Environmental Pollutants Can Cause Precocious Puberty [A Review]

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Abstract: In every 5000 children, one child suffers from precocious puberty. Such mini adults are not only exposed to various physiological and psychological disorders but they are also exposed to social threats. The exact triggering factors for precocious puberty are unknown but due to industrialization, various environmental pollutants designated as endocrine disruptors have been linked with precocious puberty. This review briefly discusses the relationship between various endocrine disruptors and precocious puberty.

Key words: Endocrine • Precocious • Puberty

INTRODUCTION

Puberty is multifaceted developmental processes that get startin late childhood and is characterized by maturation of the hypothalamic pituitary gonadal axis. In addition to the appearance of secondary sexual characteristics, there is acceleration of growth as well as the achievement of fertility [1-3]. On the other hand, precocious puberty is the appearance of secondary sex characteristics, earlier than the age of 8 years or the onset of menarche earlier than the age of 9 years in girls [4-5]. It is reported that, precocious puberty is more common in girls as compared to boys and still there is an increasing trend due to certain exogenous and endogenous factors [2]. The onset of precocious puberty is 1 case in every 5,000 children. Also it takes place in girls more than boys in 10:1 ratio [6].

Lawson Wilkins Pediatric Endocrine Society during 1999 suggested, lowering the average age of the arrival of puberty,between 8 to 7 among white girls as well as up to 6 years among African American girls [7]. Premature menarche is a serious threat for breast cancer, as a result precocious onset would seem to raise that threat [8-9]. Similarly, there is an accelerated bone growth during early puberty as compared to normal girls and therefore unable to achieve the average adult height [6, 10].

In children, the exact cause for this progressive decline in the age of puberty is not fully understood but it is accepted as the result of complex interaction between environmental, genetic and endocrine factors. Similarly, due to rapid growth in industrialization new and more toxic pollutants are dumped into the environment, some of which are endocrine disruptors (ED) that negatively affect our endocrine system. Several EDs such as phytoestrogens, topical and natural estrogens, pesticides, industrial chemicals and phthalates have been identified as possible agents affecting pubertal development in humans [11]. These synthetic or natural hormone disruptors accumulate in the environment in the long term and are introduced into the human body through water, air, foodstuffs, or through equipment's used in the office and home. Similarly, EDs can be transferred from the mother to the fetus via placenta or to the baby via breast milk [12]. They influence puberty through their estrogenic, antiestrogenic androgenic, antiandrogenic effects or through their direct effects on the gonadotropin-releasing hormone (GnRH). These chemicals may exert their estrogenic effects either directly by binding to estrogen receptors, increasing aromatase activity and increasing estrogen sensitivity or indirectly by their effect on GnRH, leading to an increase in endogenous estrogen production. All of these effects may result in precocious
The aim of this review was to briefly discuss various environmental pollutants that can cause precocious puberty.

**Natural Endocrine Disruptors:** The best known chemicals in this group are phytoestrogens, which are relatively weak compared to endogenous estrogen. They are found in several nutrients that are frequently consumed in daily life (i.e. carrots, garlic, apple, coffee, cherry, parsley, legumes). Phytoestrogens have estrogenic effects when consumed in huge amounts and antiestrogenic effects at low concentrations [14].

**Genistein and Daidzein:** A Korean study reported that both genistein and daidzein exposure in girls induces precocious puberty. In their study, they recruited 180 girls with Central Precocious Puberty (CPP) and 91 as age match control group and found significantly higher plasma level of genistein and daidzein in CPP as compared to age matched control group [15].

**Estrogenic Mycotoxin:** In one study mycoestrogen, zearalenone (ZEA) was found to be a triggering factor for CPP as, it is chemically similar to some anabolic agent used in animal breeding. They found that, weight and height velocity were higher in girls exposed to ZEA as compared to control group [16]. ZEA in exposed group represent a growth promoter.

**DDT (Dichlorodiphenyltrichloroethane):** DDT is used for agriculture as pesticides. Since 1970s, DDT was banned because of its risky threat on the environment but, still used in some countries due to considerable decrease in malaria cases in many areas [17]. DDT affects neuroendocrine pathways by competing with estrogen hormone [18] and stimulating the release of Gonadotropin Releasing Hormone (GnRH) [19]. DDT is associated to priormenarche in girls approximately 3 to 4 years before compare to average [20] but in boys, it has not shown any considerable effects on puberty [21]. However, DDT in post pubertal boyshas harmful effect on semen quality [22]. DDE (dichlorodiphenyldichloroethylene) the breakdown of DDT, is an additional frequently seen estrogendisruptor and contain the identical risk in humans as DDT however, dissimilar in structure due to which little bit modify the actions [23]. Clinical examination of 145 children in Belgium for precocious puberty, it was found that children born in foreign countries where DDT was broadly used showed a strong link with precocious puberty [24]. Vasiliu, Karmass and Muttineni, examined the consequence of DDE in children of fishermen wives living in Michigan lake and demonstrated greater levels of DDE throughout pregnancy and it was noted that exposure of fetuses to DDE was linked with decrease in the age of menarche [25]. It was also reported that 4 month old girl presented with sexual maturity containing menstruation, breast improvement, uterine length of 69mm at ultrasonography as well as considerably high estrogen bioactivity but no growth acceleration, pelvis masses or adrenal tumors and pubic hair. Similarly, in her father there was a dramatic decrease in libido. Latter on the cause was found to be DDD and DDT pesticides that accumulate in the family farm. The precocious sexual development was possibly caused by the estrogen activity of the environmental contamination by tons of pesticides accumulate in the family farm [26].

**Dioxin:** Dioxin acts as an estrogen disruptor and copies the actions of estrogen [27]. Small quantities of dioxins can be produce through different process including chlorinbleaching of pulp and paper, certain types of chemical manufacturing as well as processing, combustion process and through our food supply such as milk [28]. Exposure to dioxin causes unusual breast growth in pre pubertal girls while no considerable effect on pre pubertal boys [29]. It was also reported that perinatal exposure to a low dose of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) induces precocious puberty including early maturation of the hypothalamic–pituitary axis, the gonads as well as genitals, in female Long-Evans hooded rats [30].
**BPA (Bisphenol A):** BPA (Bisphenol A) is used to construct polycarbonate plastics as well as epoxy resins, used to construct many daily used domestic products containing plastic containers like baby formula bottles, dental sealants, as well as polycarbonate laboratory flasks. Different mechanism of action of BPA is proposed by different scientists. It was suggested that the neurotoxic effects of BPA can be mediated either by competing with estradiol for binding with ERα’s, [31] or through ERK/NK-kappa pathway [32]. The action of BPA are fewereffective than estrogen as well as show antagonistic consequence in the existence of estrogen on peroxidase activity as well as progesterone levels however it effect on uterine weight [33]. BPA cause precocious puberty in girls as well as enhancement of abnormality in boys [34]. Neonatal exposure to medium and high doses of BPA can induce precocious puberty in rats, but it may not result from the change in hypothalamic Kiss-1 mRNA expression. In contrast, low dose has no effect on puberty timing [35]. In a study of 103 girls, containing 52 controls, 51 with Central Precocious Puberty (CPP) having age 7 to 9 years were recruited. Pubertal staging, anthropometry, bone maturation were assessed. Gonadotropin releasing hormone-stimulation test were conducted to determine the basal along with peak levels of luteinizing hormone (LH). Serum bisphenol A levels were analyzed by gas chromatography/mass spectrometry method. Geometric mean serum BPA levels were higher in CPP girls as compared to control group [36].

**Phthalate Esters:** Phthalate esters are plasticizers which contaminating foods as well as drinks which are contained in plastic bottles [39]. It disrupts the endocrine system by mimicking estrogen along with binding to ERα as well as b [40]. Phthalates can cause decrease in testosterone production, testicular dysgenesis syndrome as well as decrease in the anogenital distance in 2 to 36 months old boys [41-42]. Exceptionally, only some reports are accessible that has found phthalate effected pubertal boys while the effects on pubertal girls contain defeminization and thelarche, or early thelarche as well as estrogen on peroxidase activity as well as secondary breast development [43]. In Puerto Rico, it has been reported that phthalate levels in the blood of girls who exhibited premature breast development were 68% higher than those of control group [44]. Studies in 2008 and 2009 [45] in Korea reported a significant relationship between the phthalate levels in the plasma and precocious puberty in patients.

![Structure of Phthalate esters](image)

**Methoxychlor:** It is an organochlorine and has been introduced for use instead of DDT. Animal’s studies showed that methoxychlor accumulates in fat tissues and like DDT and its metabolites it has similar estrogenic effect [46] but there are no studies on the effects of this pesticide on precocious puberty in humans.

**Polybrominated Biphenyls (PBBs):** (PBBs) added to plastics and used for production of different products including, computer monitors, televisions, textiles as well as plastic. These are colorless to off-whites solids and introduce into environment as mixtures of different individual brominated biphenyl for PBBs components identified as congeners [37]. Exposure to milk contaminated with PBB is responsible for earlier menarche, thelarche as well as pubarche in girls but no significant effect of PBBs was observed in boys [38].

**CONCLUSIONS**

Long term exposure to endocrine disruptors such as genistein, daidzein, ZEA, DDT, DDE, dioxin, BPA, PBBs, phthalate esters and methoxychlor can cause precocious puberty. Although, they are children but look like mini adult and are therefore at risk for sexual harassment. Such girls can also develop various forms of cancer, sexually transmitted diseases and even pregnancy as they have no information about safe sex. To prevent the incidence of precocious puberty, we should not use food pack in plastic container. There should be proper care and education for such children to adjust them safe in society.

**REFERENCES**


