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Effects of blood lead and cadmium levels on the functioning of children with behaviour disorders in the family environment

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Abstract

Introduction and objective: The developing brain of a child is extremely prone to damage resulting from exposure to harmful environmental factors, e.g. heavy metals. Intoxication of children's organisms with lead and cadmium affects their intellectual development. Even a relatively small amount of this metal in children's blood can lead to developmental dysfunctions. The aim of this study was to analyse the correlation between blood lead and cadmium levels in children with behaviour disorders and their functioning in the home. Material and methods: This survey-based study was conducted among 78 families with children diagnosed as having behaviour disorders. It was performed using the ADHD-Rating Scale-IV. To determine lead and cadmium levels the laboratory procedure was based on Stoppler and Brandt's method. Results: The mean blood lead level was 19.71 µg/l and the mean blood cadmium level was 0.215µg/l. Higher blood lead levels in children correlates positively with incidences of hyperactive and impulsive behaviour in the home, as assessed by parents ($p=0.048$). Statistically significant effects of cadmium on children's behaviour were not noticed. Conclusions: The effect of lead on the developing organism of a child has such behavioural consequences as attention disorders, hyperactivity and impulsive behaviour which, in turn, may interfere with children's functioning in the home. A negative effect of cadmium on the functioning of children with behaviour disorders in the home was not proved.

Key words

lead, cadmium, child behaviour disorders

INTRODUCTION

Developmental disorders are a consequence of interaction between genetic, chemical and social factors. Genetic factors aside, the environment is more and more often regarded as potentially detrimental to children's health and contributing to such present-day problems as obesity, asthma and neoplasms, as well as behavioural and learning disorders. Exposure to chemical toxic substances should receive particular attention since it can be avoided. The developing brain of a child is extremely prone to damage resulting from lengthy exposure to harmful environmental factors [1]. The effects of lead on a child's development can be observed as early as in the prenatal period. Research conducted among pregnant women showed that higher lead levels in women's blood in the first and second trimester are main contributors to the risk of premature birth [2].

The latest research on children demonstrated that their blood lead levels were continuously decreasing. This is most probably the effect of imposing a ban on using this metal in petrol, paints for places of residence, and soldered parts of dishes and pipes delivering water. In 1991-1994, the National Health and Nutrition Examination Surveys (NHANES) carried out research on children aged 1-5 years, which proved that 4.4% of them had lead concentrations higher or equal to 100 µg/l, with the geometric mean being equal to 27 µg/l. More recent data, obtained in the years 1999-2002, showed that lead concentrations above 100 µg/l were noted in 1.6% of 1-5-year-old children, and the average concentration in the analysed population was 19 µg/l [3]. Nevertheless, approximately 310,000 children in the USA from the age of 1-5 have lead levels exceeding 100 µg/l [4].

The most recent outcomes suggest that intoxication of children's organisms with lead affects their intellectual development, and not only when it occurs in high doses. Even a relatively small amount of this metal in children's blood can lead to developmental dysfunctions. Numerous studies conducted recently proved that exposure to lead in the early period of life, resulting in blood lead concentration even below 20 µg/l, may cause a considerable decrease in the intelligence quotient (IQ). Analysis of data shows that there is no safe lead level in blood, i.e. the one which would not have an effect on the neurobehavioural functioning of a child [5]. Research on children's non-verbal intelligence suggests that there is a correlation between blood lead levels and lower IQ scores [6].

In the general population, the main sources of exposure to cadmium are cigarettes, food (mainly crustaceans, giblets,

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some vegetables) and air pollution in highly industrialized areas [7]. Cadmium, next to lead and mercury, is regarded as one of the main contributors to diseases associated with heavy metal poisoning [8]. In 1999, the Agency for Toxic Substances and Disease Registry (ATSDR) placed cadmium among 7 substances in the environment which are particularly dangerous for human health. The whole list included 275 items at that time [9]. It was demonstrated in animals that intrauterine exposure to cadmium had a significant impact on their birth weight, body mass gain and ability to stay alive. It also contributed to slower ossification and neurobehavioural development disorders [10]. The research carried out by Barański reported the potential influence of cadmium on the neurobehavioural functioning of the offspring of rats exposed to cadmium oxide in the doses of 0.02-0.16 mg Cd/m^3 for 5 months before pairing them up, before and after insemination, and from the 1st-20th day of pregnancy [11]. Other research on animals showed that intoxication with cadmium had a neurotoxic effect and resulted in behaviour disorders [12]. This element has the most direct influence on brain metabolism, hindering many enzymes containing sulfhydryl groups. As a consequence, lengthy exposure to cadmium negatively affects levels of norepinephrine, serotonin and acetylcholine [13]. It was also observed in humans that early childhood, which is the time of dynamic brain development, can be a critical stage because of particular susceptibility to a neurotoxic effect of cadmium [14].

The aim of this study was to analyse the correlation between blood lead and cadmium levels in children with developmental disorders and their functioning at home.

MATERIALS AND METHODS

The study was conducted with the consent of the Bioethical Commission of the Pomeranian Medical University in Szczecin (Permit No. BN-001/113/08, dated 24 November 2008).

The study involved 78 children – 16 girls and 62 boys. The basic inclusion criterion was a diagnosis of behaviour disorders such as hyperactivity, impulsiveness and attention deficit disorder, diagnosed by a psychologist or school educationalist. The parents gave their written consent to children's participation in the study; they were informed about its anonymous character and the possibility of resigning at any moment without the necessity of giving reasons. The mean age of the children was 8 years. Age groups were created so that the appropriate balance between them was maintained – the youngest respondents, aged between 2 and 5, constituted 35.6% of all children, those aged between 5 and 10-31.5%, and the oldest, aged between 10 and 18, were 32.9%.

This survey-based study was performed using the standardised and valid ADHD-Rating Scale-IV, which is a reliable and easy-to-administer instrument for diagnosing attention deficit disorder and behavioural problems in children [15]. Each version includes descriptions of 18 behaviours being a manifestation of hyperactivity, impulsiveness and attention deficit disorder. Individuals responded to each item on the 4 point Likert scale. For the purposes of this study, the authors used direct observations made by the parents of all participants (Parent ADHD Rating Scale-IV). The scale was divided into 2 subscales: 1) evaluating escalation of symptoms associated with attention deficit disorder; 2) concerning hyperactivity and impulsiveness of a child.

To determine lead and cadmium levels, a 5 ml venous blood sample was collected from each child with the use of a closed system (Vacutainer). Next, the frozen material was transported in refrigerating units to the Institute of Industrial Medicine and Community Health at the Department of Chemical Damage in Sosnowiec. Lead and cadmium levels were measured in the Laboratory of Metal Analyses. The procedure employed in the laboratory is based on Stoppler and Brandt's method. Lead and cadmium levels were measured in the fluid above the sediment in full blood samples deproteinized with nitric acid. The measurement was performed using graphite furnace atomic absorption spectrometry (GFAAS) and an atomic absorption spectrometer PerkinElmer 4100ZL. Zeeman background correction was employed to compensate for non-specific absorption. The quality of measurements performed in this centre is systematically verified by internal quality control, and participation in the national and international systems of measurement quality control at the Institute of Industrial Medicine in Lodz, the Istituto Superiore di Sanita in Rome, and the Centers for Disease Control and Prevention (CDC) in Atlanta, USA.

In accordance with the guidelines of the laboratory, lead concentration in full blood was regarded normal if its average level was below 100 µg/l. In 1991, this value was accepted as a limit by CDC and the World Health Organization (WHO) [16]. Nevertheless, studies carried out during the last 20 years show undeniably that this value cannot be regarded as safe. Whether a safe limit can be established or not is a very disputable question. Some researchers claim that it is impossible to use this concept with reference to lead levels in children's blood since even minimum amounts of this metal may considerably affect neurobehavioural development of a young organism [17, 18, 19, 20].

In accordance with the guidelines of the Institute of Industrial Medicine and Community Health, a normal cadmium level in full blood is 0.5 µg/l, on average. However, as with lead, we cannot be absolutely certain that there will not be any negative effects even if the blood cadmium level is lower.

Pearson's linear correlation coefficient was used in this study to analyse the correlation between the assessment of children's behaviour according to the questionnaire and children's lead (Pb) and cadmium (Cd) levels. The Tables include Pearson's linear correlation coefficients (r) and the test probability or p-value calculated for these coefficients. The accepted significance level was equal to 0.05.

The children included in the study were characterised by the proportion. Pb and Cd levels were determined using median, lower and upper quartiles, arithmetic mean and standard deviation.

The Mann-Whitney test was used to assess statistically significant differences between the assessment of children's behaviour according to the questionnaire and children's blood lead levels, classifying them for one of two groups:

- group 1 – with lower lead levels – children with lead levels up to 19,9 µg/l;
- group 2 – with higher lead levels – children with lead levels of 20 µg/l or more.

All data transformations and preliminary calculations were carried out with Microsoft Excel 2007. Statistical analysis was performed using the selected modules of STATISTICA 7.1.

RESULTS

The lowest blood lead level in the group examined was 6 µg/l and the highest 101 µg/l. The mean level of this element was 19.71 µg/l. Lead concentration in particular patients differed from the mean value by +/- 13.59 µg/l, on average.

The lowest cadmium level noted in the children was 0.05 µg/l, and the highest – 2.91 µg/l. The mean level of this element was 0.22 µg/l +/- 0.34 µg/l (Tab. 1).

Table 1. Basic descriptive statistics of lead and cadmium levels in children's full blood (µg/l)

Heavy metal levels for N=73	Min.-Max.	Median	Q_1-Q_3	$\bar{X}$±SD
Pb (µg/l)	6-101	16	12-22	19.71±13.59
Cd (µg/l)	0.05-2.91	0.16	0.12-0.22	0.22±0.34

Min.-max. – min. and max. values
Q_1-Q_3 – lower and upper quartiles
±SD – mean value and standard deviation

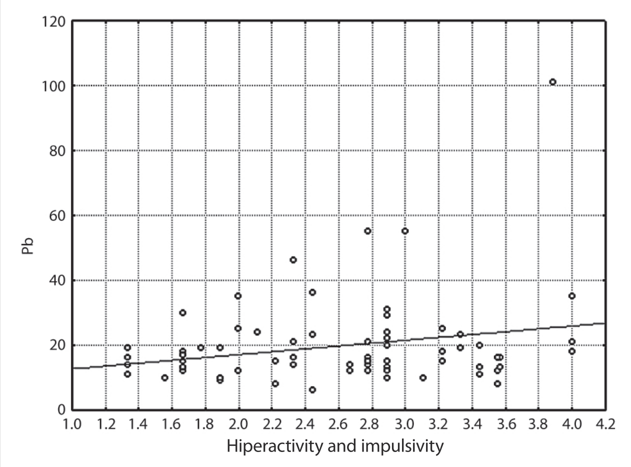

Figure 1. Correlation between children's blood lead levels and intensification of their hyperactive and impulsive behaviour at home

The children's behaviour at home were assessed with the ADHD-Rating Scale-IV. The questionnaire evaluated 2 aspects of a child's behaviour: 1) attention deficit disorder and 2) hyperactivity and impulsiveness.

We analysed the correlation between blood lead and cadmium levels and the frequency of undesirable behaviour making children's normal functioning at home difficult. To evaluate the intensity of behaviour suggesting attention disorders (Part I) and hyperactivity and impulsiveness (Part II), the parents responded to each item on the 4 point Likert scale in 'the home questionnaire' (Parent ADHD Rating Scale-IV). The obvious but slight correlation between lead levels and hyperactivity and impulsiveness results ($p < 0.05$) in 'the home questionnaire' was noticed. This permits the assumption that higher lead levels correlate with a lower assessment of children's behaviour (with the prevalence of hyperactivity and impulsiveness) (Tab. 2).

Table 2. Correlation between results of 'home questionnaire' and children's blood lead and cadmium levels

N=73	Pb (µg/l)		Cd (µg/l)	
	r	p	r	p
Attention deficit disorder	0.2292	p>0.05	-0.0660	p>0.05
Hyperactivity and impulsiveness	0.2369	**p<0.05**	-0.0334	p>0.05

r – Pearson's Linear Correlation Coefficient
p – significance level

Figure 1 is a graphic illustration of the correlation between blood lead levels and the intensification of symptoms suggesting hyperactivity and impulsiveness.

Results concerning the influence of the children's blood lead levels on attention deficit disorder symptoms demonstrated by them at home did not prove any statistically significant correlations ($p > 0.05$).

The children were divided into 2 groups, depending on their blood lead levels: Group 1 – consisted of children with blood lead levels up to 19.9 µg/l; Group 2 – those with blood lead levels above 20 µg/l. The Mann-Whitney U test for 2 independent samples was used in the analysis.

'The home questionnaire' revealed statistically significant differences between the groups. They referred to the assessment of both areas of the children's behaviour, i.e. hyperactivity and impulsiveness, and attention deficit disorder ($p < 0.05$). The individuals with higher lead levels had worse results in both areas (Tab. 3).

Table 3. Results of Mann-Whitney U test for 'home questionnaire' diagnosing behaviour problems in both groups of children (depending on blood lead level)

	n1	n2	z	p
Attention deficit disorder	48	24	**-2.31**	**<0.05**
Hyperactivity and impulsiveness	48	23	**-1.96**	**<0.05**

n1 – number of children in group I
n2 – number of children in group II
z – Mann-Whitney U test statistic
p – significance level for *z*

Figure 2 illustrates the comparison between the escalation of attention deficit disorder symptoms at home in both groups of children.

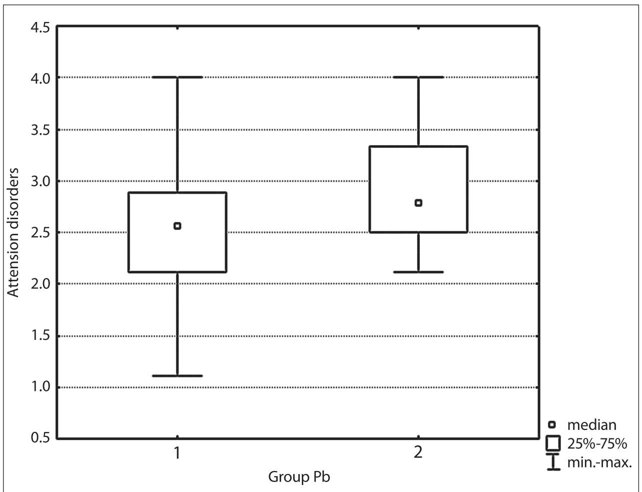

Figure 2. Outcomes of the 'home questionnaire' concerning attention deficit disorder in both groups of children (depending on blood lead levels)

Figure 3 is a graphic illustration of the correlation between the children's blood lead levels and the escalation of hyperactivity and impulsive behaviour.

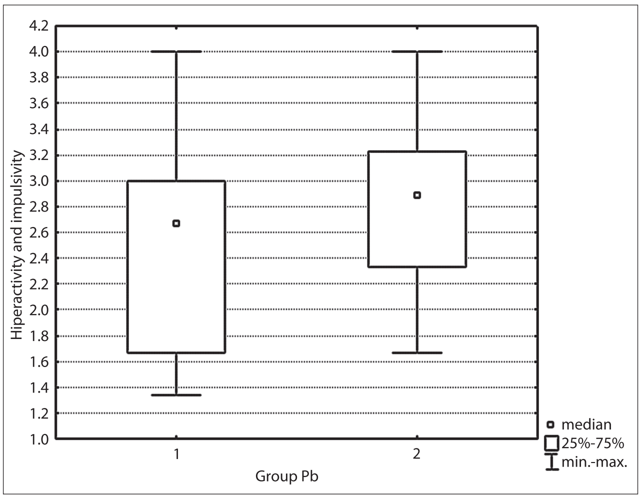

Figure 3. Outcomes of the 'home questionnaire' concerning hyperactivity and impulsive behaviour in both groups of children (depending on blood lead levels)

DISCUSSION

During the last century, the progress of industrialization and urbanization resulted in economic growth and better health of people in many regions of the world. Thanks to wider access to safe drinking water, improvements in food nutrition, vaccinations and waste utilization, former infectious diseases in children were brought under control. The infant mortality rate was also noticeably reduced. A common danger to children's health in the contemporary world, however, is an exposure to chemical substances, both natural and those produced by man. About 15,000 chemical substances are widely spread in the environment: air, water, soil and food, of which almost all were developed during the last 50 years. These chemical compounds also include those having a neurotoxic effect, among them lead, cadmium, mercury, pesticides, solvents and polychlorinated biphenyls [21].

Lead is a heavy metal having a very toxic influence on human organisms at any age. In the light of numerous studies it is undeniable that exposure to high doses of lead may have serious negative consequences for the neurocognitive and behavioural development of a child [22, 23]. Research conducted in 1972 demonstrated that more than 50% of overactive children had blood lead levels between 250-550 μg/l [24]. Since placing limits on the common use of lead, the mean levels of this metal in children's blood have considerably decreased.

Data provided by the Third National Health and Nutrition Examination Survey (NHANES III) indicate that blood lead levels in the majority of children in the USA exposed to this element are lower than 100 μg/l, and show a continuous downward trend [25].

As demonstrated by numerous studies, exposure to lead may have significant neurodevelopmental consequences, including lower IQ, reduced frustration tolerance, attention deficit, hyperactivity and weak reaction control. A study performed in the USA on a group of 97 children with ADHD and a 53-person control sample revealed a significant correlation between an increased blood lead level and higher incidence of ADHD symptoms [26]. Other American researchers discovered a significant correlation between increased blood lead levels and the incidence of ADHD in 4,704 children [27]. Analysis of hair lead levels in ADHD children also showed that the concentration of this metal was considerably higher than in the control group [28, 29].

The research on 150 American children proved that the presence of lead in their blood considerably contributed to a higher incidence of hyperactive and impulsive behaviour. However, such a correlation was not found with reference to attention deficit disorder, compared to the control group [30]. A similar correlation was reported in this study. According to the parents, the degree of hyperactivity and impulsiveness was considerably higher in the children who had elevated blood lead levels.

Data analysis performed within the National Health and Nutrition Examination Survey (NHANES III) demonstrated that the elevated blood lead levels significantly correlated with the incidence of ADHD. Children with lead levels higher than 20 μg/l were at 4.1 times greater risk of developing symptoms associated with psychomotor hyperactivity than individuals with lower levels of this metal [31]. In the presented study, blood lead levels exceeding 20 μg/l were found in 32.9% of children, while levels higher or equal to 10 μg/l were noted in 94.5% of the participants (the mean lead level in this group was 19.7 μg/l). In 2007, Surkan et al. published an analysis of differences in intelligence levels, school achievements, attention levels and working memory between children allocated to one of three categories depending on their blood lead levels: I – lead levels between 10 and 20 μg/l, II – 30-40 μg/l and III – 50-100 μg/l. It was found that the children in group III had numerous deficits in areas such as intelligence, visual and spatial abilities, and school achievements. Also comparison of results obtained from the children in groups I and II proved some differences suggesting that lead concentrations between 30-40 μg/l were less safe for the normal development of a child than the level of this metal equal to 10-20 μg/l [32]. In the presented study, the children were divided into 2 groups: 1) individuals with blood lead levels below 20 μg/l; 2) those with the levels equal to and higher than 20 μg/l. Some differences between these groups were noticed, especially in the assessment of hyperactivity, impulsive behaviour and attention deficit disorder in the home, which were significantly more intensive in the group with higher blood lead levels.

Recently, research has been conducted in Szczecin and its environs on a group of 141 healthy children aged 5-18 years. The aim was to assess lead levels in the children's serum, erythrocytes and hair. The mean lead concentration in erythrocytes was 2.78 μg/dl [33]. Other studies performed on 174 healthy children living in this area proved that the mean lead concentration was 0.73 μg/dl in serum, 2.41 μg/dl in erythrocytes and 1.6 μg/g in hair (dry mass) [34]. The comparison of our results with those mentioned above is not possible since we used different methodology, based on the analysis of heavy metal levels in full blood collected from ill children.

Cadmium is a heavy metal having a toxic and carcinogenic effect on the human organism [35]. Numerous epidemiological studies conducted in the 1970s and 1980s provided evidence for the profound effect of this metal on children's behaviour and neurological development [36]. Research on children whose development was slower compared to their peers revealed that cadmium levels in their hair were considerably higher [37]. Other authors have noted that the presence of this metal correlated positively with learning difficulties and dyslexia in children [38]. The cohort study carried out by R. Thatcher et al. demonstrated that cadmium affects children's intelligence level (IQ score) [39]. Apart from the correlation between IQ and cadmium levels, other researchers noticed that this metal had an effect on children's visual, locomotive and cognitive abilities [40]. The results reported by R. Pihl and M. Parkes show that the presence of cadmium, cobalt, manganese, chromium or lithium in blood results in a 98% certainty that a child is going to have learning problems [41]. Research conducted among 149 children aged 5-16 years demonstrated that the presence of cadmium considerably affected test results measuring their intelligence, physical fitness and academic achievement [42].

The results of research conducted in a similar area and a similar, in terms of age, group of healthy children demonstrated that the average cadmium level in erythrocytes was 0.311 μg/dl [33]. Other comparable studies that have been carried out in the surroundings of Szczecin showed that the mean cadmium level in serum of healthy children was 0.12 μg/dl, in erythrocytes 0.21 μg/dl, and in hair 0.1 μg/g (dry mass) [34]. The direct comparison of our results with those obtained by other authors is not possible since we used different methodology based on the analysis of this metal content in full blood. We determined levels of heavy metals in full blood using a method recommended by the accredited laboratories of the Institute of Industrial Medicine and Community Health in Sosnowiec.

CONCLUSION

The effect of lead on the developing organism of a child has such behavioural consequences as attention deficit disorder, hyperactivity and impulsiveness which, in turn, may result in functional problems in the home.

Negative effect of cadmium on the functioning of children with behaviour disorders in the home was not proved.

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