CANCER PREVENTION: CURRENT RESEARCH JOURNAL Open Access

SCIENTIFIC LITERATURE

REVIEW ARTICLE

Prevention from the Pollution of Carcinogenic Endocrine Disrupting Chemicals in Water Sources

Wei Zhang, Qing Xiu Liu and Jun Sheng Lin*

School of Medicine, Huaqiao University, China

ARTICLE INFO

Article history:
Received: 30 May 2017
Accepted: 17 July 2017
Published: 20 July 2017

Keywords:
Endocrine disrupting chemicals;
Hormone-sensitive cancers;
Cancer causation;
Cancer prevention;
Water body;
Pollution

Citation this article: Zhang W, Liu QX, Lin JS. Prevention from the Pollution of Carcinogenic Endocrine Disrupting Chemicals in Water Sources. Cancer Prev Curr Res J. 2017; 1(1):111.

Correspondence:
Jun Sheng Lin,
School of Medicine, Huaqiao University, Quanzhou 362021, China,
Tel: +86-0595-22690889;
Email: junshenglin@hqu.edu.cn

ABSTRACT

Endocrine Disrupting Chemicals (EDCs) are exogenous chemicals in our environment that interfere with any aspect of hormone action causing a variety of disorders even increasing incidence rate of hormone-sensitive cancers. This mini review mainly focuses on the recent studies on the carcinogenesis of EDCs and the ideas how to reduce EDCs pollution in the aquatic environment. Advanced technologies for sensitive detection, continuous monitoring and efficient removal of EDC pollutants are required to minimize the exposures of humans to these chemicals. It is also required a sustainable regulation updating system to stop new pollutants entering our daily environment. All these efforts can be made by collaboration with science, industry, government and community.

Abbreviations: AhR: Aryl hydrocarbon Receptor; AR: Androgen Receptor; AREs: Androgen-Response-Elements; BC: Breast Cancer; BPA: Bisphenol A; DDT: Dichloro Diphenyl Trichloroethane; EDCs: Endocrine Disrupting Chemicals; ER: Estrogen Receptor; EREs: Estrogen-Response-Elements; PAE: Phthalates; PCB: Polychlorinatedbiphenyl; TC: Testicular Cancer

Introduction

Endocrine Disrupting Chemicals (EDCs) are environmental micro pollutants (natural or anthropogenic) that alter the function of the endocrine system, by interfering with hormone biosynthesis, metabolism, or action, and consequently causing disturbances in the endocrine system even cause increased incidence of cancers. Nearly 800 chemicals are known to have more or less interference effects on endocrine system [1]. It has been alerted regarding the potential adverse effects of EDCs on health of human and wildlife [2]. Although the presence of endocrine disruptors in water sources is usually very low, EDCs have been constantly released and spread into our daily environment, and still are going on. The technologies for treatment of domestic and industrial wastewaters are remained to be improved, but EDCs can be ubiquitously found in the aquatic environment (such as surface waters, groundwater, waste water, runoff, and landfill leachates), even transform into new contaminants [3]. The environmental EDCs remained in landfill leachate, are inevitably

discharged into rivers, groundwater and sea. Water body contaminated with EDCs has been posing a serious health risk including tumorigenesis [4]. It is not easily to detect the trace of EDCs in the environment, but through the food chain in the ecosystem of bioaccumulation, after a few trophic levels, endocrine disruptors can achieve remarkable concentration in wildlife animals even in humans. Due to its ubiquitous nature and continuous exposure, 91.3% of U.S. adults that were sampled had a measurable amount of BPA in their urine; higher exposures observed in women and low-income individuals [5,6]. Multiple-source data of epidemiologic studies and animal experiments have demonstrated that EDCs polluted in water body in relation to carcinogenesis of hormone-related cancers including breast, testicular, prostate, uterine and ovarian cancers [7,8]. Evidences of direct and indirect links between exposure to EDCs polluted in water and hormone-dependent cancers have been reported and, in turn, attracted more and more researchers to further investigate for identification and to find the related mechanisms. More and more researchers and policymakers have been paying attention to develop technologies and to concern new regulation for prevention of EDCs-sensitive cancers.

Carcinogenesis of EDCs

The cellular and molecular mechanisms of EDCs causing hormone-sensitive breast, uterine, ovarian, and prostate cancers have been well reviewed by a Scientific Statement [9]. Scientists have continued to add our knowledge that EDCs indeed can be found in human body and related to disorders including cancers. PAEs, BPA, and their metabolites were found in the umbilical cord blood, amniotic fluid, placenta, and breast milk. These data evidenced that EDCs might have a vast influence on the development of fetus and newborns [10]. It has been commendably clarified that EDCs can transfer from mother to fetus through the placenta, as well as to newborns via breast nursing. As we have known that fetal or perinatal exposure to even very low doses of EDCs may increase the risk of cancer-developing [11]. Various EDCs acted through multiple mechanisms, for example, by chemicals that bind both ER and AhR. EDCs are also involved in enhancing the progression and metastasis by effecting on the tumor microenvironment [12,13].

EDCs interfere a variety of genomic and non-genomic activities, depending on the pathway that is disrupted. EDCs can lead to tumor cell proliferation in the genomic pathways in which AR/ER dimers directly bind to Androgen-Response-Elements (AREs)/Estrogen-Response-Elements (EREs) flowing ligands binding or interact with other transcription factors by action of transcription factor cross-talk [14,15]. Stimulation of AR- and ER-mediated gene transcription (cyclin D and VEGF etc.) by EDCs could also contribute to enhancement of hormone-induced tumor cell proliferation [16,17]. In addition, EDCs can compete with androgen/estrogen in ARs/ERs binding and induce androgenic/estrogenic effects [18]. The activation of these pathways, mediated by steroidal receptor (AR or ER) or by Growth Factor Receptors (GFR) may be responsible for stimulation of proliferation and/or cell migration in cancers [15,17,19].

EDCs have the ability to bind with deferent receptors and consequently effect on gene expression and cancer cell growth [19]. On the other hand, it also has been shown to evoke inflammatory responses (likely mediated by the NF-kB signaling) with increased release of cytokines and growth factors (EGF, FGF, VEGF, etc.). Therefore, EDCs increase cell proliferation, decrease and alter the architecture of the organ/tissue, causing an increasing risk of carcinogenesis.

Breast Cancer (BC) risks have both heritable and environment/lifestyle components. The heredity actually plays a minor role (contribution of 5–27%), whereas the environment/lifestyle is considered as the majority of risk. EDCs can act directly or indirectly on mammary tissue to increase sensitivity to chemical carcinogens [20]. The timing of the exposure to environmental factors is indispensable for cancer development [10]. During a sensitive development window, EDCs exposures could alter the mammary gland by increasing the risk of cancer [21]. Rodent models and human epidemiological investigations provide us evidences that some endocrine disruptors (such as BPA, organochlorine pesticides and

PCBs) can impact the development and function of normal mammary gland, and many of those relate to increasing the risk of BC [22-24]. These clues suggest that traditional toxicology tests may lack lots of important indicators on the mammary gland. It is better to normalize chemical detection scheme for determination of threshold toxic level during the critical stage of development, as well as for assessment of male mammary gland. The pervasive presence of EDCs means the continuous exposure of fetuses, newborns, children, adolescents, and adults to these chemical mixtures. It has been demonstrated that there is a possible link between environmental exposures with EDCs and a risk of Testicular Cancer (TC), especially, that exposure to EDCs in early life may be involved in the etiology of TC [25]. Comprehensive precaution programs to reduce the EDCs exposure to these vulnerable populations may be critical in preventing estrogen-related cancers.

Some of the EDCs have been banned and their global use has decreased. However, their persistence in the environment, such as DDT, has resulted in continued human exposure [26]. As the slow-dividing progenitor cells are more vulnerable to the environmental factors [27], exposure of human mesenchymal stem cells to these EDCs for long term causes a series of alterations in self-renewal, differentiation, and proliferation which may partially lead to the homeostatic imbalance and increased cancer incidence [26].

Reduction of EDCs Polluted in the Aquatic Environment

As a result of civilization, urbanization and industrialization, humans are continuously exposed to an environment with pollution. We have to envisage the serious problem of EDCs contamination in the aquatic environment. Eco-friendly strategies to control EDCs polluted in water body are urgently required.

1. More sensitive detection technologies are required

Better understanding about the carcinogenic effects of EDCs polluted in water body as well as their molecular mechanism(s) in hormone-sensitive cancers would be useful in developing prevention and treatment strategies. A large number of EDCs continuously enter water systems from various sources, such as landfill leachate, human excretion, wrongful disposal, and industrial wastes, can persist for a long time. The toxic activity of individual compound can be at the concentrations as low as pg L-1- ng L-1 [28]. However, synergistic effects of mixtures of EDCs have been demonstrated in animal models [29,30]. Which alerts that disorders of body functions could be caused by interaction of hundreds of chemicals each at levels below toxicity? Importantly, there is still a lack of testing systems suitable for identification of the effects in disturbing the function of the endocrine system. Therefore, we should pay more attention on the development of methods including quantitative high-throughput screening platform to identify multiple EDCs on key molecular targets in endocrine system at the same time, such as quantitative high-throughput screening to identify activators of AR and alkali assay to screen for molecules that interfere with aromatase activity [31-33]. More sensitive technologies for quick detection of toxic EDCs used in daily life are also demanded. The current framework of internationally recognized EDCs testing systems has to be further improved. Knowing more about carcinogenic effect of EDCs is useful in sensitizing the scientific community and the manufacturers to the importance of finding alternatives to their indiscriminate use to protect human health and the ecosystem. In addition, proper evaluation of particular EDCs would help establish removal or reduction strategies and provide guidance of policy modifications for controlling these chemicals while enhancing the recyclability of water.

2. Continuous monitor systems are required

Occurrence of EDCs in the landfill leachate from municipal solid waste landfill has become a serious problem. However, monitoring EDCs is still limited, especially in the developing countries. This may be connected to the fact that it is difficult to detect the trace compounds in landfill leachate, due to its very complex matrix. The levels of the most EDCs in the environment are currently not efficiently monitored and/or regulated. In the case of landfill, the insulation system between the land filled wastes and the soil environment should be

effectively monitored, because EDCs can easily penetrate into ground and surface water once the insulation system is leaking at any point [34]. In addition, the existing wastewater treatment plants were not traditionally designed to remove EDCs, therefore contribute to the introduction of different levels of a variety of EDCs from different plants into the environment. Sewage treatment plant effluents and wastewater discharges are considered to be a major source of EDCs that directly release into the aquatic environment. There is a pressing need for sensitive, quick and inexpensive methods to monitor the quality of treated wastewater effluents. Previous reports indicated that combination of in vitro/in vivo testing and instrumental analysis to monitor the occurrence of EDCs in wastewater is feasible [35,36]. Bioassays are also recommended as they can account for the overall effect of complex mixtures [37]. Moreover, continuous real-time and online systems for concentration monitoring and analyses should be conducted comprehensively [38].

3. Reducing the discharge of pollutants into environment should be compulsory

There is a need to coordinate guidance on the regulation for the reduction of EDCs, but this has been hindered by the lack of consensus among scientists [39]. Governments should consult with the organizations representing medicine, chemistry, and environment science, to set up sustainable strategies and regulations to prohibit the discharge of the pollutants into our environment, thereby reducing the risk of hormone-related cancers in humans.

4 Efficient removal of pollutants from our daily environment

Previous reports indicated that traditional wastewater treatment processes are not efficient enough to prevent contamination of environmental surface waters [36]. At present continuously emerging technologies from different disciplines can be cross-used to develop advanced treatment processes to overcome the limitation of traditional technologies for EDCs removal from wastewater treatment system. For examples, membrane-based treatment including reversing osmosis, bio-based degradation, UV-fenton, Tertiary ozonation, and other advanced chemical and physical treatment processes can be combined to remove and reduce the EDCs in water body during the wastewater treatment process [40-43].

Conclusion

EDCs are readily available in the aquatic environment and long term exposure is inevitable. It is considered that the exposure to these chemicals could increase the risk of hormone-dependent cancers. Advanced technologies for sensitive detection, continuous monitoring and efficient removal of EDC pollutants are required to minimize the exposures of humans to these chemicals. It is also required a sustainable regulation updating system to prohibit new pollutants entering our daily environment. All these efforts can be made by collaboration/cooperation from science, industry, government and community.

Acknowledgements

This work was supported by the National Key R&D Program of China (Grant No.2016YFE0101700) and Huaqiao University Grant (13Y0391).

References

1. Bergman A, Heindel JJ, Kasten T, Kidd KA, Jobling S, et al. (2013). The impact of endocrine disruption: a consensus statement on the state of the science. Environmental health perspectives. 121: A104-A106.

2. Plahuta M, Tisler T, Toman MJ, Pintar A. (2017). Toxic and endocrine disrupting effects of wastewater treatment plant influents and effluents on a freshwater isopod Asellus aquaticus (Isopoda, Crustacea). Chemosphere. 174: 342-353.

3. Bhatnagar A, Anastopoulos I. (2017). Adsorptive removal of Bisphenol A (BPA) from aqueous solution: A review. Chemosphere. 168: 885-902.

4. Weber AA, Moreira DP, Melo RM, Vieira AB, Prado PS, et al. (2017). Reproductive effects of oestrogenic endocrine disrupting chemicals in Astyanax rivularis inhabiting headwaters of the Velhas River,

Brazil. The Science of the total environment. 592: 693-703.

5. Johns LE, Ferguson KK, Meeker JD. (2016). Relationships Between Urinary Phthalate Metabolite and Bisphenol A Concentrations and Vitamin D Levels in U.S. Adults: National Health and Nutrition Examination Survey (NHANES), 2005-2010. The Journal of clinical endocrinology and metabolism. 101: 4062-4069.

6. Perera F, Nolte EL, Wang Y, Margolis AE, Calafat AM, et al. (2016). Bisphenol A exposure and symptoms of anxiety and depression among inner city children at 10-12 years of age. Environmental research. 151: 195-202.

7. Morgan M, Deoraj A, Felty Q, Roy D. (2016). Environmental estrogen-like endocrine disrupting chemicals and breast cancer. Molecular and cellular endocrinology.

8. Ahmad MI, Usman A, Ahmad M. (2017). Computational study involving identification of endocrine disrupting potential of herbicides: Its implication in TDS and cancer progression in CRPC patients. Chemosphere. 173: 395-403.

9. Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, et al. (2015). Executive Summary to EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocrine reviews. 36: 593-602.

10. Rutkowska AZ, Szybiak A, Serkies K, Rachon D. (2016). Endocrine disrupting chemicals as potential risk factor for estrogen-dependent cancers. Polskie Archiwum Medycyny Wewnetrznej. 126: 562-570.

11. Quagliariello V, Rossetti S, Cavaliere C, Di Palo R, Lamantia E, et al. (2017). Metabolic syndrome, endocrine disruptors and prostate cancer associations: biochemical and pathophysiological evidences. Oncotarget. 8: 30606-30616.

12. Burks H, Pashos N, Martin E, McLachlan J, Bunnell B, et al. (2016). Endocrine disruptors and the tumor microenvironment: A new paradigm in breast cancer biology. Molecular and cellular endocrinology.

13. Lee HM, Hwang KA, Choi KC. (2016). Diverse pathways of epithelial mesenchymal transition related with cancer progression and metastasis and potential effects of endocrine disrupting chemicals on epithelial mesenchymal transition process. Molecular and cellular endocrinology.

14. Katz TA, Yang Q, Trevino LS, Walker CL, Al-Hendy A. (2016). Endocrine-disrupting chemicals and uterine fibroids. Fertility and sterility. 106: 967-977.

15. Deb P, Bhan A, Hussain I, Ansari KI, Bobzean SA, et al. (2016). Endocrine disrupting chemical, bisphenol-A, induces breast cancer associated gene HOXB9 expression in vitro and in vivo. Gene. 590: 234-243.

16. Park MA, Hwang KA, Lee HR, Yi BR, Jeung EB, et al. (2013). Benzophenone-1 stimulated the growth of BG-1 ovarian cancer cells by cell cycle regulation via an estrogen receptor alpha-mediated signaling pathway in cellular and xenograft mouse models. Toxicology. 305: 41-48.

17. Di Donato M, Cernera G, Giovannelli P, Galasso G, Bilancio A, et al. (2017). Recent advances on bisphenol-A and endocrine disruptor effects on human prostate cancer. Molecular and cellular endocrinology.

18. Park MA, Hwang KA, Choi KC. (2011). Diverse animal models to examine potential role(s) and mechanism of endocrine disrupting chemicals on the tumor progression and prevention: Do they have tumorigenic or anti-tumorigenic property?Laboratory animal research. 27: 265-273.

19. Kampa M, Notas G, Castanas E. (2017). Natural extranuclear androgen receptor ligands as endocrine disruptors of cancer cell growth. Molecular and cellular endocrinology.

20. Macon MB, Fenton SE. (2013). Endocrine disruptors and the breast: early life effects and later life disease. Journal of mammary gland biology and neoplasia. 18: 43-61.

21. Osborne G, Rudel R, Schwarzman M. (2015). Evaluating chemical effects on mammary gland development: A critical need in disease prevention. Reproductive toxicology. 54: 148-155.

22. Zhang XL, Liu N, Weng SF, Wang HS. (2016). Bisphenol A Increases the Migration and Invasion of Triple-Negative Breast Cancer Cells via Oestrogen-

related Receptor Gamma. Basic & clinical pharmacology & toxicology. 119: 389-395.

23. Fischer C, Mamillapalli R, Goetz LG, Jorgenson E, Ilagan Y, et al. (2016). Bisphenol A (BPA) Exposure In Utero Leads to Immunoregulatory Cytokine Dysregulation in the Mouse Mammary Gland: A Potential Mechanism Programming Breast Cancer Risk. Hormones & cancer. 7: 241-251.

24. Arrebola JP, Belhassen H, Artacho-Cordon F, Ghali R, Ghorbel H, et al. (2015). Risk of female breast cancer and serum concentrations of organochlorine pesticides and polychlorinated biphenyls: a case-control study in Tunisia. The Science of the total environment. 520: 106-113.

25. Giannandrea F, Fargnoli S. (2017). Environmental Factors Affecting Growth and Occurrence of Testicular Cancer in Childhood: An Overview of the Current Epidemiological Evidence. Children. 4: 1.

26. Strong AL, Shi Z, Strong MJ, Miller DF, Rusch DB, et al. (2015). Effects of the endocrine-disrupting chemical DDT on self-renewal and differentiation of human mesenchymal stem cells. Environmental health perspectives. 123: 42-48.

27. Weng YI, Hsu PY, Liyanarachchi S, Liu J, Deatherage DE, et al. (2010). Epigenetic influences of low-dose bisphenol A in primary human breast epithelial cells. Toxicology and applied pharmacology. 248: 111-121.

28. Blavier J, Songulashvili G, Simon C, Penninckx M, Flahaut S, et al. (2016). Assessment of methods of detection of water estrogenicity for their use as monitoring tools in a process of estrogenicity removal. Environmental technology. 37: 3104-3119.

29. Rider CV, Furr JR, Wilson VS, Gray LE. (2010). Cumulative effects of in utero administration of mixtures of reproductive toxicants that disrupt common target tissues via diverse mechanisms of toxicity. International journal of andrology. 33: 443-462.

30. Hass U, Scholze M, Christiansen S, Dalgaard M, Vinggaard AM, et al. (2007). Combined exposure to anti-androgens exacerbates disruption of sexual differentiation in the rat. Environmental health perspectives. 115 Suppl. 1: 122-128.

31. Baravalle R, Ciaramella A, Baj F, Di Nardo G, Gilardi G. (2017). Identification of endocrine disrupting chemicals acting on human aromatase. Biochimica et biophysica acta.

32. Lynch C, Sakamuru S, Huang R, Stavreva DA, Varticovski L, et al. (2017). Identifying environmental chemicals as agonists of the androgen receptor by using a quantitative high-throughput screening platform. Toxicology. 385: 48-58.

33. Metcalfe CD, Kleywegt S, Letcher RJ, Topp E, Wagh P, et al. (2013). A multi-assay screening approach for assessment of endocrine-active contaminants in wastewater effluent samples. The Science of the total environment. 454-455: 132-140.

34. Kapelewska J, Kotowska U, Wisniewska K. (2016). Determination of personal care products and hormones in leachate and groundwater from Polish MSW landfills by ultrasound-assisted emulsification microextraction and GC-MS. Environmental science and pollution research international. 23: 1642-1652.

35. Ko EJ, Kim KW, Kang SY, Kim SD, Bang SB, et al. (2007). Monitoring of environmental phenolic endocrine disrupting compounds in treatment effluents and river waters, Korea. Talanta. 73: 674-683.

36. Kusk KO, Kruger T, Long M, Taxvig C, Lykkesfeldt AE, et al. (2011). Endocrine potency of wastewater: contents of endocrine disrupting chemicals and effects measured by in vivo and in vitro assays. Environmental toxicology and chemistry. 30: 413-426.

37. Marshall M, Pineda M, Yargeau V. (2017). Sensitivity of the LuminoTox tool to monitor contaminants of emerging concern in municipal secondary wastewater effluent. The Science of the total environment. 598: 1065-1075.

38. Febbraio F. (2017). Biochemical strategies for the detection and detoxification of toxic chemicals in the environment. World journal of biological chemistry. 8: 13-20.

39. Solecki R, Kortenkamp A, Bergman A, Chahoud I, Degen GH, et al. (2017). Scientific principles for the identification of endocrine-disrupting chemicals: a consensus statement. Archives of toxicology. 91: 1001-1006.

40. Hou C, Lu G, Zhao L, Yin P, Zhu L. (2017). Estrogenicity assessment of membrane concentrates from landfill leachate treated by the UV-Fenton process using a human breast carcinoma cell line. Chemosphere. 180: 192-200.

41. Bertanza G, Papa M, Pedrazzani R, Repice C, Dal Grande M. (2013). Tertiary ozonation of industrial wastewater for the removal of estrogenic compounds (NP and BPA): a full-scale case study. Water science and technology : a journal of the International Association on Water Pollution Research. 68: 567-574.

42. Bilal M, Asgher M, Iqbal HM, Hu H, Zhang X. (2017). Bio-based degradation of emerging endocrine-disrupting and dye-based pollutants using cross-linked enzyme aggregates. Environmental science and pollution research international. 24: 7035-7041.

43. Sun J, Wang J, Zhang R, Wei D, Long Q, et al. (2017). Comparison of different advanced treatment processes in removing endocrine disruption effects from municipal wastewater secondary effluent. Chemosphere. 168: 1-9.