Parkinson’s disease among Inuit in Greenland: organochlorines as risk factors

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ABSTRACT

Objectives. In the present study we investigate organochlorines as possible risk factors for Parkinson’s disease (PD) in an arctic population. This has never been done before. Study design. Case-control study of Inuit in Greenland. Materials and methods. Plasma from 31 PD (20 males and 11 females) (mean age 69 yr) and 122 controls (57 males and 65 females) (mean age 61 yr) was analysed for 31 PCBs and pesticides by dual-column GC-ECD and GC-NCl/MS. Results. Plasma concentrations of PCBs and pesticides were markedly increased in both PD and controls. The concentrations did not differ between the PD cases and controls. However, the mean DDE concentration was higher in PD than in controls (42.1 and 15.0 µg/l, respectively, and with a wide range among the PD cases). The difference was significant for log transformed DDE values after control for age and sex (p= 0.005). Conclusion. A few epidemiological studies indicate a possible connection between exposure to pesticides and PD. The idea that exposure to organochlorines may be an important risk factor for PD among the Inuit in Greenland requires more investigations.

Keywords: Parkinson’s disease, Inuit, organochlorines, case-control study

INTRODUCTION

Parkinson’s disease (PD) was described for the first time in 1817 by James Parkinson, but the diagnosis is still clinical. It is the second most common neurodegenerative disorder with a prevalence of 100-150 per 100,000 in Caucasians. The male:female ratio reveals a slight male preponderance.

The aetiology is unknown. Pathogenesis/pathophysiology: Using neuropathology as the "gold standard", only 76 out of 100 patients with the clinical diagnosis of PD were diagnosed correctly (1). The degeneration of dopaminergic neurons in the substantia nigra results in a loss of dopaminergic input to the striatum. Neurotoxins like 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) cause mitochondrial dysfunction and this in turn will mean an increase in free radicals, neuronal death and accumulation of defect α-synuclein, a protein found in dopaminergic neurons (2, 3). Malfunction of α-synuclein which is thought to play a role in normal dopamine vesicle function...
and gives rise to increased dopamine in cytoplasm, which means more free radicals (Figure 1) (3,4).

The only risk factor neurologists agree on is age. Possible risk factors are organochlorines (5), MPTP (2), work in agriculture and horticulture (5), living in rural areas, well water and heavy metals (6) as well as polymorphisms in enzymes metabolising neurotoxins (7). It has recently been shown in the Norwegian population that persons with the tau H1 haplotype have an increased risk of PD (8) and in a study from Iceland a susceptibility gene for PD has been found (9).

The background for our study was an investigation showing a high prevalence of idiopathic PD in the Faroe Islands compared to the island of Als in Denmark (10) as well as high blood values of pesticides in the population of the Faroe islands (11). Furthermore, the prevalence of PD among the Inuit in Greenland is almost twice the prevalence of PD on the island of Als (12). Finally, the Arctic has for decades been contaminated by polychlorinated biphenyls (PCBs) and organochlorinated pesticides with accumulation in the marine food chain. The indigenous population with its high consumption of marine animals is therefore highly exposed to these contaminants. As a result, exceptionally high blood concentrations of several organochlorines have been found among the Inuit of Greenland (13).

The objective of the present study was to investigate organochlorines as possible risk factors for PD in an arctic population.

**MATERIALS AND METHODS**

Study design: case-control study of Inuit in Greenland.

Plasma from 31 PD cases (20 males and 11 females) (mean age 69 yr) and 122 controls (57 males and 65 females) (mean age 61 yr) was analysed for 31 PCBs and pesticides, including toxaphenes, and their metabolites by dual-column gas chromatography with dual electron-capture detection or gas chromatography with negative chemical ionisation mass spectrometry. The quantitation was performed using the method developed by the laboratory of the Centre de Toxicologie du Québec, Québec, Canada. Non-parametric statistics (Mann-Whitney test) and general linear models of log transformed DDE values were applied using SPSS version 12.0.

**RESULTS**

There were almost twice as many male as female cases, with a male:female ratio of 1.8. Plasma concentrations of PCBs and pesticides were markedly increased in both PD cases and controls in comparison with European and North American general populations. The concentrations did not differ between the PD cases and the controls except for DDE. The mean DDE concentration was higher in PD (42.1 µg/l; range 0.3-273; s.d. 63) than in controls (15.0 µg/l; range 0.8-43; s.d. 8.2). The distribution of DDE was highly skewed and comparisons were performed accordingly using non-parametric statistics in addition to analyses of log transformed DDE values to approach a normal distribution. Using the Mann-Whitney test the difference between cases and controls was barely significant (p=0.06) without adjustment for confounders. In a general linear model of log transformed DDE concentrations with age and sex as confounders, the difference was statistically significant (p=0.005). A closer look at the distribution of DDE concentrations revealed that all individuals with very high DDE concentrations (=>50 µg/l) were PD cases. If these were excluded from the analyses there was no difference between cases and controls.

**DISCUSSION**

Organochlorines are found in the lipid phase of tissues, including the brain. Some of them are metabolised in humans, e.g. DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethylene). One of its metabolites, DDE (1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene), comes exclusively from ingested food and has a half-life of many years. Organochlorines are generally only excreted to a small extent. A dose-response relation regarding their harmfulness has never been shown in
humans, but all of them should be considered injurious. In 2000 Tüchsen and Jensen (5) published the first cohort investigation showing that working in agriculture and horticulture may be associated with a high risk of PD. Our study is the first that deals with the possible connection between PD and organochlorines in an Inuit population. The neurotoxin MPTP is known to be capable of causing parkinsonism. The chemical structure of some of the pesticides is very alike that of MPTP, which together with the results of the cohort study (5) and animal studies points to pesticides as being one of the possible triggers for PD, maybe in some cases on a susceptible genetic background (8, 9). The prevalence of PD among the Inuit is twice that found in the island of Als, Denmark. Our hypothesis that exposure to organochlorines may be an important risk factor for Parkinson’s disease among the Inuit in Greenland requires more investigations, which are in progress.

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