Exposure to organochlorine pollutants and human sperm Y:X ratio

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Introduction

During recent years there have been concerns that exposure to persistent organochlorine pollutants (POPs), might contribute to a change in the sex ratio of offspring in exposed populations [1]. Results from studies regarding POPs and sex ratio are contradictory[2,3,4,5,6,]. Short-term paternal exposure to high levels of POPs, as in Seveso or in the Yucheng incident lead to an increased proportion of female offspring, whereas results from studies comprising subjects consuming highly contaminated fish from the Great Lakes, Michigan U.S., showed that paternal exposure to POPs was linked to a higher proportion of male offspring. The mechanisms behind these changes in sex ratio are unknown. One hypothesisis that the POP exposure changed the proportion of sperm bearing Y and X chromosomes [7].

In Sweden the consumption of fatty fish from the Baltic Sea, at the Swedish east coast, is a major source of exposure to POPs. Fishermen from the east coast have averagely higher serum levels of PCBs and total-TEQ than both west coast fishermen and the general population [8,9,10]. In the present study, we aimed to investigate whether there is an association between POP exposure and the Y:X chromosome ratio in the sperm of Swedish fishermen.

Subjects and Methods

Semen and blood samples from 149 Swedish fishermen from the east and west coasts, aged 27-67 years, were analyzed. The proportion of Y- and X-chromosome bearing sperms in semen samples was determined by two-color fluorescence *in situ* (FISH) analysis [11].

We choose to analyse 2,2´,4,4´,5,5´-hexachlorobiphenyl (CB-153) and dichloro-diphenyl dichloro-ethene (p,p´-DDE) in serum as proxy markers for POP exposure. The CB-153 and p,p´-DDE concentrations were adjusted for total serum lipid concentration determined by enzymatic methods and expressed as ng/g lipid.

In linear regression models, we evaluated whether there was an association between CB-153 and p,p´-DDE serum concentrations on the fraction of sperm bearing the Y chromosome. The exposure variables were analysed as continuous (untransformed and log transformed) as well as categorized into five equally sized groups due to exposure levels. Age, smoking status, abstinence time and sex hormone levels were considered as potential confounders (Table 1). If these variables showed any association ($p<20$) with Y chromosome fraction they were included in the model, one at the time together with the exposure variable. For CB-153 and especially p,p´-DDE the log transformed variables better fulfilled model assumptions compared to the untransformed variables.

Results and Discussion

The log transformed lipid adjusted p,p'-DDE concentration was significantly ($p<0.001$) associated with the Y chromosome fraction (slope [ß] for ln[p,p'-DDE] 0.66, 95% confidence interval [CI] 0.30, 1.01). According to the regression model this means that a p,p'-DDE concentration of 242 ng/g lipid (the median level) corresponds to an Y chromosome fraction of 51.2 % and a p,p'-DDE concentration of 472 ng/g lipid (lower limit value for highest exposure category) corresponds to 51.7 %. However, p,p-DDE explains only 7.5% of the total variance for Y:X chromosome fraction.

Also the log transformed lipid adjusted CB-153 concentration was significantly ($p=0.05$) associated with the Y chromosome fraction (ß for ln[CB-153] 0.42, 95% confidence interval [CI] 0.01, 0.83). According to the regression model this means that a CB-153 concentration of 200 ng/g lipid (the median level) corresponds to a Y chromosome fraction of 51.3 % and a CB-153 concentration of 328 ng/g lipid (lower limit value for highest exposure category) corresponds to 51.5 %. However, CB-153 explains only 2.0% of the total variance for Y:X chromosome fraction.

Our main finding was that higher exposure to POPs was associated with a slightly higher proportion of Y chromosome bearing sperm. The mechanism behind the observed findings is still unknown. One hypothesis is based on the observations that apoptosis in the spermatogenic cells is under influence of sex hormones and gonadotropins and that the Y-and X-chromosome bearing spermatids may differ in their susceptibility to sex hormones [7] such that POPs with hormonal activity will have a differential effect on apoptosis. Another hypothesis is that there is a loss of the X chromosome due to an effect on formation of micronuclei during the process of meiosis caused by POPs [12]. Such mechanisms would be mirrored by changes in the ratio between Y and X chromosome bearing spermatids in the seminal fluid. No previous study of POP exposure and Y:X ratio has been performed and more research are needed to elucidate the intratesticular mechanisms affecting the distribution of Y and X bearing sperm.

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Table I. Outcome, exposure and potential cofounders of the study population of Swedish fishermen (n=149)

Mean	SD	Median	Range
Outcome variable			
Fraction of Y chromosomes (%)	51.2	1.74	51.1	47.5 - 56.8
Exposure variables			
CB-153 (ng/g lipids)	258	208	200	40.5 - 1460
p, p´-DDE (ng/g lipids)	356	335	242	40.4 - 2250
Potential confounders			
Age (yrs)	47	9.2	48	27 - 67
Abstinence time (days)	3.8	2.5	3.0	0.5 - 15
Testosterone (nmol/L)	13	4.9	12	4.2 - 32
SHBG (nmol/L)	32	12	31	6.8 - 71
Testosterone/SHBG	0.4	0.2	0.4	0.2 - 1.5
FSH (IU/L)	4.1	2.3	3.5	0.9 - 16
LH (IU/L)	3.0	1.2	2.8	1.0 - 6.2