THE INFLUENCE OF PCB AND CHLORINATED PESTICIDES ON BONE MINERAL DENSITY IN MEN

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Introduction

Persistent organochlorines (POCs), such as PCBs and DDT, are present at relatively high concentrations in food and show estrogenic, anti-estrogenic or anti-androgenic activity in biological test systems[1,2]. As it is known that bone mineral density (BMD) in men is influenced by sex hormones[3,4,5], we looked for associations between BMD and serum concentrations of hormone-mimicking POCs in 115 men from the general Swedish population.

Materials and Methods

Originally, 790 men (aged 40-74) were randomly sampled from the population register. They lived in the county of Uppsala, in central Sweden just north of the capital Stockholm. Among these men, 286 agreed to participate in an extensive survey of food habits, to donate blood and to have their BMD measured. Serum for organochlorine analysis was sampled from the first 115 of the participating men (mean age at 63 years (41-75 years)) when they visited the hospital for blood sampling. The study was approved by the local Ethics Committee.

Quantitative bone measurements were performed by dual energy absorptiometry (DXA) (DPX-L, Lunar Co, Madison, WI, USA) and quantitative ultrasound (QUS) (Achilles Plus, Lunar Co, Madison, WI, USA). Five variables were measured. The variables BMD (g/cm^2) of the whole body (WBBMD), the lumbar spine (LSBMD) at the L2-L4 region, and of the femoral neck (FNBMD) were measured by DXA. We measured the propagation of the ultrasound beam by speed of sound (SOS, m/s) and the broadband ultrasound attenuation (BUA, dB/MHz) on the left *os calcis*.

The following POCs were analysed in serum: ten PCB congeners (IUPAC no 28, 52, 101, 105, 118, 138, 153, 156, 167 and 180), five DDT isomers (*p,p'*-DDT, *p,p'*-DDD, *p,p'*-DDE, *o,p'*-DDT and *o,p'*-DDE), hexachlorobenzene (HCB), three hexachlorocyclohexane isomers (α-HCH, β-HCH and γ-HCH), *trans*-nonachlor and oxychlordane (Table 1). Serum samples were analysed using a gas chromatograph equipped with dual capillary columns and dual electron capture detectors (ECD, ^{63}Ni), after appropriate extraction, cleanup and quality assurance steps[6].

The associations between concentrations of POCs and the five DXA and QUS variables were studied by linear regression. In multivariate analysis, we considered the following possible confounding variables: age (continuous), body mass index (BMI, continuous), height (continuous), smoking status (never, former, current), cortisone use (never, ever), diabetes (yes, no) and long-term physical activity by tertiles. The physical activity variable was based on reports of estimated leisure physical activity on a four point scale in each of three periods – teenage, age 18-30 and recent years- which were summed and condensed into tertiles. In order to detect non-linear associations, the study subjects were divided into quartiles according to their

concentrations of POCs. Adjusted means (least-square means) of the dependent variables were calculated for each quartile of the independent variables, on the basis of the regression estimates with all confounding factors held at their mean values. The distribution of several of the independent variables was strongly skewed, but statistical analysis of untransformed and ln-transformed POC concentrations gave similar results.

Table 1. Serum concentrations (ng/g lipid) of persistent organochlorines in 115 men from the general Swedish population

	n above LOQ[a]	Mean	SD	Range
CB 28	97	5.8	9.1	<2.0-78.1
CB 52	37	4.2	3.1	<2.0-16.4
CB 101	93	4.2	3.1	<2.0-18.3
CB 105	103	6.6	4.8	<2.0-28.1
CB 118	115	41.9	23.1	4.3-143
CB 138	115	141.6	66.0	3.1-335.0
CB 153	115	294.3	120.8	22.8-627.0
CB 156	115	22.9	7.1	7.9-49.6
CB 167	111	10.0	4.7	<2.0-29.7
CB 180	115	216.1	74.2	71.4-480.0
p,p'-DDT	111	19.8	13.5	<4.0-78.6
p,p'-DDD	20	2.8	2.0	<4.0-15.4
p,p'-DDE	115	783.8	684.8	25.0-4030.0
o,p'-DDT	3	2.2	1.6	<4.0-15.7
o,p'-DDE	0			
HCB	115	84.0	136.4	23.1-1468.0
α-HCH	9	1.2	0.7	<2.0-6.1
β-HCH	115	18.1	29.0	12.4-187.0
γ-HCH	29	1.7	1.6	<2.0-12.1
trans-Nonachlor	115	30.5	15.6	7.9-89.5
Oxychlordane	115	13.7	7.0	4.3-35.7

[a]LOQ=Limit of quantification. When results were below LOQ they were set to 50% of that limit in the calculation of means and SD.

Results and Discussion

In the multiple regression analyses, a few statistically significant associations were found between concentrations of single POCs and DXA or QUS variables, (results not shown). Overall, our findings did not indicate strong associations between organochlorine concentrations in serum and BMD, BUA and SOS among the study participants. The only consistent finding in both the regression analysis and the analysis of adjusted means was the negative associations between concentrations of *p,p'*-DDE with all five DXA and QUS variables (Table 2, Fig. 1). The multivariately adjusted mean of BMD in femoral neck, lumbar spine and whole body was slightly lower (3-8%) at the two highest *p,p'*-DDE concentration quartiles than at the lowest

quartile (not statistically significant). A similar result was found for BUA and SOS in the ultrasound measurement of *os calcis*. The decrease in BUA and SOS between the first and third quartile was statistically significant.

Table 2. Regression coefficients and p values in multivariate regression analyses of associations between serum concentrations of *p,p'*-DDE and DXA or QUS variables[a]

Compound	Bone[b]	Coefficient (x 10^{-3})	SE (x 10^{-3})	p
p,p'-DDE	Femoral neck BMD	-0.02	0.02	0.40
	Lumbar spine BMD	-0.01	0.03	0.63
	Whole body BMD	-0.01	0.02	0.40
	BUA	-2.3	1.8	0.21
	SOS	-4.6	5.7	0.42

[a]Adjusted for age (continuous), BMI (continuous), height (continuous), smoking (never, former, current), cortisone use (never, ever), diabetes (yes, no) and long-term physical activity (tertiles). [b]BMD variables: n=114-115; BUA and SOS: n=107.

A large number of statistical comparisons were made and it can not be excluded that the few significant results were due to chance. However *p,p'*-DDE acts as a weak anti-androgen in biological test systems, by blockage of the androgen receptor. Recent studies indicate that androgens may have positive effects on BMD by decreasing the bone resorption. It is hypothetically possible, therefore, that the anti-androgenic *p,p'*-DDE causes negative effects on bone density. This hypothesis is supported by a small experimental study on male pigeons, where *p,p'*-DDE reduced the medullar bone formation during estrogen treatment. *p,p'*-DDE was the compound showing the highest serum concentrations among our men (Table 1), but the decrease in adjusted means of BMD, BUA and SOS between the first and fourth quartiles of *p,p'*-DDE concentrations was not large enough to be statistically significant in our relatively small study.

In conclusion, our results indicate that the studied POCs do not exert major effects on bone density in our study group. The finding of a slightly decreased bone density among men with elevated serum concentrations of *p,p'*-DDE has to be confirmed in a larger study on the same population of men, or in studies of male populations with higher body burdens of POCs.

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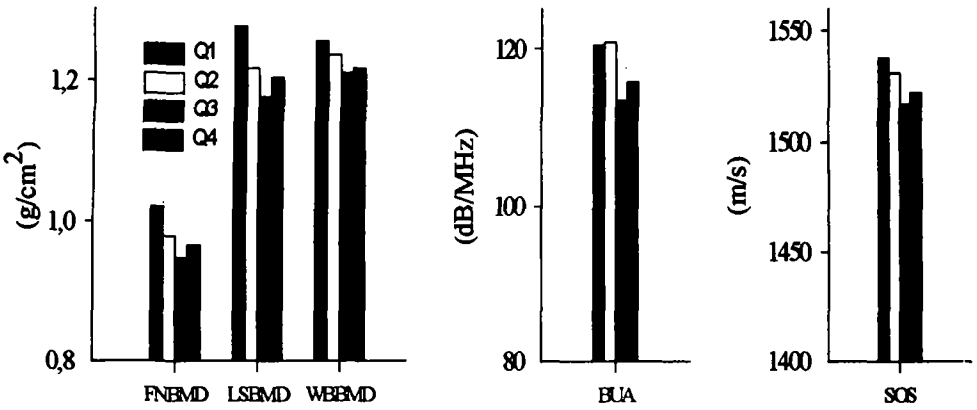

Figure 1. *p,p'*-DDE. Adjusted means of femoral neck BMD (FNBMD, n=115), lumbar spine BMD (LSBMD, n=114), whole body BMD (WBBMD, n=115) and broad-band attenuation (BUA, n=107) and speed of sound (SOS, n=108) in os calcis for each exposure quartile (Q1,Q2, Q3 and Q4) of *p,p'*-DDE. The means were adjusted for age (continuous), BMI (continuous), height (continuous), smoking (never, former, current), cortisone use (never, ever), diabetes (yes, no) and long-term physical activity (tertiles). The adjusted means of BUA and SOS in the third *p,p'*-DDE quartile was significantly different from the adjusted mean of the first quartile ($p<0.05$).

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