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Levels of cadmium and lead in blood: an application of validated methods in a group of patients with endocrine/metabolic disorders from the Rome area

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Abstract

Lead (Pb) and cadmium (Cd) are environmental pollutants, known to cause adverse health effects in humans even following long-term exposure to low doses. These metals, individually or in combination with other persistent environmental contaminants, have been claimed to have the potential to cause alterations in the function of the endocrine system. Human exposure to Pb and Cd is generally assessed by monitoring their concentrations in blood, taking into account the influence of various factors, such as age, gender, smoking habit, occupation, alcohol consumption, diet and air pollution. Following the phase-out of leaded gasoline in the European Union and improvements in food-packaging and contamination control, a decrease in blood Pb levels of the general population has been observed in several European countries and the USA. We report the preliminary results of a study, performed within the framework of the project "Human Exposure to Xenobiotics with potential Endocrine Activities: Evaluation of Reproductive and Developmental risks". We measured the concentrations of Cd and Pb in the blood of a group of patients with endocrine/metabolic disorders. The analytical procedures, based on atomic absorption spectrometry, were validated according to the EURACHEM guidelines. The median values and ranges were 0.48 μg l^{-1} (0.20–1.73 μg l^{-1}) and 21.8 μg l^{-1} (12.0–65.7 μg l^{-1}) for Cd and Pb, respectively; the Cd levels were significantly higher in smokers. Overall, the concentrations of Cd and Pb found in our series of patients were comparable to levels currently expected in the general population.

Keywords: Method performance; Uncertainty of measurement; Human study; Endocrine disrupter; Environmental contaminant

1. Introduction

Lead (Pb) and cadmium (Cd) are two naturally occurring heavy metals, for which most of the widespread presence in the human environment comes from anthropogenic activities. Both metals are known to cause adverse health effects in humans [1–3]. The concentration of Pb (B–Pb) and Cd (B–Cd) in blood, which is considered the most reliable biomarker of recent Pb and Cd exposure, is influenced, besides diet and air pollution, by different factors such as gender, age, smoking habits (one cigarette usually contains 1–2 μg Cd, of which about 10% may be inhaled) and alcohol consumption [1–3]. Among the potential effects on human health of long-term exposure to low levels of Pb, cognitive disorders [4–6], effects on renal function [7] and blood pressure [8] have been reported. In most industrialized countries in Europe and in the USA, the improvement of working conditions and the actions taken to minimize the environmental exposure to Pb, such as the phase-out of leaded gasoline and improvements in food preparation and packaging, have led to a substantial reduction of B–Pb levels as observed in both workers and the general population [9–11]. However, limits for B–Pb in the general population have also been reduced (Table 1), owing to

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Table 1
Limits for Pb in blood (μg/l) in the general population recommended by EEC Directive 312/77, the U.S. Centers for Disease Control and Prevention (CDC) and the Commission on Human Biological Monitoring (CHBM) of the German Federal Environmental Agency

	Type	All	Children	Women in the reproductive age	Males and females >45 years
EEC Directive [12] 1977	limits (centiles)	200 (50th) 300 (90th) 350 (98th)			
CDC (USA) [13] 1985	action level		250		
CDC (USA) [14] 1991	action level		100		
CHBM (DE) [15] 1999	reference value		60		
	alert level		100	100	150
	action level		150	150	250

evidence of early adverse effects, especially concerning subtle cognitive alterations in children [12–15].

Cadmium accumulates in human tissues and organs (kidneys, liver, muscles) and its biological half-time is very long (from 5 to 30 years). Cadmium exposure has been associated mainly with effects on renal function [3,16].

Recent experimental studies have focussed on the adverse effect of exposure to low doses of Pb and Cd on the endocrine system. These metals, individually or in combination with other persistent environmental contaminants such as halogenated organic compounds (polychlorinated biphenyls, dioxins, hexachlorobenzene, etc.), may cause adverse effects on thyroid function [17]. Both Pb and Cd may bind and activate estrogen receptors, constituting a new class of nonsteroidal environmental estrogenic agents which in turn are claimed to contribute to the high incidence of hormone-related diseases [18–20]. In other studies Cd has induced a dose-dependent inhibition of the biosynthesis of progesterone [21,22]. On this basis, both Pb and Cd are claimed to act as endocrine disrupters, therefore attention is still paid to the potential health effects of long-term exposure to low levels of these metals.

Biological monitoring of the general population and of groups considered at risk provides essential information for both the evaluation of exposure and risk characterization. In this study we measured the concentrations of Cd and Pb in blood in a group of patients with endocrine/metabolic disorders, using analytical methods based on electrothermal atomic absorption spectrometry. Since the quality of analytical results is an essential pre-requisite for the assessment of health risks, methods were validated in-house according to the EURACHEM guideline [23] and the requirements of ISO/IEC 17025 [24] and ISO 15189 [25], including estimates of uncertainty of measurement according to the EURACHEM/CITAC Guide [26]. In this paper, we present the preliminary results of this survey and evaluate them in the light of (a) data obtained in a group of healthy male subjects undergoing routine medical controls between 1999 and 2000, and (b) data previously reported in the literature for the general population living in Italy, other European countries and the USA.

2. Materials and methods

2.1. Subjects and sample collection

The group of patients consisted of 33 subjects (7 males and 26 females), aged from 17 to 55 years, attending an outpatient clinic for endocrine/metabolic disorders in Rome, Italy, who were enrolled between 2001 and 2003 within the framework of the project "Human exposure to xenobiotics with potential endocrine activity: evaluation of reproductive and developmental risks". Enrolled patients were suffering from obesity in most cases, frequently associated with other endocrine and/or metabolic disorders, and gave fully informed consent to the study.

The examination included a medical history and a physical examination. The following data were collected: date of birth, gender, weight, height, place of residence, smoking habit, nursing (natural or artificial), type of diet, alcohol consumption, physical activity, drug assumption and variation in weight. Furthermore, a venous blood sample was drawn after overnight fasting, collected in plastic tubes with K_2EDTA, to determine the concentration of metals (Pb and Cd) and organic contaminants (chlorinated pesticides and selected polychlorinated biphenyls).

For Pb and Cd determination, an aliquot of each sample was transferred in an Eppendorf vial and stored at −20 °C until analysis. To avoid Pb and Cd contamination, plasticware was periodically checked for Pb or Cd leakage.

In addition, Pb was measured in blood samples from 78 healthy adult male subjects undergoing routine medical controls between 1999 and 2000 in Rome, Italy.

2.2. Instrumentation

Lead and Cd in blood were determined using an atomic absorption spectrometer SIMAA 6000 (Perkin Elmer, Ueberlingen, Germany) equipped with Zeeman background correction, a Transverse Heated Graphite Atomizer, EDL System 2 lamps for Pb and Cd. Automatic pipettes (Gilson, France) and an automatic diluter system Microlab® 500 Series (Hamilton Company, USA), both calibrated at regular intervals, were used to dilute samples.