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A literature Study on Association of Environmental Toxic Compounds with Thyroid Disruption

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Abstract

The literature evidences showed a drastic effect of environmental chemicals compounds on the status of thyroid hormones. Most of the environmental chemical compounds mentioned in study show structural resemblance with thyroid hormones. Therefore, these chemicals can mimic the activity of thyroid hormones. Some chemical compounds also exhibit other mechanism; however, the exact mechanism of action is not cleared yet. Most commonly these chemicals include a dose dependent inhibition of thyroid hormones. No doubt these chemical compounds have beneficial roles at industrial scale where these are used in the preparation of various useful things but we cannot ignore their life-threatening consequences.

Keywords: Thyroid hormones, Environmental chemicals, Thyroid disruption.

INTRODUCTION

Several review studies have evaluated the literature evidences on adverse human health effects due to environmental exposure of toxic chemical compounds [1-5]. In this study, there is discussion about epidemiological literature findings relevant to the examination of toxic impact of different environmental chemicals on thyroid function.

Dioxins and Thyroid Hormones

Polychlorinated dibenzo dioxins are very toxic environmental pollutants. These pollutants are generated during synthesis of herbicides in industry. In a study of Air-force Vietnam-war vetrans, the exposure of tetrachloro dibenzo para dioxin revealed a remarkably high level of thyroid stimulating hormone in body fluids which represents a clear picture of reduction in thyroid hormones [6]. The exposure tetrachloro dibenzo para dioxin in dam during gestation period lead towards an increase in the level of thyroid stimulating hormone while decrease in thyroid hormones [7]. In rats, the exposure of tetrachloro dibenzo para dioxin also shown similar results [8]. A very important point is that the reduction in tetra-iodothyronine and elevation in thyroid stimulating hormone levels depend upon administered doses of tetrachloro dibenzo para dioxin [9].

Phthalates and Thyroid Hormones

According to in-vivo and in-vitro investigations the phthalates exert a determinantal effects on thyroid hormone activity. When rats fed on 2-ethylhexa phthalate, a most commonly used compound, the levels of tetraiodothyronine and tri-iodothyronine decreased in plasma. On the other hand, the rats receiving 2-ethylhexa phthalate intravenously revealed an increase in concentration of tetraiodothyronine and tri-iodothyronine. Furthermore, the exposure of another commonly used phthalate such as dibutyl phthalate to male rats induced a dose dependent reduction in plasma tri-iodothyronine and tetraiodothyronine levels [10].

Bisphenol-A and Thyroid Hormones

The Biphenyl-A is extensively utilized in the manufacturing of plastic articles which are being used in our daily routines. The human population is extensively exposed to this chemical compound [11]. Up till now, only a few studies have been conducted on thyroid-disrupting capability of biphenyl-A in human population. However, Zoellar et al found that the prenatal exposure of biphenyl-A was associated with remarkably high level of tetraiodothyronine but this study was conducted in pups [12].

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Few derivatives of biphenyl- such as tetrachloro bisphenol-A, tetrabromo bisphenol-A and tetramethyl bisphenol-A increased the production of thyroid hormones by enhancing its discharge from GH3-cells, growth hormone producing cells. These compounds also mimic the activity of thyroid hormones [13]. However, the field voles and polecats did not reveal any remarkable influence on thyroid hormones. [14]. This class of compounds is also found to be associated with the regulation of expression of various thyroid genes in central nervous system [15].

Proposed mechanism of actions of Bisphenol-A

- Biphenyl-A can interact with signaling pathway of thyroid hormones both in-vivo and in-vitro. However, due to complex interaction, it is difficult to understand [16].

- Biphenyl-A antagonizes tri-iodothyronine mediated thyroid receptor's activation.

- Biphenyl-A increased N-CoR (corepressor) interaction in culture medium in order to decrease tri-iodothyronine mediated gene activation. The biphenyl-A exposure in rats gives a similar thyroid profile as shown in case of thyroid-resistance syndrome [17].

Brominated Flame-retardants and Thyroid Hormones

It is a class of compounds consisting of 80 different chemical congeners. The most prominent are tetra bromo bisphenol-A, polybrominated diphenyl ethers and hexabromo cyclododecane [18]. The Brominated Flame-retardants are widely used in preparation of building materials and electronic equipment [19]. These are also used in furniture, plastics, insulating materials and textile industry. Both Brominated Flame-retardants and, polychlorinated biphenyl, a chemical compound having thyroid hormones disrupting potential, have almost similar structures. Due to restrictions on the use of polychlorinated biphenyls its concentration is slowly depleting from the environment. On the other hand, the level of brominated flame-retardants in the environment is increasing day by day [20].

Triclosan and Thyroid Hormones

Triclosan is an antibacterial compound which is usually chlorinated at various positions. Now a days it is being used in household products. The usage of triclosan became a cause of water contamination in many countries of the world. This chemical compound is also detected in breast milk of human and in fish [21].

According to literature evidences the oral administration of triclosan produced a dose-dependent reduction of thyroid hormones in rats [22]. In this aspect a study exhibited an inverse relationship between plasma free thyroid hormones, such as tri-iodothyronine and tetraiodothyronine, and Urinary triclosan in pregnant women of Shanghai in China [23]. Due to structural similarity the triclosan shows endocrine disrupting capability [21].

Pentachlorophenol

Few human studies are available on this pollutant. However, the available literature has revealed the negative association between thyroid hormones and pentachlorophenol in newborns. This chemical compound can increase the risks of neurodevelopmental defects in newborns. Unfortunately, this chemical compound has ability to move across barriers, therefore, it can penetrate into the blood of developing fetus and somehow alters thyroid hormone's availability [24].

Nitrates

Nitrate exists as a univalent ion (NO¬3-). It is also present in drinking water as a contaminant. These univalent anions create hindrance in normal uptake of iodide by thyroid gland as a result decrease in the concentration of thyroid hormones [25]. In turn the low levels of thyroid hormones are associated with various subclinical disorders [26]. The normal limit values for nitrate ion in ground water is up to 50mg/l (WHO 2007). The limit value for nitrate ion in Europe is also the same as mentioned previously (50mg/l). In 2003, the Europe-Environment Agency has reported that nitrate levels increased in about 67% of the drinking water in Europe [27].

In 1945, Comly reported first adverse effect of nitrate when he noticed cyanosis in old infants in Lowa [28]. The nitrates disrupt the uptake of iodine [29]. The exposure of drinking water contaminated with nitrate to male rats not only decreased concentrations of thyroid hormones but also made thyroid gland heavier (Goiter). Side by side, a reduction in body weight was also revealed in this study [30]. Similarly, when female rats exposed to a dose of 50mg/l of nitrate, the alterations in thyroid hormones and weight of thyroid gland have been reported [27]. The studies on human did not give any solid evidence. However, kilfoy et al found that the chances of thyroid cancer increased due to dietary intake of nitrate among men but NIH-AARP cohort showed no signs of cancer among women [31]. Besides it was also revealed that nitrate also decreased the concentration of insulin-like growth factor-1(IGF-1) [29].

UV-filters

UV-filters are used in the preparation of plastic and cosmetic articles [10]. These can also disturb normal homeostasis of thyroid hormones [32]. UV-filters are released into rivers via wastewater where these chemicals become a part of fish bodies. One thing of great importance is that human milk also contains UV-filters. A number of UV-filters have been produced and are being used on a large scale and many cause disruptions of endocrine system [33]. In this study we focus only upon some important UV-filters possessing thyroid disrupting potential such as BP-2, OMC and 4-MBC. An experimental study conducted on rats, treated with benzophenone-2(BP-2) revealed an increase in thyroid stimulating hormone levels and a decrease in tetraiodothyronine level besides the activity of thyroid-peroxidase, an enzyme responsible for the thyroid hormone's synthesis [32]. In another study conducted on rats, treated with 4-methyl bezylidene-comphor (4-MBC), revealed an increase in tri-iodothyronine level. Furthermore, the administration of another chemical Octyl-methoxycinnamate in rats revealed a decrease in thyroid hormones levels following a dose-dependent relationship [32].

Perchlorates

The perchlorates are used for the treatment of hyperthyroidism. These chemicals can also inhibit the uptake of iodine in thyroid tissues [34]. The inhibition of thyroid hormones production in thyroid gland can cause hypothyroidism. Normally, the uptake of iodide and perchlorates into the cells is dependent upon thyroid stimulating hormone's concentration [35]. The newborns are at greater risk of developing thyroid hormone's deficiency and due to high level of perchlorate women's milk the perchlorate may affect thyroid hormone's signaling during infant development [16]. The neonates of mothers who drink water containing perchlorate during pregnancy reflected an increase in thyroid stimulating hormone levels [36].

In the beginning the perchlorate was used in high doses i.e., up to 2000mg/day for the treatment of Graves disorder. But this high dose can also provide harm to bone marrow thus increasing the chances of agranulocytosis and aplastic anemia. Later on, in 1984, the authors reported that the perchlorate could be used successfully for the treatment of hyperthyroid Graves disorder with dose of 900mg/day or less for a period not exceeding from one year, in this case no adverse effect had been reported [10]. In 1974, it was reported that the administration of 600mg/day dose of perchlorate to five volunteers for a period of one-week enhanced non-thyroxin I2 discharge by 65%, exhibiting an entire blocking of I2 uptake by thyroid gland. In 1992, five healthy volunteers were given a 900mg/day dose of perchlorate salt (potassium perchlorate) for four weeks but surprisingly they did not reveal any iodine depletion. These studies were carried out in areas of

moderate I2 deficiency but not in regions where I2 intake was sufficient. The salts of perchlorates are soluble in water. These salts have been found in ground and surface waters in many states. Multiple surveys of drinking water and wells indicated that the levels of perchlorates are being exceeded every day. Lowrence et al also found the side effects of perchlorate when these compounds were consumed in low amounts on thyroid gland as it was a matter of great concern for the environment-protection agency (EPA). The spring water containing perchlorate in minor amounts (10mg/L) was ingested by 9 normal male volunteers that reflected a decrease in thyroid uptake by 38% below the baseline value but rebounded by 25% over the normal baseline value after withdrawal [37].

CONCLUSION

The environmental chemicals which are mentioned in literature review can disrupt levels of thyroid hormones in body fluids. According to evidences these typical chemical compounds decrease the normal levels of thyroid hormone

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Conflict of Interest

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