# Electrocardiographic Profile of Agrochemical Poisoning

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**ABSTRACT**

Systemic toxicity in agrochemical poisoning is common worldwide. Even though there are few chemicals causing cardiovascular toxicity, they are commonly reported due to their wide usage. In this review, we evaluated the evidence of the association between pesticide exposure and cardiovascular toxicity with special consideration of electrocardiogram changes in humans. We conducted a comprehensive methods search using Medline (PubMed), ProQuest, EBSCO host Medical, Scopemed and Google Scholar in November 2016. All studies included were studied in humans focused on cardiovascular toxicity that was published between 2000 and 2016.

**Keywords:** cardiovascular toxicity, electrocardiograph, agrochemical, pesticide, insecticide, rodenticide

## INTRODUCTION

Agrochemical is the term given to various chemicals widely used as a prophylactic treatment to maintain high agricultural production.[1] These agrochemicals constitute pesticide, herbicides, rodenticides etc. Pesticides are chemicals that may be used to kill fungus, bacteria, insects, plant diseases, snails, slugs, or weeds among others. Insecticides are a type of pesticide that is used to specifically target and kill insects. Herbicides are used to kill undesirable plants or weeds.[2] Farmers are the population most exposed to the pesticide, herbicide and rodenticide. Poisoning is, therefore, common among them either by occupational exposure to pesticides or suicidal or accidental consumption. Application of these agrochemicals in most cases results in high risk of exposure to living beings which constitutes major occupational hazards which may result in poisoning and death and, in certain cases, work-related cancer and reproductive impairments.[3,4] It is also seen among the common people due to their availability of household pesticides, rodenticides etc.[5,6] Further, it has been reported that every year 3 million acute poisoning cases are caused by agrochemicals worldwide, out of which 2 million are suicide attempt and rest are occupational or accidental poisoning cases.[7,8]

The agrochemicals manifest numerous health effects with local and systemic toxicity.[5,9] The diagnosis of abnormal electrocardiogram (ECG) changes encountered in a specific agrochemical poisoning and their management is challenging even to experienced physicians. The ECG having a valuable source of information must be used as an indispensable tool in the emergency department for the detection and diagnosis of cardiovascular toxicity. Knowledge of the characteristic ECG abnormalities may provide early clues to the detection of specific agrochemical poisoning, the prompt recognition of which can be lifesaving.

We conducted a comprehensive methods search using Medline (PubMed), ProQuest, EBSCO host Medical, Scopemed and Google Scholar in November 2016. All studies included were focused on cardiovascular toxicity in humans that were published between 2000 and 2016.The present article makes an attempt to appraise the importance of clinical toxicology by describing various agrochemical poisons, their mechanism of action and their electrocardiographic changes.

## REVIEW OF LITERATURE

The results of the review are presented in Table-1.

### Organophosphates and Carbamates

Organophosphate compounds and carbamates are used extensively worldwide for agricultural, industrial, and domestic pest control. Organophosphates like Dichlorvos, Chlorpyrifos, Malathion, Dimethoate etc. and carbamates like propoxur (Baygon), carbaryl, methomyl etc. are commonly used. The toxicological mechanism is acetylcholinesterase inhibition by phosphorylation of a serine in the active site resulting in an excess of the neurotransmitter acetylcholine, which results in accumulation of acetylcholine and overstimulation of muscarinic and nicotinic receptors in synapses throughout the autonomic and central nervous systems and at neuromuscular junctions. ECG abnormalities like sinus bradycardia, sinus tachycardia, prolonged QTc, elevated ST segment and low amplitude or inverted T waves, first-degree AV block was observed.[10-12] Sinus tachycardia and ST-T changes in Dichlorvos poisoning were also reported.[13] Methomyl, carbamate insecticide poisoning demonstrated cardiac arrest.[14]

### Organochlorines

Organochlorines like gamma benzene hexachloride, endosulfan and dichlorodiphenyl-trichloroethane (DDT) are heavily chlorinated aromatic compounds that are nonvolatile and poorly water soluble. They act by binding to sodium channels in neurons and increasing the permeability of sodium. But in high concentrations, it causes myocardial instability. Endosulfan is an insecticide and acaricide. ECG showed sinus tachycardia with ST depressions with multiple episodes of bradycardia and cardiac arrest.[15]

### Pyrethroids

Pyrethrins are naturally occurring esters of chrysanthemum resin that possess insecticidal activity, whereas pyrethroids are synthetic derivatives of pyrethrins. Pyrethrins and pyrethroids delay closure of sodium channels. The delay results in prolonged depolarization, repetitive firing, and eventually conduction

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| Agrochemicals | Common Uses | Mechanism of Action | Common Chemicals | Common ECG Abnormalities |
|---|---|---|---|---|
| Organophosphate | Pesticides | Acetylcholinesterase inhibition | Dichlorvos, Chlorpyrifos, Malathion, Dimethoate | Sinus bradycardia, sinus tachycardia, prolonged QTc, elevated ST segment and low amplitude or inverted T waves, first degree AV block |
| Carbamates | Pesticides | Acetylcholinesterase inhibition | propoxur (Baygon), carbaryl, methomyl | Sinus bradycardia, sinus tachycardia, prolonged QTc, elevated ST segment and low amplitude or inverted T waves, first degree AV block |
| Organochlorines like gamma benzene hexachloride, endosulfan and dichlorodiphenyltrichloroethane (DDT) | Insecticide, acaricide | Binds to sodium channel and increasing the permeability of sodium. | Gama benzene hexachloride, endosulfan and dichlorodiphenyl-trichloroethane (DDT) | sinus tachycardia, ST depressions, bradycardia, cardiac arrest. |
| Pyrethroids | Insecticide | Delay closure of sodium channels, resulting in prolonged depolarization, | Pyrethroids | Conduction blockade or transient complete heart block. |
| Neonicotinoid | Insecticide | Nicotinic acetylcholine receptor agonist | Imidacloprid | Sinus tachycardia, mild QT prolongation, bradycardia, arrhythmia, cardiac arrest |
| Glyphosate | Pesticide, herbicide | Destroying mitochondrial cell walls and interfering with cellular energy production | Glyphosate, glufosinate | QTc interval |
| Amitraz | Acaricide, ectoparasite repellant, insecticide | α -adrenergic agonist activity, inhibits monoamine oxidase (MAO) enzyme activity and prostaglandin E2 synthesis | Amitraz | Sinus bradycardia |
| Phosphide | Rodenticide | Inhibit cytochrome C oxidase | Zinc Phosphide | Ventricular arrhythmias |
| | Rodenticide, Insecticide | | Aluminum phosphide | ST segment elevation/ depression, T wave inversions, PR prolongation, broad QRS complexes, right or left bundle branch block, supraventricular ectopics or fibrillation |
| | Pesticides, Rodenticide, fireworks | | Yellow Phosphorous | Tachycardia, arrhythmias and persistent Left Ventricular Dysfunction, with deep inverted T waves in ECG |
| Heterocyclic organic compound | Rodenticide | GABA-A receptor antagonist and disables chloride channels | Tetramine (tetramethylene disulphotetramine) | Sinus tachycardia |

**Table-1:** Agrochemical poisoning manifesting cardiovascular toxicity

blockade or transient complete heart block.[16]

**Neonicotinoid**

Neonicotinoid, a systemic insecticide that possesses nicotinic action as nicotinic acetylcholine receptor agonist exhibited severe sinus tachycardia, mild QT prolongation.[17] In Imidacloprid, belonging chloronicotinyl nitroguanidine class though rare, cardiovascular manifestations like tachycardia, bradycardia, arrhythmia, and cardiac arrest were also described.[18,19]

**Glyphosate**

In acute glyphosate pesticide ingestion which produces toxicity by destroying mitochondrial cell walls and interfering with cellular energy production, QTc interval was noticed. Glyphosate and analogue, glufosinate are a widely used herbicide. They are commonly used with surfactants.[20]

**Amitraz**

Amitraz is a non-systemic acaricide, an ectoparasite repellent and insecticide. It has α-adrenergic agonist activity. It also inhibits monoamine oxidase (MAO) enzyme activity and prostaglandin E2 synthesis, though some of these effects may be dose dependent. Poisoning presented with the presence of sinus bradycardia.[21,22]

**Phosphides**

Phosphides are mainly used as rodenticides. Toxicity is caused by the liberation of phosphine gas which blocks cytochrome C oxidase inhibiting oxidative phosphorylation resulting in myocardial damage and circulatory failure. Zinc phosphide is a rodenticide and is commonly implicated in suicidal poison ingestion. Phosphine is shown to exhibited fatal ventricular arrhythmias.[23] Rice tablets or celphos or aluminum phosphide is an effective insecticide and rodenticide. The ECG changes observed were ECG changes varying from ST segment elevation/depression, T wave inversions, PR prolongation, broad QRS complexes, and right or left bundle branch block, supraventricular ectopics or fibrillation.[24-26] Yellow Phosphorous, is widely used as a rodenticide and in fireworks. Its toxicity is also secondary due to the release of phosphine gas. Cardiotoxicity manifested as tachycardia, arrhythmias and persistent Left Ventricular Dysfunction, with deep inverted T waves in ECG.[27]

**Heterocyclic organic compounds**

Tetramine (tetramethylene disulphotetramine, TETS) known as illegal rodenticides acts as a GABA-A receptor antagonist and disables chloride channels. ECG revealed sinus tachycardia in toxicity.[28]

## RECOMMENDATIONS

Occupational exposure is certainly among the primary source of exposure mainly farmers and their families. Therefore, awareness of the ways in which agrochemical exposure occurs and the danger it poses are a crucial component of comprehensive care. Education about their safety is an important measure for preventing exposure. They must be educated how to reduce take-home exposure such as removing work clothes and shoes before entering their home; shower or bath upon returning home and before touching other people; and store and launder dirty work clothes separately from other clothing. Accidental poisonings can be avoided by proper labeling and storage of containers mainly out of sight and *out of reach* of *children*. Usage of chemical-resistant gloves reduces contamination. In acute pesticide poisoning, concerning both accidental death and suicides, there must be a method adopted by national governments to control their accessibility. Agrochemicals most toxic to humans if restricted can reduce the possible fatality. Further the government must also advise the agrochemical industries for the production of new agrochemical with low environmental and human risk. Provision of cost-effective schemes for farmers by the government with economic support and psychological counseling of the suicide-attempted victims is also required.

## CONCLUSION

This systematic review provides clear evidence that certain agrochemical poisoning manifests cardiovascular toxicity across vulnerable populations. We hope this will stimulate further evaluation of cardiovascular toxicity incidence and mortality in agrochemical-exposed cohorts and focuses on a prerequisite for special training and fellowship courses for the healthcare providers for handling these cases.

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