THE ASSOCIATION BETWEEN INTRAUTERINE EXPOSURE TO PERSISTENT ORGANOCHLORINE POLLUTANTS AND TYPE 1 DIABETES: A CASE-CONTROL STUDY

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ABSTRACT

It is of great importance to investigate suggested triggering factors for the risk of developing type 1 diabetes. The present study aimed to investigate the hypothesized association between persistent organochlorine pollutants (POP) and type 1 diabetes. It was performed as a case-control study within a biobank in Malmö, which is located in the Southern part of Sweden. The study included 150 cases (children who had developed type 1 diabetes) and 150 controls. As biomarkers for POP exposure we used 2,2',4,4',5,5'-heaxchlorobiphenyl (CB-153) and the major DDT metabolite 1,1-dichloro-2,2-bis (*p*-chlorophenyl)-ethylene (p,p'-DDE). The hypothesis that in utero exposure to POPs will trigger the risk for developing type 1 diabetes was not supported by the results from the current study. When comparing the quartile with the highest maternal serum concentrations of CB-153 with the other quartiles, an odds ratio (OR) of 0.73 (95% confidence interval [CI] 0.42, 1.27) was obtained. Similar results was obtained for p,p'-DDE (OR 0.56, 95% CI 0.29, 1.08).

INTRODUCTION

The incidence of type 1 diabetes in Europe is increasing at a rate of about 3 % per year and there is also an increasing incidence throughout the world.[1-4] During the last 20 years, the incidence of type 1 diabetes has increased with about 50 percent. Although that there is a genetic explanation to the disease, such an increase could not be explained only by so called "risk genes". It is reasonable to believe that environmental exposures may trigger the risk of developing type 1 diabetes. An environmental exposure that has been suggested as a triggering factor for developing childhood type 1 diabetes is persistent organochlorine pollutants (POPs), such as polychlorinated biphenyls (PCBs), dioxins and the pesticide DDT. There are circumstantial evidence supports that *in utero* exposure to dioxin-like compounds might act as a triggering factor for developing childhood type 1 diabetes. It is the overall objective of this study to assess possible impacts of *in utero* exposure to POPs on type 1 diabetes.

MATERIAL AND METHODS

Study population and design

The vast majority of the deliveries in the city of Malmö, located in the southern part of Sweden with 270.000 inhabitants, take place in the Department of Obstetrics at Malmö University Hospital. Child births at neighboring cities or at home is very rare. Since 1970, venous blood samples from mothers and umbilical cord blood samples from the children have been collected from the majority of delivering women and their children. These samples from approximately 70,000 deliveries have been stored in a freezer at –20 C° and the biobank comprised the study population for the current case-control study.[5]

Cases

Among the children from the study population, born from February 1970 to December 1990, 150 have (82 boys and 68 girls) developed type 1 diabetes before calendar year 2002 (cases). The median age at diagnoses was 11 years (range 1.9 – 27)

Controls

For each case, a non-diabetic offspring from the study population, matched for gender and date of birth (with the exception for two controls the differences were ±9 months), was selected as a control.

Biomarkers of exposure
In the present study 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) and the major DDT metabolite 1,1-dichloro-2,2-bis (*p*-chlorophenyl)-ethylene (p,p'-DDE) has been used as a biomarker for PCB exposure.

Statistical analyses
The association between the absolute levels of maternal POP concentrations and the risk to develop type 1 diabetes was evaluated by conditional logistic regression (EGRET), given odds ratios (OR) as the risk measure with 95% confidence intervals (CI). The exposure variables (CB-153 and p,p'-DDE) were categorized into quartiles based on the distributions among the controls. The lowest exposure categories were handled as the reference categories.

RESULTS

Exposure levels
The median maternal serum concentrations of CB-153 were 2.4 ng/mL (range 0.1, 11.4) among the cases and 2.6 ng/mL (0.2, 7.2) among the controls. The corresponding figures for p,p'-DDE were 9.2 ng/mL (range 0.5, 79) and 9.6 ng/mL (0.9, 129), respectively.

CB-153 and type 1 diabetes
When comparing the group with the highest maternal serum concentrations of CB-153 with the group with the lowest concentrations, an OR of 0.64 (95% CI 0.32, 1.29) was obtained (Table). The upper three exposure quartiles did all give ORs below unit, although not statistically significant, when they were compared with the lowest exposure quartile. When the upper three exposure quartiles were collapsed into one group, which was compared to the lowest exposure quartile, an OR of 0.73 (95% CI 0.42, 1.27) was obtained.

p,p'-DDE and type 1 diabetes
As was observed for CB-153, the upper three exposure quartiles did all give ORs below unit when they were compared with the lowest exposure quartiles (Table). When the upper three exposure quartiles were collapsed into one group, which was compared to the lowest exposure quartile, an OR of 0.56 (95% CI 0.29, 1.08) was obtained, corresponding to a p-value of 0.08.

Table. Associations between maternal serum levels of PCB-153 and p,p'-DDE, respectively, and the risk for developing type 1 diabetes among their infants. Odds ratios (OR) and 95% confidence intervals (CI) were obtained from conditional logistic regressions.

	Cases	Controls	OR	95% CI
PCB-153 (ng/mL)				
<1.9 (ref)	47	39	1.00	-
1.9 – 2.6	39	36	0.85	0.45, 1.63
2.7 – 3.4	33	38	0.67	0.35, 1.31
>3.4	31	37	0.64	0.32, 1.29
p,p'-DDE (ng/mL)				
<5.8 (ref)	47	36	1.00	-
5.8 – 9.6	36	40	0.58	0.28, 1.20
9.7 – 16.8	28	37	0.51	0.24, 1.07
>16.8	39	37	0.64	0.28, 1.46

DISCUSSION
The hypothesis that in utero exposure to POPs will trigger the risk for developing type 1 diabetes was not supported by the results from the current study. The risk estimates do, although not statistically significant, actually went in the opposite direction. It is, however, not reasonable to believe that POPs should protect against type 1 diabetes. Thus one might speculate that CB-153 as well as p,p'-DDE might act as an indicator for some

other exposure. In Sweden, an important source for POPs is through high intake of fatty fish from the Baltic Sea. High intake of such fish does also result in a high intake of polyunsaturated fatty acids, which has been supposed to protect against the risk of developing type 1 diabetes.[6] Whether that is the case in the present study remains unknown.

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