Persistent Organic Pollutants and Endometriosis Risk

Project Scope

Endometriosis, a chronic disease affecting approximately 5 percent of U.S. reproductive-aged women, causes chronic pelvic pain, dysmenorrhea, and infertility. Some recent epidemiologic studies suggest that endocrine-disrupting chemicals in the environment may increase endometriosis risk, presumably through estrogenic mechanisms. Other studies, however, have failed to confirm this relationship. Thus, the investigators conducted this study to examine the relationship between endometriosis and exposure to organochlorine compounds and polychlorinated biphenyls (PCBs, potential endocrine disruptors) in a large health maintenance organization (HMO) population. An additional question of interest was whether these associations are modified by polymorphisms in genes involved in estrogen metabolism.

The specific objectives of the study were to determine whether:

- The risk of endometriosis in the study population is associated with serum levels of 14 organochlorine pesticides, or urine levels of the pesticide methoxychlor
- The risk of endometriosis is associated with serum levels of total PCBs and 35 individual PCB congeners
- The risk of endometriosis resulting from organochlorine pesticide or PCB exposure differs among women with differing CYP1A1, CYP1A2, COMT, and GSTM1 genotypes
- The risk of endometriosis resulting from organochlorine pesticide or PCB exposure differs among women with differing levels of other exposures affecting estrogen levels

Grant Title and Principal Investigator

Persistent Organic Pollutants and Endometriosis Risk

Victoria Holt – Fred Hutchinson Cancer Research Center

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Key Findings

- The purpose of the study was to investigate the relationship between endometriosis and exposure to organochlorine compounds (including the pesticide methoxychlor) and polychlorinated biphenyls in a large population-based study, and determine whether these associations are modified by polymorphisms in genes involved in chemical detoxification and estrogen metabolism.
- Analyses of blood and urine samples for PCBs, pesticides, and metabolites, as well as genotyping of subjects for GSTM1 and COMT polymorphisms, are ongoing.
- No association has been found between self-reported exposure to all pesticides combined and endometriosis risk (Odds Ratio [OR]=0.96, 95% Confidence Interval [CI]=0.70-1.33); however, exposure to herbicides and fungicides appeared to increase disease risk.
- There was little apparent modification of these risks by the genetic polymorphisms so far evaluated.
- The effect of serum levels of several organic pollutants on endometriosis risk will be evaluated.
- The results of this study will indicate whether exposure to organochlorine compounds and polychlorinated biphenyls increases endometriosis risk and whether the risk is modified by genetic polymorphisms.

Project Period: March 2002 to March 2004

The study funded under this grant is part of a larger case-control study on the risk factors for endometriosis, sponsored by the National Institute of Child Health and Human Development, that was conducted within a large Washington State HMO. The study provided extensive interview data on a variety of subject characteristics, including occupational and nonoccupational chemical exposures. Results of laboratory analyses of two polymorphic genes (GSTM1 and COMT) involved in the metabolism of environmental

toxins and estrogens are available for 295 cases and 581 controls from that study, and the research under the STAR grant involved the genotype determination of two polymorphic cytochrome p450 genes (1A1 and 1A2) in these subjects as well.

Relevance to ORD's Multi-Year Research Plan

This research contributes directly to Long Term Goal 2, identified in ORD's Multi-Year Plan, which is to determine the extent of the impact of endocrine disrupters on humans, wildlife, and the environment. This study improves our understanding of relationship between endometriosis and exposure to organochlorine compounds and polychlorinated biphenyls in a large health maintenance organization (HMO) population. No evidence was found the genetic variations in metabolic enzymes affected the association between chemical exposures and endometriosis risk.

Project Results and Implications

The final results of research under this grant have not yet been published, Initial findings from the interview data on pesticide exposures indicate no association between self-reported exposure to all pesticides combined and endometriosis risk (Odds Ratio [OR]=0.96, 95% Confidence Interval [CI]=0.70-1.33). However, exposure to herbicides and fungicides appeared to increase disease risk. Specifically, any (occupational or nonoccupational) exposures to herbicides was associated with a significant increase in endometriosis risk (OR=1.65; 95% CI=1.03-2.64). A stronger risk elevation was observed when occupational herbicide exposure was evaluated separately (OR=2.87, 95% CI=0.98-8.40), but the association was not significant at p = 0.05, owing to the relatively small number of subjects with occupational exposures. Similarly, any self-reported exposure to fungicides was associated with more than a doubling of risk of endometriosis (OR=2.15; 95% CI=0.99-4.70), and there was a stronger risk elevation with occupational fungicide exposure (OR=2.80, 95% CI=0.95-8.23). No statistically significant relationships were found between these risks and any genetic polymorphisms.

At the time this summary was written, investigators were determining lipid-adjusted serum levels of total polychlorinated biphenyls (PCBs), PCB congeners, hexachlorobenzene, β-hexachlorocyclohexane (β-HCH), λ-HCH, aldrin, hepachlor epoxide, oxychlordane, transnonachlor, p,p'-dichlorodiphenyl dichloroethylene (p,p'-DDE), o,p'-DDE, dieldrin, endrin, o,p'-dichlorodiphenyl trichloroethane (o,p'-DDT), p,p'-DDT, and mirex residues from 283 cases (women with endometriosis) and 581 controls. In addition, 450 urine samples (150 cases and 300 controls) will be tested for levels of the methoxychlor metabolite 2,2-bis-(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE). The results of these analyses will be used to evaluate the relationships between organochlorine exposures, genetic polymorphisms, and endometriosis risk.

Investigators

Victoria Holt – Fred Hutchinson Cancer Research Center, Washington

For More Information

NCER Project Abstract and Reports:

http://cfpub2.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.abstractDetail/abstract/2361/report/0