Општа медицина 2013;19(1-2):26-30 UDC 613.95:613.14

Velickova N, Ruskovska T,
Kamceva G, Ivanovska V

Faculty of medical science, University "Goce Delcev", Stip, R. Macedonia

Biological and genotoxic monitoring as integral part of predictive and preventive medical surveillance of children living in polluted area

Key words:
lead,
pollution,
children,
blood

Abstract

Introduction: Presence of many elements and their compounds in the environment pose a significant health risks to the exposed individuals and contributes to the burden of disease in society. An example for one of these black points wich destroyed the health of the people is lead and tine smelter in Veles (city in R of Macedonia). It is obvious that there is environmental-health risk with enough evidence for the pollution of the environment, as well as impact of higher blood level of lead in selected children.

Objective: To registred and define the environmental health risk on children in Veles.

Method: In this study we compare two groups of 100 children (average 10 years old). Exposed group comprised children living in Veles (contaminated area), and control group were children who live in village Ivankovci.

Results: Student's t-test indicates statistically significant differences ($t=15.14$; $p<0.001$), between average concentration of lead in the air in Veles (0.94 mg/m^3) and Ivankovci (0.03 mg/m^3); statistically significant differences ($t=5.74$; $p<0.001$), between average concentrations of BLL (37.27 µg/ml) in exposed group and control group (18.20 µg/ml); statistically significant differences ($t=2.35$; $p<0.05$), between average concentrations of hemoglobin in exposed group (children who live in Veles) and control group and the other hematological parameters between two groups.

Discussion: The significance of these results show that children are exposed to mixtures rather than single chemicals. This complexity is a major reason why mixtures are not well studied. In this study are illustrated some of the principles and approaches that can be used to study the effects of mixtures. The multidisciplinary elaboration of the topic, suggests the need for a more serious approach to this important phenomenon (genotoxicological impact of heavy metals) and also is a specific model that is capable of application in other related research.

Conclusion: Registered changes had reversible character. Manifested signs of disease were not registered, because of yet successful compensatory mechanisms in the examined children.

Correspondence to:
Nevenka Velickova
Faculty of medical science
University "Goce Delcev" - Stip
R. Macedonia
nevenka.velickova@ugd.edu.mk

Introduction

Many elements and compounds from the environment pose a significant health risks to exposed individuals (in our research children), and contribute to the burden of disease for society[11]. Socioeconomic factors influence both lead exposure and many health outcomes, including intellectual development, growth, and numerous chronic diseases. "Lead is a developmental toxicant" and the "harmful effects of lead on children's development can occur without signs or symptoms" (*Centers for Disease Control and Prevention).* Lead is the most extensively studied environmental neurotoxicant. Animal and *in vitro* studies have provided an abundance of information concerning biochemical and physiologic changes caused by lead[1, 2, 9, 10, 12]. Athough the precise mechanisms of action and their relative importance in different manifestations of lead toxicity are not known for certain, *in vitro* studies demonstrate that lead can interfere with fundamental biochemical processes. At the most basic level, many of the proposed mechanisms of lead toxicity involve binding to proteins and/or interference with calcium dependent processes[3]. For some of harmful effects of lead, such as anemia, the lead-associated biochemical changes that contribute to the effect in humans are fairly well understood.

In that context of special interest is to determine the influence of lead, like heavy metals, in the same time the silent but the strongest factors for different diseases. This research gets the meaning and enriches the fund of knowledge in genotoxicology. In this study, the possible clinical aspects of lead on the children health are elaborated, with special reference to hematological effects, esp. anemia as a result of heavy metals intoxication.

Method

In this study we compared two groups of 100 children (mean age 10 years). Exposed group were children who live in Veles (contaminated area) and control group were children who live in village Ivankovci (14.27 km from Veles, not contaminated area). Veles with its geographic position, atmospheric specificities, urban and industrial concentration and wrong location of the lead and zink smelter has all predispositions for huge and continious air pollution with lead as specific agent. One can conclude that there is an obvious environmental-health risk in Veles. It is representative block ecologic points with enough evidence for the pollution, as well as the impact of higher blood-lead levels in the selected children. We have used biochemical analysis (inductively coupled plasma spectrometry (ICP) as one of the most sensitive analytical techniques for the determination of elements in biological materials, and the basic haematological parameters, using descriptive statistical analysis (StatView).

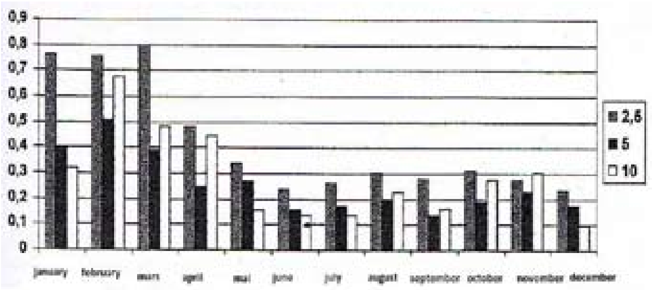
Results

Results indicate higher concentration of lead in the area (0.94 mg/m^3), that is 35% higher of maximal limited concentration of lead (0.7 mg/m^3).

Concentration of lead in suspended particles in the air mg/m^3

Month	Veles	Ivankovci
January	1.48	0.0143
February	1.94	0.0233
Mars	1.677	0.00446
April	1.044	0.02113
Mai	0.776	0.07716
June	0.536	0.024
July	0.59	0.02433
August	0.711	0.02633
September	0.579	0.0175
October	0.7608	0.03383
November	0.8114	0.04766
December	0.4426	0.012
Average	**0.94565**	**0.031189**
SD	**0.489585**	**0.038118**
min	**0.4426**	**0.0**
max	**1.94**	**0.288**
MLC	0.7	

Student t-test indicates statistically significant differences ($t=15.14$; $p<0.001$), between average concentration of lead in the air in Veles (0.94 mg/m^3) and Ivankovci (0.03 mg/m^3) (Graficon 1).



Graficon 1. Concentation of lead (mg/m^3) at measuring position at department of public health - Veles; according to diameter of suspended particles in the air.

Student t-test indicates statistically significant differences ($t=5.74$; $p<0.001$), between average concentrations of BLL (37.27 μg/ml) in exposed group (children who live in Veles) and control group (children who live in Ivankovci) (18.20 μg/ml) (Table 1).

Table 1. Levels of lead in blood in exposed and control group

	X	min	max	SD
Veles	37.277749	2.57	92.55	17.93559
Ivankovci	18.20290	0.03	36.4	11.56369

Student t-test indicates statistically significant differences (t=2.35; p<0.05), between average level of hemoglobin in exposed group (children who live in Veles) and control group (chidren who live in Ivankovci) (Table 2).

Table 2. Levels of hemoglobin in blood in exposed and control group

	X	min	max	SD
Veles	132.1281	112	162	9.119305
Ivankovci	127.2903	116	139	6.320304
Referent value		115	155	

Student t-test indicates statistically significant differences (t=0,31; p<0,05), between average number od redblood cells in exposed group (children who live in Veles) and control group (chidren who live in Ivankovci) (Table 3).

Table 3. Levels of red blood cells in exposed and control group

	X	min	max	SD
Veles	4,892463	2,95	6,8	0,414764
Ivankovci	4,844839	4,44	5,9	0,337746
Referent value		4,2	5,5	

Prior reviews that compiled extensive evidence from *in vitro*, animal, and human studies established lead as a multi-organ toxicant, including studies showing effects of lead blood levels near 10 g/dL[1,9,12]. These studies include that lead is a developmental toxicant and that harmful effects of lead on children's development can occur on respiratory, neural, renal and hematopoetic system (Table, 4, 5, 6, 7).

Table 4. The most common respiratory disease in children

Respiratory disease	**Veles**		**Ivankovci**	
	N	**%**	**N**	**%**
Without disease	150	73,9	27	87,09
Bronchitis	32	15,8	3	9,68
Bronchopneumonia	18	8,9	1	3,23
Asthma	3	1,5	/	/

Table 5. The most common neuropsychiatric disorders in children

Neuropsychiatric disorders	**Veles**		**Ivankovci**	
	N	**%**	**N**	**%**
Without disease	200	98,5	30	96,77
With Neuropsychiatric disorders	3	1,5	1	3,23

Table 6. Distribution of renal disease at children

Renal diseases	**Veles**		**Ivankovci**	
	N	**%**	**N**	**%**
Without disease	202	99,5	31	100
Disease	1	0,5	/	/

Table 7. Distribution of anemia at children

Anemia	**Veles**		**Ivankovci**	
	N	**%**	**N**	**%**
Without anemia	199	98	31	100
Anemia	4	2	/	/

Lead interferes with heme synthesis partly by binding to sulfhydryl groups in the aminolevulinic acid dehydratase enzyme[1], which is especially sensitive to inhibition by lead (less than 0.5 µmol/l *in vitro*). This inhibition causes accumulation of delta aminolevulinic acid, a potential neurotoxic agent. Lead also inhibits ferrochelatase, an enzyme catalyzing the incorporation of iron into protoporphyrin to form heme. This inhibition also may involve lead binding to protein sulfhydryl groups. These findings are compatible with previous studies in literature quoted on the paper. The significance of these results is doubtful. Lead interferes with the activity of several major enzymes involved in heme biosynthesis[3,6,8]. The only well-defined clinical symptom associated with inhibition of heme biosynthesis is anemia. But in the real world, people are exposed to mixtures rather than single chemicals. Although various substances may have totally independent actions, in many cases two substances may act at the same location in a way that can be either additive or non-additive[5,7]. Many even more complex interactions can occur if two chemicals act in different but related targets[4]. In extreme cases there may be synergistic effects, in which case the effect of two substances is greater than the sum of their individual effects. In real life, the majority of people are exposed to multiple chemicals. This complexity is a major reason why mixtures are not well studied.

Conclusion

Biological and genotoxic monitoring is becoming an integral part of preventive medical surveillance on the children and other human populations, with actual or potential genetic hazards. Despite the theoretical value, the study has practical importance because it indicates the necessity of introducing a permanent biological and other monitoring on children in polluted area. They would contribute to better protection in this segment. The multidisciplinary elaboration of the topic suggests the need for a more serious approach to this important phenomenon (genotoxic impact of heavy metals on children) and also represents a specific model that is capable of application in other related researches.

Биолошки и генотоксични мониторинг интегрални део предиктивног и превентивног медицинског надзора деце која живе у загађеним подручјима

Величкова Н, Русковска Т, Камчева Г, Ивановска В.

Медицински факултет, Универзитет , 'Гоце Делчев'', Штип, Република Македонија

Кључне речи:
олово,
загађење,
деца,
крв

Сажетак

Увод. Многи елементи и њихова једињења, присутни у окружењу представљају значајан ризик по здравље изложених појединаца и доприносе оптерећењу друштва болестима. Пример за једну од ових црних тачака која је разорила здравље људи је топионица олова и цинка у Велесу (Р. Македонија) очигледно је да постоји ризик по здравље са довољно доказа за загађење природне средине, као и утицај виших нивоа олова у крви одабране деце

Циљ рада. Регистровати и дефинисати амбијенталне ризике по здравље деце у Велесу

Метод. У овој студији упоређујемо две групе од 100 деце (у просеку старе 10 година). Експонирана група су деца која живе у Велесу (контаминирано подручје), а контролна група деца која живе у селу Иванковци.

Резултати. Студентов *t*-тест показује значајну разлику (t=15,14; p<0,001) између просечних концентрација олова у ваздуху у Велесу (0,94 mg/m^3) и Иванковцима (0,03 mg/m^3); статистички значајну разлику између просечних концентрација олова у крви експониране групе (37,27 $\mu g/ml$) и контролне групе (18,20 $\mu g/ml$), статистички значајну разлику између просечних концентрација хемоглобина у експонираној групи (деца која живе у Велесу) и контролној групи и других хематолошких параметара између две групе.

Дискусија. Значај ових резултата показује да су деца изложена мешавинама, а не једној хемикалији. Ова комплексност је најважнији разлог због ког мешавине нису добро проучене. У овој студији су илустровани неки принципи и приступи који могу да се користе у проучавању ефекта мешавина. Мултидисциплинарна разрада теме указује на потребу озбиљнијег приступа овом значајном феномену (генотоксиколошком утицају тешких метала), а такође представља специфичан модел примењив у другим сличним истраживањима.

Закључак. Регистроване промене су реверзибилног карактера. Није регистрована манифестна појава болести због још увек успешних компензаторних механизама код испитиване деце.

Литература
References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological profile for lead*. U.S. Department of Health and Human Services. Public Health Service. Atlanta, Georgia, 1999.
2. Davis JM, Otto DA, Weil DE, Grant LD. *The comparative developmental neurotoxicity of lead in humans and animals*. Neurotoxicol Teratol. 1990;12:215-229.
3. Goldstein GW. *Evidence that lead acts as a calcium substitute in second messenger metabolism*. Neurotoxicology. 1993;14: 97-101.
4. Hammond PB, Bornschein RL, Succop PA. *Dose-effect and dose-response relationships of blood lead to erthryocytic protoporphyrin in young children*. Environ Res. 1985;38: 187-196.
5. Rabinowitz MB, Leviton A, Needleman HL. *Occurrence of elevated protoporphyrin levels in relation to lead burden in infants. Environ Res*. 1986;39:253-257.
6. Rabinowitz, M. B., Leviton, A., Needleman, H. L. *Variability of blood lead concentrations during infancy*. Arch Environ Health. 1984;39:74-77.
7. Rabinowitz MB, Leviton A, Needleman HL, Bellinger DC, Waternaux C. *Environmental correlates of infant blood lead levels in Boston*. Environ Res 1985;38:96-107.
8. Roels HA, Lauwerys R. *Evaluation of dose-effect and dose-response relationships for lead exposure in different Belgian population groups* (*fetus, child, adult men and women*). Trace Elem Med. 1987;4(2):80-87.
9. U.S. Environmental Protection Agency. *Air quality criteria for lead*. Research Triangle Park, *NC*. EPA. Office of Research and Development. EPA Publication No. 600/8-83-028F. 1986.
10. U.S. Environmental Protection Agency. *Risk Analysis to Support Standards for Lead in Paint, Dust, and Soil: Supplemental Report* (EPA 747-R-00-004). Aviable at: *http://www.epa.gov/opptintr/lead/403risksupp.htm. 2000.*
11. U.S. Public Health Service. *Smoking and Health* - Report of the Advisory committee to the Surgeon General of the Public Health Service. Publication No. 1103. Washington, D. C.
12. World Health Organization. *Environmental Health Criteria 165 Inorganic Lead*. International Programme on Chemical Safety. Geneva. 1995.

Примљен • Received: 28/05/2012
Прихваћен • Accepted 17/09/2012