



Review on effect of carbamate pesticide on male reproductive system of mammals

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Abstract

Pesticides are combination of chemicals used to avoid pest infestation and they act as biocides that kill all life forms. Most popular pesticides include carbamates, pyrethroids, organochlorine and organophosphate. The rate of damage that pesticides impose in reproduction organs and tissues entirely depends upon dosage of pesticide and their contact procedure. Direct or indirect exposure of humans to pesticides leads to severe health problems such as cancer and abnormalities of endocrine, neurological, and reproductive systems i.e., Testicular function. Carbamate is one of relevant chemical among EDCs (Endocrine Disrupting Chemicals) including carbaryl, propamocarb, pimecarb, methiocarb, benomyl, bendiocarb, aminocarb, carbofuran, carbosulfan, methomyl, thiodicarb and aminocarb adversely affect male reproductive system by effecting normal functioning of spermatogenesis and subsequent changes in reproductive ducts. Carbamate affect the normal functioning of reproduction system by destroying the endocrine system either increasing or decreasing the level of hormones such as testosterone, LH, FSH, progesterone and estradiol. Carbamate pesticides are main cause of infertility and can be controlled by awareness schemes and by promoting preventive measures.

Keywords: pesticides, carbamate, reproductive system, fecundity, testosterone, spermatogenesis

Introduction

Pesticides are man-made chemicals or combination of chemicals that are used to avoid pest infestation and popularly act as biocides that kill all life forms ^[1].

In recent years, the use and need of these chemicals well known as pesticides become so extensive ^[2]. Because they are used to enhance yield and quality of food. They are also used to control vector-borne diseases (such as malaria, encephalitis, dengue and filariasis) ^[6].

In 1960s, for the first time, they have adverse effects on environment ^[3]. They are also responsible for pollution of natural resources because they are considered to be strong class of biodegradable pollutants ^[21]. As pesticide practice for acquiring better crop yield possess contamination of food stuff so their long-term persistence in food chain endanger humans ^[4], domestic animals, birds, wild-life, livestock and fish.

Humans exposed directly or indirectly to pesticides causes various severe health issues like cancer, endocrine, neurological, and reproductive abnormalities ^[7]. Other complication include disrupted testicular function along with non-reproductive specific health problems such as cancer. Chronic exposure of pesticide leads to Parkinson and Alzheimer disease. They are also responsible for respiratory problems such as asthma, and cardiovascular diseases. They also cause aging in humans ^[1]. The other minor health issues because of interaction within pesticide include flue, mild headache and some skin problems ^[12].

In modern agriculture and food marketing, pesticides used to prevent unwanted insect to enhance production, processing, storage and transport. One or more active ingredients are present in pesticides that target the different insects ^[1]. The

carbamates, pyrethroids, organochlorine (such as DDT, aldrin, dieldrin, and hexachlorocyclohexane) and organophosphate are popular pesticides ^[2]. Although environmental, dietary and occupational are three major means of exposure of pesticides and among them occupational is the more common. Some pesticides mimic certain steroid hormones due to their structural similarity and act as endocrine disruptors. They have ability to bind with the hormone receptors ^[1] and effect natural hormones involved in maintenance of homeostasis, development and reproduction of both male and female. These EDs (Endocrine Disrupting Chemicals) are considered exogenous agents that alter the normal synthesis, transport and action of natural hormones ^[8]. For example, parathion and methyl parathion have ability to bind with estrogen receptors due to similarity to estrogen, hence disrupt the normal process of transcription of gene and adversely affect spermatogenesis by increasing apoptosis of germ cell. Through evidence, it has been proved that they have directly affect by acting as Endocrine-Disrupters and indirectly by interfering mechanism of certain hormones (such as testosterone) at neuroendocrine level and central nervous system as toxicants. They (such as carbofuran) induce oxidative stress by changing antioxidant or producing free radical leading to scavenging of certain enzymes such as catalase and superoxide dismutase ^[1]. The rate of damage that they inflict in reproduction organs and tissues entirely depends upon dosage of pesticide and their contact procedure. Carbamate can also effect, the normal functioning of reproduction system by destroying the endocrine system either increasing or decreasing the level of hormones such as testosterone, LH, FSH, progesterone and estradiol.

Effect of carbamate pesticides on male reproductive system

Carbamate

Carbamates are extracted from a West African plant named as Calaber bean that contains physostigmine, is derived from carbamic a methylcarbamate. Carbamate acid, it was used as an insecticide in 1950s and approximately 25 carbamate compounds are in use as pesticides. Carbamate is one of relevant chemical among EDCs including carbaryl, propamocarb, pimecarb, methiocarb, benomyl, bendiocarb, aminocarb, carbofuran, carbosulfan, methomyl, thiodicarb and aminocarb adversely affect male reproductive system by effecting normal functioning of spermatogenesis and subsequent changes in reproductive ducts. Carbamate is well known due to their action, effectiveness, and application in modern agriculture. Carbamates are esters of N-methyl carbamic acid. Carbamate also demonstrated as Acetylcholinesterase inhibiting agents(Ache) and carbamate effect the neurotransmission as it inhibits the enzyme (Acetylcholine esterase) that perform breakdown of neurotransmitter at nerve synapses, so enhance stimulation of level and duration of Ache at nerve endings [8]. Its toxicity depends on amount of its exposure.

In past 50 years, the use of the toxins in agriculture remarkably reduced the average number of sperms in men. The toxins that humans are exposed to can affect directly by damaging testis or indirectly by altering spermatogenesis (through disturbing hormonal regulation).

Carbaryl

Carbaryl is a widely used insecticide of carbamate family since 1956. A well-known brand Sevin manufactures carbaryl and it is used in dozens, approximately 2 million pounds of carbaryl is used in agricultural crops every year and 2 to 4 million pounds in yards and gardens (journal of pesticides reforms). The reproductive cells and tissues of mammals directly affected carbaryl induce changes in spermatogenesis and effecting regulation of hormones. When the rats effected by carbaryl was observed, they showed that carbaryl causes histopathological changes in rat testis tissue and does not causes any change in weight of testis [10]. The adverse effect of carbaryl on male reproductive system induce sperm abnormalities such as sperm count, sperm motility and sperm shape.

Hormonal effect the carbaryl

Due to exposure to carbaryl, reduction in levels of different harmones such as testosterone, progesterone and estradiol in male reproductive system of mammals [11].

The rat exposed to carbaryl shows remarkable increases in level of LH and FSH. The high level of LH in carbaryl exposed rats claimed that there is an increases in ledyng cell No. but it also inhibit the spermatogenesis. The secretion of testosterone depends on ledyng cells reduce in carbaryl exposed animals. Testosterone is very important for normal production of sperm but carbaryl exposed rat have reduced level of testosterone with ultimately effect spermatogenesis and causes infertility [13].

Carbaryl-exposed mammals have reduced diameter of seminiferous tubules which is due to decline in spermatogenic

cells or atrophy [9]. Carbaryl causes cells death by effecting mitochondrial function hence reduces ATP synthesis and also by blocking metabolism of nucleic acid and protein [14, 15].

Propoxur

Propoxur is well known carbamate insecticide used for variety of pests in both agriculture and non-agricultural applications. Propoxur is highly toxic for reproductive parameters through oral administration, such as an increase of testis weight, change in characteristics of sperm e.g decrease in motile spermatozoa and loss of germ cells are reproductive parameters effected by propoxur [16].

Propoxur also cause decrease in serum and total concentration of protein and cholesterol in intra-testicular space. However reproductive performance in term of fertility have less effect of propoxur and maintained after 90th day of treatment [17].

Propoxur-toxicity induce mechanism

In propoxur treated rat, the rate of vacuoles gradually increases at ad-luminal region while cell death within premature spermiation and loss of germ cells lead to disorganization of seminal epithelium. Furthermore rate of effect of these events on sperm motility is propoxur dose-dependent [17].

Methymol

Methymol is an insecticide of carbamate family. Methymol induce degenerative changes such as testicular lesions that lead to interruption in differentiation action of germ cells at specific stage. Hence loss of reproductive functions e.g fecundity index, motility of sperm, sperm count, level of testosterone in serum and male sexual glands significantly reduces and cause sperm anomalies [18].

Carbendazim

Carbendazim induce morphological changes: Through an experiment of Massaki Nakai, it has been shown that carbendazim treated rat have shading of elongating spermatids in all stages of spermatogenesis. Nurse cells surround the elongating spermatids. At this region cleavage occur while having undamaged ectoplasm, cleaved cytoplasm along with intact-microtubules in sloughed immature germ cells show decrease in body density along with cluster of mitochondria. Decrease in germ cell body density associated with swelling cisternae of Endoplasmic Reticulum. Hence disruption of Sertoli cell take place [19].

Male infertility also caused in carbendazim treated rat as sloughed germ cells block the efferent, ductules and lead to atrophy of seminiferous tubules [20]. In conclusion, it is demonstrated that carbendazim effect the reproductive system of male directly by effecting the meiotic spermatocytes and indirectly by causing abnormalities of Sertoli cell [19].

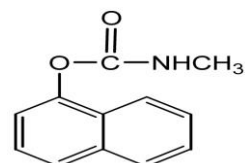


Fig 1: Structure of Carbaryl

Conclusion

In modern agriculture, the use of carbamate pesticides becomes extensive while having need to take steps for worker's welfare by industry authorities. Hazard impact on human health is higher in those countries where there are poor safety measures and poor management of work places. However it is difficult to eliminate pesticides from environment but to minimize its effects, protective equipments should be used by workers in farms. Workers using well-protected measures show less adverse effects to their reproductive system as compare to workers with poor safety management. Lack of economic investment, un comfort to handle modern equipment and ignorance about health concerning issues due to illiteracy are main reasons to avoid use of protective equipments and poor management.

Carbamate pesticides are considered to be main cause of infertility and can be controlled by awareness schemes and by promoting preventive measures. Due to lack of strong uniform management system of pesticide by government, the regulation of safe methods are not practiced mostly. As pesticides penetrate into food chain being a content of food and vegetables, it directly and indirectly effect our organisms in every trophic level. In humans pesticides cause a number of health hazards as mentioned previously so randomly effect normal population due to their penetration in food and vegetables and certain diseases Parkinson, Alzheimer disease and are also responsible for respiratory problems such as asthma, and cardiovascular diseases. Pesticides also induce Aging in humans, Assessments of pesticides risk attributes, dose-dependency with level of danger and identification of critical issues towards reproductive health are some steps to eliminate the effect of pesticides contamination.

References

- Mehrpour O, Karrari P, Zamani N, Tsatsakis AM, Abdollahi M. Occupational exposure to pesticides and consequences on male semen and fertility: a review. *Toxicology letters*. 2014; 230(2):146-156.
- Jamal F, Haque QS, Singh S, Rastogi SK. Retracted: The influence of organophosphate and carbamate on sperm chromatin and reproductive hormones among pesticide sprayers, 2016.
- Srinivasa J, Maxim P, Urban J, D'Souza A. Effects of pesticides on male reproductive functions. *Iranian Journal of Medical Sciences*. 2015; 30(4):153-159.
- Khan M, Zia J, *et al*. Pesticide residue in the food chain and human body inside Pakistan. *Journal- Chemical Society of Pakistan*. 2008; 31(2):284-291.
- Gupta VK, Ali I, Saini VK. Adsorption of 2, 4-D and carbofuran pesticides using fertilizer and steel industry wastes. *Journal of Colloid and Interface Science*. 2006; 299(2):556-563.
- Abhilash PC, Singh N. Pesticide use and application: an Indian scenario. *Journal of hazardous materials*. 2009; 165(1-3):1-12.
- Agnihotri AG. Pesticide: safety evaluation and monitoring. *Indian Agricultural Research Institute, Division of Agricultural Chemicals*, 1999.
- Kaur RP, Gupta V, Christopher AF, Bansal P. Potential pathways of pesticide action on erectile function—A contributory factor in male infertility. *Asian Pacific Journal of Reproduction*. 2015; 4(4):322-330.
- Fattahi E, Jorsaraei SGA, Gardaneh M. The effect of Carbaryl on the pituitary-gonad axis in male rats. *Iranian journal of reproductive medicine*. 2012; 10(5):419.
- Pant N, Srivastava SC, Prasad AK, Shankar R, Srivastava SP. Effects of carbaryl on the rat's male reproductive system. *Veterinary and human toxicology*. 1995; 37(5):421-425.
- Meeker JD, Ryan L, Barr DB, Hauser R. Exposure to nonpersistent insecticides and male reproductive hormones. *Epidemiology*, 2006, 61-68.
- ICAR. Report of the special committee on Harmful Effects of pesticides, ICAR, New Dehli, 1967, 78.
- Amin S, Zhang Y, Felson DT, Sawin CT, Hannan MT, Wilson PW, Kiel DP. Estradiol, testosterone, and the risk for hip fractures in elderly men from the Framingham Study. *The American journal of medicine*. 2006; 119(5):426-433.
- Eraslan G, Kanbur M, Silici S. Effect of carbaryl on some biochemical changes in rats: the ameliorative effect of bee pollen. *Food and chemical toxicology*. 2009; 47(1):86-91.
- Moreno AJ, Serafim TL, Oliveira PJ, Madeira VM. Inhibition of mitochondrial bioenergetics by carbaryl is only evident for higher concentrations—relevance for carbaryl toxicity mechanisms. *Chemosphere*. 2007; 66(3):404-411.
- Kenfack A, Ngoula F, Chombong JK, Vemo NB, Ndukum JA, Ngouateu OB, *et al*. Effects of propoxur on male fertility in wistar rat exposed neonatally. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017; 3(4):898-902.
- Ngoula F, Watchob P, Bousekob TS, Kenfack A, Tchoumbouéa J, Kamtchouing P. Effects of propoxur on the reproductive system of male rats. *African journal of reproductive health*. 2007; 11(1):125-132.
- Shalaby MA, El Zorba HY, Ziada RM. Reproductive toxicity of methomyl insecticide in male rats and protective effect of folic acid. *Food and Chemical Toxicology*. 2010; 48(11):3221-3222.
- Nakai M, Moore BJ, Hess RA. Epithelial reorganization and irregular growth following carbendazim-induced injury of the efferent ductules of the rat testis. *The Anatomical Record*. 1993; 235(1):51-60.
- Hess RA, Moore BJ, Forrer J, Linder RE, Abuel-Atta AA. The fungicide benomyl (methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate) causes testicular dysfunction by inducing the sloughing of germ cells and occlusion of efferent ductules. *Fundamental and Applied Toxicology*. 1991; 17(4):733-745.
- Gupta VK, Ali I, Saini VK. Adsorption of 2, 4-D and carbofuran pesticides using fertilizer and steel industry wastes. *Journal of Colloid and Interface Science*. 2006; 299(2):556-563.