.001$, $Z = 3.28$) (Table 2).

Thallium in Smokers and Drug Users

Nine persons in the smoking group were also consumers of opium and opium residues. The thallium level in this group of combined abuse consumers was statistically higher than the mean in other smokers, viz. 37.5 μg/L ± 13.09 μg/L vs. 4.93 μg/L ± 4.45 μg/L ($P = 0.001$, $Z = 4.67$). Upon excluding the 9 abusers of opium and opium residues from the smoker group, the thallium level of smokers was significantly higher than that of nonsmokers, viz. 4.93 μg/L ± 4.45 μg/L vs. 2.39 μg/L ± 0.63 μg/L) ($t = 2.79$, $P = 0.006$) (Table 3).

Multiple Regression Analysis

In cigarette smokers, linear regression results showed that about 80 percentile of thallium rate's variance is explained with opioid abuse, insomnia, and COPD variables. Correlation coefficient and linear regression model results are shown in Tables 4 and 5.

Discussion

The results showed that urine thallium levels in smokers (mean about 5 μg/L) with no history of drug abuse were significantly higher than in nonsmokers. The relatively small thallium amounts in nonsmokers may be due to uptake from natural environment, crops, fruit, and livestock that enters the human body through food cycle [31]. Karbuska [31] reported that thallium levels are higher in hard water due to its high solubility compared to other heavy metals. The thallium levels in the patients with combined abuse of cigarettes and narcotics were in average seven times higher than in the other smokers. Our observations were consistent with the results from the Agency of Toxic Substances and Disease Registry that reported two times higher thallium levels in smokers than in nonsmokers [26]. Also, Ghaderi et al. [24] reported urinary thallium of drug abusers about 20 times higher than the levels in their group of healthy people with a mean of 1 μg/L. The content of heavy metals such as lead and thallium in abused drugs have been studied [24, 25, 32–37], and there are reports of poisoning by thallium due to use of illegal drugs (opium, opium residues, and heroin) in Iran [24, 25]. Higher levels of urinary thallium among smokers consuming opium and opium residues are likely due to added impurities to the illegal drugs, apparently representing a significant health hazard [24, 38].

Tobacco leaves are widely used in order to manufacture cigarettes. Numerous studies have shown heavy metals such as zinc, cobalt, nickel, lead, cadmium, and thallium in cigarettes and cigarette filters [6, 39–43]. The toxicity of cigarette smoke is influenced (determined) by its tar amount. Comparison between ultra-light cigarette consumers (less than 8 mg tar) and light consumers (higher than 8 mg tar) in this study showed that lower thallium level was present in the urine of ultra-light cigarette consumers. Other studies have confirmed that cigarettes with higher tar levels had higher content of toxic metals such as thallium [6, 44]. The toxic smoke enters into the body through the lungs and stomach [45], and these compounds are slowly eliminated via the urine and stool [26]. High levels of toxic metals in smoke from electronic cigarettes have also been reported, in some cases [46, 47]. Heavy metals of cigarette smoke enter easily into the human respiratory system and result in a variety of symptoms both from the airways and the heart [7, 8]. The relationship between long-term smoking and thallium levels confirms the previous data on tissue retention of thallium and other heavy metals [15].

The most common clinical symptoms in the present study included aggressiveness, weakness, hair loss, sweating, constipation, and abdominal pain, which were essentially in

Table 2 Quantity level of urinary thallium

Variables		Mean (SEM)	Range	Value	*P*
Groups	Smokers ($n = 56$)	10.16 (1.82)	0–61.54	6.63 (Z)	0.001
	Control ($n = 53$)	2.39 (0.63)	0–23.8		
Brands					
	Iranian ($n = 29$)	9.37 (2.1)	5.07–13.67	0.44 (t)	0.65
	Foreign ($n = 27$)	11.01 (3.1)	4.67–17.36		
Cigarette consumers					
	Ultra-light ($n = 22$)	5.02 (1.83)	1.21–8.83	3.28 (Z)	0.001
	Light ($n = 34$)	13.49 (2.63)	8.13–18.85		

Table 3 Thallium in smokers and drug users

Variables	Number	Mean (SD)	Value	*P*
Opium and opium residues use				
Yes	9	37.5 (13.09)	4.67 (Z)	0.001
No	47	4.93 (4.45)		
Hookah smoking				
Yes	20	12.73 (3.3)	1.05 (t)	0.299
No	36	8.73 (2.17)		
COPD diagnosis				
Yes	11	17.77 (6.14)	0.88 (Z)	0.375
No	45	8.30 (1.64)		

Table 4 Correlation coefficients between effective variables on thallium urinary in group cigarette smoking ($n = 56$)

Variables	Age	Using duration year	Using daily	Opioid abuse	Depression	Sweating	Insomnia	Tar rate	COPD
Urinary thallium	0.43**	0.53**	0.21	0.88**	0.28*	0.20	0.26*	0.30*	0.27*

* $p < 0.05$; ** $p < 0.01$

accordance with the previous studies that reported polyneuropathy, muscle weakness, abdominal pain, and hair loss [15, 48–50]. However, here, it should be taken into account that smokers are exposed to a variety of toxic substances, and combined abuse with narcotics may not have been correctly stated by all patients. Neuropsychological effects of thallium exposure have been reported previously [51], with depression [52], memory deficits [24, 53], and sleep disorders [54]. Also, 6% of smokers had experienced seizures, apparently resulting from combination with tramadol abuse or illegal drugs [55–58].

Generally, as mentioned earlier, results showed that opioid abuse, insomnia, and COPD were variables that together strongly predict the majority of thallium level variance in smokers. This is in line with the results of the previous studies, urinary thallium level in opioid abusers [24], smoking and COPD [59], and thallium and insomnia [60].

Counterfeit cigarettes on Iranian markets are among the determinants of heavy metal content of cigarettes. Sixty percent of Iranian smokers in Tehran prefer foreign brands. And counterfeit foreign brands are prevalent among Iranian smokers [61]. Several studies have shown the presence of heavy metals in different brands of cigarettes [6, 41, 62–65]. A comparative study by Pappas et al. on original and counterfeit brands of cigarettes manufactured in the USA showed that cadmium, lead, and thallium levels were higher in counterfeit brands compared to those in original brands [6]. The need for governmental monitoring and control over major thallium sources including cigarettes can reduce the heavy metal exposure of the population. Increasing awareness in our community about cigarette tar of various brands can be part of these policies. Another approach to reduce the burden of these health effects is to apply taxes and increase prices of such drugs and tobacco [66].

Table 5 Results of multiple regression model analysis (urinary thallium level as dependent)

Steps	Parameter entered	Regression coefficient	Adjusted R square	Std. error estimate	t value	P
1	Opioid abuse	0.882	0.774	6.50	14.17	0.001
2	Insomnia	0.898	0.798	6.14	2.60	0.012
3	COPD	0.907	0.812	5.92	2.33	0.031

Conclusions

Thallium and other toxic metals, e.g., lead and arsenic, accumulate in the body. Increased biological levels of these metals following cigarette smoking are significant and represent a health hazard not only for smokers but also for people who are exposed passively. Although in smokers, individuals that have opioid abuse, insomnia, and COPD are in high risk of thallium toxicity and should be checked for medical health in medical settings. Cigarette smoke is carcinogenic, and long-term abuse may also result in undesired effects on the airways, heart, and brain. In accordance with this, tobacco control policies should be given high priority. Tobacco control will also reduce the burden of toxic heavy metals in the population. Correct information by media on dangers of smoking and drugs, and their contaminations with toxic metals, are essential for public health.

Limitations

Cause-effect relationships between toxic metal exposure in smokers and the reported symptoms among this group cannot be confirmed by the data presented here. It should be taken into account that smokers are exposed to a variety of toxic substances, and the combined abuse with narcotics may be more usual than our obtained information's indicate. Further studies are important to identify causative factors for the relatively high frequency of neurological and gastrointestinal symptoms in smoking individuals.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Petersen PE (2003) Tobacco and oral health—the role of the World Health Organization. Oral Health Prev Dent 1:309–316
2. Organization WH (2015) WHO global report on trends in prevalence of tobacco smoking 2015. World Health Organization. http://apps.who.int/iris/bitstream/10665/156262/1/9789241564922_eng.pdf
3. Funck-Brentano C, Raphaël M, Lafontaine M et al (2006) Effects of type of smoking (pipe, cigars or cigarettes) on biological indices of tobacco exposure and toxicity. Lung Cancer 54:11–18
4. Sawa T, Ohshima H (2006) Nitrative DNA damage in inflammation and its possible role in carcinogenesis. Nitric Oxide 14:91–100
5. Hecht SS (1999) Tobacco smoke carcinogens and lung cancer. J Natl Cancer Inst 91:1194–1210
6. Pappas R, Polzin G, Zhang L, Watson C, Paschal D, Ashley D (2006) Cadmium, lead, and thallium in mainstream tobacco smoke particulate. Food Chem Toxicol 44:714–723
7. Xiao T, Guha J, Boyle D et al (2004) Naturally occurring thallium: a hidden geoenvironmental health hazard? Environ Int 30:501–507
8. Xiao T, Guha J, Boyle D, Liu C-Q, Chen J (2004) Environmental concerns related to high thallium levels in soils and thallium uptake by plants in southwest Guizhou, China. Sci Total Environ 318:223–244
9. Health UDo, Services H (2006) The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General, vol 1. US department of health and human services, centers for disease control and prevention, Coordinating center for health promotion, National center for chronic disease prevention and health promotion, Office on smoking and health 709, Atlanta, pp i25–i29
10. Navas-Acien A, Silbergeld EK, Sharrett AR, Calderon-Aranda E, Selvin E, Guallar E (2005) Metals in urine and peripheral arterial disease. Environ Health Perspect 113:164–169
11. Skalnaya MG, Tinkov AA, Demidov VA, Serebryansky EP, Nikonorov AA, Skalny AV (2016) Hair ultra-trace elements in relation to age and body mass index in adult women. J Elem 21:211–220
12. Campbell C, Bahrami S, Owen C (2016) Anagen effluvium caused by thallium poisoning. JAMA Dermatol 152:724–726
13. Galván-Arzate S, Santamaría A (1998) Thallium toxicity. Toxicol Lett 99:1–13
14. Bank WJ, Pleasure DE, Suzuki K, Nigro M, Katz R (1972) Thallium poisoning. Arch Neurol 26:456–464
15. Jha S, Kumar R, Kumar R (2006) Thallium poisoning presenting as paresthesias, paresis, psychosis and pain in abdomen. J Assoc Physicians India 54:53–55
16. Kuo HC, Huang CC, Tsai YT, Chu CC, Hsieh ST, Chu NS (2005) Acute painful neuropathy in thallium poisoning. Neurology 65:302–304
17. Saddique A, Peterson C (1983) Thallium poisoning: a review. Vet Hum Toxicol 25:16–22
18. Winter ST, Laron Z, Michaelson IC (1954) Renal and vascular disturbances in a case of thallium poisoning. Arch Dis Child 29:443–446
19. Ćurković M, Sipos L, Puntarić D, Dodig-Ćurković K, Pivac N, Kralik K (2013) Detection of thallium and uranium in well water and biological specimens of an Eastern Croatian population. Arh Hig Rada Toksikol 64:385–394
20. Hall B (1985) Critical periods during development as assessed by thallium-induced inhibition of growth of embryonic chick tibiae in vitro. Birth Defects Res A: Clin Mol Teratol 31:353–361
21. Léonard A, Gerber GB (1997) Mutagenicity, carcinogenicity and teratogenicity of thallium compounds. Mutat Res 387:47–53
22. Parker J, Scheck M (1981) Thallium chondrodystrophy in chick embryos: ultrastructural changes in the epiphyseal plate. Calcif Tissue Int 33:57–69
23. Questel F, Dugarin J, Dally S (1996) Thallium-contaminated heroin [5]. Ann Intern Med 124:616
24. Ghaderi A, Vahdati-Mashhadian N, Oghabian Z, Moradi V, Afshari R, Mehrpour O (2015) Thallium exists in opioid poisoned patients. Daru 23:1–4
25. Afshari R, Mégarbane B, Zavar A (2012) Thallium poisoning: one additional and unexpected risk of heroin abuse. Clin Toxicol (Phila) 50:791–792
26. Body LM (1992) How might I be exposed to thallium? The Agency for Toxic Substances and Disease Registry (ATSDR), Atlanta, Georgia. www.atsdr.cdc.gov/ToxProfiles/tp54-c1-b.pdf
27. Ediger R (1975) Atomic absorption analysis with the graphite furnace using matrix modification. At Absorption Newsl 14:127–130
28. Christian GD, Purdy WC (1966) Coulometric determination of thallium in blood and urine. Am J Clin Pathol 46:185–188
29. Savory J, Roszel NO, Mushak P, Sunderman FW (1968) Measurements of thallium in biologic materials by atomic absorption spectrometry. Am J Clin Pathol 50:505–509
30. Fuller CW (1976) The effect of acids on the determination of thallium by atomic absorption spectrometry with a graphite furnace. Anal Chim Acta 81:199–202
31. Karbowska B (2016) Presence of thallium in the environment: sources of contaminations, distribution and monitoring methods. Environ Monit Assess 188:640
32. Aghaee-Afshar M, Khazaeli P, Behnam B, Rezazadehkermani M, Ashraf-Ganjooei N (2008) Presence of lead in opium. Arch Iran Med 11:553–554
33. Salehi H, Sayadi AR, Tashakori M et al (2009) Comparison of serum lead level in oral opium addicts with healthy control group. Arch Iran Med 12:555–558
34. Mojtaba A, Ramin A (2012) A comparison of blood-lead level (BLL) in opium-dependant addicts with healthy control group using the graphite furnace/atomic absorption spectroscopy (GF-AAS) followed by chemometric analysis. Iran Red Crescent Med J 2012:488–491
35. Khatibi-Moghadam H, Khadem-Rezaiyan M, Afshari R (2016) Comparison of serum and urine lead levels in opium addicts with healthy control group. Hum Exp Toxicol 35:861–865
36. Mehrpour O, Karrari P, Abdollahi M (2012) Chronic lead poisoning in Iran; a silent disease. Daru 20:8
37. Karrari P, Mehrpour O, Abdollahi M (2012) A systematic review on status of lead pollution and toxicity in Iran; guidance for preventive measures. Daru 20:2
38. Ghaderi A, Afshari R (2016) Alteration of abused drugs should be added to the medical curricula. Futur Med Educ J 6:3–4
39. Nada A, Abdel-Wahab M, Sroor A, Abdel-Haleem A, Abdel-Sabour M (1999) Heavy metals and rare earth elements source-sink in some Egyptian cigarettes as determined by neutron activation analysis. Appl Radiat Isot 51:131–136
40. Verma S, Yadav S, Singh I (2010) Trace metal concentration in different Indian tobacco products and related health implications. Food Chem Toxicol 48:2291–2297
41. Chang MJ, Naworal JD, Walker K, Connell CT (2003) Investigations on the direct introduction of cigarette smoke for trace elements analysis by inductively coupled plasma mass spectrometry. Spectrochim Acta B At Spectrosc 58:1979–1996
42. O'Connor RJ, Schneller LM, Caruso RV et al (2015) Toxic metal and nicotine content of cigarettes sold in China, 2009 and 2012. Tob Control 24:iv55–iv59
43. Caruso RV, O'Connor RJ, Travers MJ, Delnevo CD, Edryd Stephens W (2015) Design characteristics and tobacco metal concentrations in filtered cigars. Nicotine Tob Res 17:1331–1336
44. Pérez-Bernal JL, Amigo JM, Fernández-Torres R, Bello MA, Callejón-Mochón M (2011) Trace-metal distribution of cigarette ashes as marker of tobacco brands. Forensic Sci Int 204:119–125
45. Armitage AK, Turner DM (1970) Absorption of nicotine in cigarette and cigar smoke through the oral mucosa. Nature 226:1231–1232

46. Goniewicz ML, Knysak J, Gawron M et al (2014) Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. Tob Control 23:133–139
47. Williams M, Villarreal A, Bozhilov K, Lin S, Talbot P (2013) Metal and silicate particles including nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. PLoS One 8:e57987
48. Lech T, Sadlik JK (2007) Thallium intoxication in humans. Toxicol Lett 172:S85
49. Misra UK, Kalita J, Yadav RK, Ranjan P (2003) Thallium poisoning: emphasis on early diagnosis and response to haemodialysis. Postgrad Med J 79:103–105
50. Karrari P, Mehrpour O, Afshari R, Keyler D (2013) Pattern of illicit drug use in patients referred to addiction treatment centres in Birjand, Eastern Iran. J Pak Med Assoc 63:711–716
51. Tsai YT, Huang CC, Kuo HC et al (2006) Central nervous system effects in acute thallium poisoning. Neurotoxicology 27:291–295
52. Shiue I (2015) Urinary heavy metals, phthalates and polyaromatic hydrocarbons independent of health events are associated with adult depression: USA NHANES, 2011–2012. Environ Sci Pollut Res Int 22:17095–17103
53. Thompson C, Dent J, Saxby P (1988) Effects of thallium poisoning on intellectual function. Br J Psychiatry 153:396–399
54. Kazantzis G (2000) Thallium in the environment and health effects. Environ Geochem Health 22:275–280
55. Mehrpour O (2013) Addiction and seizure ability of tramadol in high-risk patients. Indian J Anaesth 57:86–87
56. Taghaddosinejad F, Mehrpour O, Afshari R, Seghatoleslami A, Abdollahi M, Dart RC (2011) Factors related to seizure in tramadol poisoning and its blood concentration. J Med Toxicol 7:183–188
57. Goodarzi F, Mehrpour O, Eizadi-Mood N (2011) A study to evaluate factors associated with seizure in tramadol poisoning in Iran. Indian J Forensic Med Toxicol 5:66–69
58. Farzaneh ES, Mostafazadeh BA, Mehrpour O (2012) Seizurogenic effects of low-dose naloxone in tramadol overdose. IJPT 11:6–9
59. Lundbäck B, Lindberg A, Lindström M et al (2003) Not 15 but 50% of smokers develop COPD?—report from the obstructive lung disease in Northern Sweden studies. Respir Med 97:115–122
60. Peter ALJ, Viraraghavan T (2005) Thallium: a review of public health and environmental concerns. Environ Int 31:493–501
61. Heydari G, Tafti SF, Telischi F et al (2010) Prevalence of smuggled and foreign cigarette use in Tehran, 2009. Tob Control 19:380–382
62. Iskander FY (1986) Cigarette ash as a possible source of environmental contamination. Environ Pollut B 11:291–301
63. Pourkhabbaz A, Pourkhabbaz H (2012) Investigation of toxic metals in the tobacco of different Iranian cigarette brands and related health issues. Iran J Basic Med Sci 15:636–644
64. Karbon MH, Ali FH, Hasan EJ, Znad DE, Zamil SK, Lafi AF (2015) Evaluation of the level of some heavy metals in tobacco of domestic and imported cigarette brands used in Iraq. Baghdad Sci J 12:582–590
65. Çiftçi H, Ölçücü A (2007) Determination of iron, copper, cadmium and zinc in some cigarette brands in Turkey. J Int J Sci Technol 2:29–32
66. Guindon GE, Tobin S, Yach D (2002) Trends and affordability of cigarette prices: ample room for tax increases and related health gains. Tob Control 11:35–43