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Review

Pesticides and Their Effects on Worker Health

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Abstract

There are more than 1000 types of pesticides used worldwide, especially in agriculture, as well as in homes, offices, landscaping and gardens. The use of pesticides is inevitable in obtaining sufficient and healthy products from agriculture for nutrition in life sustaining. In people exposed to pesticides; Acute and chronic harmful effects are observed depending on the type of pesticide used, the dose used and the duration of use. It has been shown that chronic exposure can cause diseases such as diabetes, thyroid dysfunction, asthma, and cancer. Necessary precautions should be taken when using pesticides to eliminate or reduce their harm to human health. Reducing pesticide use is the responsibility of both the producer, the consumer and the state. To protect workers from pesticides, appropriate measures should be taken according to risk assessment at each stage. In order to eliminate the risk in the workplace environment, it should be replaced with another substance if possible, and if not, exposure should be reduced by using the necessary prevention and protection methods. Since pesticide use is widespread in our country, we wanted to examine its effects on human health in the light of the literature.

Keywords: Agricultural worker, exposure, pesticide, protection

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In agriculture, pesticides play an important role in increasing the yield and obtaining quality products, in the fight against diseases, pests and weeds.[1] A pesticide is any substance or mixture of chemical or biological ingredients intended to expel, destroy or control any pest or to regulate plant growth.[2] According to the World Health Organization (WHO), there are more than 1000 pesticides used worldwide. In addition to the benefits of pesticides, they can cause damage to human health and the environment. The toxicity of a pesticide depends on its function and other factors. For example, insecticides tend to be more toxic to humans than herbicides. Toxicity may depend on the amount of exposure and the route by which exposure occurs. Many of the older and cheaper pesticides, such as dichlorodiphenyltrichloroethane (DDT), can remain in soil and water for years. These chemicals are banned by countries that have signed the 2001 Stockholm Convention, an international agreement aimed at eliminating and restricting the production and use of persistent organic pollutants. Because pesticides are toxic and spread into the environment, their production, distribution and use require strict regulation and control. Moreover regular monitoring of food and environmental residues is also necessary. WHO has two goals regarding pesticides. These; to protect public health by prohibiting pesticides that are most toxic to humans and permanent in the environment, and by setting maximum limits for pesticide residues in food and water.[3]

In the world and in our country, insecticides, fungicides and herbicide group pesticides are widely used depending on the pest group.[1] In our country, pesticide use is more intense in regions where fruit and vegetable production is high.[4]

Pesticides are classified as in Table 1.[5-11]

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Table 1. Pesticide Groups

Insecticides	**Organochlorines**
	Chlordane
	Aldrin
	DDT
	Lindan
	Heptachlor
	Toxaphene
	Organophosphates
	Chlorpyrifos
	Fonofos
	Malathion
	Phorate
	Terbufos
	Carbamates
	Carbaryl
	Carbofuran
	Pyrethroids
	Permethrin
Herbicides	**Dinitroanilines**
	Pendimethalin
	Trifluralin
	Thiocarbamate
	EPTC
	Phenoxy
	2,4,-D
	2,4,5-T(2 4 5-trichlorophenoxyacetic)
	Triazine
	Atrazine
	Cyanazine
	Metribuzin
	Chloroacetanilide
	Alachlor
	Metolachlor
	Imidazolinone
	Imazethypyr
	Phosphinic
	Glyphosate
	Benzoic
	Dicamba
	Urea
	Chlorimuron-ethyl
Fungicides	**Acylalanine**
	Metalaxyl
	Aliphatic nitrogen
	Dodine
	Amide
	Carpropamid
	Anilide
	Carboxin
	Carbamate
	Dicarboximide
	Famoxadone
	Dichlorophenyl
	Organobromine
	Metil Bromür
	Phthalimide
	Captan
Acaricides	Organochlorine
	Dicofol
	Carbamate
	Carbofuran
	Methiocarb
Rodenticides	**Crystalline Alkaloid**
	Strychnine
	Anticoagulant
	Bromadiolone
	Coumachlor

Uses of Pesticides and Occupational Exposure

Especially in the agricultural area; It is used to control various pests and disease carriers (eg mosquitoes, ticks, rats and mice) in homes, offices, shopping malls and in streets, parks, gardens and landscapes. Moreover, pesticides are used in electrical equipment, refrigerators, paint, carpet, paper, cardboard and food packaging materials, fish farming, forestry, timber protection, animal husbandry, industrial insect control, construction industry (wallpaper adhesives, paints, plastering, etc.), sea and water, insect control, food storage. Occupationally, those working in these fields may be exposed to pesticides directly or indirectly. Especially agricultural workers (e.g. greenhouse workers), park, garden, landscape workers, forestry workers, gardeners, pest control workers are at great risk.[5-6,12-13] Agricultural workers; It is defined to include ranchers, farm workers, field workers, agricultural implement users, and agricultural pesticide handlers (mixers, loaders, cleaners and sprayers). Take-home exposure in farm worker families should also be considered.[14] Exposure in farm workers may vary depending on the product processed, climate, vocational training, task performed, method of application, use of personal protection equipment (PPE), control measures, and hygiene applied.[15]

Exposure to Pesticides and Affecting Factors

Exposure to pesticides; It can be transmitted by contact with the skin, splashing into the eyes, by inhalation, swallowing contaminated food, and ingestion by smoking.[13] Windward spread of pesticides, pesticide mixing and spraying, inappropriate use of PPE, inadequate information, inadequate hand washing and showering, wearing dirty clothing, inappropriate eating, drinking and smoking with dirty hands in the workplace, warm air, spraying against the wind and factors such as reuse of pesticide containers cause exposure to pesticides and increase adverse effects.[16] Inadequate ventilation in the closed area, high indoor temperature and humidity increase exposure.[13] Exposure is more common in regions with low socioeconomic status.[16]

Effects on Human Health

Pesticides can cause acute health effects (e.g. skin and eye irritation, headache, vertigo and nausea) and chronic health effects (e.g. cancer, asthma and diabetes) in humans. These health effects may vary with the duration and amaount of exposure, the type of pesticide (with regard to toxicity and persistence), and the environmental characteristics of the affected areas.[5]

Acute Health Effects

Acute and intense exposure as a result of accident during the production, application, storage and transportation of

pesticides can cause allergic reactions. Allergic reactions to pesticides can be life-threatening. Even a small amount of contact with the chemical can initiate an allergic reaction and allergic dermatitis and anaphylaxis can be seen.[17]

Mild and Moderate Symptoms; Flu-like symptoms, headache, dizziness, skin rash, joint numbness. Nausea, vomiting, diarrhea, abdominal pain, increased salivation, excessive sweating, tearing, tremor, nervousness.

Severe Severe Symptoms; Increase in mild and moderate symptoms, excessive increase in body fluids, convulsions, severe unconsciousness, coma, death.[17]

Chronic Health Effects

It can be seen in those who work with pesticides for a long time in unsuitable conditions. It has effects on endocrine, skin, respiratory system, neurological system, gastrointestinal system, urinary system, hematopoietic system. It can cause diabetes, Parkinson's, irritant and allergen-induced asthma. Exposure during pregnancy may cause childhood leukemia and lymphomas. Some cancers have been associated with DNA damage, oxidative stress.

The chronic effects of pesticides on human health are summarized in Table 2.

Endocrine System

Diabetes (Type 2)

It has been observed that exposure to organochlorine (OC) pesticides increases the risk of T2 Diabetes (T2D). Exposure to different types of OC pesticides was associated with a significantly higher risk of T2D. The T2D pathogenesis of pesticide exposure is largely unknown. Inflammation in adipose tissue, ectopic lipid deposition (lipotoxicity) in the liver, muscle and pancreas, and mitochondrial dysfunction are the primary mechanisms underlying the pathogenesis of T2D, all of which have been associated with OC pesticides.[18]

In Thailand, patients diagnosed with diabetes in the population of agricultural workers, most of whom are rice farmers, were evaluated on the basis of questionnaires. Diabetes prevalence was found to be positively correlated with insecticides, herbicides, fungicides, and rhodanticides. Three types of insecticides have been associated with organochlorine (endosulfan), an organophosphate (mevinphos), a carbamate (carbaryl carbaryl/Sevin), as well as a fungicide (benlate).[19]

Thyroid Dysfunction

In a survey of pesticide applicators in the USA, insecticide (aldrin) and herbicide (pendimethalin) were associated with subclinical hypothyroidism and elevated TSH levels. Pendimethalin was found to be significantly associated with anti-TPO positivity.[20] Exposure to four organochlorine insecticides (aldrin, chlordane, heptachlor, and lindane), four organophosphate insecticides (coumaphos, diazinon, dichlorvos, and malathion), and three herbicides (dicamba, glyphosate, and 2,4-D) in a cohort study of farmers occupationally exposed to pesticides associated with increased hypothyroidism. A high risk of hypothyroidism was observed in the elderly population who reported that they used aldrin, heptachlor, and lindane organochlorines continuously.[21]

Thyroid Cancer

In a cohort study of licensed pesticide applicators in the USA, it was stated that the use of fungicide metalaxyl and organochlorine insecticide lindane may be associated with an increased risk of thyroid cancer, although there is insufficient evidence.[22] A positive correlation was found between the insecticide chlordane metabolite and thyroid cancer.[23]

Pancreatic Cancer

In his survey-based study conducted on licensed pesticide applicators in the USA; A significant exposure-response relationship of pendimethalin (Herbicides -Dinitroanilines) and EPTC (Herbicides -Thiocarbamate) with pancreatic cancer was observed. Pendimethalin contains N-nitrso-compounds or nitrosamine. Nitrosamines are potent animal carcinogens and can form N-nitroso-compounds, Pendimethalin and EPTC, which are suspected carcinogens for humans.[24]

Hematopoietic System

Lymphoma, Multiple Myeloma

In the survey-based research conducted on people who have worked as a farmer or gardener for at least 6 months and have been exposed to pesticides; Positive associations were observed between Hodgkin Lymphoma (HL) and occupational exposure to all organic insecticides, triazole fungicides and urea herbicides. Exposure to insecticides, fungicides, and herbicides was associated with a three-fold increased risk of Multiple Myeloma.[10] Exposure to insecticides, fungicides, and herbicides was associated with a three-fold increased risk of Multiple Myeloma.[10] In a case-control study conducted in Sweden, two types of pesticides (phenoxyacetic acid and DDT) were observed as risk factors in farmers in multiple myeloma patients.[25]

Neurological System

Epilepsy

Hospital registry data of the Spanish healthcare system between 1998 and 2010 were analyzed. A significant increase

Table 2. Harms of Pesticides on Human Health

System Affected Disease	Profession	Pesticide	Pathogenesis
Endocrine system			
Diabetes (Type 2)	Agriculture worker	Insecticide (Organochlor (OC)) Chlordane, Oxychlordane Insecticides organochlorine (endosulfan), organophosphate (mevinphos9 carbamate (carbaryl carbaryl/ Sevin), Herbicides Fungicides Rodenticides	Inflammation in adipose tissue, lipid accumulation (lipotoxicity) in liver, muscle and pancreas, and mitochondrial dysfunction
Thyroid dysfunction	Pesticide applicators Pesticide applicators	Insecticide (Aldrin) Herbicide Pendimethalin Insecticide Organochlorine Aldrin, Chlordane, Heptachlor, Lindane Organophosphate Coumaphos, Diazinon, Dichlorvos Malathion Herbicide Dicamba Glyphosate 2,4-D	Subclinical hypothyroidism High TSH levels Anti-TPO Positivity Hypothyroidism Hypothyroidism Hypothyroidism
Thyroid Cancer	Licensed Pesticide applicators	Insecticide Organochlorine lindane Fungicide Metalaxyl Insecticide, Orgonochlorine Chlordane	
Pancreatic cancer	Licensed Private and Commercial Pesticide applicators	Herbicide Pendimethalin Thiocarbamate (EPTC)	Carcinogenic
Hematopoietic System		Insecticide	
Hodgkin Lymphoma	Farmer or gardener	Herbicide Urea Fungicide Triazole	
Multiple Myeloma	Farmer or gardener Farmer	Insecticides Herbicides Fungicides Insecticide DDT Herbicide Phenoxyacetic acid	
Neurological System		İnsecticide	Overstimulation of central muscarinic
Epilepsy		Organophosphate Organochlorine Pyrethroid DDT	acetylcholine receptors (mAChRs) Neurotoxic Hypersensitivity with the Na channel
Parkinson's disease	Pesticide applicators and Their Partner (mostly farmers)	Insecticide Organophosphate Terbufos Herbicide Trifluralin 2,4,5-T Dikamba, Imazethapyr Metolachlor Metribuzin Fungicide Benomyl	

Table 2. CONT.

System Affected Disease	Profession	Pesticide	Pathogenesis
Sleep-Apnea syndrome	Agriculture Worker	Insecticide Carbamate organophosphate	Acetylcholinesterase inhibition
Autoimmune Disorders			
Rheumatoid Arthritis	Male Pesticide Applicators	Insecticide Organachlor Toxaphen Herbicide Atrazine	
Respiratory system			
Asthma		Organophosphates and pyrethrins	Acute Exposure
Asthma		Herbicide 2,4,5-TP,EPTC paraquat Insecticide (organochlorines: chlordane, heptachlor and lindane and organophosphates: diazinon, parathion and coumaphos), Fungicide (captain), Fumigant (mixture of ethylene dibromide and 80/20 - carbon tetrachloride and carbon disulfide) Insecticide Organochlorine: DDT and Organophosphates; phorate and malathion Herbicide (petroleum oil)	Allergic Asthma Non allergic asthma
Reproductive System			
Prostate cancer	Pesticide applicators	Herbicide Thiocarbamate (butylate)	Destruction of DNA repair pathways
Urinary System			
Chronic renal failure	Farmer	Herbicide Pendimethalin Atrazine Dicamba	DNA damage and oxidative stress
Renal Cell Cancer	Pesticide Applicators	Insecticide Chlorpyrifos Chlordane Herbicide 2,4,5-T Atrazine cyanazine paraquat	Histopathological changes Carcinogenic Carcinogenic DNA damage Mutagenicity Oxidative stress

in the risk of epilepsy was observed in areas where pesticides were used more. In the discussion section, the causes of epilepsy are explained as follows: Seizures may occur as a result of overstimulation of central muscarinic acetylcholine receptors by causing inhibition of acetylcholinesterase by organophosphates. Pyrethroid and DDT insecticides cause hyperexcitability by interacting with the sodium channel. Most organochlorines and type II pyrethroids block the GABA receptor and cause a hyperexcitability syndrome accompanied by convulsions.[26]

It has been observed that the risk of epilepsy is higher in greenhouse workers who are exposed to pesticides more than agricultural workers in the open fieldthose, especially in those who do not use gloves and face protection.[27]

Parkinson's Disease (PD)

Pesticide applicators and their spouses (mostly farmers) were assessed in a questionnaire-based study. Five herbicides (dicamba, imazethapyr, metolachlor, trifluralin, and metribuzin) were found to be associated with an increased risk of PD among those who did not wear chemical resistant gloves. In the study, it was found that the continuous use of the insecticide terbufos and the herbicides trifluralin and 2,4,5-T(2 4 5-trichlorophenoxyacetic) was associated with an increased risk of PD.[28]

A study examining the relationship between occupational exposure to insecticides, herbicides and fungicides, and airborne endotoxin and PD showed a significant association between the fungicide benomyl and the risk of PD.[29]

Sleep-Apnea Syndrome

In a survey-based study of male pesticide applicators in the agricultural sector in the USA, exposure to carbofuran (from the carbamate group) was shown to be positively associated with sleep apnea. Organophosphates are irreversible acetylcholinesterase inhibitors. Carbofuran are reversible inhibitors. Acetylcholine accumulates in nerve junctions, leadS to overstimulation of acetylcholine receptors and subsequent toxicity and potential disruption of the sympathetic, parasympathetic, and peripheral nervous systems. Thus, carbamates may play a role in the initiation and/or progression of central sleep apnea. In the study, no relationship was found between organaphosphates with similar effects and sleep apnea syndrome.[30]

Autoimmune System

Rheumatoid Arthritis (RA)

In a survey-based study of male pesticide applicators; A positive correlation was found between exposure to toxfen (organachlor) and atrazine (herbicide) and RA.[9]

Respiratory system

Asthma

High levels of pesticide exposure have been associated with both allergic and non-allergic asthma. Asthma may develop as a result of acute exposure to organophosphates and pyrethrins.[31] 48 pesticides were evaluated for asthma risk among farmers. Three herbicides (2,4,5-TP, EPTC and paraquat), six insecticides (organochlorines: chlordane, heptachlor and lindane and organophosphates: diazinon, parathion and coumaphos), one fungicide (captan), and two fumigants (ethylene dibromide and 80/20 mixture – carbon tetrachloride and carbon disulfide) has been positively associated with allergic asthma. One herbicide (petroleum oil) and three insecticides (organochlorine: DDT and organophosphates; phorate and malathion) have been associated for non-allergic asthma. Allergic asthma odds ratios for five pesticides (2,4,5-T, parathion, coumaphos, captan and 80/20 mixture) were found to be statistically significant.[32]

Reproductive System

Prostate Cancer

Butylate, a thiocarbamate herbicide, is used in corn and grassy and broadleaf weeds and nuts. A survey-based study conducted in licensed pesticide applicators in the USA investigated the relationship with prostate cancer in butylate users. In the study, a possible association was observed between the use of butylate and an increased risk of prostate cancer, especially in those with a family history of prostate cancer.[33]

Urinary System

Kidney Effects

The use of pendimethalin (herbicide), atrazine (herbicide) has been associated with a high probability of chronic kidney disease (CKD). Use of atrazine in the previous year was associated with a lower eGFR and higher probability of CKD compared to never used. Two herbicides, pendimethalin and atrazine, were thought to be associated with varying kidney function among pesticide applicators. The use of pendimethalin, atrazine, and dicamba herbicides has been found to reduce eGFR. Although the exact mechanism of action is not known, it has been mentioned in the research that it may cause kidney damage through DNA damage and oxidative stress.[7]

Renal Cell Cancer

Evaluated in a survey-based study of pesticide applicators in the USA. Evidence of associations with RCC was found for four herbicides (2,4,5-T, atrazine, cyanazine, and paraquat) and two insecticides (chlorpyrifos and chlordane). Cyanazine, mutagenicity and DNA damage; Atrazine causes endocrine disruption of the hypothalamic-pituitary-adrenal axis, DNA damage and oxidative stress. 2,4,5-T; In the IARC evaluation of TCDD, it causes sufficient carcinogenicity in experimental animals. TCDD binding causes and activation of the aryl hydrocarbon receptor. Paraquat; In animal studies, it causes glomerular lesions and renal tubular necrosis resulting from oxidative stress-induced cellular damage. Histopathological changes were observed in the kidneys of rats administered chlorpyrifos.[34]

Occupational Health and Safety in Pesticide Application

Reducing pesticide use is a shared responsibility of all society as scientists, farmers, consumers, governments and the private sector.[35] In order to protect workers from diseases caused by pesticides, appropriate measures should be taken at every stage according to the risk assessment. The way to eliminate the risk in the workplace environment is the absence of this substance in the workplace environment. For this, it should be replaced with another substance, if possible. If not possible, the risk in the environment should be reduced by using the necessary prevention and protection methods.[36]

Storage

They should be stored in their original packaging with approved product labels. There should be sufficient storage

space, sufficient shelves, appropriate placement (for example, liquid ones at the bottom, dry ones at the top, to prevent liquid from leaking…). There should be appropriate markings on the outside of the tank.

Carrying

It should be carried in a suitable closed container, such as a trailer, outside the vehicle, not close to the driver in the vehicle.

Preparation

In mixing and loading processes, closed systems that do not allow the worker to contact the chemical should be used as much as possible. When open mixing and loading, instructions should be followed and direct contact with the pesticide concentration and final spray mix should be avoided. Appropriate protective measures should be taken. When pesticide is spilled, it should be absorbed by surrounding it with non-reactive absorbent (inert absorbent) materials (carpenter sawdust, clay, etc.) or sand.

Application

During all operations, the contamination of pesticide by skin and respiration should be prevented by using personal protective equipment such as suitable gloves, masks, work clothes-overalls, glasses, etc.

Health Surveillance

Recruitment and periodic examinations should be done. Monitoring records should be kept in accordance with national legislation and practice. Employers considering using organophosphorus or n-methyl carbamate pesticides should develop a cholinesterase monitoring plan for pesticide applicators.[37] Inhibition of acetylcholinesterase with organophosphorus, chlorinated and carbamate pesticides and accumulation of acetylcholine creates a toxicity picture with cholinergic findings. It is recommended to measure cholinesterase levels at regular intervals by defined centers in workers in the pesticide industry.[38]

A number of direct and indirect exposure assessment methods have been developed to classify workers' pesticide exposure. In direct methods, respiratory or dermal exposure of workers was assessed by sampling biomarkers or metabolites in the target population in blood, urine, or skin. However, direct measurements of exposure are generally only possible in prospective cohort and cross-sectional studies. As a result, indirect methods have been developed and applied for pesticide exposure assessment. These include job title-based assessments, self-reported exposures, and self-administered or interviewed questionnaires and records.[15]

Human Bio Monitoring

It is mentioned that the urinary 3-phenoxy benzoic acid concentration level is used to determine the pyrethroid deltamethrin exposure among greenhouse farm workers, and the urinary metabolites dialkyl phosphate (DAP) and dimethylalkylphosphate (DMAP) level are used in biological monitoring to determine the exposure of organophosphate pesticides. For organophosphate pesticides in flower growers, erythrocyte acetylcholinesterase (AChE) and plasma butyrylcholinesterase (BuChE) levels are measured.[13]

Conclusion

Care should be taken to ensure that pesticides used in agricultural practices are targeted and not harmful to humans and other living things. Due to the harmful effects of pesticides on human health, it is very important to take measures to reduce pesticide exposure. Necessary warnings should be on pesticide packages. The training of practitioners is important.

It should not be forgotten that pesticides are widely used in both professional and life areas. While pesticides are easily identified in the history in acute intense exposure, exposure can easily be missed in chronic exposure if they are not brought to mind or not. When caring for patients in the clinic, at least when asked about their occupation, a job description suggesting pesticide exposure is helpful. For this reason, it is extremely important to always ask about his profession in the clinic.

Disclosures

Ethics Committee Approval: Ethics committee approval was not obtained because our study was a review.

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