INCREASED CONCENTRATIONS OF POLYCHLORINATED BIPHENYLS AND HEXACHLOROBENSENE IN MOTHERS TO MEN WITH TESTICULAR CANCER

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Introduction

An increasing incidence of testicular cancer has been reported from several western countries during the last decades[1]. Thus, in Sweden the annual age-adjusted incidence of testicular cancer increased significantly by 2.2% during the time period 1980-1999[2]. This is the most common cancer among young males. Cryptorchidism is an established risk factor. An increased risk has also been reported for the descendent testis[3], suggesting common risk factors. Some prenatal risk factors seem to be common for both crypthorchidism and testicular cancer, such as high levels of oestrogen in the first trimester[4].

Prenatal exposures have been discussed to be of etiological significance, such as environmental pollutants with estrogenic potency, i.e., xenoestrogens[1]. Impacts of increasing levels of xeno-estrogens have been observed in aquatic systems. In humans concern has been focused on ”endocrine disrupting chemicals” with either estrogenic or antiestrogenic effects, which may be related to an increasing incidence of hypospadia in newborn boys[5]. Indications of a decrease in sperm counts have been observed in recent years, but the hypothesis of an association with exposure to xenoestrogens is still a controversial question. Testicular cancer has usually not been regarded to be an occupational disease[6]. Increased risk has been associated with employment in agriculture and natural gas extraction, in professionals and administrators[7] and exposure to polyvinyl chloride[8 9]. The aim of this study was to investigate concentrations of certain persistent organic pollutants (POPs) in blood from men with testicular cancer compared with controls and their mothers.

Materials and Methods

Incident cases with testicular cancer were recruited during the time period 1997-2000 from the Department of Urology at Huddinge (n=17) and Karolinska Hospital in Stockholm (n=5), Department of Oncology at the University Hospitals in Örebro (n=13), Linköping (n=13) and Lund (n=10), Sweden. Consecutive patients at the clinic of the respective physician were asked to participate. No case refused to participate. The patient as well and his mother was asked to give blood for chemical analysis of POPs.

For each case a control subject free from testicular cancer was drawn from the Swedish population registry. This national registry covers the whole population and is continuously updated as to e.g., emigration and deaths. Due to the unique Swedish ID-numbers all inhabitants can be traced. The controls were drawn within 5-year age strata to the cases, i.e. 20-24 years, 25-29 years etc. After that

the mother of the control subject was identified using the population registry. As one criterion the mother should be within the same 5-year age stratum as the mother to the respective case. If this was not the situation a new set of controls, male control and his mother, was drawn. Thus both the male cases and controls and the mothers were within the same 5-year old groups respectively.

Blood was drawn from all study subjects during the same time period (1997-2000). They were instructed to have only a light meal before this was done. Plasma was frozen for later analysis. Furthermore, all study participants were asked to answer a questionnaire on e.g., occupations, weight and length including weight one year before blood was drawn. The mothers also answered questions on reproductive history, such as number of children and year of birth of all children.

Chemical analysis

All blood samples were coded with an id-number that did not reveal sex or if it was a case or a control. Approximately 20 ml of blood was used for analyses of 36 congeners of polychlorinated biphenyls (PCBs), p,p'-dichlorodiphenyl-dichloroethylene (p,p'-DDE), hexachlorobenzene (HCB) and six chlordane congeners. The plasma samples were fortified with ^{13}C-labelled internal standards. The lipid fraction, including the organochlorines, was first removed from plasma by use of Hydromatrix column. The lipid content was then determined gravimetrically and further cleaned up by multi-layer silica chromatography. Congener specific analyses and quantification of the organochlorines was done by high-resolution gas chromatography and mass spectrometry, HRGC-MS, running in EI and SIM-mode. The methods detection level was in the range of 0.3-1 ng/g for the various analytes and samples. All results are expressed in ng/g lipid.

Statistical methods

Unconditional logistic regression analysis was performed using the SAS system (SAS Institute, Cary, NC) for calculation of odds ratio (OR) and 95 % confidence interval (CI). In the analyses adjustment was made for age and Body Mass Index (BMI) at the time of sampling. The median concentration in the controls was used as cut off value in these calculations. The SAS system was also used for descriptive statistics and Wilcoxon rank sum tests.

Results

In total 61 case and control pairs were recruited. For technical reasons blood from 58 cases was analysed. Of the case mothers 44 agreed to participate compared with 45 of the control mothers.

Cases and controls

The 58 cases with testicular cancer had a mean age of 31 years (median 30, range 18-45) and 61 controls had a mean age of 32 years (median 31, range 19-47).

Mothers to cases and controls

Blood was obtained from 44 mothers to the cases and 45 mothers to the controls. Both groups of mothers were of similar age overall, although mothers to seminoma cases tended to be somewhat older than the other ones.

In Table 1 results on concentrations of organochlorines for the sons are displayed. The only significant difference was an increased concentration of cis-nonachlordane in cases with testicular cancer. This yielded OR=2.7 (CI=1.2-5.7) if the median concentration among the controls was used as cut off value.

Table 1. Concentrations of organochlorine compounds (ng/g lipid) in cases with testicular cancer and controls. Wilcoxon P-value is given

	Number	Mean	Median	Min	Max	P-value
Sum of PCBs						
— cases	58	395	357	96	1099	0.91
— controls	61	394	364	110	1083	
HCB						
— cases	58	26	24	5.3	58	0.33
— controls	61	24	22	8.8	47	
p,p-DDE						
— cases	58	152	117	35	529	0.27
— controls	61	140	98	29	601	
Sum of chlordanes						
— cases	58	25	21	8.0	72	0.40
— controls	61	22	21	8.2	70	

Table 2 displays the results of concentrations of organochlorines in mothers of cases and controls. Significantly increased concentrations were found for the sum of PCBs, HCB, trans-nona-chlordane, cis-nonachlordane and sum of chlordanes.

Table 2. Concentrations of organochlorine compounds (ng/g lipid) in mothers to cases with testicular cancer and controls. Wilcoxon P-value is given

	Number	Mean	Median	Min	Max	P-value
Sum of PCBs						
— case mothers	43	859	792	236	2114	0.0004
— control mothers	41	592	563	141	1193	
HxCBz						
— case mothers	44	47	39	12	120	0.004
— control mothers	45	34	31	8.9	81	
p,p-DDE						
— case mothers	44	566	315	109	3339	0.48
— control mothers	45	428	324	51	1431	
Sum of chlordanes						
— case mothers	44	47	34	14	131	0.03
— control mothers	45	32	31	5.8	76	

Results of calculations of OR and CI in the group of mothers showed: For sum of PCBs OR=3.8 (CI=1.4-10), HCB OR=4.4 (CI=1.7-12), trans-nonachlordane OR=4.1 (CI=1.5-11) and cis-nona-chlordane OR=3.1 (CI=1.2-7.8) were obtained. Also the other organochlorines yielded increased ORs, although not significantly so.

Conclusions

Interestingly, significantly increased concentrations were found among case mothers for the sum of PCBs, HCB, cis-nonachlordane and the sum of chlordanes. Using the median concentration among the control mothers as cut off value significantly increased ORs were found among case mothers to sons with embryonal cancer for the sum of PCBs, HCB, trans- and cis-nonachlordane. No increased risk was found for DDE. Decreasing levels of certain organochlorines such as PCBs have been found in Swedish breast milk since the 1980's. However, the highest concentrations were found in early 1970's[10]. Since the median age among the cases was 30 years most of them were born during the time period with high concentration in the population. Prenatal and lactation exposure appears to be an important source of the adverse health effects of POPs seen in infants, such as cognitive motor deficits from PCBs[11]. Testicular cancer could also be such an adverse health effect.

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