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IS ENVIRONMENTAL CADMIUM A SERIOUS HAZARD TO CZECH POPULATION?*

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Abstract. The main objective of the study was to asses whether the environmental cadmium exposure in the Czech Republic is high enough to be able to affect significantly the human reproduction. Cadmium levels were measured in the blood and follicular fluid of 220 women in *in vitro* fertilization (IVF) therapy, using atomic absorption spectrometry. The mean value of cadmium in venous blood was 0.85 ng. ml-1 with significantly higher values among smokers (1.18 ng.ml-1, SD = 1.6, 95%CI: 0.6–1.1) as compared to non-smokers (0.46 ng.ml-1, SD = 0.4, 95%CI: 0.4–0.6) ($p < 0.0001$). In all, 1518 blood-free follicles were assessed to determine cadmium residues in follicular fluid. The mean cadmium value was 0.34 ng.ml-1(SD = 0.45, 95%CI: 0.28–0.41). No association was found between the cadmium levels in blood and follicular fluid, and similar cadmium levels were observed in the follicular fluid of women with different smoking habits. The calculated dietary cadmium intake was similar in all our patients and had no relation to either blood or follicular cadmium levels. The follicular cadmium levels were approximately 20 times lower as compared to those found in the group of Canadian women. Our study confirmed the previous findings on the low exposure of the Czech population to environmental cadmium.

Key words:
Cadmium, Residues, Blood, Follicular fluid, Environment

INTRODUCTION

Cadmium is widely dispersed in the human environment. The two important sources of non-occupational cadmium exposure are dietary intake and cigarette smoking. While only 6–10% of ingested cadmium is absorbed in the digestive system, the respiratory system uptakes 40–60% of inhaled cadmium [1]. In blood, cadmium is bound to erythrocytes and its levels are related to exposure during the last few weeks or months prior to the examination. Cadmium can be accumulated in various human organs, predominantly in the renal cortex and bones [2], but also in the liver [2], ovary, [3], follicles [4], and placenta [5,6].

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Cadmium residues are determined in humans in order to monitor the level of the population exposure to this toxic metal and to assess its toxic effects. It has been estimated in the animal studies that the reproductive organs are particularly susceptible to toxic effects of cadmium, which may produce selective damages to vascular endothelium and obstruction of the microcirculation in the testes, placenta and ovarium, resulting in necrosis [7,8]. Other experiments have shown that exposure to cadmium can reduce meiotic maturation of oocytes leading to a decreased number of ovulated oocytes which were frequently diploid [7]. A significant reduction of oocyte meiotic maturation has also been observed in smoking women [9]. The increasing number of infertile patients and the necessary treatment with the assisted reproduction techniques (ART) prompted our research aimed at investigating a possible impact of cadmium on the *in vitro* fertilization (IVF) outcomes, since the Czech Republic is generally regarded as a heavily polluted area.

MATERIALS AND METHODS

A group of 220 women (from Brno and Prague) who had applied for the ART infertility treatment was included in a three-year study. All the admitted patients were interviewed for their medical and personal histories including data on the age, education, occupation and smoking habits. Their dietary practices were recorded in a special questionnaire [10] designed to provide a semiquantitative estimation of cadmium intake from a diet. For the assessment of cadmium levels, macroscopical blood-free follicles and samples of venous blood, supplemented with citrate, were collected. Since some samples showed inter-follicular variation in the same women, cadmium content was assessed in each follicle. The evaluation of the total cadmium residue in each patient was based on the median, the arithmetic and geometric means, and minimum/maximum values. Cadmium residue levels were measured by the method of graphite furnace-atomic absorption spectrometry (AAS) using deuterium background correction with a Pd matrix modifier. Decomposition of follicular fluid, using microwave digestion, was performed [11]. The laboratory where the measurements were performed is not accredited and does not participate in the international comparative studies. The system of quality assessment (quality control) for follicular fluid has not as yet been developed and therefore the assessment could not be performed. The results were processed and evaluated using the SPSS statistical software, version 9. Differences were tested using Student's t-test, ANOVA and chi-square test, and correlation was evaluated by means of the Pearson and Spearman coefficients.

RESULTS

In blood, the mean cadmium level was 0.85 ng.ml-1 (SD = 1.0, 95% CI: 0.4–0.9). Cadmium blood levels were significantly ($p < 0.001$) higher in smokers than in non-smokers, i.e., 1.18 ng.ml-1 (SD = 1.6, 95% CI: 0.6–1.1) vs. 0.46 ng.ml-1 (SD = 0.4, 95% CI: 0.4–0.6). On the other hand, tobacco smoke exposure had no effect on cadmium levels in follicular fluid: all the three groups of women (current smokers, ex-smokers and never smokers) showed similar Cd levels (Table 1). In the majority of follicles (72.9 %) cadmium levels were below the detectable limit (i.e., below 0.1 $ng.ml^{-1}$). No relation was found between cadmium levels in venous blood and follicular fluid. No age-related association with the levels of follicular cadmium were shown. Although the women in our study manifested different smoking and nutrition habits, they showed similar cadmium intake from a diet, as indicated by the semiquantitative index value. The cadmium dietary intake influenced neither Cd plasma levels nor Cd concentration in the follicular fluid. The mean values of cadmium in follicular fluid of Czech women were approximately 20 times lower than those observed in a sample of Canadian women who had cadmium levels in follicular fluid analyzed for the first time [4].

DISCUSSION AND CONCLUSIONS

The differences found between the Canadian and our study were highly significant, thus it was necessary to discuss them all. Zenzes et al. [4] were the first authors who analyzed and described cadmium levels in human follicular fluid and so far no other findings have been reported. The

Table 1. Cadmium residues in follicular fluid

Cd content(ng.ml^{-1})	Total	Smoking habit			
		never	ex-	current	p<
Arithemtic mean	0.34	0.38	0.33	0.25	NS
SD	0.45	0.57	0.16	0.19	
95% CI	0.28	0.27	0.28	0.19	
	0.41	0.48	0.39	0.31	
min	0.1	0.1	0.1	0.1	
max	5.0	5.0	0.7	1.0	
Median	0.31	0.34	0.29	0.23	NS
SD	0.42	0.53	0.15	0.20	
95% CI	0.24	0.24	0.24	0.17	
	0.36	0.43	0.34	0.29	
Geometric mean	0.30	0.33	0.28	0.22	NS
SD	0.43	0.54	0.14	0.17	
95% CI	0.24	0.23	0.24	0.16	
	0.36	0.43	0.33	0.27	

average values of cadmium residues measured in follicles obtained from 51 Canadian women participating in IVF program were 6.73 ng.ml^{-1} for non-smokers and 7.93 ng.ml^{-1} for smokers. The differences were significant, including smoking-dose effect on cadmium levels. Our results are supported by the study of IVF patients from Prague [12], as the authors found only slightly higher levels of cadmium residues in follicles (1.19 ng.ml^{-1}). The age-dependent positive correlation for follicular cadmium levels was also analyzed. Unfortunately, in the group residing in Prague, the smoking status of patients has not been investigated. In both Czech studies, the low cadmium concentrations in follicular fluid of women were in agreement with low cadmium levels found in their blood samples (0.85 ng.ml^{-1} for the Brno group, 2.83 ng.ml^{-1} for the Prague group). Even though the Prague value is higher, it is low in comparison with common values elsewhere [4]. We do not assume that the different laboratory treatment of follicular fluid samples used in the first stage of the procedure could be the reason for a large difference in the values. Both Zenzes and Drbohlav analyzed only the first follicular fluid sample for each patient and separated proteins by precipitation. The whole procedure comprised several stages in which undiluted and diluted samples and those with added amounts of cadmium were analyzed and compared. The first stage of our procedure was based on microwave digestion of the protein matrix, which ensured the complete decomposition of protein in a very short time and thus allowed to avoid the risk of the second sample contamination [11]. Another aspect to be considered is the difference in exposure to the environmental cadmium levels between the Czech and the Canadian populations. The Canadian authors quoted after the Report of the National Research Council of Canada, published in 1979, daily values of 50 to 98 μg cadmium intake from the diet. They were higher by 25 to 50% if compared to the dietary intake in the United States, Germany or Japan [8]. In the Czech Republic the daily intake of cadmium was calculated from the food commodities measured in 12 selected towns. None of the values obtained from these measurements were higher than the exposure limit. An estimation of an average cadmium alimentary intake for a Czech adult is 21 μg/day. For the whole population, the daily intake remains within the range of 26–43% of the limit [1]. Within the Czech food consumption basket, the higher Cd residue levels are found in rice: the consumption of 1 kg presents an exposure dose of 55 μg/kg b.w. In other important sources – the grain foodstuffs and potatoes – cadmium residues are significantly (two times) lower [1]. Plants are exposed to cadmium namely by its absorption from the contaminated soil. Different amount of cadmium in superphosphates used as fertilizers and produced at different world natural deposits can explain the differences in food contamination by cadmium. In the majority of developed countries, non-smokers

with non-occupational exposure to cadmium have blood cadmium levels lower than 1 $ng.ml^{-1}$, with minor variations related to regional differences in dietary practices and, consequently, to cadmium dietary intake.

In the same geographic area, smokers always show significantly higher cadmium levels in blood and other body tissues than non-smokers [8,13]. Smoking only one cigarette, a smoker usually uptakes 0.1 to 0.2 μg, which makes approximately 10% of the total amount of cadmium in the cigarette. The exposure level is dose-dependent and can also be affected by the tobacco quality. Regarding this issue, an important source of cadmium are the cigarettes produced in Serbia; in this region, cadmium blood levels in smokers are similar to the values measured in occupationally exposed workers and are five times higher on average than the levels in smokers living in other countries [14]. The blood cadmium levels in our patients were 0.85 $ng.ml^{-1}$ on average, significantly higher in blood of smokers as compared to non-smokers. In the literature, there is a lack of data on cadmium levels in follicular fluid. The unique Canadian study [4] has not investigated blood cadmium levels. The low level of cadmium exposure in the Czech Republic has been repeatedly described in the studies concerned with the cadmium residues measurement in blood and tissue samples obtained from children and adults living in different regions. All values of cadmium residues were within the ranges found in the areas of foreign countries free from the environmental pollution. In smokers, cadmium levels were two or three times higher, and in occupationally exposed workers, 10–100 times higher than in non-occupationally exposed non-smokers [15].

In summary, environmental cadmium seems not to be a serious biologic source of the Czech population exposure. The former results of low levels of cadmium residues found in different body tissues have been recently confirmed in the studies focused on the measurement of cadmium residues in follicular fluid.

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