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Original Article

Association of organochlorine pesticides and risk of epithelial ovarian cancer: A case control study

Tusha Sharma [a], *Basu Dev Banerjee* [a,*], *Darshana Mazumdar* [b], *Vipin Tyagi* [a], *Gaurav Thakur* [a], *Kiran Guleria* [b], *Rafat S. Ahmed* [a], *Ashok Kumar Tripathi* [a]

[a] *Environmental Biochemistry and Molecular Biology Laboratory, Department of Biochemistry, University College of Medical Sciences (University of Delhi) and GTB Hospital, Dilshad Garden, Delhi 110095, India*

[b] *Department of Obst. and Gynecology, University College of Medical Sciences (University of Delhi) and GTB Hospital, Dilshad Garden, Delhi 110095, India*

ARTICLE INFO

Article history:
Received 3 November 2014
Accepted 23 January 2015
Available online 7 February 2015

Keywords:
Ovarian cancer
Risk assessment
Environmental toxins
Organochlorine pesticide

ABSTRACT

Background/aims: Organochlorine pesticides (OCPs) belongs to the class of hydrocarbons characterize by its cyclic structure. Due to their persistence nature OCP gets accumulated in the food chain and cause possible adverse health effects specifically various hormone mediated disorders. Ovarian cancer is also one of the hormone dependant cancer and begins with the transformation of cells that comprises the ovaries including surface epithelial, germ cells, etc. It has been suggested that endocrine disruption, exposure to xenobiotic and subsequent oxidative stress may antedate ovarian cancer and contribute to its pathogenesis. However, no report regarding any association of OCP level with etiology of epithelial ovarian cancer is so far available among North Indian population.

Methods: A total of 120 subjects were included in this case control study, consisting of 60 histological proven cases of epithelial ovarian cancer and 60 controls subjects. Quantification of OCP levels was done by Perkin Elmer Gas Chromatograph (GC) equipped with 63Ni selective Electron Capture Detector.

Results: Levels of β-HCH, endosulfan I, p'p'-DDT, p'p'-DDE and heptachlor were found significantly high in cases of epithelial ovarian cancer as compare to control. A significant association was also observed between higher levels of β-HCH and heptachlor and EOC with odds ratio of 2.76 and 2.97 respectively.

Conclusion: Results indicate the plausible role of OCPs with the pathogenesis of epithelial ovarian cancer among north Indian population. Moreover, it is one of the first report suggesting significant level of heptachlor among north Indian women population with epithelial ovarian cancer.

* *Corresponding author*. Environmental Biochemistry and Molecular Biology Laboratory, Department of Biochemistry, University College of Medical Sciences (University of Delhi) and GTB Hospital, Dilshad Garden, Delhi 110095, India.
E-mail address: banerjeebd@hotmail.com (B.D. Banerjee).

http://dx.doi.org/10.1016/j.jrhm.2015.01.006

1. Introduction

Organochlorine pesticides (OCPs) belongs to the class of hydrocarbons characterize by their cyclic structure. In Indian scenario these compounds are widely used for pest control in agriculture and public health program. Due to their persistence nature OCP gets accumulated in the food chain and causes possible adverse health effects specifically hormone mediated disorders like reproductive health including preterm birth, Intra uterine growth retardation, birth defect like hypospadias, cancer.[1–5] Experimental studies suggest that a number of OCP demonstrate weak estrogenic or antiestrogenic effects.[6] These chemicals may interfere with the functioning of endocrine system by mimicking hormone, blocking the effects of normal endogenous hormone or may alter/modify the synthesis, metabolism/transport of hormones.[6] The U.S. Environmental Protection Agency restricted and banned the use of most of OCPs during the 1970s and 1980s. However, some OCP continue to be used in some developing countries including India for vector control and health programs and the significant levels of various pesticides has also been observed in fresh water sediment of most populated and intensive used rivers in India.[7,8] Thus, the health effects of OCP exposure remain an important global public health concern as xenoestrogen.

It is believed that these compounds may act as a tumor promoter through hormone mediated effects or may act as endocrine disruptors. Epidemiological studies have also linked OCP with various hormone mediated cancer like prostate,[5] testicular, breast and endometrial cancer[9–11] but there is scarcity of information about ovarian cancer among Indian or other population with reference to organochlorine pesticides exposure. Ovarian cancer is also one of the hormone dependant cancer and begins with the transformation of cells that comprises the ovaries including surface epithelial cells, germ cells & the sex cord or stromal cells. The surface epithelial cells are purported to be the primary locus for ovarian cancer with almost 90% of all ovarian cancer thought to be derived from the simple epithelium. Epithelial ovarian cancer contributes to a large portion of mortality and morbidity among all cancer occurring in women. It has been suggested that endocrine disruption, genetic predisposition, altered immune surveillance, inflammation, exposure to xenobiotic and subsequent oxidative stress may antedate ovarian cancer and contribute to its pathogenesis. However, no report regarding any association of OCP level with etiology of epithelial ovarian cancer is so far available among North Indian population. Hence, this study has been carried out to identify the possible association of OCP with the incidence of epithelial ovarian cancer.

2. Material & method

2.1. Study population

A total of 120 subjects were included in this case control study, consisting of 60 histological proven cases of epithelial ovarian cancer and 60 controls subjects. Controls were randomly selected attending the outpatient clinics of obstetrics and gynecology department with non specific complaints such as vaginal discharge with or without other minor illness like cold, cough and fever with similar age group on the basis of their consent for participation under this study. Normal bilateral ovaries were confirmed on trans-vaginal ultrasonography before consider as healthy control. Subjects of carcinoma ovary were included on the basis of clinical examination, imaging and confirmed by cytological or histopathological examination. Women with other type of ovarian cancer (which were not epithelial in origin like germ cells or stromal cells) or other illness like deranged liver function, diabetes, etc. were excluded from the study because a positive association has been observed with higher levels of OCPs and these diseases in this laboratory as a part of our ongoing research (unpublished data). Women who were using talcum powder and tobacco were excluded from both the study as these may be possible etiological agent for epithelial ovarian cancer. Further, with known occupational exposure to pesticide such as agriculture field, industrial worker, involve in any vector control program who are at risk of having any chemical and metal exposure were excluded from both the study group. This study was performed at the Department of Biochemistry, Department of obstetrics and gynecology, University College of Medical Sciences (University of Delhi) and Guru Teg Bahadur Hospital, New Delhi, India. Necessary ethical clearance was obtained from the Institutional Ethical Committee for Human Research. A written informed consent was obtained from each subject prior to their inclusion in the study as per ethics norms. Information regarding age and relevant clinical information were obtained as per pre-designed questionnaire. A total of 1 ml peripheral blood was collected in EDTA vial and used for OCP residues extraction and quantification.

2.2. OCPs residue extraction and quantification

HPLC-grade solvents were used and checked for any contamination before extraction. OCPs extraction was done using hexane and acetone (2:1) according to earlier published method from this laboratory.[5] Blood (1 mL) was taken in a 50 mL conical flask. Hexane (6 mL) and acetone (3 mL) were added and the contents were shaken at room temp for 30 min in a mechanical shaker. The extract was centrifuged for 10 min at 2000 rpm and clear top layer of hexane was collected. The remaining portion was again extracted twice using same process and the newly extracted hexane layer was added to the previous solvent fractions. Clean up of the samples was done by column chromatography following USEPA method 3620B. Elute was collected in a 100 mL beaker and evaporated to concentrate the sample and redissolved in hexane for further analysis. Flow diagram has been provided as Fig. 1.

Quantification of OCP levels was done by Perkin Elmer Gas Chromatograph (GC) equipped with 63Ni selective Electron Capture Detector. The column used was Elite-GC DB-5, 60 m and 0.25 mm ID. The carrier and makeup gas was nitrogen with a flow rate of 2 mL min^{-1} and 35 mL min^{-1}, respectively, employing the split less mode. Final extract (1 lL) was injected at a temperature of 170 °C with a hold time of 1 min. The temperature was raised from 170 °C to 225 °C at a rate of 5 °C