IJISET - International Journal of Innovative Science, Engineering & Technology, Vol. 10 Issue 01, January 2023
ISSN (Online) 2348 – 7968 | Impact Factor – 6.72
www.ijiset.com

Endocrine Disrupting Chemicals and Development of Ovarian Cancer

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Abstract

Endocrine-Disrupting Chemicals are exogenous chemical compounds ubiquitously found in everyday life of the modern world. Many common organic pollutants function as endocrine disruptors in human and animals, interfering with the interference of sex hormone signaling and reproductive function. These exogenous chemical compounds enter the human body and acts as endogenous hormones viz. BPA mimics the actions of estrogen on multiple levels by activating estrogen receptors. Presence of detectable levels of polychlorinated biphenyls, pesticides, phthalates and other toxicants in women is strongly correlated with incidence of ovarian cancer which cancer is the most frequent female gender related neoplasm whose growth mostly depends on estrogen. It is group of disease that develop in the ovaries or in the fallopian tubes and the peritoneum. In the present review we aim to point out disruptions in ovarian processes caused by EDCs that may originate adverse outcomes such as steroidogenesis, epigenetic modifications, infertility, cell proliferation, uterine wall destruction and over all ovarian cancer by these exogenous chemicals.

Keywords: Endocrine-Disrupting Chemicals, EDCs, Ovarian cancer, exogenous chemical compounds, Organic pollutants

1. Introduction

Endocrine disrupting chemicals, a heterogeneous group of exogenous chemicals that can interfere with any aspect of endogenous hormones, represent an emerging global threat for human metabolism. Endocrine disrupting chemicals (EDCs), natural or synthetic, mimic, enhance, or inhibit endogenous hormones. One such process is female reproductive function, the major reproductive organ being the ovary. Production of steroid hormones by the ovary plays a key role in the female phenotype maintenance, as well as is critical for regular ovarian processes, including follicle growth, oocyte maturation and ovulation. The scientific studies report that ovarian steroid hormone production is being recognized as an important target for the action of endocrine disrupting chemicals (EDCs). Disruptions in ovarian processes by EDCs can lead to adverse outcomes such as anovulation, infertility, estrogen deficiency, and premature ovarian failure among others.The impact during critical development windows promote the disruption of individual or multiple systems involved in metabolism via

epigenetic changes. These changes can permanently alter the epigenome in the germline, enabling changes to be transmitted to the subsequent generations [1]. Further, exposure to insecticides leads to reproductive incapacitation primarily through disturbances in ovarian physiology. Disturbed ovarian activities encompass the alterations in hormone synthesis, follicular maturation, ovulation process, and ovarian cycle, which eventually lead to decline in fertility, prolonged time-to-conceive, spontaneous abortion, stillbirths, and developmental defects. Insecticide-induced ovarian toxicity is effectuated by endocrine disruption and oxidative stress, which occurs due to suppression of antioxidant defence system, upsurge of reactive oxygen and nitrogen species, potentiates DNA damage and expression of apoptotic and inflammatory markers. Apart from this, persistent industrialization of modern society has raised increasing concern over the impact of industrial byproducts as common use of such pollutants function as endocrine disrupting chemicals in humans and animals, as they interfere with sex hormone signaling and reproductive function [2]. Further, exposure to endocrine disrupting chemicals in the form of pesticides, fungicides, herbicides, plasticizers, cosmetics, etc. and their ability to cause epigenetic modifications has hypothesized their catalytic role in ovarian cancer progression. The fact that these chemicals have been detected in the biological samples of general population, and even directly in the follicular fluid of women, emphasizes the demands for testing the influence of EDCs on ovarian steroidogenesis. Moreover, animal models have demonstrated disturbances in the development of ovaries and steroid hormonal levels in response to such synthetic chemicals [3]. The present review is an attempt to address the Impact of endocrine disruptive chemicals on the development of ovarian cancer cells.

2. EDC’S and Ovarian cancer.

Concerning the impact of endocrine disrupting substances on ovarian and other cancers, a large number of reports and studies have been compiled (4).The authors examined whether EDCs act as estrogen mimics, interfere with apoptosis, change cell signalling pathways, or impact estrogen metabolism while reviewing the potential targets of EDCs within the ovary. They concluded that despite the controversy surrounding the study of EDCs, it is crucial to do so because human society continues to release significant amounts of industrial chemicals into the environment. By understanding how these chemicals work, we may be able to treat any potential negative effects. They also emphasized that investigating how EDCs affect the ovary may result in unanticipated discoveries regarding ovarian function and dysfunction. Finally, the authors stated that comprehending the science behind endocrine disruption.

Endocrine disruptors' impact on ovarian function, as well as their effects on metabolism, nuclear receptor signaling, and steroidogenesis [5]. The effects of EDCs on ovarian function and describes how these alter hormone availability or alter the binding and activity of the hormone at the receptor level to interfere with hormone signaling via two mechanisms. The study includes reports on the endocrine-disrupting potential of various pesticides, including dichlorodiphenyltrichloroethane and methoxychlor, plasticizers, including bisphenol A and phthalates, dioxins, polychlorinated biphenyls, and polycyclic aromatic hydrocarbons, including benzo[a]pyrene, as well as other chemicals.

The effect of di-n-butyl phthalate and hexabromocyclododecane, the growth and promotion of BG-1 ovarian cancer cells via upregulation of the cyclin D and cyclin-dependent kinase-4 gene. Treatment with di-n-butyl phthalate(DBP) or Hexabromocyclodecane (HBCD) resulted in increased cell proliferation of BG-1 cells as observed with 17-β estradiol (E2) and both, DBP and HBCD, upregulated the expression levels of cell cycle-regulatory genes. However, the expression of the p21 gene was not altered by DBP or HBCD [3]. The results suggest that DBP and HBCD are EDCs have apparent estrogenic activities by stimulating the cell proliferation of BG-1 cells and by inducing the expression of cyclin D and cdk 4 and DBP and HBCD have sufficient potency to disrupt the endocrine system and to stimulate cell growth in ER-positive cancer cells.

Production of steroid hormones by the ovary plays key role in the female maintenance, as well as is critical for the regular ovarian processes, including follicle growth, requisite for the female reproductive health. The effects of selected EDCs i.e. pesticides, phthalate and phenol derivatives, and halogenated arylhydrocarbons on the processes of ovarian steroidogenesis [6].

Chemicals that disrupt the endocrine system can stimulate the growth of ovarian cancer cells through the ER.The chemokine CXCL12 (C-X-C motif fector 1)Signaling Axis for CXCR4 (C-X-C Chemokine Receptor type 4). According to the reports, "endocrine disrupting chemicals" (EDCs) exhibit mitogenic activities in ovarian cancer cells by triggering the ER and upregulating CXCL12 expression. Genestein, bisphenol A, and HPTE are EDCs that act similarly to estradiol in that they promote both cell proliferation and the induction of CXCL12 mRNA and protein. The ER antagonist ICI 182,780 completely reversed the effects, proving that the observed effects of these drugs were receptor-mediated. Moreover, the results suggest that the ER-CXCL12-CXCR4 signalling axis may represent a promising target for development of therapeutics for ER+ ovarian cancer.

Analysis of the impact of industrial groups and pollutant substances, as well as the relative risk of ovarian cancer mortality and death in areas around installations. Excess ovarian cancer mortality was found near all industries put together, but particularly near refineries, fertilizer plants, glass and paper production facilities, the food and beverage industry, waste treatment facilities, the pharmaceutical industry, and ceramics factories [7]. Installations releasing metals and polycyclic aromatic chemicals were also found to be associated statistically. The survey's findings suggest that living close to an industrial area may increase one's risk of developing ovarian cancer and dying from it.

Endocrine-Disrupting Chemicals cause Epigenetic Modifications in Ovarian Cancer. Endocrine disruptors do have a potential carcinogenicity and their high proportions in human body may cause epigenetic modifications, prompting ovarian surface epithelium to grow in an abnormal manner [8].

Different risk factors, both genetic and environmental, that could lead to the development of ovarian cancer. This highlights various factors that can trigger the development of ovarian cancer viz.TP53, BRCA genes, cigarette smoke and talc powder and how they are able to

promote ovarian cancer [9]. This may prove useful in devising a better screening, treatment and preventive measure towards the ovarian cancer and an exciting opportunity to advance knowledge of ovarian cancer to efficiently aid medical practitioners and researchers to device better prevention and treatment plan to combat ovarian cancer.

The effects of a mixture of endocrine-disrupting chemicals (EDCs) which are persistent hormonally active environmental toxicants present in ovarian follicular fluid (FF) on secretion of(insulin-like growth factor 1) IGF1 by COV434 and KGN cells used as in vitro models of juvenile and adult GCTs, respectively.

The EDC mixture under investigation contained polychlorinated biphenyl 153, perfluorooctanoate, perfluorooctanesulfonate, 2,2-dichlorodiphenyldichloroethylene, and hexachlorobenzene.It was discovered that treating KGN cells with the EDC combination as well as with the individual test compounds significantly increased IGF1 secretion. Additionally, after exposure to the EDC mixtures, KGN cells' IGFBP3 gene expression decreases. This effect involves the estrogen receptor alpha pathway. The EDC mixture also increased the proliferation of HGrC1 human non-cancer granulosa cells when it was added to the conditioned medium of KGN cells [10]. The results indicate that the mixture of EDCs found in FF increases secretion of IGF1 by KGN cells and thus indirectly contributes to progression of adult GCTs, and increases proliferation of non-cancer granulosa cells.

By activating the estrogen receptors and, the synthetic plastic bisphenol, which is based on carbon and is used to make cans, reusable water bottles, and medical equipment, mimics the effects of estrogen on various levels. BPA controls a number of processes, including cell migration, apoptosis, and proliferation, which results in neoplastic changes. It carries out these functions by activating a number of oncogenic signaling pathways, including the STAT3, PI3K/AKT, and MAPK pathways. BPA has also been linked to preneoplastic lesions, as well as benign lesions like endometrial hyperplasia, the development of ovarian cysts, an increase in the ductal density of mammary gland cells, and other modifications of the reproductive system in both males and females [11]. Breast or ovarian cancer could continue to develop from the benign lesions.

The detrimental effects of insecticides on female reproductive efficiency and ovarian function. Due to disruptions in ovarian physiology, insecticide exposure in females impairs their ability to reproduce. Endocrine disruption and oxidative stress contribute to the toxic effects of insecticides on ovarian tissue [12]. Endocrines of oogenesis and the potential effects of EDCs on various intra-ovarian entities, including gonadotropin action, steroidogenic potential, growth factor expression, and maturational competence modulation(13). A further topic of discussion is the relative significance of free radical-induced stress, inflammation, and elevated cell death in the regulation of ovarian functions and how they affect a female's ability to reproduce.

A possible human carcinogen's dietary intake of acrylamide and the risk of developing breast, endometrial, and ovarian cancer. In non-experimental studies, a dose-response meta-analysis was done to determine the relationship between estimated dietary intake of acrylamide and risk of female breast, endometrial, and ovarian cancers. Particularly among non-smokers,

consumption of acrylamide was found to be slightly associated with an increased risk of ovarian cancer. While the association was more linear and positive among never smokers, the risk of endometrial cancer was highest at intermediate levels of exposure [14].

The frequent use of straighteners/relaxers or pressing products in the past year to be associated with an increased risk of ovarian cancer. Ever use of permanent hair dye was positively associated with non-serous but inversely associated with serous. Many findings suggested that frequent use of hair straighteners/relaxers or pressing products, which are primarily used by African American/Black women, and possibly permanent hair dye, may be associated with the occurrence of ovarian cancers [15].

3. Conclusion

Reproductive health has become a major global concern as a result of the current lifestyle and growing urbanization, which has led to exposure to a wide range of environmental toxins that have the potential to interfere with endogenous hormone-controlled reproductive processes. These endocrine-disrupting substances (EDCs) have the potential to seriously perturb ovarian homeostasis, resulting in problems like anovulation, infertility, estrogen deficiency, and early ovarian failure. The current review makes an effort to address the effects of EDCs on the hormonal system, their potential carcinogenicity, and their high concentration in the human body, which may result in epigenetic modification, mutations, and steridogenesis, causing cell surface epithelium to grow abnormally. Ovarian cancer cells grow primarily as a result of hormone-disrupting substances. In daily life, numerous harmful chemicals are consumed.

4. References

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