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THE EFFECTS OF CHRONIC LEAD POISONING ON THE VALUES OF HYPERTENSION IN CHILDREN

Zivkovic Jovan,[1] Savic Zoran[2]

[1] Faculty of Medicine, University of Priština, based in Kosovska Mitrovica
[2] Health Center Kosovska Mitrovica

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Abstract: **Introduction:** During the treatment of Roma children from Kosovska Mitrovica suffering from chronic lead poisoning (which began in the second half of the last decade), hypertension has also been observed. The examination and treatment were conducted under the patronage of World Health Organization, Ministry of Health of the Republic of Serbia and local administration. **Aim of this work** is show correlation between lead levels in blood and hypertension in children. **Materials and methods:** Lead from capillary blood flow was measured by Lead care analyzer. Extracted blood from a vein measured lead level in the toxicological laboratory of the Institute „Karajović" Belgrade. The pressure was measured by standard devices with changeable cuffs and has been expressed in mmHg. Hypertension has been observed in 159 children. They were divided into four groups. First group: non-Roma children (n = 32) with blood lead level of up to 10 mcg/dl. Second group: Roma children (n = 31) with blood lead level of up to 10 mcg/dl. Third group: Roma children (n = 53) with blood lead levels of 10–45 mcg/dl. Fourth group: Roma children (n = 43) with blood lead levels more than 45 mcg/dl, with an average value of 61.6 mcg/dl. **Results:** There is a statistically significant difference in the elevation of systolic blood pressure between group (chi-square = 31,179; p < 0,001), the first ($\bar{x}$ = 107,2 mmHg) and the fourth group ($\bar{x}$ = 114,6 mmHg), the second ($\bar{x}$ = 104,5 mmHg) and fourth group, third ($\bar{x}$ =106,4 mmHg) and fourth group. There is a statistically significant difference in the elevation of diastolic blood pressure between group (chi-square = 32,028; p < 0,001), the first ($\bar{x}$ = 67,7 mmHg) and the fourth group ($\bar{x}$ =73,4 mmHg), the second ($\bar{x}$ = 66 mmHg) and third group ($\bar{x}$ = 69 mmHg), second and fourth group, third and fourth group of children. It is concluded that when the value of lead in the blood was higher its effect on blood pressure was more pronounced. **Conclusion:** Most children with lead levels over 45 mcg/dl have developed an increased blood pressure as well, which required further observation and testing. Twelve of the children from the fourth group have significant hypertension. But, none of the children have shown severe hypertension values.

Key words: children, lead in the blood, hypertension.

INTRODUCTION

Lead has been known to man before all other metals. It has been used widely for a very long time. Ever since the ancient and Roman times, the production and use of lead have been constantly increasing throughout history (with only slight oscillations). Many of the ancient civilizations, such as Egypt, Greece, Rome and Phoenicia, were familiar with lead (1). There is historical evidence that indicates the exploitation of lead in pre-Roman times in the northern region of Kosovo and Metohija (today's territory of Trepča). Year 1927 is considered a milestone — the English company "Trepca Mines Limited" began working on the opening of the mine, while the production started in 1939 when the lead smelter was built (2). Lead can enter the body by inhalation and ingestion, while the absorption of lead through undamaged skin is insignificant. Lead can also be transported transplacentally (3). When lead is inhaled, the absorption occurs within the whole respiratory tract, especially in bronchioles and alveoli (4). After the absorption, lead is transported by blood, mostly by erythrocytes (about 95% of the intake), then by protein fractions of plasma, and minimally in terms of ionic transport. Ionized lead represents metabolically active nucleus of the entire amount of lead in the body responsible for toxic effects. Lead toxicity may have multiple mechanisms. As other heavy metals, lead

forms a series of complexes with ligands that contain sulphur, nitrogen or oxygen. The interaction of lead with sulphur groups, amine and simple amino acids (inhibition of enzyme activity) is especially significant (5, 6).

Chronic lead poisoning is common, especially in children. Lead affects many systems and organs in human body: hematopoietic system, hearing, peripheral and autonomic nervous system, skeletal system, liver, kidneys, reproductive system, metabolism of vitamin D, etc (7). There is no hard evidence of heart damage due to chronic lead poisoning. Lead poisoning causes spasms of the smooth muscles of blood vessels (especially of smaller blood vessels of the central nervous system, kidneys and bowels). The main effect of lead poisoning on the cardiovascular system is hypertension with all its consequences (8).

Hypertension is a health problem of national significance. It is one of the main risk factors for atherosclerosis and consequential cardiovascular, cerebrovascular and renal diseases, which are the leading cause of morbidity and mortality in our country, as well as other developed countries and many developing countries.

The primary goal of pediatricians and other child care medical personnel is to recognize children and adolescents who either have the risk factors for developing hypertension, or have already developed it, and take preventive and therapeutic measures in a timely manner (since hypertension in childhood and adolescence is one of the strongest predictors of adult hypertension) (9).

AIM OF THE STUDY

The aim of this study is to process and represent the test results of examined children chronically poisoned by lead in Kosovska Mitrovica, using statistical-epidemiological methods, as well as to show correlation between lead levels in blood and hypertension in children.

MATERIALS AND METHODS

Examination and treatment of Roma children, identified as the group with the highest risk for lead poisoning by the World Health Organization, started in the second half of the last decade. The investigation included almost all Roma children from North Kosovska Mitrovica within the age group of 1–14. The research also included two control groups- Roma children from Leposavić and non-Roma children from Kosovska Mitrovica.

Lead Care Analyzer (No 70–2233) at Kosovska Mitrovica Public Health Institute was used for determination of capillary blood lead levels. Venous blood lead levels were determined in toxicological laboratory of the Institute for Occupational Health “Karajović”, Belgrade.

Basic hematological and biochemical analyses were performed in the central laboratory of Health Center Kosovska Mitrovica (Le, Le formula, Er, Hb, Hct, MCV, MCH, MCHC, Tr, feritin, AST, ALT, Urea, Cr, serum Fe). Children with lead levels above 40 microgr/dl were treated with “Chemet”, a medication used for the first time in Europe with these children.

For analysis of obtained data, descriptive-statistical methods were used, as well as methods for testing the statistical hypotheses. Among the descriptive methods, measures of central tendency (arithmetic mean) were used and measures of variability (standard deviation) and relative numbers. The methods used for testing statistical hypotheses were: Kruskal-Wallis with Mann-Whitney post hoc test and chi-square test. For analysis of correlation, the Spearman’s rho test was used. For variable of age in children, ANOVA was performed. Distribution of results was normal. For the rest of analysis Kruskal-Wallis test was performed. After the application of Bonferroni correction, there was no change in significance. Statistical processing was done by SPSS21 software program. Statistical hypotheses were tested at a significance level of 0.05.

During the investigation, the blood pressure of 159 children (ages 5–14) was monitored in order to determine the effects of chronic lead poisoning. The groups were formed based on the recommendation by The World Health Organization. The children were divided into four groups. The first group (n = 32) consisted of non-Roma children with blood lead levels of up to 10 mcg/dl (the average lead level of 7.78 mcg/dl). Roma children from Kosovska Mitrovica and Leposavic were first joined based on the capillary blood lead level, and then divided into the remaining three groups: the second group (n = 31) consisted of Roma children with blood lead levels of up to 10 mcg/dl (the average lead level being 7.7 mcg/dl); the third group (n = 53) consisted of Roma children with blood lead levels between 10 and 45 mcg/dl (the average lead level value of 25.47 mcg/dl); the forth group (n = 43) consisted of Roma children with blood lead levels greater than 45 mcg/dl (the average lead level of 61.70 mcg/dl).

Each child’s blood pressure was measured several times and the average values were calculated. The blood pressure was measured using the auscultatory method. The values are expressed in millimeters of mercury (mmHg).

The following table provided by WHO was used for blood pressure interpretation:

Table 1. *Normal blood pressure values in children (mmHg)*
(upper limits of normal blood pressure — recommended by WHO)

AGES	**BOYS**		**GIRLS**	
Years of age	Systolic	Diastolic	Systolic	Diastolic
5	104	65	103	66
6	105	68	104	68
7	106	70	106	69
8	107	71	108	71
9	109	72	110	72
10	111	73	112	73
11	113	74	114	74
12	115	74	116	75
13	117	75	117	76
14	120	75	119	77

Table 2. *Average values of arterial blood pressure (mmHg) and blood lead levels (mcg/dl)*
(SBP — systolic blood pressure, DBP — diastolic blood pressure, Pb — blood lead level)

Ages	Group I			Group II			Group III			Group IV		
years of age	SBP	DBP	Pb	SBP	DBP	Pb	SBP	DBP	Pb	SBP	DBP	Pb
5	102	62	7	99	60	7	100	64	25	106	69	60
6	103	65	7	100	62	8	102	65	25	108	70	60
7	104	65	8	101	63	7	103	65	25	110	69	62
8	105	68	8	103	65	8	103	67	26	110	70	62
9	105	68	7	105	66	7	105	69	26	112	72	61
10	108	69	8	106	68	7	106	70	25	115	72	62
11	110	70	9	107	68	7	108	72	25	115	75	62
12	110	71	9	107	70	8	110	72	26	120	75	65
13	113	71	7	110	70	8	110	73	26	120	78	65
14	118	72	7	112	70	8	114	73	26	125	81	65

These values represent the lower limits of high blood pressure in accordance with the age and gender of the children. Each value, equal or higher, represents marginal blood pressure, HTN degree I or II and requires further examination.

It is evident from Table 1 that gender does not affect the blood pressure values, and was therefore disregarded from further research (recommended by WHO).

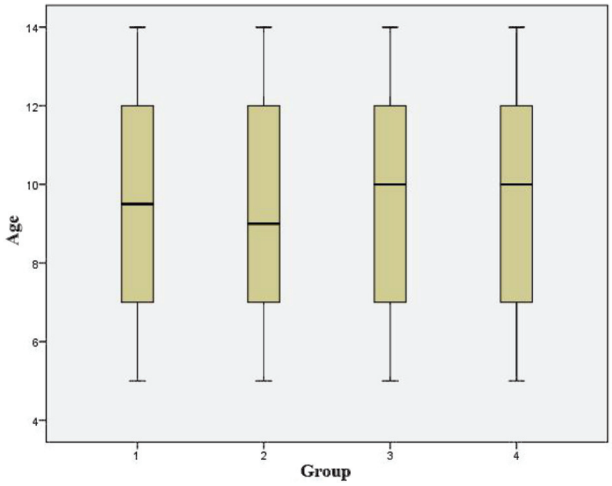
RESEARCH/INVESTIGATION RESULTS

Blood pressure values and average blood lead levels in examined children are outlined in Table 2.

The average age of examinees in the research was 9.6 ± 2.9 years of age. The youngest examinee was 5 years old, while the oldest was 14 years of age (Table 3, Graph 1).

Table 3. *Ages of examined children*

Group	**n**	**$\bar{x}$**	**SD**	**Med**	**Min**	**Max**
1	32	9.4	2.9	9.5	5	14
2	31	9.3	2.9	9	5	14
3	53	9.7	2.9	10	5	14
4	43	9.5	2.9	10	5	14
Total	159	9.6	2.9	10	5	14



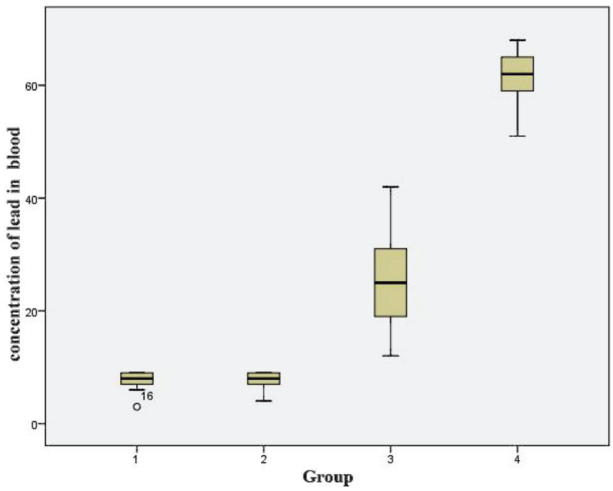
Graph 1. *The average age of examined children*

The first control group consisted of children of similar age as other examined children.

Average values of blood lead levels in examined groups of children are presented in Table 4 and Graph 2.

Table 4. *Blood lead levels*

Group	n	$\bar{x}$	SD	Med	Min	Max
1	32	7.9	1.4	8	3	9
2	31	7.6	1.4	8	4	9
3	53	25.4	7.5	25	12	42
4	43	61.6	4.2	62	51	68
Total	159	28.2	22.3	20	3	68



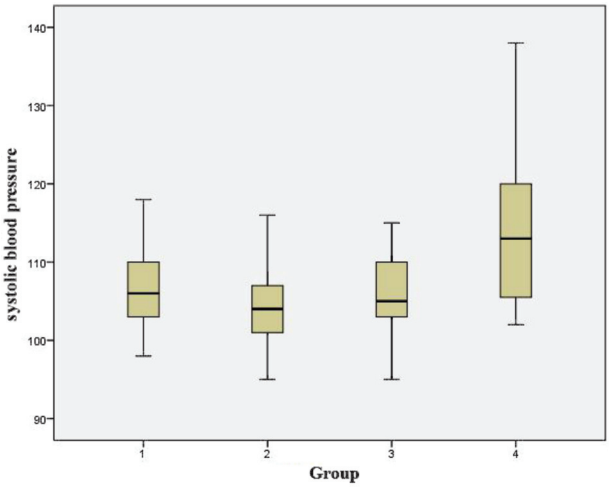
Graph 2. *Blood lead levels*

Blood lead levels in the third group of children exceed the (upper) limits of normal values (25.4). The treatment with diet was applied. Blood lead levels in the children from the fourth group was very high (61.6). These children were treated with Chemet.

Average values of systolic blood pressure of examinees are shown in Table 5 and Graph 3.

Table 5. *Average values of systolic blood pressure*

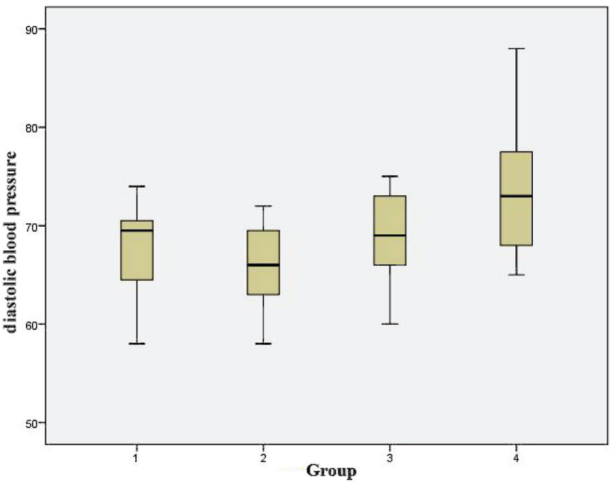
Group	n	$\bar{x}$	SD	Med	Min	Max
1	32	107.2	5.2	106	98	118
2	31	104.5	4.6	104	95	116
3	53	106.4	4.9	105	95	115
4	43	114.6	9.5	113	102	138
Average	159	108.4	7.5	106	95	138



Graph 3. *Values of systolic blood pressure*

Table 6. *Average values of diastolic blood pressure*

Group	n	$\bar{x}$	SD	Med	Min	Max
1	32	67.7	4.2	69.5	58	74
2	31	66	4.0	66	58	72
3	53	69	3.7	69	60	75
4	43	73.4	5.9	73	65	88
Total	159	69.4	5.3	69	58	88



Graph 4. *Values of diastolic blood pressure*

The values of diastolic blood pressure in children from the fourth group are increased with regard to their

age. The increase of diastolic blood pressure is less noticeable than the increase of systolic blood pressure.

DISCUSSION

Lead can enter the body by ingestion and inhalation. It is distributed to almost all tissues and organs and has adverse effects on them. These effects are mostly reversible, however, in cases of longer and intense poisoning, irreversible changes can occur. In children, the central nervous system is the most vulnerable and severe changes can be manifested. Chronic lead poisoning is more common than acute lead poisoning in children. The clinical picture does not show anything specific that can indicate chronic poisoning. The only means of diagnosing chronic lead poisoning is by determining the blood lead level. All other examinations are of less importance, or even irrelevant.

However, the fact that there were about 200 deaths from chronic lead poisoning among children per year in the United States during the mid 20th century is astonishing. The children who suffered from chronic lead poisoning lived in wooden houses painted with lead colors (lead-based paint) (10).

The investigation of blood lead levels of 92 immigrant children from Africa, and 401 control group children, was conducted in 2004 in New Hampshire. The blood lead levels above 10 mcg/dl were found in 29% of immigrant children and only in 1.5% of the control group children. The reasons were the residential area (residence near the industrial zone), lifestyle and diet (11).

An examination conducted in India in 2007 included 107 children who lived near the lead mine. Blood lead levels between10 and 20 cmg/dl were found in 43% of the children, while 39% of the children had blood lead levels greater than 20 mcg/dl. Only 18% of the examined children had normal blood lead values (12).

Similar research was published in 2008 in Columbia. The examined group consisted of 110 children whose parents were involved in battery recycling. Blood lead levels between 10 and 20 mcg/dl were found in 25% of the children. Almost half of the children (49%) had blood lead level of 20 mcg/dl. Only 26% of examinees had the allowed blood lead level values (13).

Two separate investigations were conducted in Germany (Duisburg). The first one, performed in 1983, included 843 children with place of residence in the city centre and 872 children from the suburbs. The average blood lead level in children from the city center was 5.3 mcg/dl, as opposed to 1.8 mcg/dl found in children who lived in the suburbs. The second investigation took place in 2008. The children who lived in the city center had the average blood lead level of 2.2 mcg/dl, while the average blood lead level in children from the suburbs was 1.4 mcg/dl. The reduction was achieved by the use of unleaded fuel and driving restrictions in the city center (14).

According to the standards of the World Health Organization (WHO), the optimal blood lead level is up to 5 mcg/dl. The values up to 10 mcg/dl can be tolerated. Blood lead levels of 10–45 mcg/dl indicate chronic lead poisoning. These values do not require medicamentous treatment, but only the change of residence and proper diet. Blood lead values of above 45 mcg/dl demand urgent medical treatment.

During the 50 years of his work, Howard performed longitudinal monitoring of 192 lead-intoxicated (former) children. He concluded that there was a high risk for the development of hypertension (15).

Ho H. and associates concluded that the long term exposure of children to lead and the accumulation of lead in bones represent high risk factors for developing hypertension (16).

The US national poison control center (DCC) published that the blood lead level higher than 10 mcg/dl was found in 310.000 children in the period 1999–2002 (17).

Kopp and associates came to a conclusion that the exposure of children to lead can induce significant changes in cardiovascular system functioning and hypertension. Myocarditis, ECG changes, increased catecholamines, hypertension, hypercholesterolemia, atherosclerosis, and vascular degeneration signs are associated with lead poisoning which has been proved in clinical and experimental studies. Morphological and biochemical postmortem changes in the myocardium have been proved in humans, whereas cardiovascular changes have been established in animals (18).

The American Academy of Pediatrics announced in the journal “Pediatrics” in 2005 that the lead level in blood decreases in children in America, but 25% of them still lives in houses painted with lead paint. In the samples taken it was recorded over 10 mcg/dl lead level, resulting in weakened cognitive functions and other consequences (19).

Binns et al are announcing that the Center for Disease Control and Prevention (CDC) reported that in studies from 1991 children with increased lead in the blood showed that physical and mental health of children may be affected even when lead level is below 10 mcg/dl. In children throughout the USA with increased lead level in blood were recorded weakened cognitive functions, functions of motor skills, reduced physical abilities and changed behavior. Accordingly CDC proposed training measures, prevention and enhancement of awareness of health centers, families and local health programs (20).

Lyn Patrick amounts that even smaller amounts of lead in the blood, over a long period of time, result in disorders in cognition, neuro-behavioral disorders, neurological damages, hypertension, and kidney failure (21).

Shiring Weng et al during the six years of monitoring the levels of lead in the blood in middle age people found a significant interaction with hypertension and increased level of serum creatinine. They conclude that diabetes and hypertension are the consequences of short-term and long-term exposure to lead (22).

Barbosa et al claim that there is no lower limit safety of lead level in blood. Bad influence on health, including intellectual deterioration in young children, occurs when the lead level is less than 10 mcg/dl (23).

By examining the blood lead levels in Roma children who live in camps in Kosovska Mitrovica, and by comparing the obtained results with the results of many authors who investigated this problem, the same conclusion is reached: the two main risk factors for chronic lead poisoning in children are the place of residence and lifestyle. Primitive battery recycling has a special significance as a risk factor for chronic lead poisoning in children.

Our results of the blood lead levels in Roma children show that the children from the first and second group do not suffer from chronic lead poisoning. The children from the third group suffer from low-intensity chronic lead poisoning. However, chronic lead poisoning in children from the fourth group is of very high, even alarming, intensity (up to 65 mcg/dl).

In the course of our research, no statistical significance in the age of examined groups was established ($F = 2.332$; $DF = 3$; $p = 0.916$).

Statistical significance was found in the level of diastolic blood pressure among the examined groups (chi-square = 32.028; $p < 0.001$), especially between the first and the fourth group ($p = 0.001$), the second and the third group ($p = 0.002$), the second and the fourth group ($p < 0.001$), and finally the third and the fourth group ($p = 0.001$). The median diastolic blood pressure value is statistically significant in the fourth group of examinees.

There is a positive correlation between the values of blood lead levels and diastolic blood pressure ($r = 0.48$; $p < 0.001$). High blood lead level is followed by the increase in diastolic blood pressure.

Statistical significance was established in blood lead levels among the examined groups (chi-square = 140.2; $p < 0.001$). The median blood lead value is statistically significant between the first and the third, the first and fourth, the second and third, the second and the fourth, and the third and the fourth group ($p < 0.001$).

Statistical significance was found in the level of systolic blood pressure among the examined groups (chi-square = 31.179; $p < 0.001$), especially between the first and the fourth group ($p = 0.001$), the second and the fourth group ($p < 0.001$) and the third and the fourth group ($p < 0.001$). The median systolic blood pressure value is statistically significant in the fourth group of examinees. A positive correlation between the values of blood lead levels and systolic blood pressure ($r = 0.42$; $p < 0.001$) has also been proven. High blood lead level is followed by the increase in systolic blood pressure.

CONCLUSION

There is evidence of significant lead poisoning in Roma children who live in camps in the north region of Kosovo and Metohija. Lead poisoning was determined by the reliable methods of measuring the blood lead levels.

Chronic lead poisoning, especially if significant, leads to the increase of blood pressure values, both systolic and diastolic.

The higher the blood lead levels, the greater the effects on the blood pressure. The blood pressure values in the majority of children with high blood lead levels (higher than 45 mcg/dl) required detailed examination and further observation.

Abbreviations

WHO — Word Health Organization
CDC — Center for Disease Control and Prevention
Er — red blood cell (RBC)
Le — white blood cell(WBC)
Le — formula = WBC formula
Hb — hemoglobin
Hct — hematocrit
MCV — mean corpuscular volume
MCH — mean corpuscular hemoglobin
MCHC — mean corpuscular hemoglobin concentracion
Tr — trombocit
AST — aspartat aminotransferaza
ALT — alanin aminotransferaza
Fe — iron
Pb — lead
Cr — creatinin
HTN — high hypertension
SBP — systolic blood pressure
DBP — diastolic blood pressure

Sažetak

DEJSTVO HRONIČNOG TROVANJA OLOVOM NA VREDNOST KRVNOG PRITISKA KOD DECE

Živković Jovan,[1] Savić Zoran[2]

[1] Medicinski fakultet Univerziteta u Prištini, sa sedištem u Kosovskoj Mitrovici
[2] Zdravstveni centar Kosovska Mitrovica

Uvod: Tokom projekta lečenja romske dece, iz Kosovske Mitrovice, hronično trovanih olovom (započetog u drugoj polovini prošle decenije), praćena je i hipertenzija. Ispitivanje i lečenje je vršeno pod patronatom Svetske zdravstvene organizacije, Ministarstva zdravlja Srbije, lokalne administracije. **Cilj** rada je da se utvrdi korelacija između povišenog nivoa olova u krvi dece i hipertenzije. **Materijal i metode:** nivo olova iz kapilarne krvi je određivan na aparatu Lead care analyzer. Nivo olova iz venske krvi određivan je u toksikološkoj laboratoriji Instituta „Karajović“ u Beogradu. Pritisak je meren standardnom metodom. Praćena je tenzija kod 159-ro dece. Podeljena su u četiri grupe. Prva grupa: ne-romska deca (n = 32) olovo u krvi do 10 mcg/dl. Druga grupa: romska deca (n = 31), olovo do 10 mcg/dl. Treća grupa: romska deca (n = 53) olovo u krvi 10–45 mcg/dl. Četvrta grupa: romska deca (n = 43), olovo u krvi veće od 45 mcg/dl, sa srednjom vrednošću 61,6 mcg/dl. **Rezultati:** Postoji statistički značajna razlika u visini sistolnog krvnog pritiska između ispitivanih grupa (hi-kvadtat = 31,179; p < 0,001). Između prve (X =107,2 mmHg) i četvrte grupe (X = 114,6 mmHg), druge (X = 104,5mmHg) i četvrte grupe, treće (X = 106,4 mmHg) i četvrte grupe. Postoji statistički značajna razlika u visini dijastolnog krvnog pritiska između grupa (hi-kvadrat = 32,028; p <0,001). Između prve(X = 67,7 mmHg) i četvrte grupe(X = 73,4 mmHg) druge (X = 66 mmHg) i treće (X = 69 mmHg) druge i četvrte, treće i četvrte grupe dece. **Zaključak:** Što je veća vrednost olova u krvi njegovo dejstvo na krvni pritisak je izraženije. Deca sa olovom iznad 45 mcg/dl imaju povećane vrednosti krvnog pritiska i kod njih je indikovano dalje praćenje i detaljnije ispitivanje. Dvanaestoro dece iz četvrte grupe ima signifikantnu hipertenziju. Ni jedno dete nema vrednosti ozbiljne hipertenzije.

Ključne reči: deca, olovo u krvi, hipertenzija.

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Correspondence to /Autor za korespondenciju
Prof dr Jovan Živković
Donjovrežinska 10/13
18000 Niš,
Mob. Tel.063/408-694
Email: drjovanzivkovic@gmail.com