



Endocrine Disrupting Chemicals and Health Effects

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Abstract

Endocrine disrupting chemicals are compounds that change the normal functioning of the endocrine system in both humans and in natural life. These chemicals have been called endocrine disruptors because they are thought to mimic natural hormones, inhibit the action of hormones, or alter the normal regulatory function of the immune, nervous, and endocrine systems. Many chemicals are identified as endocrine disruptors, and people are exposed to these chemicals in the environment (via water, air, and soil) or through food. Although the effects of endocrine disruptors in natural life have been studied since 1940, it has been seen as a working area where we have heard its name quite a lot in recent years. Studies on the effects of endocrine disruptors on human and environmental health have become quite popular in recent years. In this article, it is aimed to introduce endocrine disruptive chemicals, their effects, mechanisms of action, possible risks and solutions on human and environmental health by using a comprehensive literature.

Key words: Endocrine disrupting Chemicals, Environmental Risks, Environmental Health

INTRODUCTION

An endocrine disrupting component is defined by the European Environmental Protection Agency (EPA) as an agent that prevents the synthesis, secretion, transport, binding or destruction of natural hormones in the body responsible for the protection of homeostasis, reproduction, development / or behavior. To make a simpler definition are chemicals or chemical mixtures that cause normal hormonal function deterioration in the body (Kavlock vd., 1996).

Endocrine disrupting chemicals can be classified in the following two ways (Diamanti-Kandarakesis et al., 2009):

(i) Natural Endocrine Inhibitors

• Natural chemicals in human and animal foods (eg phytoestrogens: genistein and coumestrol)

(ii) Synthesized

These can be grouped as follows:

• Synthetic chemicals used as industrial solvents and their by-products (eg polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), dioxins

• Plastics (eg bisphenol A (BPA))

• plasticizers

• Pesticides eg dichlorodiphenyltrichloroethane (DDT)

• fungicides (eg, vinclozolin) and

• Some pharmaceutical agents eg diethylstilbestrol (DES)

B. Endocrine disrupting chemicals can also be grouped according to their origin (Caliman and Gavrilescu, 2009):

(i) Natural and artificial hormones (eg, phyto-estrogens, 3-omegafatty acids, birth control pills and thyroid drugs).

(ii) Drugs with hormonal side effects (eg, naproxen, metoprolol and clofibrate).

(iii) Industrial and household chemicals (eg, phthalates, alkylphenolytoxylate detergents, fire retardants, plastyates, solvents, 1,4-dichloro-benzene and polychlorinated bisphenols (PCBs)).

(iv) By-products of industrial and domestic processes (eg polycyclic aromatic hydrocarbons (PAH), dioxins, pentachlorobenzene).

2. The role of the Endocrine disrupting chemicals in Environment

As mentioned earlier, we are constantly intertwined with

endocrine disrupting chemicals in our daily lives. According to the results obtained from various studies, endocrine disrupting chemicals exist in the air we breathe, in the water we drink and in the soil where grow the foods we eat. Some of the environmental pollutants are endocrine disruptors known as neuroendocrine disruptors, and they mimic or modulate the synthesis and metabolism of neuropeptides, neurotransmitters or neurohormones (Cristina et al., 2012). They cause various modifications of various physiological, behavioral, or hormonal processes, such as the reproductive, development, ability to deal with changes and many other abnormalities in the animal's body (Cristina et al., 2012). It is known that endocrine disruptors work by changing hormonal and homeostatic systems in living systems. These systems are of primary importance as they are involved in the regulation of metabolism, sexual development, insulin production and use, growth, stress response, sex behavior, reproduction and even in the development of fetal processes.

The wildlife is not exposed to pollutants individually, but is exposed to a complex mixture of endocrine disruptors. The way wildlife is exposed to endocrine disruptors is critical and important. Most endocrine disruptors are disturbed in the environment, for example by sunlight, bacteria and chemical processes, while others remain in the environment at different time intervals.

Due to sewage treatment process, urban and agricultural wastes and industrial wastes, waters and surface areas are continuously exposed to endocrine disrupting substances. In addition, the exposure can occur from oil tankers, ships, fuel extraction process, oil waste and many other sources. Although endocrine disrupting chemicals are not persistent in water for a long time, the continuous introduction of these chemicals into the aquatic environment causes the aquatic habitat to be in constant contact with endocrine disruptors (Kidd ve ark., 2012).

However, three sources can be considered as potential exposure sources for animal lives. The primary source of exposure should be considered a water source. Some endocrine disruptors have been found to be highly soluble in water and present in water at the level of ppt and ppb. Fish can take these pollutants from their gills, while wild

birds and mammals can take these pollutants with drinking water. Some endocrine disruptors can accumulate in organisms as they can be found due to soil and sediment, and these endocrine disruptors can enter a complex food chain network. Endocrine disruptors are also known to show high affinity to fats and have a tendency to accumulate in organisms. Therefore, they can reach to high-organizational creatures by way of food chain (Kidd *et al.*, 2012).

After exposure, endocrine disrupting chemicals circulate in the body and undergo metabolic and excretion procedures. Some endocrine disruptors accumulate in places where they are excreted from the body because they show high affinity to the adipose tissues. In the case of fish and birds, endocrine disrupting chemicals may be thrown from the body. The liver of animals is known as the place where endocrine disrupting chemicals are metabolized and then excreted in the feces or urinary tract (Kidd *et al.*, 2012).

There are different varieties of exposure to endocrine disrupting substances and spread all over the world. However, there are significant differences between countries in terms of the use of these substances. In some countries, the use of these substances is still prohibited in some countries.

Globally, endocrine disruptors are mainly steroid hormones, synthetic steroids, polychlorinated dibenzodioxines, biphenyls and etc. (Diamanti-Kandarakis *et al.*, 2009). As seen in previous studies, these chemicals appear to have significant toxicities in humans as well as in wild animals. However, alkylphenol ethoxylate, gonadotropin compounds, insecticide, etc. endocrine disruptors have not been discussed much in previous studies. These endocrine disruptors are either naturally produced or produced in industries depending on various applications (Endocrine Disruptors, 2001).

Many of these endocrine disruptors might end up in the aquatic environment and make water a potential source of EDCs. The reasons are may be incomplete removal of the contaminants during sewage treatment processes, soil run off or indiscriminate discharges of them into the waterways (Veerasingam and Ali, 2013). Some water treatment systems, such as agglomeration, precipitation, filtration and chlorination, can not remove or remove these contaminants from the water (Westerhoff *et al.*, 2005; Gibs *et al.*, 2007; Kim *et al.*, 2007; Schenck *et al.*). When endocrine disrupting chemicals are released to water sources such as lakes and rivers, it can be seen that even if present in low concentrations, they may cause toxic effects on the environment.

Wastewater from pharmaceuticals and other industries can be a major source of exposure due to potential adverse effects on the environment (Stumm-Zollinger and Fair, 1965). They may contain natural human hormones, hormones from pharmaceutical products such as birth control pills, and potential endocrine disruptive chemicals derived from different detergents, soaps, plastics, food and personal care products. Industries can also be considered as a potential source of endocrine disruptors. Products such as pesticides containing DDT, bisphenol A and plastic products containing phthalates, and personal care products containing antimicrobials are regularly produced in industry (Gore *et al.*, 2014).

In addition to water and industrial resources, agriculture and animal husbandry can act as a very important source of endocrine disrupting chemicals. Sex steroids such as estradiol, progesterone and testosterone, which are defined as endocrine disruptors, have growth-enhancing effects in humans and animals. As a result, these chemicals have been used for many years in agricultural practice. It is known that it is used to regulate weight gain in animal breeding and to increase nutritional efficiency. However, these chemicals have dangerous effects on the environment because hundreds of animals can live in an area and result in

high concentrations of these chemicals to the environment. However, EPA researchers have documented that chemical mixtures in some wastewater may cause infirmation of fish populations under treatment plants (Kim *et al.*, 2005).

Evidence from different studies has shown that industrial endocrine disruptors have a significant impact on the environmental health and urgent measures should be taken to correct this situation.

2. Adverse Effects of Endocrine Disruptors on Human Health

From a physiological perspective, an endocrine-disrupting substance is a compound, either natural or synthetic, which, through environmental or inappropriate developmental exposures, alters the hormonal and homeostatic systems that otherwise enable the organism to communicate with and respond to its environment.

Different studies on animal organs, clinical observations and epidemiological studies have demonstrated the potential role of endocrine disruptors causing reproductive systems, prostate, breast, lung, liver, thyroid, metabolism and obesity (Polyzos *et al.*, 2012).

Some endocrine disruptors known to cause harmful effects to human health are prohibited in the United States. Even some prescription drugs have unexpected effects on the endocrine system. In 1971, since the US Food and Drug Administration was related to rare vaginal cancer, DES (diethylstilbestrol) stopped the writing of physicians. Due to US suspected harmful health and environmental effects, the production of PCBs was stopped in 1977; Exports and imports of PCBs; It was stopped at the end of 1979.

Epidemiological studies of the last 50 years have increased the likelihood of many diseases such as prostate, breast, testicular cancer, as well as diabetes, obesity and decreased fertility. Some studies have shown that some cancers related to hormones are mostly industrialized areas.

2.1 Cancer: In Great Britain, from 1978 to 2007, the overall incidence of cancer has increased by 25%, with a 14% increase in men and a 32% increase in women (Sam and Nicolas, 2012).

2.2 Diabetes: The United States Patient Control and Prevention Center (CDC) showed that the prevalence of diabetes increased by 176% from 1980 to 2011 (Center for Disease Control and Prevention, 2014). Childhood obesity is more than double in children and has tripled in adolescents over the last 30 years. In the United States, the prevalence of obesity in children 6-11 years of age increased from 7% in 1980 to 18% in 2012. Similarly, in adolescents, prevalence increased from 5% to approximately 21% (Center for Disease Control and Prevention, 2014).

2.3 Disorders in Thyroid Function: Thyroid hormones play very important roles in human physiology. For example; brain development, metabolism control and some other important physiological events in adults. Therefore, if changes in the functions of the thyroid gland occur, negative effects can occur in adult physiology, development and metabolism due to disorders in thyroid hormones (Diamanti-Kandarakis *et al.*, 2009).

There are a number of literature that suggest that endocrine disrupting chemicals directly disrupt normal functions of thyroid glands. The primary environmental chemicals identified as thyroid disruptors may include PCBs; bisphenol A (4,4-isopropylidenediphenol BPA); perchlorate, tetrachlorodibenzo-p-dioxin [TCDD]; polychlorinated dibenzofuran [PCDF] (both commonly referred to as dioxins); pentachlorophenol (measured in mammals as the source chemical hexachlorobenzene [HCB]), a common pesticide that breaks down into pentachlorophenol; triclosan; polybrominated diphenyl ethers [PBDE] and tetrabrominated diphenyl ethers commonly known as flame retardants; naturally occurring chemicals such as

soy isoflavones, thiocyanate in cruciferous vegetables and etc. Phthalates (di [2-ethylhexyl] phthalate [DEHP], dinocetylphthalate [DnOP], diisodecyl phthalate [DIDP], dinhexyl phthalate [DNHP] and dinbutyl phthalate [DBP], which are used as plastic softeners in feeding tubes and plastic containers), also in animal studies It has been shown to alter thyroid functions. Also paraben is used in cosmetics, dichlorodiphenyltrichloroethane [DDT], pesticides, HCB, methoxychlor, chlorine, and endosulfan have thyroid-disrupting effects in animals and humans (Patrick, 2009).

The first step in thyroid hormone synthesis is the uptake of iodide into the thyrocyte by the sodium/iodide symporter (NIS). Iodine is essential for thyroid hormone synthesis, and today iodine deficiency has become a worldwide problem. Therefore, chemicals that interfere with NIS may inhibit thyroid hormone synthesis, thereby increasing the iodine deficiency problem. The best example of this is perchlorate, which is used in air cushion, rocket launchers, air cushion systems. Since the chemical is highly stable in the environment, it has become a worldwide pollutant in drinking and irrigation water and food. In experimental studies, it was observed that serum perchlorate had a half-life of about 8 hours and a dose of approximately 5.2 g / kg d was sufficient to start reducing the uptake of iodide to the thyroid gland (Diamanti-Kandarakis et al., 2009).

Thyroperoxidase is a protein that contains both and is responsible for the oxidation of iodide to iodine before it is transferred to thyroid hormone and can be blocked by many components.

2.4 Corticoid Dysfunction: Many evidence has shown that corticoid hormonal function may be affected by endocrine disruption. For example, hexachloro-benzene causes oxidative stress, deterioration of arachidonic acid metabolism and porphyria (Lelli et al., 2007).

2.5 Metabolic Disorders: Peroxisome is a proliferating active receptor (PPAR), alpha, beta and gamma, and consists of three types of isotypes that play a very important role in controlling cellular differentiation programs and in the transcriptional control of lipid and carbohydrate metabolism (Casals-Casas et al., 2008). PPAR alpha is found in the liver and is mainly associated with the presence of endocrine disruptors (Feigee et al., 2006).

2.6 Interference with hormonal feedback regulation and neuroendocrine cells: Neuroendocrine systems that function as a link between the central nervous system and the peripheral endocrine system control homeostatic processes including reproduction, growth, metabolism, energy balance and stress response.

Endocrine disrupting chemicals cause a deterioration in the thyroid system of hypothalamic pituitary, which plays a role in metabolism and energy balance by acting on neuroendocrine system. For example, PCBs reduce thyroxine and thyroid stimulating hormone (TSH) in response to thyrotropin releasing hormone that causes hypothalamic and pituitary deregulation (Gore, 2010). Furthermore, exposure to endocrine disrupting chemicals, which may be hormonal active substances, may lead to inappropriate hypothalamic programming and, consequently, a decrease in reproductive success in adulthood (Gore, 2008).

2.7 Effects on the Nervous System: The nervous system is the most important body system and ensures that all parts of the body are secreted and work perfectly. It can be affected by endocrine disrupting chemicals and these effects are induced by various chemicals. The hormonal balance and function in the body can be changed due to the direct effect of endocrine disrupting chemicals on the endocrine glands. In contrast, the compounds may initially affect the central nervous system (CNS), eg neuroendocrine disruptors that may affect the endocrine system. These cause neuroendocrine deterioration, and indications can lead to

changes in metabolic rate, indirect effect on behavior, change in sexual differentiation in the brain, sexual dimorphic reproduction and inefficient neural endpoints, as well as some neuroterogenic effects. There are many studies on the effects of these chemicals on behavior, learning, memory, attention, sensory function and neurological development as a result of exposure to endocrine disruptive chemicals. Examples of neuroendocrine disruptors include PCBs, Dioxins, DDT and related chlorinated pesticides and metabolites, mercury, lead, organotin, insect growth regulators, dithiocarbamates, synthetic steroids, tamoxifen, phytoestrogens, and heavy metals such as atrazine herbicides (Mellanen et al., 1996).

2.8 Effects on the Male and Female Reproductive System: Some of the diseases we experience throughout life, some of which are related to endocrine disruptors, can be sexually dimorphic. Therefore, it can be expected that endocrine disruptors may produce different disorders in men and women in which they can act as estrogen and / or androgen antagonists (Diamanti-Kandarakis et al., 2009).

Adolescence: The age of menarche has decreased from 16 or 17 years to 13 years since the last century. Adolescence may be associated with many other disorders, such as early onset insulin resistance, metabolic syndrome, breast and reproductive system cancers.

Primary ovarian failure: Studies have shown that primary ovarian failure occurs in approximately 1% of the female population under the age of 40 years. The causes of this disease have been associated with endocrine disrupting chemicals (Costa et al., 2014).

Irregularities in the menstrual cycle: Endocrine disrupting chemistries can interfere with the hormonal regulation of the menstrual cycle and may lead to long cycles, thus reducing the likelihood of conception (Costa et al., 2014).

Polycystic ovary syndrome (PCOS): This is a common endocrine disorder in women. The disease is characterized by anovulation and hyperandrogenism and is associated with higher prevalence of obesity, insulin resistance and metabolic abnormalities (Costa et al., 2014).

Men may also suffer from abnormal abnormalities in their sexual organs, such as sperm anomalies, hypospadias, and ectopic testicles. There is a strong likelihood that these diseases are due to perinatal exposure of endocrine disrupting chemicals at sensitive stages of sexual differentiation of the developing fetus (Fechner et al., 2011; Santodonato, 1997).

Sperm quality: Several studies have reported that endocrine disrupting chemicals cause a decrease in sperm quality (since the 1930s) in many countries such as sperm count, normal sperm rate, and sperm volume, and this can be expected to affect fertility. However, various studies also refute this downward trend in human sperm quality. Even though there is no worldwide decline in sperm quality, there are clear differences in sperm quality both within and between countries. However, until now, no research has examined the relationship between endocrine disrupting chemicals and sperm quality (Endocrine Disruptors, 2001).

Fertility: In males, the fertility rate has declined in recent years in some countries, such as Denmark, France and the United Kingdom (Comhaire et al. 2007; Bay et al., 2006). Some human and experimental animal studies have shown that occupational or environmental exposure to certain chemicals, such as pesticides and PCBs, can reduce fertility. However, any relationship with endocrine deterioration remains speculative (Nicolopoulou-Stamati and Pitsos, 2001).

3. CONCLUSIONS

As a result, we can list the following determinations regarding endocrine disrupting chemicals

- Increased endocrine-related disease,
- Increased global rate of endocrine related cancers,
- Increased Obesity and Type II diabetes,
- Increased risk of prostate cancer among workers due to pesticides, especially PCBs and arsenic.

As we know that endocrine disrupting chemicals are stable compounds with a low degree of biodegradability, sewage water needs to be treated. Manufacturing industries with various uses of endocrine disrupting chemicals should be encouraged to have a Wastewater treatment plant at their production sites. More epidemiological data should be available to interpret the impact of endocrine disruptors on human health or diseases. Environmental causes of trends in endocrine diseases and disorders should be addressed. The public should be made aware of the harmful effects of endocrine disruptors by using written and electronic media.

Endocrine disrupting chemicals need to be promoted public awareness before affecting large-scale human and wildlife. Heavy metals such as lead and others such as POPs, tributyltin, di (2-ethylhexyl) phthalate, nonylphenol are prohibited in many countries, but sometimes these prohibitions only relate to specific uses. Particularly due to lack of occupational safety, the proportion of prostate cancer increases due to endocrine disrupting chemicals. Understanding the current need to improve the health of human and wildlife with the prevention of environment-borne diseases is extremely important.

The researchers noted that all organs should take into account the characteristics of the endocrine system and its mechanism to fully comprehend how endocrine disrupting chemicals damage human and wildlife to assess the behavior of endocrine disrupting chemicals.

It is necessary to raise awareness about exposure to endocrine disrupting chemicals between different governments and private sectors to reduce the exposure. More co-operative work should be done to further test the toxic effects of endocrines, as well as to help close gaps through information sharing between developed and developing countries.

People should be brought together to be aware of the harmful effects of these toxic substances and to learn about endocrine disruptors. This will also help policy makers in determining the optimum levels of exposure to these chemicals. The public should also be encouraged to assist policymakers in the effective implementation of policies created in the awareness and minimization of these chemicals by deterring people from the production, import and use of these toxic substances. All these gaps need to be dealt with urgently by the government, the NGO and the private sector. It may also be necessary to give specific ideas to policy makers to review our legislative process so that these endocrine problems can be reduced. Awareness of workers' safety and health at the workplace should be ensured by the workers, as well as by the state institutions.

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