Scientific Notes of Taurida V.I. Vernadsky National University
Series «Biology, chemistry». Vol. 26 (65). 2013. No 1. P. 242-247.

UDK 616.1/9-02:614.7

CARDIAC AUTONOMIC ACTIVITY AND TOXIC ELEMENTS (PB AND CD)

Tymchenko S.L.

State institution "Crimea State Medical University after S.I. Georgiyevsky", Simferopol, Ukraine
E-mail: rivka@pisem.net

Studies conducted among adults professionally exposed to heavy metals suggest a negative impact of Pb and Cd on heart rate variability (HRV) while the results among children regarding background exposure are less consistent. Measurement of Pb and Cd in hair was performed in 56 children (12-13 year old) using X-ray spectrophotometry. HRV was assessed using 5-min recordings through a standardized protocol. Multiple linear regressions were performed. Median hair lead and cadmium levels were 2,59 μg/g (interquartile range (IQR): 1,06-5,25) and 0,02 μg/g (IQR: 0,0005-0,11), respectively. Child hair Pb and Cd were associated with high frequency (HF) ($b = -0.26$ and $b = -0.33$, $p < 0.05$), while Cd with low frequency (LF) ($b = -0.36$, $p = 0.006$). Results of the present study suggest that lead and cadmium exposure during childhood influence HRV.
Keywords: lead, cadmium, children, heart rate variability, autonomic nervous system.

INTRODUCTION

Numerous toxic pollutants, such as heavy metals being released into the environment as a result of anthropogenic transformation of the environment may present a hazard to human health. Anthropogenic sources of these metals include industrial emissions, fossil fuel burning, waste incineration, consumer products, and mining and smelting wastes [1-4]. Human exposure to cadmium and lead is primarily a result of inhalation of metal particles in air, ingestion of contaminated food or drinking water, or in children ingestion as a result of hand-to-mouth behavior [3-4]. Measurements of these substances in various tissues and body fluids are used to provide biomarkers of human exposure to environmental pollutants. In particular, trace element analysis of human hair is considered as an indicator of long-term human body burden, unlike blood, which reflects only the immediate effects of environmental exposure and does not necessarily reflect the current organism burden, because it undergoes homeostatic mechanisms which instantly balance the concentration of elements [5-6].

Numerous epidemiological studies suggest negative impact of lead and cadmium exposure on cardiovascular risk factors such as blood pressure (BP) and heart rate variability (HRV) [7-14]. The letter reflects cardiac autonomic regulation. Studies of combined background exposure to various metals that may influence mechanisms of cardiac regulation and produce adverse health effects are generally lacking. Thus the present study considers the interrelationship of Pb and Cd to heart rate variability in 12-13 year old children with no occupational exposure to metals.

MATERIALS AND METHODS

Hair samples were collected from 12-13 year old male and female children (n=56) from Simferopol (Ukraine), who had never been occupationally exposed to metals. All of them were comparable in health, hygiene and living conditions. Written informed consent was obtained from a parent of each participant before inclusion in the study. Hair samples were cut from the nape of the neck as close to the scalp as possible and the Pb and Cd measurements were performed by X-ray spectrophotometry (ElvaX-Med) method.

HRV spectral indices were derived from 5-minute recordings by three-lead electrocardiography (Cardio, Ukraine) in supine position. Only normal-to-normal (NN) beat intervals were used in the analysis. Frequency domain parameters included: very low frequency (VLF, ≤0.04 Hz), low frequency (LF, 0.04–0.15 Hz), high frequency (HF, 0.15–0.4 Hz), total power (TP, ≤0.4 Hz), LF/HF ratio, LF norm (LF/LF + HF), and HF norm (HF/LF + HF) were measured.

Statistical methods. Because of the skewed distribution of most of the measured parameters, the results are presented as median and range. The Spearman's rank correlation (*r*, *P*) was calculated for associations between each of the measured parameters. Multiple linear regression was used to calculate the interrelationship of the parameters considered possible explanatory variables with respect to heart rate variability parameters.

RESULTS AND DISCUSSION

Table 1 shows data for measured HRV parameters and metals concentrations in hair in the study population. Mean age was 12.6± 0.4 years and the group was composed of 29 girls (52%) and 27 boys (48%). The results showed that the mean concentration of lead and cadmium in hair of children, aged 12-13 years, was 5.35±1.12 and 1.33±0.35 μg/g, respectively, with no significant differences between boys and girls ($p > 0.05$). The mean content of cadmium and lead in hair of the analyzed individuals was comparable to the data obtained in inhabitants of a non-industrialized agricultural regions [15] and fell within the normal range of concentrations of this element in hair, i.e. below 3.0 and 5.0 μg/g respectively.

But when comparing these results with other literature data concerning element concentrations in hair of children living in other regions of Ukraine, the mean concentrations of discussed elements established in this study seem to be higher than values published [16].

HRV spectral parameters are presented in Table 1 and all were similar in girls and boys ($p > 0.05$).

More information about elements' relationships and HRV parameters can be derived from correlations. There was no significant correlation for Pb and Cd in hair. For Cd there was no significant correlation between any of the HRV parameters investigated (Table 2). For hair lead, a significant negative correlation was found with LF and HF ($-0.56<r<-0.59$, $p < 0.0001$).

Table 1

Descriptive data for the HRV parameters and hair Pb and Cd concentration measured in 12-13 year old children

Parameter	Mean±SD	Percentile				
		5th	25th	50th (median)	75th	95th
Pb, μg/g	5.35±1.12	0.34	1.06	2.59	5.25	22.43
Cd, μg/g	1.33±0.35	0.0001	0.0005	0.02	0.11	7.49
TP, мs^2	4970.85±832.74	895.00	1848.00	3707.50	7157.00	12828.00
VLF, мs^2	1573.25±143.93	400.00	775.50	1300.00	1971.50	3800.00
LF, мs^2	2755.48±237.87	164.00	1108.00	2782.50	3850.00	6381.00
HF, мs^2	3252.43±272.05	340.00	1350.00	3300.00	4975.00	6200.00
LF/HF	0.93±0.09	0.43	0.62	0.77	1.31	1.85
LFn, %	45.54±2.33	30.0	38.00	43.50	57.00	65.00
HFn, %	54.50±2.33	35.00	43.00	56.50	62.00	70.00

HRV: heart rate variability; Pb: lead; Cd: cadmium; TP: total power; VLF: very low frequency; LF: low frequency; HF: high frequency; LFn: low frequency, normalized value; HFn; high frequency, normalized value.

Table 2

Correlations between heavy metals and HRV indexes in children

	Pb	Cd	TP	VLF	LF	HF	LF/HF	LFn	HFn
Pb	1	-0.10	-0.12	-0.16	-0.56***	-0.59***	-0.16	-0.17	0.17
Cd	-0.10	1	-0.06	0.03	0.03	0.01	0.08	0.07	-0.08

HRV: heart rate variability; Pb: lead; Cd: cadmium; TP: total power; VLF: very low frequency; LF: low frequency; HF: high frequency; LFn: low frequency, normalized value; HFn; high frequency, normalized value;

*** $p < 0.0001$

Another finding of this study is the negative correlation observed between lead and cadmium in hair for HF ($b = -0.26$ and $b = -0.33$, $p < 0.05$), which is a specific index of parasympathetic activity [17] and a negative correlation of Cd and LF ($b = -0.36$, $p = 0.006$), which reflects the baroreflex function [18]. Despite the fact that these two correlations seem to be contradicting, they may suggest that cadmium appears to show a double mode of interaction with lead and the way it affects the HRV. These results corroborated those reported in other studies for cadmium [19]. In other words, biologically controlled Pb and Cd concentrations became out-of-control (or an opposite direction) on metal overload, thus, abolishing (or makes random) observed primary effect, that might suggest an autonomic dysfunction in children with high levels of these metals.

In the present study, we did not observe significant associations between Pb and parameters representing parasympathetic activity. In contrast, we observed significant associations with HRV parameters representing overall HRV, which includes variations due to sympathetic (LF) and parasympathetic (HF) activity. Thus our results do not allow us to draw a definitive conclusion about a direct impact of lead and cadmium on the sympathetic activity. However, a possible influence of cadmium on this branch of the ANS must be considered. Furthermore, a decrease in overall HRV parameters could be the result of impairment in the baroreflex function, which can increase the cardiac sympathetic tone [20].

CONCLUSION

Most of the examined individuals had from 0.34 to 5.25 μg/g lead and from 0.001 to 0.11 μg/g cadmium in their hair.

Regarding the hair Cd and Pb levels of all studied children, no impaired cardiac autonomic activity was observed. But revealed correlations suggest that cadmium and lead present potential health risks to children who are exposed at even low levels. Therefore, it is important to monitor Cd and Pb exposure of children not only to recognize acute health risks due to these heavy metals, but also to identify and to avoid their exposure as early as possible.

ACKNOWLEDGEMENTS

This paper is dedicated to prof. Evstafyeva H., Ph.D., who essentially contributed to the study realization.

References

1. Overview of human health and chemical mixtures: problems facing developing countries / L. Yáñez, D. Ortiz, J. Calderón [et al.] // Environmental Health Perspectives. — 2002. — Vol. 110 (6). — P. 901–909.
2. Ziemacki G. Heavy metals: sources and environmental presence / G. Ziemacki, G. Viviano, F. Merli // Annali dell'Istituto Superiore di Sanita. – 1989. – Vol. 25 (3). – P. 531-535.
3. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for Cadmium (Draft for Public Comment). — Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, 2008. — Режим доступу до профайлу: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=48&tid=15
4. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for Lead. — Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, 2007. — Режим доступу до профайлу: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=96&tid=22
5. Agency for Toxic Substances and Disease Registry (ATSDR). Summary report on Hair analysis panel discussion exploring the state of the science — Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, 2001. — Режим доступу до профайлу: http://www.atsdr.cdc.gov/hac/hair_analysis/pdfs.html
6. Rahman A. Zinc, manganese, calcium, copper, and cadmium level in scalp hair samples of schizophrenic patients / A. Rahman, M.A. Azad, I. Hossain // Biological Trace Element. – 2009. – Vol. 127 (2). – P. 102-108.
7. Low level exposure to cadmium and early kidney damage: the OSCAR study / L. Järup, L. Hellstrom, T. Alfven [et al.] // Occupational and Environmental Medicine. — 2000. — Vol. 57. — P. 668–672.
8. Eum K.D. Cadmium in blood and hypertension / K.D. Eum, M.S. Lee, D. Paek // Science of the Total Environment. — 2008. — Vol. 407(1). — P. 147–153.

9. Air pollution and heart rate variability: effect modification by chronic lead exposure / S.K. Park, M.S. O'Neill, P.S. Vokonas [et al.] // Epidemiology. — 2008. — Vol. 19 (1). — P. 111-20.
10. An epidemiological re-appraisal of the association between blood pressure and blood lead: a meta-analysis / T.S. Nawrot, L. Thijs, E.M. Den Hond [et al.] // Journal of Human Hypertension. — 2002. — Vol. 16. — P. 123–131.
11. Autonomic and central nervous system effects of lead in female glass workers in China / K. Murata, S. Araki, K. Yokoyama [et al.] // American journal of industrial medicine. — 1995. — Vol. 28 (2). — P. 233-244.
12. Blood lead and blood pressure in young children / P. Factor-Litvak, JK. Kline, D. Popovac [et al.] //. Epidemiology. — 1996. — Vol. 7. — P. 633–637.
13. Den Hond E. The relationship between blood pressure and blood lead in NHANES III. National Health and Nutritional Examination Survey / E. Den Hond, T. Nawrot, J.A. Staessen // Journal of Human Hypertension. — 2002. — Vol. 16. — P. 563–568.
14. Effects of inorganic lead exposure on the autonomic nervous system and on the variability of heart rate among workers at a battery plant / G. Muzi, N. Murgia, M. Dell'Omo [et al.] // Giornale italiano di medicina del lavoro ed ergonomia. — 2005. — Vol. 1. — P. 46-50.
15. Nowak B. Contents and relationship of elements in human hair for a non-industrialised population in Poland / B. Nowak // Science of the Total Environment. – 1998. – Vol. 290 (1). – P. 59-68.
16. Накопичення кадмію та його вплив на організм дитини / Ю.В. Марушко, О.Л. Таринська, Т.І. Олефір [та ін.] // Клінічна педіатрія. – 2010. – № 5 (26). – С. 49-52.
17. Impact of diet-induced weight loss on the cardiac autonomic nervous system in severe obesity / P. Poirier, T.L. Hernandez, K.M. Weil [et al.] // Obesity Research. – 2003. – Vol. 11 (9). – P. 1040-1047.
18. Low-frequency power of heart rate variability is not a measure of cardiac sympathetic tone but may be a measure of modulation of cardiac autonomic outflows by baroreflexes / D.S. Goldstein, O. Bentho, M.Y. Park [et al.] // Experimental Physiology. – 2011. – Vol. 96 (12). – P. 1255-1261.
19. Jhun H.J. The association between blood metal concentrations and heart rate variability: a cross-sectional study / H.J. Jhun, H. Kim, D.M. Paek // International archives of occupational and environmental health. — 2005. — Vol. 78 (3). — P. 243-247.
20. Effect of baroreceptor denervation on the autonomic control of arterial pressure in conscious mice / F.L. Rodrigues, M. de Oliveira, H.C. Salgado [et al.] // Experimental Physiology. – 2011. – Vol. 96 (9). – P. 853-862.

Тымченко С.Л. Механизмы регуляции деятельности сердца и токсичные элементы (свинец и кадмий) / С.Л. Тымченко // Ученые записки Таврического национального университета им. В.И. Вернадского. Серия «Биология, химия». – 2013. – Т. 26 (65), № 1. – С.242-247.

Исследования эффектов свинца (Pb) и кадмия (Cd) в условиях профессионального воздействия среди взрослого населения свидетельствуют о значительном отрицательном воздействии данных металлов на вариабельность сердечного ритма (ВСР), в тоже время результаты подобных исследований среди детей в условиях фоновой экспозиции весьма малочисленны. Средние значения Pb и Cd в волосах 56 детей (12-13 лет) методом рентгенспектрофотометрии составили 2,59 мкг/г (интерквартильный размах (ИКР): 1,06-5,25) и 0,02 мкг/г (ИКР: 0,0005-0,11) соответственно. Регистрацию ВСР проводили используя 5 минутные записи по стандартизированному протоколу. Результаты множественной регрессии выявили наличие корреляционных связей между содержанием Pb и Cd в волосах и высокочастотной составляющей спектра: HF ($b = -0.26$ и $b = -0.33$, $p < 0.05$), и негативной корреляционной связи для Cd и низкочастотной составляющей: LF ($b = -0.36$, $p = 0.006$). Результаты настоящего исследования позволяют предположить, что экспозиция данными металлами способствует изменению ВСР.

Ключевые слова: свинец, кадмий, вариабельность сердечного ритма, дети, вегетативная неравная система.

Тимченко С.Л. Механізми регуляції серцевої діяльності і токсичні елементи (свинець і кадмій) / С.Л. Тимченко // Вчені записки Таврійського національного університету ім. В.І. Вернадського. Серія „Біологія, хімія". – 2013. – Т. 26 (65), № 1. – С. 242-247.

Дослідження ефектів свинцю (Pb) і кадмію (Cd) в умовах професійної дії серед дорослого населення свідчать про значну негативну дію даних металів на варіабельність серцевого ритму (ВСР), в той час результати подібних досліджень серед дітей за умов фонової експозиції є нечисленні. Середні значення Pb і Cd у волоссі 56 дітей (12-13 років) методом ренгенспектрофотометрії склали 2,59 мкг/г (інтерквартильний розмах (ІКР): 1,06-5,25) і 0,02 мкг/г (ІКР: 0,0005-0,11) відповідно. Реєстрацію ВСР проводили використовуючи 5 хвилинні записи по стандартизованому протоколу. Результати множинної регресії виявили наявність кореляційних зв'язків між вмістом Pb і Cdy волоссі з високочастотною складовою спектру: HF ($b = -0.26$ і $b = -0.33$, $p < 0.05$), і негативного кореляційного зв'язку для Cd і низькочастотної складової: LF ($b = -0.36$, $p = 0.006$). Результати даного дослідження дозволяють припустити, що експозиція даними металами сприяє змінам ВСР.

Ключові слова: свинець, кадмій, діти, варіабельність серцевого ритму, автономна нервова система.

Поступила в редакцию 14.02.2013 г.