PERSISTENT ORGANOCHLORINE POLLUTANTS IN OBESE WOMEN AFTER DIET INDUCED WEIGHT LOSS: FIVE YEARS FOLLOW UP STUDY

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SUMMARY

Aim: Persistent organochlorine pollutants (POPs) from the environment are still bioaccumulating in human tissues. The aim of our study was to analyze the development of plasma POPs levels in obese women in relationship with their weight loss success in five year follow-up study.

Methods: 20 obese women aged 25–73 years were studied just before and after having completed a 3 month controlled low calorie diet (LCD) intervention (5 MJ daily), and again after 6 and 60 months since the beginning of the study. Body weight and plasma levels of 7 POPs were measured: polychlorinated biphenyls (PCB) 153, 138, 180; 2,2-bis(4-chlorophenyl)-1,1,1-trichloroethylene (p,p´-DDE); 2,2-bis(4-chlorophenyl)-1,1,1-trichloroethane (p,p´-DDT), hexachlorocyclobenzene (HCB), hexachlorocyclohexane β (HCH β).

Results: Data shows that after 3 months of a completely controlled restrictive diet regimen, the weight loss was associated with an increase in POP plasma levels. However, after a five year follow-up, there were no differences in POPs plasma levels between those who kept losing weight or maintained the initial weight (WL/M) and the group of weight gainers (WG), except for HCB where the WG had a significantly higher level ($p < 0.05$).

Conclusions: These results suggest that contrary to the long-term weight gain, the long-term weight loss or weight maintenance caused by diet restriction is associated with lower plasma levels of HCB.

Key words: persistent organic pollutants, hexachlorocyclobenzene, low calorie diet, body weight changes

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INTRODUCTION

Persistent organochlorine pollutants (POPs), organochlorine pesticides and polychlorinated biphenyls (PCBs) are synthetic chemicals that have been released into the environment in hundreds of metric tons for many years and have been used in diverse applications such as industry and agriculture. Although they were banned in most countries, their residues are still widespread in the environment. Because of their high lipophilicity and structural stability, they still can be found accumulated in biological systems. They show a carcinogenic and an endocrine disruption potential. Recently, based on epidemiological studies, there has been concern about their speculated association with metabolic disturbances like diabetes mellitus type 2, rheumatoid arthritis, disturbances of cognitive function, etc. Contaminated food, especially fatty fish, meat and milk products, is still a main source of the exposure of general population (1).

Among chlorinated pesticides, p,p´-DDT has been used most extensively. Its metabolite p,p´-DDE together with hexachlorocyclobenzene (HCB) are, at the present day, the most frequently prevalent residues in the adipose tissue of humans (2).

PCBs form a subgroup of halogenated aromatic hydrocarbons. There are theoretically 209 single congeners. They have been used, to a great extent, in diverse technical applications from the 1930s to the 1970s (3). Despite production bans in many industrial countries in the 1970s and 1980s, about 113 different PCB congeners were still detectable in the environment in 1998 (4). Their concentration in human tissue is generally monitored by using examinations of human breast milk and data from Europe show their decreased concentration. 'Non-dioxin-like' PCB 153, 138, and 180 are the main congeners which show the highest concentration and are most frequently found in breast milk (5). In the former Czechoslovakia, PCB was marketed as technical mixtures under the trade name "Delor" produced in the amount of about 21,500 tons in Eastern Slovakia from 1959 to 1984, when the production was finally abolished (6). About 11,600 tons were used inside the former Czechoslovakia (7). Therefore, the industrial areas of the Czech Republic have one of the highest PCB burdens of all European countries (8).

After human exposure, POPs are accumulated in the body, especially in the adipose tissue. They have relatively long half-lives before disappearing from the tissue or from the body. The variability of the stored amount depends on dietary exposure (food habits, and the quality and quantity of POPs in available food) and on individual disposition to store these substances (genetic traits and size of adipose tissue and its dynamic changes) (9). Their distribution in the body is affected by changes in body weight. Weight loss resulted in an acute increase of their concentration in reduced adipose tissue, brain, and serum/plasma without changing the total amount, as it was documented in case of hexachlorocyclohexane (HCH) (10). However, dramatic weight loss, which occurred as a consequence of bariatric surgery treatment, showed not only an increased level of serum and adipose tissue POPs concentrations together with a reduced amount of white adipose tissue, but a decreased total body burden for POPs after 12 months post-surgery as well (11). The objective of our study was to analyze in five year follow up study the development of plasma POPs levels in obese women in relationship to their weight loss success, caused by restrictive diet regimen.

MATERIALS AND METHODS

Twenty obese adult women, aged 25–73 years (BMI > 30 kg/m^2) were randomly selected from the patients of the Centre for Obesity Treatment (Faculty Hospital in Pilsen, Czech Republic) during their first visit in 2006. Informed consent was obtained from all patients involved in the study. Anthropometry: body weight (BW) and height were measured, and a plasma analysis of 7 POPs (p,p´-DDE, p,p´-DDT, HCB, HCH ß, PCB 153, 138, 180) was performed in all the subjects. Obese patients were studied just before (Time 1, T1) and after the 3 month (Time 2, T2) of low calorie diet (LCD) intervention (5 MJ daily, protein 20% of total energy, fat 25–30% of total energy). Their diaries were checked on a monthly basis using nutritional software NutriDan 1.2 (DADI Ltd., Pilsen, 2002, Czech Republic). After that period they were instructed to continue their diet and were checked again 6 months (Time 3, T3) and 60 months (Time 4, T4) after the beginning of the study.

Venous blood was collected in time T1, T2, T3, and T4 from fasted (12 hours) subjects between 7.00 a.m. and 10.00 a.m. Plasma samples were divided into 50 µl aliquots and stored at −80°C for subsequent analysis of PCB 153, 138, 180, p,p´-DDE, p,p´-DDT, HCH ß and HCB. Plasma levels of these pollutants were determined by a high resolution gas chromatography with electron capture detection (HRGC/µECD; Agilent Technologies 6890 Series, Palo Alto, CA, USA), Capillary Column DB-5 (0.25 mm x 60 m x 0.25 µm); J&W Scientific, USA (12). The values (in ng/kg fat) of the detection limit (LOD) were the following: PCB 153 (<20), PCB 138 (<60), PCB 180 (<40); p,p´-DDE (<10); p,p´-DDT (<50), HCB (<20), HCH β (<40).

Statistics

POPs concentration values below the detection limit were treated as one-half the value of the detection limit (LOD). The descriptive statistics including the median and range (minimum –maximum) were calculated only for the congeners detected in at least 50% of samples.

Due to the not normal distribution of most of the examined variables, the non-parametric Wilcoxon Rank-Sum Test was performed to compare the POP concentration increase during a 60 month period between WG and WL/M groups. All statistical computations were performed with the MATLAB Statistics Toolbox.

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The approval of the protocol examination was authorized by the Medical School and Faculty Hospital Ethics Committee in Pilsen.

RESULTS

Basic characteristics of plasma concentration development of each measured POP in whole sample during the five-year follow up are summarized in Table 1, BW development in Table 2. During this time, i.e. from 2006 to 2011, only plasma levels of HCH β and DDT decreased. The median and range of all others

Table 1. *Development of plasma concentration of PCB congeners and chlorinated pesticides/metabolites; (n = 20)*

	T1	T2	T3	T4
HCH-beta	20	570	350	230
	20–2,390	140–4,370	170–5,350	100–440
HCB	175	450	270	935
	10–880	40–2,440	120–1,570	100–4,470
p,p´-DDE	160	385	27	1,435
	5–700	100–1,500	150–1,410	210–8,180
p,p´-DDT	25	46	41	100
	25–1,740	37–610	41–410	100–290
PCB 138	30	150	160	705
	30–140	80–340	110–330	350–1,110
CB 153	140	190	205	780
	10–500	60–620	130–420	280–1,260
CB 180	20	110	90	765
	20–140	60–180	70–230	150–1,520

Median; minimum–maximum, expressed in ng/kg, T1 – initial measurement, prior diet restriction, T2 – measurement after 3 months of LCD intervention, T3 – measurement after 6 months from the beginning of the study, T4 – measurement after 60 months from the beginning of the study

Table 2. Development of body weight

T1	T2	T3	T4
108.2	101.6	99	108.8
82.8–130.5	74.7–118.5	73–115	77.9–120.4

Median, minimum–maximum, expressed in kg, T1 – initial measurement, prior diet restriction, T2 – measurement after 3 months of LCD intervention, T3 – measurement after 6 months from the beginning of the study, T4 – measurement after 60 months from the beginning of the study

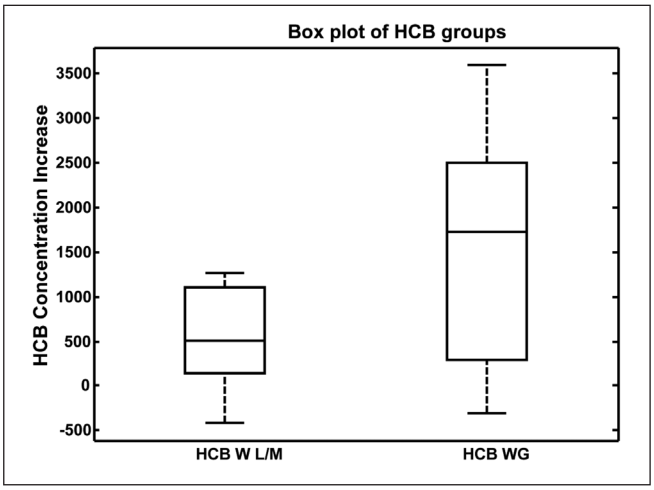

***Fig. 3.** The box plot of HCB, in ng/kg lipids; median is depicted as the central line.*
$p < 0.05$, Wilcoxon's test

examined POPs increased. The highest plasma levels detected were DDE and HCB (Fig. 1). The medians of HCB and DDE are also depicted as the central line in the box plots in Figure 3.

To show the dependency of the increase of pollutant concentration between T4 a T1 on relative weight growth, the linear regression of the increase of pollutant concentration $(POP_{T4}–POP_{T1}) \cdot 10^6$ on relative weight growth $(BW_{T4}–BW_{T1})/BW_{T1} \cdot 100$ is represented in Fig. 2.

Depending on body weight difference between time 4 and time 1, the sample was divided into two cohorts: women whose BW decreased or remained relatively stable ($BW_{T4}–BW_{T1} < 1.5$ kg) (weight losers/maintainers – WL/M, $N = 11$); and the others

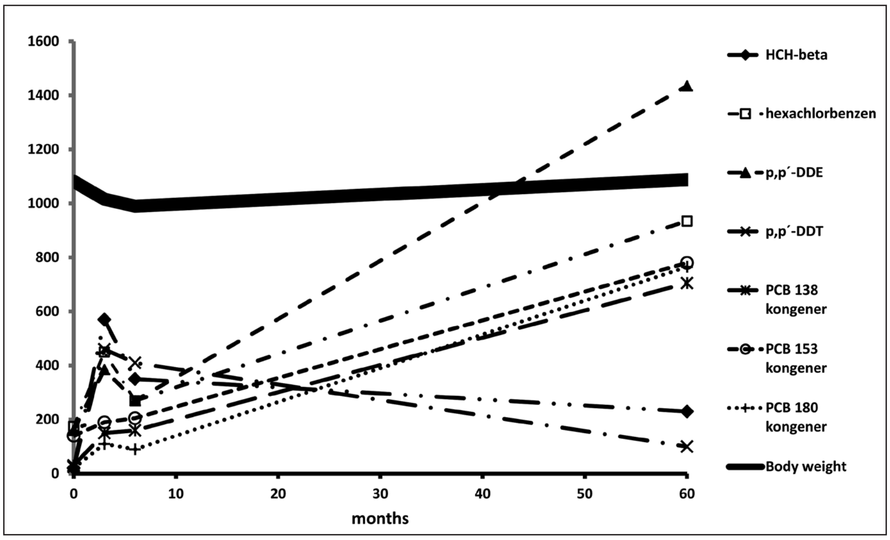

***Fig. 1.** The development of plasma POPs levels (medians, in ng/kg lipids) and body weight (in kg·10) during five-year follow-up.*

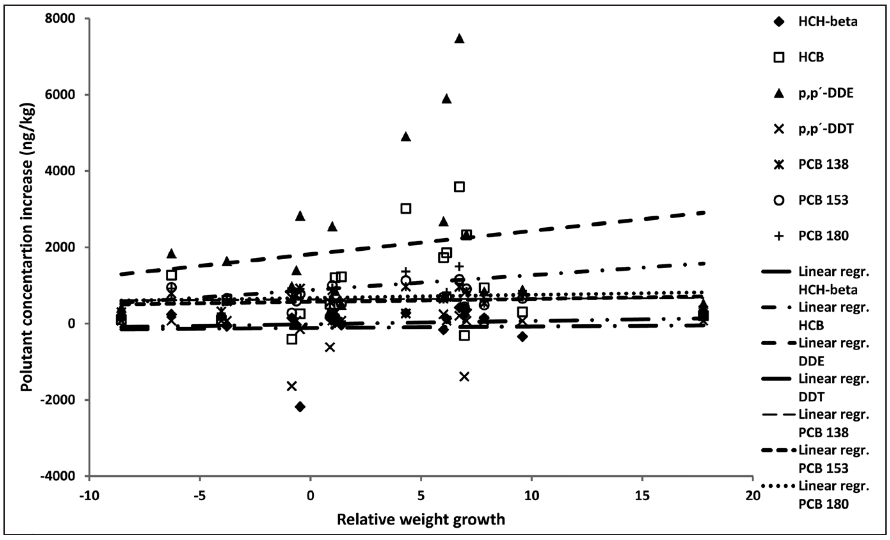

***Fig. 2.** The linear regression of the increase of pollutant concentration $(POP_{T4}–POP_{T1}) \cdot 10^6$ on relative weight growth $(BW_{T4}–BW_{T1})/BW_{T1} \cdot 100$.*

(weight gainers WG, N=9). WL/M had lower plasma level of HCB in comparison to WG in T4 ($p<0.05$), although they did not differ in T1 (Table 2, Fig. 3). A similar tendency, however without statistical significance ($p<0.1$), was also observed in DDE. Some tendency was also observed for other POPs but without statistical significance ($p>0.1$). These results suggest that long term weight loss or weight maintenance tend to be positively associated with a lower plasma level of HCB contrary to the HCB plasma level in weight gainers.

DISCUSSION

During a five years follow up study from 2006 to 2011, there were increased medians levels of 5 from 7 examined POPs. Many studies confirmed age as a predictor of POPs levels (13, 14). In case of body weight and body composition maintenance, the increase of POPs plasma levels is the result of an imbalance between increased body burden from everyday exposure to food and their slower degradation and elimination from the body. Taking into account that biological half-time of many POPs is around ten years; there is a high probability of an accumulation of these POPs in the body, especially in lipophilic tissue. Intergeneration differences along with the gradual reduction of body burden, reflect a gradual decrease of background exposure from the environment as a result of the Stockholm Convention (15). It depends on the amount of particular POP which has been released into the environment and also on its chemical properties for degradation. Based on our data, only DDT and HCH ß have been reduced during the five-year follow up study. The situation in POPs body distribution is more complicated with the changing of the fat/fat-free mass compartments, as it occurs with the development of overweight and obesity. There are studies which suggest an inverse association between PCB levels and BMI gain over the last ten years (16). On the other hand, weight loss, and especially drastic weight loss, is associated with increased plasma/serum levels in the liver, brain, and in a reduced size of white adipose tissue. The knowledge of these dynamics along with total POPs body burden development is very important for an obesity treatment strategy.

CONCLUSION

The results of our study, where the subjects tried to keep lifestyle modification based on energy and total fat restriction in their diet, show that after 3 months of completely controlled regime, the weight loss was associated with an increase in POP plasma levels. However, after the five-year follow up, there were no differences in POPs plasma levels between the group of long-term successful WL/M and the group of WG, except for HCB where the WG had a significantly higher level.

Conflict of Interests

None declared

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