International Journal of scientific research and management (IJSRM)
||Volume||2||Issue||6||Pages|| 1000-1004||2014||
Website: www.ijsrm.in ISSN (e): 2321-3418

Indiscriminate chemical use in Kerala: Special emphasis to reproductive changes by endocrine disrupting chemicals

Rejitha Joseph[1]. and Soumya[2] Sankar.

([1]MVSc Scholar, Dept of Veterinary Physiology, Kerala Veterinary and Animal Sciences University

[2] MVSc Scholar, Dept of Animal Husbandry and Extension, Kerala Veterinary and Animal Sciences University)

Corresponding author: Rejitha Joseph, Puthenpurackal (H), ACN-100, Angamaly Central Nagar, Angamaly P.O., Kerala, 683572.

E-mail id.: drrejithajoseph@gmail.com

Abstract
Some of the insecticides and pesticides are known as endocrine disrupting (ED) chemicals that have the property to alter normal functioning of endocrine system. In this paper the hazardous properties of some pesticides liberally used in Kerala and their physiological effects with special emphasis to disorders in reproductive system are reviewed. The aim of the present review is to give an overview of various ways in which EDs may disrupt the reproductive hormonal function. Endocrine disturbing chemicals disturb the mechanism of hormone synthesis, storage, release and action through getting into various steps and modulating various enzymes involved. Altered hormonal profile result in sub fertility or infertility of individuals and effect of chemicals on gametes are resulting in genetic defect. General awareness on adverse effect of pesticide, controlled use of pesticide and biological pest control has to be disseminated among the farmers of Kerala. It is necessary to establish a double pricing system to agricultural products of organic farming in Kerala for promoting organic farming among the farmers.

Key words: Pesticides, Endocrine disrupting chemicals, Kerala

Introduction

Pesticides and insecticides are used in agricultural and medical practice to control unwanted organisms, weeds, ectoparasites and vectors of disease. The main acute health effects are difficulty in breathing, headaches and irritation of skin and mucous membranes, whereas chronic adverse effects are neurological and psychological effects, suppressed immune system, cancer, reproductive disorders and genetic defects. The expression of these effects depends on the type of the chemical and on level and duration of exposure. Detrimental effects of ED pesticides on wildlife and population level impact was reported by some of the scientists (Grote *et al.*, 2004, Reeder *et al*., 2005).Pesticide exposure in women may be resulted in reproductive problems such as decreased fertility, spontaneous abortions, still birth, premature birth, low birth weight, developmental abnormalities, ovarian disorders and disruption of hormonal function.

Role of hormone on reproduction

Hormones are playing an important role in development, growth and maintenance of reproductive organs and establishment of reproductive vigor and viability of germ cells. In males and females, secretion of Gonadotropic Releasing Hormones from hypothalamus (GnRH) results in the release of Follicle Stimulating

Hormone (FSH) and Luteinizing Hormone (LH) from the anterior pituitary gland. In males, LH enhances the production and secretion of testosterone from the gonads/testes via leydig cells. In females, LH stimulates the production of oestrogens and progesterone from the gonads/ovary through theca interna cells and luteal cells. Concentrations of LH or frequency of LH surge increase in males during prepuberal period and rhythm of surge release and subsequent increase in testosterone concentration maintained throughout the life period. But in case of female the concentration of LH increases during ovulation and with the formation of the corpora lutea with progesterone secretion. The target tissue of FSH is sertoli cells in the case of males and granulose cells in the case of females. FSH stimulates the maturation of germ cells within the gonads. In the male FSH also stimulates the secretion of inhibin and in female it stimulates follicular development and oestradiol synthesis. which has a negative feedback directly to the anterior pituitary. Oxytocin from hypothalamus and prolacin from anterior pituitary also plays an important role in female reproductive system.

The main male sex hormone testosterone is required for spermatogenesis. Testosterone is produced by the leydig cells within the testes. The principal action of testosterone is anabolic growth, spermatogenesis endorsement and promotion of accessory sex glands secretion. Reproductive role of oestrogens like estradiol, estrone and estriol stimulate follicular growth and maturation; prepare female genitalia for copulation and growth of zygote. It also contributes to the growth and development of mammary tissue and prepares the uterus for parturition. Progesterone prepares the uterus after conception, the mammary tissues for milk production. Preparation of uterus after conception includes enhanced growth of endometrial gland and nourishment of embryo.

Effects and Mechanism of action of EDs

The effects of pesticides or insecticides on reproductive system are through its action as endocrine disruptors. Endocrine disruptors are usually natural or synthetic chemicals that mimic, increase or inhibit the action of endogenous hormones. Mechanisms involved in disruption of hormonal function are by interfering1. Hormone synthesis 2. Hormone storage and release 3. Hormone transport and clearance 4. Hormone receptor recognition and binding 5. Hormone post-receptor activation (Sonnenschein and Soto, 1998).

Interferences with hormone synthesis can be exemplified by pesticides like prochloraz and other imidazole fungicides, which can inhibit estrogen biosynthesis by inhibiting the enzyme aromatase and thereby preventing the conversion of androgens to estrogens (Bretveld *et. al.,* 2006). Heptachlor may act as an inducer of testosterone. Some pesticides like atrazine, simazine, primicarb, propamocarb, iprodion and propazine can stimulate aromatase acivity (Vinggaard *et al.* 2000). Ketoconazole have an inhibitory action on progesterone synthesis.

Mechanism of action of formamidine pesticides like chlordimeform and amitraz is interruption of norepinephrine binding to alpha – 2-adrenoceptors (Costa *et al*., 1988), which result in reduced pulsatile release of GnRH and blockage of ovulatory surge of LH. Viability and quality of the oocyte could affect by disordered timing of LH surge. Malathione exposure at the onset of estrus can inhibit the release of progesterone (Prakash *et al.,* 1992).

DDT analogs, endosulfan and mirex are potent inducers of hepatic microsomal monooxygenase activity which degrades endogenous androgens, resulting in suppressed androgen receptor (Massaad *et al*., 2002). Organophosphate pesticides can affect enzymes that stimulate contractions of the uterus. The study showed an inverse association between chlorpyrifos levels (in umbilical cord blood in a dose–response relationship) and birth weight and length in newborns born before the ban, suggesting that diazinon levels may also be associated with

reduced birth weight and length (OCFP 2012 pesticide preview).

Hypospadias, an abnormal positioning of the opening of the urethra in males, is one of the birth defects most commonly studied in the pesticide exposure. There is some reports suggests that an increased risk of hypospadias with maternal occupational pesticide exposure (Rocheleau, 2009).

Sex hormones play a strong role in fetal genitourinary development and utero exposure to endocrine-disrupting chemicals could contribute to hypospadias. Organochlorines persist in fat tissue and can be transmitted to fetuses placentally and to infants via breast milk. Many chemicals like Cyhalothrin, Mancozeb, Malathion modulate the action thyroid hormone and act as disrupters of normal reproduction (Foster, *et al*., 1995).

Name of chemicals used mainly in kerala	**Mode of action**
Carbaryl (Sevin , Hexavin, Carvint)	Estrogen mimic
Carbosulfan – (Marshal)	Affect androgen- and androgen-receptor dependant mechanisms. Interfere with cellular microtubule formation in oestrogen-sensitive cells
Malathion (Cythion, Malamar, Star Mal, Malatox)	Increased apoptosis of spermatids during spermatogonial proliferation
Dichlorvos (Vapona, Nuvan, Luvon)	Competitive inhibitor of androgen receptors, inhibits oestrogen-sensitive reporter binding to androgen receptors. Some of them induce the production of aromatase the enzyme which converts androgen to oestrogen
Quinalphos (Quinalphos, Kinalux, Ekalux)	Increases the expression of oestrogen responsive genes.
Dimethoate (rogor, corothioate, nugor, hilthoate)	Decreases the blood level concentration of LH.
Chlorpyriphos (Dursban, classic , Radar)	Antagonises androgen activity
Acephate (Astaf, Starthene)	Disturbs hormone expression in the hypothalamus
Carbendazim	Increases oestrogen production by increasing aromatase activity
Diuron	Inhibits the actions of androgens.
Cypermethrin	Mimics the action of oestrogen. Metabolites also have oestrogenic effects
Fenvalerate	Inhibits the proliferation of oestrogen-sensitive cells, antagonizes the action of progesterone.
Methyl parathion	Gonadotrophic hormone inhibition
Chloripyriphos	Antagonises androgen activity
Endosulphan	Antagonises the action of androgens via binding competitively to their receptors and inhibiting the genetic transcription. Mimics the actions of oestrogens indirectly by stimulating the production of their receptors. Weak aromatase inhibitor.
DDT	Mimics the action of oestrogen, antagonises the action of androgens via binding competitively to their receptors and inhibiting the genetic transcription. Promotes the proliferation of androgen-sensitive cells. Mimics the actions of oestrogens indirectly by stimulating the production of their receptors.
Carbendazim	Affect androgen receptor. Increases oestrogen production by increasing aromatase activity

Captan	Inhibits the action of oestrogen.
2.4–D	Synergistic androgenic effects when combined with testosterone
Glyphosate	Disrupts the action of aromatase preventing the production of oestrogens.
Carbofuran	Acute doses increase levels of progesterone, cortisol and oestradiol whilst decreasing testosterone levels
Triazophos	Inhibition of natural ligands that bind to androgen receptors and androgen-binding proteins. Some induce or inhibit the production of aromatase, an enzyme that converts androgen to oestrogen
Atrazine	Androgen inhibitor with a weak oestrogenic effect. Disrupts the hypothalamic control of lutenising hormone and prolactin levels. Induces aromatase activity, increasing estrogen production. Damages the adrenal glands and impairs steroid hormone metabolism.
Pyrethroids	Antagonise or potentiate the action of oestrogen by acting on the oestrogen receptor or possibly an alternative signalling pathway. Some Inhibit the action of progesterone by affecting the hormone directly. (McKinlay *et al*., 2008)

Impact on population of Kerala

Study of Kerala Agricultural University revealed that farmers are still using chemicals for food crops include chemicals which are banned for sale in Kerala (Endosulfan), banned for use in fruits/vegetables (Monocrotophos) and those permitted for restricted use only (Methyl Parathion, Lindane and Methoxy Ethyl Mercury Chloride). Recent study on the chemical level on vegetables showed high level than permitted level in food crops. The government of Kerala has banned the sale/use of Endosulphan due to the environmental and human health problems, but that still in use among pineapple growers and mango planters (Indiradevi, 2010). The exact impact of EDs over the Kerala population is not available even though the market vegetable levels of EDs are high over the entire state.

Conclusion

In this paper, we described the different ways in which EDs may disrupt the hormonal function of reproductive system and in particular to the effects of chemicals popularly used in Kerala. Pesticides are comprises of large number of chemicals with dissimilar structures and diverse toxicity which may act through different mechanism. So it is difficult to explain the actual patho-physiological pathway and development of reproductive failure even though it affecting various metabolic pathways. Even though there are so many reports that altered hormonal profile result in sub fertility or infertility of individuals and effect of chemicals on gametes are resulting in genetic defect, a further elaborated study needs for this. General awareness on adverse effects of pesticide has to be disseminated among the farmers and a promotion of organic farming is necessary for the healthier future generation.

References

Grote, K., Stahlschmidt, B., Talsness, C.E., Gericke, C., Appel, K.E. and Chahoud, I. 2004. Effects of organotin compounds on pubertal male rats. *Toxicology* 202(3):145–158

Reeder, A., Ruiz, M.O., Pessier, A., Brown, L.E., Levengood, J.M. and Phillips, C.A. 2005. Intersexuality and the cricket frog decline: Historic and geographic trends. *Environ Health Perspect* 113(3):261–265

Sonnenschein, C. and Soto, A. M. (1998). An updated review of environmental estrogen and androgen mimics and antagonists. *J. Steroid Biochem. Mol. Bio.* 65: 143-150

Bretveld, R. W., Thomas, C.M.G., Scheepers, P.T.J., Zielhuis, G.A. and Roeleveld, N. 2006. Pesticide exposure: the hormonal function of the female reproductive system disrupted. *Reprod. Bio. Endocrino.* 4:30-46

Vinggaard, A.M., Hnida, C., Breinholt, V. and Larsen, J.C. 2000. Screening of selected pesticides for inhibition of CYP19 aromatase activity in vitro**.** *Toxicol In Vitro.* 14**:**227-234.

Costa, L.G., Olibet, G. and Murphy, S.D. 1988. Alpha 2-adrenoceptors as a target for formamidine pesticides: in vitro and in vivo studies in mice. *Toxicol Appl Pharmacol.* **93:**319-328

Prakash, N., Narayana, K., Murthy, G.S., Moudgal, N.R and Honnegowda. 1992. The effect of malathion, an organophosphate, on the plasma FSH, 17 beta-estradiol and progesterone concentrations and acetylcholinesterase activity and conception in dairy cattle. *Vet. Hum. Toxicol.* 34:116-119

Massaad, C., Entezami, F., Massade, L., Benahmed, M., Olivennes, F., Barouki, R. and Hamamah, S. 2002. How can chemical compounds alter human fertility**.** *Eur. J. Obstet. Gynecol. Reprod. Biol.* 100:127-137

Foster, W.G., McMahon, A., Younglai, E.V., Jarrell, J.F. and Lecavalier, P. 1995. Alterations in circulating ovarian steroids in hexachlorobenzene exposed monkeys. *Reprod. Toxicol.* 9:541-548

McKinlay, R., Plant, J.A., Bell, J.N.B. and Voulvoulis, N. 2008. Endocrine disrupting pesticides: Implications for risk assessment. Environ. Int. 34: 168–183

Indiradevi, P. 2010. Pesticides in Agriculture – A Boon or a Curse? A Case Study of Kerala. *Economic & Political Weekly*. 14: 26-35