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EFFECT OF SMOKING ON LEAD CONCENTRATION IN SMOKERS AND EX-SMOKERS

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ABSTRACT

Background: Tobacco smoke contains more than 4,000 different chemical ingredients. Heavy metals such as lead, cadmium and others are among them. The WHO published a lead content of 2.5-12.2 µg per cigarette, of which 2-6% was inhaled by smoking. Lead toxicity is primarily related to the interaction of lead with several enzymes containing sulfhydryl groups, resulting in mercaptides, and the enzymes themselves lose their function. **The aim** of the study was to determine the differences in the concentrations of lead in the blood and urine of smokers and ex-smokers in relation to non-smokers. **Methods:** The research included 108 respondents divided into three groups. The first group of respondents consists of regular smokers (n = 51), the second group of ex-smokers (n = 38) and the third group of respondents who have never consumed tobacco (n = 17). Determination of the level of lead was performed by the method of atomic absorption spectrophotometry with an electrothermal atomizer. **Result:** A significant positive correlation was found between the number of pack-year and the concentration of lead in the blood (Rho = 0.339; p <0.05). Lead levels in the blood of ex-smokers decrease in relation to age groups (p = 0.021). **Conclusion:** Smoking is still a significant factor that contributes to the concentration of lead in the human body.

KEYWORD: Lead concentration, Smoking, Ex-smokers, Smokers.

I. INTRODUCTION

The ingredients of tobacco smoke vary and depend on the type of tobacco, the climate in which it is planted, the method of cultivation, climatic characteristics, the drying process, and the technology used to obtain the finished product. Tobacco smoke contains more than 4,000 different chemical ingredients.[1] Heavy metals such as lead, cadmium, and others are among them. In 1977, the WHO published a lead (Pb-from the Latin plumbum) content of 2.5-12.2 µg per cigarette, of which 2-6% was inhaled by smoking. The content of Pb in cigarettes has decreased over the years due to a different cultivation technology- the value, e.g., for cigarettes from Great Britain and the USA, from 0.4 µg - to 0.9 µg per cigarette.[2]

About 76% of lead is eliminated through the kidneys and about 16% through the gastrointestinal tract. At the same time, other elimination pathways are less important (bile, sweat, milk, hair, nails, teeth).[1,3,4]

Exposure of the general population to lead is represented through air and food in approximately equal proportions. About 50% of inhaled Pb particles are resorbed. The biological half-life of Pb in the blood is about 20 days, in soft tissues, the reversible fraction in bone 30-40 days, and the irreversible fraction 10-20 years.[5,6,7,8]

Biomarkers of exposure are used to assess exposure to lead or other heavy metals and represent the measured values of metals in a biological sample. Blood, urine,

hair, and nail samples are usually used as biological samples.[9,10] Pb toxicity is primarily related to the interaction of lead with several enzymes containing sulfhydryl groups, resulting in mercaptides, and the enzymes themselves lose their function, i.e., are inactivated.[11,12] Eventually, increased lead values in biological material are associated with more potential health risks. By determining the level of Pb in the body fluids of smokers, especially ex-smokers, health risks to non-smokers can be assessed to a certain extent.[13,14,15]

The study's objectives are to determine the difference in Pb concentrations in the biological material of smokers to former smokers and non-smokers. Then, to determine the difference in the Pb concentrations in the biological material of former smokers in relation to non-smokers and the influence of smoking experience on the concentration of this heavy metal.

II. MATERIALS AND METHODS

According to the inclusion criteria, the research included 108 respondents divided into three groups. The first group of respondents consists of regular smokers (n = 51; average age 47.80 ± 5.68), the second group of ex-smokers (n = 38; average age 50.57 ± 6.16), and the third group of respondents who have never consumed tobacco (n = 17; average age 48.88 ± 5.60). The group of respondents of regular smokers was divided into three subgroups (smokers with a smoking experience of 10-15 years, smokers with a smoking experience of 15.1-25 years, and smokers with a smoking experience of over 25.1 years). The respondents of ex-smokers were divided into two subgroups (those who quit smoking 1-10 years ago and those who quit smoking 11-20 years ago). The smoking experience of former smokers was 30.94 ± 18.46 years/box per day, while for current smokers, the length of service was 32.78 ± 17.70 years/box per day.

All subjects had a detailed history: gender, age, smoking status, eating habits (consumption of fish, meat, alcohol, and coffee), type of occupation, education, and presence of acute illness or chronic illness. For smokers, data on the length of smoking experience with the average daily smoked cigarettes were taken. For the former smokers, data on the length of the smoking experience, the average daily smoked cigarettes, and the length of non-tobacco consumption. Criteria for inclusion in the study are unprofessional exposure to heavy metals, not taking supplements of trace elements and other substances as a dietary supplement, voluntary consent to participate in the study, and permanent residence in Sarajevo Canton for at least 20 years. For respondents who smoke at least ten cigarettes a day. Criteria for non-inclusion in the study are consumption of fewer than ten cigarettes per day by a group of smokers, consumption of less than ten cigarettes by ex-smokers while smoking, occupational exposure to heavy metals, the existence of metal implants, residence in Sarajevo Canton less than 20 years.

The study was conducted with the approval of the Ethics Committee of the Faculty of Medicine, University of Sarajevo (1324-AS/11) in accordance with the recommendations contained in the Declaration of Helsinki on Biomedical Research Involving Human Subjects as revised in 2013.

Sample analysis: Specific amounts of blood and urine were taken from each subject for the research. Blood for analysis was taken in 10 ml with the consent of the volunteer subjects. Patients' sera were obtained from blood samples taken from the cubital vein after fasting for 12 hours. The blood sample was analyzed immediately or left for up to 2 days at + 4ºC, and if stored for several days, then stored at -20ºC. K2-EDTA (Ethylenediaminetetraacetic Acid) was used as an anticoagulant for the blood.

Disposable urine is taken from the patient for the first sample. Urine is taken in a plastic container made of chemically inert material. Therefore, it is necessary to take about 20 cm3 of urine. This sample is labeled and left at -20 ° C.

Determination of the level of LEAD was performed in the laboratory for the toxicology of the Public Institution for Occupational Medicine of the Sarajevo Canton by the method of atomic absorption spectrophotometry with an electrothermal atomizer.

The standard supplement method was used. A pool of blood and urine was added to all solutions made for the calibration curve when determining metals in whole blood and urine. All solutions were made in deionized water of very high purity. Standards were developed for individual metals, the values of which covered the possible range of metal levels in the samples. In addition to the blank, standards for Pb of the following concentrations were developed: 0.1 mg / L, 0.2 mg / L, 0.5 mg / L, and 1.0 mg / L.

Venous blood in which Pb was determined was hemolyzed with Triton ™ X-100 solution. HNO3 precipitated blood proteins. After preparation, a portion of the sample was injected into a graphite cuvette, and Pb absorbance was measured at 283 nm. The lead level was calculated using a calibration curve made by the method of standard addition of Pb to the blood.

Table 1: Procedure for preparation of whole blood samples for lead determination.

Reagents	Blind trial	pool	*St 1	St 2	St 3	St 4	SERONORM	Sample
0.05% triton-X	400 µL	400 µL	400 µL	400 µL	400 µL	400 µL	400 µL	400 µL
pool	-	100 µL	100 µL	100 µL	100 µL	100 µL	-	-
Water	100µL	-	-	-	-	-	-	-
seronorm	-	-	-	-	-	-	100 µL	-
Sample	-	-	-	-	-	-	-	100 µL
0.02 mol/L NHO_3	50 µL	50 µL	-	-	-	-	50 µL	50 µL
*St 1	-	-	50 µL				-	
St 2	-	-	-	50 µL	-	-	-	-
St 3	-	-	-	-	50 µL	-	-	-
St 4	-	-	-	-	-	50 µL	-	-
1.58 mol/L HNO_3	450 µL	450 µL	450 µL	450 µL	450 µL	450 µL	450 µL	450 µL

* Standard

Other analyses: Complete blood count and urine creatinine concentration were determined for each of the subjects. Urine creatinine concentration is the best indicator of urine concentration, and its determination was necessary to express the concentration of heavy metals so that the concentration of heavy metals is expressed in micrograms per gram of creatinine in urine (µg / g creatinine in urine - µg / g Ucr). That means that the concentrations of heavy metals can be compared with each other regardless of the concentration of urine, which is a great advantage over the volume expression of the concentration of heavy metals, i.e. in µg / L of urine.

Statistical analysis: For statistical data processing *Microsoft Excel 2013* and *IBM SPSS Statistics 20* were used. The results are presented as the median, with the first and third quartile values (Q1 and Q3) or as an arithmetic mean with the corresponding standard deviation, depending on the data distribution. The values were compared using Student t-test or non-parametric test (Man Whitney test). The Kruskall-Wallis test or analysis of variance (ANOVA) was used to compare the values of more than two groups, depending on the data distribution. The Spearman's coefficient correlation analysis was used to correlate data. A significance level of 5% was used to determine statistical differences.

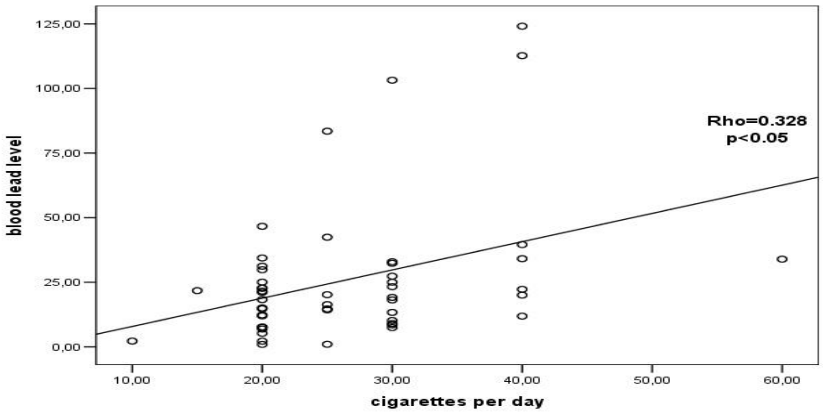
III. RESULTS AND DISCUSSION

Table 2. shows the median values of lead in blood, lead in urine and lead in urine / g creatinine in subjects stratified by smoking status. No significant difference in the examined parameters was found between the examined groups.

Table 2: Comparative analysis of lead concentrations in relation to smoking status.

Variable	Smokers	Former smokers	Non-smokers	p
Lead in the blood	21.65 (12.31-32.79)	18.0 (7.19-33.29)	18.7 (7.94-41.95)	0.094
Lead in urine	1.77 (1.36-2.17)	1.77 (1.26-2.57)	1.68 (1.24-2.15)	0,977
Lead in urine / creatinine	1.29 (0,73-2.62)	1.56 (0,91-2.78)	0,98 (0,69-2.18)	0,153

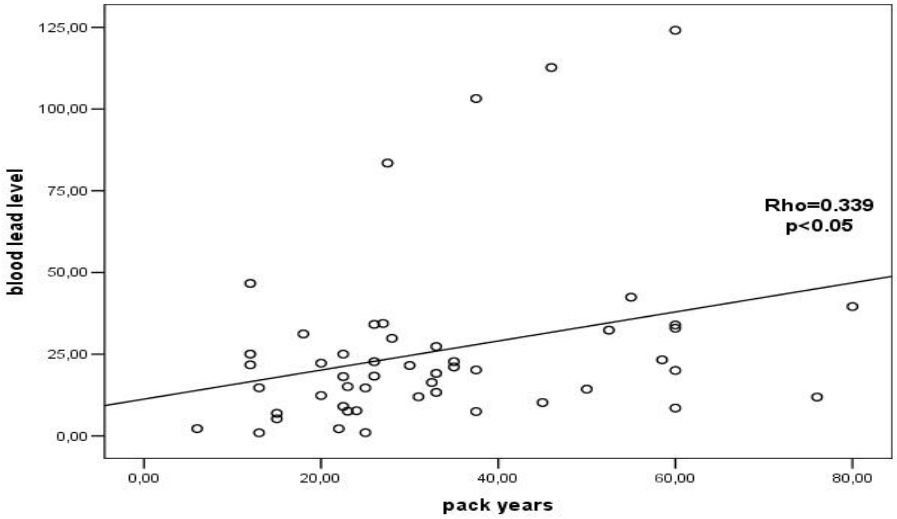
A significant positive correlation was found between the number of cigarettes consumed per day and the concentration of lead in the blood (Rho = 0.328; p <0.05) (Graph 1).



Graph 1. Correlation between the number of cigarettes consumed per day and the concentration of lead in the blood.

Rho - Spearman correlation coefficient

A significant positive correlation was found between the number of *pack-year* (It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked) and the concentration of lead in the blood (Rho = 0.339; p <0.05) (Graph 2).



Graph 2. Correlation between pack-years and blood lead concentration.

Rho - Spearman correlation coefficient.

Lead levels in the blood of smokers are constantly high and do not differ statistically in relation to age groups (p = 0.758); the same is the case with non-smokers, where the values are also independent in relation to age groups (p = 0.979). However, in ex-smokers, the lead values decrease in relation to age groups (p = 0.021) (Table 3.).

Table 3. Values of lead levels in the blood of the respondents in relation to age groups.

		X	SEM	Minimum	Maximum	F	P
Smokers	Age 41-50	24,64	3,69	0,95	103,20	0.279	0.758
	Age 51-55	31,07	12,09	5,24	124,10		
	Age 56-60	23,57	6,06	1,00	42,43		
Ex-smokers	Age 41-50	25,77	3,59	1,12	52,51	3.662	**0.021**
	Age 51-55	16,19	4,26	0,12	33,56		
	Age 56-60	11,53	3,94	0,27	39,52		
Non-smokers	Age 41-50	18,14	5,70	1,88	44,51	0.021	0.979
	Age 51-55	16,16	8,07	0,63	52,87		
	Age 56-60	17,00	.	17,00	17,00		

In the regression analysis model, a significant positive correlation was found between education and occupation and the lead concentration in urine/gram creatinine (p = 0.021; p = 0.042). (Table 4)

Table 4: Correlation of demographic characteristics, bad life habits, BMI, and hypertension with the concentration of lead in urine/gram creatinine.

Model	Non-standardized coefficient		Standardized coefficient	t	p
	B	Standard error	Beta		
Smoking	-0,363	0,430	-0,092	-0,844	0,401
Gender	-0,137	0,594	-0,025	-0,231	0,818
Age	0,056	0,051	0,119	1,094	0,277
Occupation	-2,187	0,926	-0,400	-2,361	**0,021**
Education	-1,3874	0,656	-0,367	-2,065	**0,042**
Alcohol	0,814	0,709	0,124	1,147	0,254
BMI	0,048	0,069	0,075	0,692	0,491
Hypertension	-0,052	0,670	-0,008	-0,077	0,939
Dependent variable: Lead in urine / gram of creatinine					

Our research is consistent with a study by Celic et al.[16] Lead was determined in the blood of 164 male volunteers, divided into four groups. The first group (n = 29) was a control group of non-smokers composed of office workers; the second group consisted of minibus drivers (n = 135). The group with drivers is divided into three groups according to smoking status or use of smokeless tobacco - maras powder, namely those who do not smoke tobacco or use smokeless tobacco (group 2; n = 33), cigarette smokers (group 3; n = 62) and smokeless tobacco users (group 4; n = 40). This study found a higher level of Pb in minibus drivers compared to the control group in subjects with the same smoking status. However, the difference in blood lead concentration in smokers compared to non-smokers was not statistically significant (35 ± 1.6 µg / L vs. 38 ± 2.4 µg / L, p> 0.05). In 1977, the WHO published a Pb content of 2.5-12.2 µg per cigarette, of which 2-6% was inhaled by smoking. The content of Pb in cigarettes has decreased over the years due to a different cultivation technology, so the value, e.g., for cigarettes from Great Britain and the USA, from 0.4 µg - to 0.9 µg per cigarette.[2]

This data may partly explain our results and the results of research by Celic et al.[16] because tobacco ingredients are influenced by factors such as cultivation method, soil composition, and possible pesticide and heavy metal residues, use of unleaded gasoline, climatic characteristics, drying process and technology used to obtain the finished product.[2]

The results of our research are in line with the research within the framework of heavy metal biomonitoring in Germany (Band VII: Arsen, Schwer - und Edelmetalle in Blut und Urin der Bevölkerung in Deutschland – Belastungsquellen und - pfade[17]). The study analyzed the level of heavy metals in the blood of 4,647 people. Smoking was a significant factor in the increase in the physical load of lead, with an increase in its value in the blood. Consumption of 10 cigarettes per day compared to 0 cigarettes per day, according to this study, contributes to the additional lead load by 12.2%, and consumption of 20 cigarettes/day compared to 0 cigarettes/day contributes to the additional lead load of 15.7%. As in this biomonitoring (173), our study found a positive correlation between Pb levels in the blood and the length of smoking (Rho = 0.339; p <0.05), we proved that long-term smokers had higher blood lead values than those with the shorter smoking experience. In this case, the smoking experience is expressed in the number of years / 1 pack of cigarettes per day (number of pack-year). We also demonstrated a positive correlation between Pb levels in smokers' blood and the number of cigarettes smoked per day (Rho = 0.328; p <0.05). Our results for the level of Pb in the blood are in line with the results of the research of Massadeh et al.[18] and Afridia et al.[19], who also found a positive correlation between blood lead levels and length of smoking, and the number of cigarettes consumed per day. Similar results have been found in the Apostles et al.[20], Weyermann and Brenner[21], Jakubowski et al.[22], Liou et al.[23], and Wietlisbach et al.[24] However, none of these studies included ex-smokers.

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Similar results were obtained in Bonanno et al.[25] study. These authors used data from the National Human Exposure Assessment Survey (NHEXAS - USA), which determined the level of Pb in smokers, non-smokers, and non-smokers exposed to secondhand smoke.

A study from Korean National Health and Nutrition Examination Survey (KNHANES)[26] showed that smoking, male gender, older age and the presence of COPD were associated with higher blood lead levels, while other comorbidities including diabetes, hypertension, stroke, osteoporosis, asthma, and depression were not associated (P <0.05). Our research showed that ex-smokers have lower blood lead concentrations with age, and univariate regression analysis the lead values decrease in relation to age groups. This can be interpreted as ridding the human body of lead over the years after quitting smoking. Our research also showed that education and occupation (physical or office-intellectual type of work) influence the concentration of lead in urine expressed per gram of creatinine.

IV. CONCLUSION

Regardless of the fact that the content of lead in cigarettes has been decreasing over the years due to different growing technologies, smoking is still a significant factor that contributes to the concentration of lead in the body with all the health risks associated with it.

Ethical Considerations: Ethical approval was obtained from the Ethical committee of the Faculty of Medicine, University of Sarajevo and informed consent was obtained from patients.

Conflict of Interest Statement: I didn't had any conflicts of interest to declare.

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