

EXPOSURE TO PERSISTENT ORGANOCHLORINE POLLUTANTS AND TYPE 2 DIABETES MELLITUS

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Introduction

The incidence of type 2 diabetes mellitus (T2DM) is rapidly increasing world-wide (1). T2DM is characterized by peripheral resistance to insulin action and a relative deficiency of insulin. The main factors identified as responsible for the disease are age, central adiposity, lack of physical activity, and dietary glycemic load (2). Moreover, a number of genetic factors seem to be of importance for the pathogenesis (2,3).

Persistent organochlorine pollutants (POPs), such as polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs), dichloro diphenyl trichloroethane (DDT) and its major metabolite 1,1-dichloro-2,2-bis (p-chlorophenyl)-ethylene (p,p'-DDE) have been associated with T2DM in recent epidemiological studies (4,5). In Sweden the consumption of fatty fish from the Baltic Sea (at the Swedish east coast) is the single most important source of exposure to POP.

The aim of the present study was to assess the association between biomarkers for POP and prevalence of T2DM in two independent cohorts of Swedish fishermen and their wives.

Materials and methods

In two studies we choose to analyze 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) in serum with a well described GC/MS/MS technique, as a proxy biomarker for POP exposure, because Cb-153 correlates very well with both total concentration in serum of PCBs (6-7), with the PCB derived dioxin-like effect (6) as well as with the total POP derived dioxin-like effect (8). In addition, we have used another relevant exposure biomarker, p,p'-DDE, which is present in relatively high serum concentrations in subjects consuming fatty fish from the Baltic Sea (9).

The first study included 184 Swedish fishermen's wives (median age 64 years) and 196 Swedish fishermen (median age 60 years) living at the east coast of Sweden (10). The second study included 544 fishermen's wives (median age 50 years) living at both costal stretches of Sweden (11). There was an overlap of only 23 women between the second and the first study, and none of the overlapping women had T2DM. In both studies the participants were asked if they had diabetes and if so, what type of diabetes, years since diagnosis and what kind of treatment they had.

Associations between exposure and T2DM were analyzed by logistic regression. Age, Body Mass Index (kg/m² body weight) were regarded as potential confounders. Moreover, trends of associations between POP biomarkers and T2DM prevalence were tested with Jonckheere-Terpstra test.

Results and discussion

Study 1

CB-153 was significantly associated with T2DM for the whole data set (an increase of 100 ng/g lipid corresponded to an Odds Ratio (OR) of 1.16, 95% confidence interval [CI] 1.03, 1.32, p=0.03). Among the men the corresponding OR was 1.20 (95% CI 1.04, 1.39, p=0.01) and among the women 1.06 (95% CI 0.75, 1.50, p=0.74). Regarding p,p'-DDE for the whole dataset there was a significant association between exposure and T2DM (an increase of 100 ng/g lipid corresponded to an OR of 1.05, 95% CI 1.01, 1.09, p=0.006). No gender difference of the point estimate for OR was observed.

Using the exposure data categorized into tertiles there were significant positive trends between CB-153 and p,p'-DDE exposure, respectively, and T2DM (table 1). Among the men significant positive trends between CB-153 exposure and diabetes (p=0.005) and between p,p'-DDE exposure and diabetes (p=0.04) were observed. Among the women the pattern was very similar regarding p,p'-DDE exposure and diabetes (p=0.07), whereas no such association was observed for the CB-153 exposure.

Study 2

Effects on the thyroid hormone system

In the second study including only women, CB-153 was significantly associated with T2DM, an increase of 100 ng/g lipid corresponded to an OR of 1.6, 95 % confidence interval [CI] 1.0, 2.7, $p=0.05$. When age was included in the model the association became weaker OR 1.4, 95 % CI 0.8-2.5, $p=0.25$. Regarding p,p'-DDE an increase of 100 ng/g lipid corresponded to an OR of 1.3, 95% CI 1.1, 1.5, $p=0.004$. Inclusion of age in the model did not change the association for p,p'-DDE. BMI did not fulfil the inclusion criteria for any of the models.

When the exposure variables were categorized into quartiles, significant positive trends between CB-153 and T2DM ($p=0.004$) and p,p'-DDE and T2DM ($p=0.002$) were observed (table 2).

These two independent cross-sectional studies of subjects relatively highly exposed to POPs shows an association between serum concentrations of POP biomarkers and an increased prevalence of T2DM. However, the studies comprise too few incident cases to allow a firm evaluation if there is a threshold effect for the association between POPs and T2DM. It might seem paradoxical for a hypothesized association that the body burdens of most POPs have been declining in the general population over the past decades whereas the incidence and prevalence of T2DM have increased quite dramatically in most industrialized countries during the same time period. However, the critical time window in human life for POP exposure might be open a long time before the T2DM is diagnosed. Thus, to what extent POP exposure may have contributed to the T2DM epidemic in the general population ought to be tested in large prospective study.

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Effects on the thyroid hormone system

Table 1. Prevalence of diabetes mellitus (T2DM) in relation to tertiles of of lipid adjusted serum concentrations of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) and dichloro-diphenyl-dichloro-ethane (p,p'-DDE), among 184 Swedish fishermen's wives and 196 Swedish fishermen.

Exposure (ng/g lipid)	T2DM Yes/no	p for trend *
Male		
CB-153		
-290	0/64	
>290-475	4/61	0.005
>475	8/58	
p,p'-DDE		
-410	1/63	
>410-850	4/61	0.04
>850	7/60	
Female		
CB-153		
-180	3/57	
>180-290	4/57	0.94
>290	3/60	
p,p'-DDE		
-375	1/59	
>375-860	3/59	0.07
>860	6/56	

** Jonckheere-Terpstra's test

Table 2. Prevalence of type 2 diabetes mellitus (T2DM) in relation to quartiles of lipid adjusted serum concentrations of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) and dichloro-diphenyl-dichloro-ethane (p,p'-DDE), among 543 women from Sweden.

Exposure (ng/g lipid)	T2DM Yes/No	p for trend *
CB-153		
< 58	1/135	
> 58-84	0/136	
> 84-118	7/128	
> 118	7/129	0.004
p,p'-DDE		
< 91	0/136	
> 91-144	2/134	
> 144-240	5/130	
> 240	8/128	0.002

* Jonckheere-Terpstra's test