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Cardiotoxicity of Pesticides: Are Africans at Risk?

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Abstract

Cardiovascular disease has maintained the unenviable position as the number one cause of death in the world. It is now clear that the traditional risk factors of cardiovascular disease are driven by primary factors like globalisation, urbanisation, industrialisation and agricultural practices. Pesticide use is an integral component of modern and improved agriculture. The abuse and misuse of these chemicals has caused significant poisoning worldwide and particularly in low- and middle-income countries where Africa belongs. This review surveys the widening population of people poisoned by pesticides in Africa and examines the possibility of pesticide-induced cardiotoxicity. The exposed group includes workers in pesticide industries, transporters of these chemicals, farmers, farm workers who apply these pesticides, vendors and sellers of farm produce and consumers of foodstuffs that are treated with pesticides as well as persons who consume water and inhale air filled with pesticides. There are numerous animal model studies that employ electrocardiography, echocardiography, enzyme studies and histopathology to demonstrate pesticide-induced cardiotoxicity in many parts of the world. There are also case reports and epidemiological data of pesticide-induced cardiovascular intoxication in man. With the increasing reports of pesticide-induced central system nervous toxicity in Africa, there are enough reasons to suspect cardiovascular system poisoning as well. The poorly developed clinical toxicology specialty may explain the low index of suspicion of pesticide-induced cardiovascular diseases. With the pervading ignorance, indiscriminate sale, unguarded use, lack of adequate legislation, inadequate enforcement of legal institutes associated with pesticide use in Africa, there is no doubt that the increasing prevalence and incidence of cardiovascular diseases may partly be due to exposure to these chemicals. Africans may after all be at risk of pesticide-induced cardiotoxicity, but more studies will be required to examine the pattern of cardiotoxicity as well as factors that modulate its occurence.

Keywords Pesticides · Cardiotoxicity · Africans

Introduction

Cardiovascular disease has maintained the unenviable position as the number one cause of death annually with an estimated 17.7 million people dying from CVDs in 2015 representing 31% of all global deaths a number that is expected to grow to > 23.6 million by 2030 [1, 2]. About 80% of these deaths occur in low- to middle-income countries (LMIC) where resources for prevention and management are least available. Cardiovascular disease is responsible for 10% of the disability-adjusted life years (DALYs) lost in LMIC [3]. It means that LMIC where Nigeria is located are hard-hit and carry a disproportionate burden of the world's CVDs.

The traditional risk factors which can be called intermediate factors include hypertension, diabetes mellitus, obesity, dyslipideamia, physical inactivity and recently environmental pollutants. These risk factors lead to end organ damage, which includes stroke, heart failure, arrhythmia, coronary heart disease, renal impairment and so on. But there are underlying primary factors which whip up the so-called risk factors. These are globalisation, urbanisation, industrialisation which includes agricultural practices that ensure increased and improved food supply for the rapidly growing population of the world [4].

The post World War II era saw a change in agricultural practices leading to mechanisation and the development and

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deployment of many chemicals to combat pests of human and animal diseases including plant diseases and pest control. The production of these animal and plant agricultural poisons has so much progressed that over 1 billion pounds of pesticides are used in the United State (US) each year and approximately 5.6 billion pounds are used worldwide [5]. In many developing countries, programs to control exposures are limited or non-existent. As a consequence, it has been estimated that as many as 25 million agricultural workers worldwide experience unintentional pesticide poisonings each year [6]. Comparison of these data with the WHO report in 1973 that probably half a million cases of acute serious pesticide poisoning occurred yearly and out of about 3 million cases of poison-related hospitalisation 220,000 deaths occurred will clearly state the amount of explosion of use that has occurred [7].

Nigeria is the most populated country in Africa and a mirror of what happens in the continent. In 1970, only 21 pesticide chemicals were available in Nigeria but this jumped to about 15,000 metric tonnes per annum of pesticides comprising about 135 pesticide chemicals marketed locally under 200 different produce brands and formulations were imported during 1983–1990, thus making Nigeria one of the largest pesticides users in sub-Sahara Africa [8]. By 1998, about 125,000–130,000 metric tonnes of pesticides were used every year [8].

In Africa, herbicides are used indiscriminately in farms to keep weeds and pests at bay; insecticides and herbicides are applied to agricultural produce to ensure long storage and every household uses pesticides to contain the menace of mosquitoes, spiders, rats, cockroaches, termites, soldier ants without any regulation or supervision. Backyard poultry, fishery, rabbit farms all use one form of pesticide or the other. Unfortunately, these poisons can also harm man and there are documented reports of real and potential organ toxicity associated with pesticides [9].

This review examines how widespread the misuse and abuse of these pesticides are in Africa and possible organ damage associated with its use. Though Europe presently has a well-developed regulatory policy on pesticide toxicity but Regulation (EC) No. 1272/2008 does not classify pesticides as cardiotoxic [10]. This has not been a deterrent in documenting pesticide-induced cardiotoxicity in Europe [11]. If there are documented data on the cardiotoxicity of pesticides in US and Europe where strict guidelines govern the use of these chemicals, it is unlikely that Africans are free from these poisons given the onslaught of pesticides and the lack of policy on their use [12–15].

It is now estimated that 23% of all cardiovascular diseases are due to environmental toxicants, even though their type and nature of these are not fully known [16]. Pesticides are among the environmental poisons that are currently known to cause heart disease.

Classes of Pesticides

Pesticides are defined as "chemical substances used to prevent, destroy, repel or mitigate any pest ranging from insects (i.e. insecticides), rodents (i.e. rodenticides) and weeds (herbicides) to microorganisms (i.e. algicides, fungicides or bactericides)" (Box 1) [17]. Pesticides can also be classified based on whether they are biodegradable or not (Box 2). The biodegradable pesticides are those which can be broken down into harmless compounds [18, 19]. Another way to classify pesticides is to consider their chemical forms as shown in Table 1 [18, 19]. Table 2 is classification based on the toxicity of pesticides [18, 19].

Box 1: Pesticides Grouped by Types of Pests They Kill

1. Insecticides—insects
2. Herbicides—plants
3. Rodenticides—rodents (rats and mice)
4. Bactericides—bacteria
5. Fungicides—fungi
6. Larvicides—larvae

Table 1 Classification of pesticides based on chemical composition

Groups of pesticides	Compounds	Notes
Organophosphate	Azinphos-methyl, chlorfenvinphos, diazinon, dichlorvos, dimethoate, fenitrothion, malathion, parathion, parathion-methyl, trichlorfon	Insecticide, little persistent
Carbamate	Aldicarb, aminocarb, carbaryl, carbofuran, dimetan, dimetilan, isolan, methomyl, propoxur, pyramat, pyrolan, zectran	Insecticide, little persistent
Organochlorine	DDT and analogues, benzene hexachlorides, cyclodienes, toxaphenes	Insecticide, persistent
Glyphosate		Herbicide, little persistent
Bipyridyl	Paraquat, Diquat, diethamquat, cyperquat, difenzoquat, morfamquat	Herbicide, little persistent
Botanical	Nicotine, rotenone, pyrethrum	Insecticide

Table 2 Index classification of active pesticide ingredients based on toxicity

Type	Class
1a	Extremely hazardous
1b	Highly hazardous
II	Moderately hazardous
III	slightly hazardous
U	= Unlikely to present acute hazard in normal use
FM	Fumigant, not classified
O	Obsolete as pesticide, not classified

Box 2: Pesticides Classified Based on Degradability

Persistent

The persistent pesticides are those which may take months or years to be degraded; during which time it is able to be transmitted through long distances via air, water and living creatures. The pesticides also get stored easily in fatty tissues and build up in food chains. Pesticides are regarded as persistent if they are resistant to degradation through metabolic activity, ultraviolet radiation and extreme temperatures. Typical examples of pesticides with these characteristics are the organochlorine insecticides: DDT and its metabolites, as well as the cyclodiene insecticides (dieldrin, aldrin, heptachlor, endrin, telodrin and chlordane).

- Biodegradable: The biodegradable pesticides are those which can be broken down by microbes and other living beings into harmless compounds.

In December, 2002, the United Nations Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals (UNCETDG/GHS) approved a document called “The Globally Harmonized System of Classification and Labelling of Chemicals” to provide the basis to address classification of chemicals, labels and safety data sheets [19].

The classification is based primarily on the acute oral and dermal toxicity to the rat since these determinations are standard procedures in toxicology. Where the dermal LD50 value of a compound is such that it would place it in a more restrictive class than the oral LD50 value would indicate, the compound will always be classified in the more restrictive class [19].

Provision is made for the classification of a particular compound to be adjusted if, for any reason, the acute hazard to man differs from that indicated by LD50 assessments alone [19].

Survey of Pesticides Use and Implications in Africa

In Africa, pesticides are used and misused more commonly than are reported. There are many reports indicating the use of pesticides in many African countries apart from Nigeria. These include Niger, Ghana, Morocco, Algeria, Ethiopia, Kenya, Tanzania, Uganda, Malawi, South Africa. Pesticide use in these countries is beyond cash crops and now includes non-cash crops like grains, tubers, vegetables, fruits and other staple foods [20, 21]. Nigeria and South Africa are the greatest users of pesticides.

Nigeria has depended on petroleum as the main driver of the economy for many years. However, in the past decade, the proceeds from petroleum has taken a downward turn with the gross domestic product attaining an all time low. This has rekindled interest in and a return to agriculture which was the main stay of the economy following independence in the 1960s. This renewed interest in agriculture has lead to a return to the farms in such a way that individuals, groups and government have increased cultivatable lands. The demand for pesticides has also increased commensurably.

The use of pesticides over the years has made it possible to increase crop yields and food production [22]. No doubt, pesticides has increased yield and has ensured better preservation of farm produce. But the use or rather the misuse of pesticides has also become worrisome (Table 3), [23]. Intensive use of pesticides has also caused significant contamination of the soil. To keep away weeds, many farmers have moved away from manual uprooting of weeds and now depend on herbicides to reduce man-hours and maximise profit. The problem is that these herbicides are applied wrongly over both weeds and crops leaving considerable residues in the farm produce which reach the consumer leading to significant health implications.

The first case of human exposure to pesticide in Nigeria occurred in 1958, in which all members of the family of a local chief who was a prominent cocoa farmer at Okebode in South western Nigeria were hospitalised after eating a leaf earlier sprayed with Lindane [8]. In 1963, the Insecticide Testing Unit (ITU) of the World Health Organization in Lagos, Nigeria, undertook a program to evaluate the effect of two carbamate and one organophosphorous insecticides in a village scale trail, the toxicological information gained in the trail showed that one of the carbamate tested (3-isopropylphenyl *N*-methylCarbamate) was too toxic to man to be used as a residual insecticide in houses [24].

In 2004, carbofuran pesticides residues found on several batches of noodles manufactured in Nigeria may have resulted in 23 reported cases of vomiting and one death [8]. Environmental contamination by organochlorines pesticides of aquatic bodies, lands, wildlife, foodstuff, human diet,

Table 3 Reasons for abuse, misuse and pesticide poisoning in Nigeria

Issues relating to pesticide abuse, misuse and poisoning	Comments on reasons why results on containment has remained poor
Pesticide production and importation	Some of the most hazardous pesticides are still in use in Nigeria; hazardous chemicals are illegally imported
Pesticide storage and distribution	Pesticides are stored in inappropriate conditions; transported with foodstuff; some expired pesticides are still in use
Application of pesticides	Poor training on use of pesticides in respect of kitting and use of applicators; use of wrong formulations and doses and wrong timing of application; pesticides are stored in inappropriate containers; empty pesticide containers are used for storing food
The public perception of pesticides	Very poor knowledge and awareness, non-persuasion of associated adverse effects, easily sold on the cheaper more hazardous pesticides
Legislation and enforcement	Inadequate laws; ignorance of law enforcement officers; corruption among law officers
Monitoring of locally used farm products	No monitoring is done for locally sold farm products
Response from medical personnel	Medical personnel are not adequately trained in chemical and pesticide poisoning; inadequate analytic equipments for definite diagnosis of poisoning

human blood and mother's breast milk in Nigeria and other sub-regions in Africa continent has been established [25].

There are also serious concerns about grain storage in Nigeria. Farmers and food business companies have been known to store foodstuffs with pesticides to avoid being destroyed by weevils and other pests. There numerous reports in daily newspapers in Nigeria of the use of insecticides: dichlorvos (sniper, made by Swiss-Nigeria Chemical Company, Nigeria), chlorpyrifos, cyhalothrin, dimethoate, trichlorphon and omethoate mixed with water and sprayed over grains like beans to preserve them from weevils for 6 months [26]. This is double burden of pesticide poisoning after the application of herbicides during planting. Pesticides poisoning have also occurred through storage of pesticides close to consumable foodstuff, the use of pesticides containers for household, improper disposal of used containers, conveying of foodstuffs together with pesticides in the same vehicle [26, 27].

Pesticide food poisoning in Nigeria has led to rejection of farm produce by European countries because of the high content of pesticide residues [26, 27] and these unwholesome products have been accepted and sold in local markets without restraint and with untold possibilities of pesticide poisoning. What is worrisome is that this level of pesticide food poisoning goes on without any serious objection from individuals, groups or regulatory agencies. The environmental legal framework is weak and because of the unenlightenment the law enforcement officers do nothing or even protect few people who try to stop these sharp and unhealthy practices. The food police of Nigeria, National Agency for Food, Drug Administration and Control (NAFDAC) appears to be overwhelmed and incompetent to handle the level of food poisoning going on in Nigeria and the Standard Organisation of Nigeria have never raised any query on the level of chemical poisoning in Nigeria.

In Nigeria, pesticides have been found in surface and underground water. When pesticides are applied to destroy pests and pathogens, only 15% of the applied amount hits the target, with the remaining 85% being distributed in soils and air [28].

Pesticides contaminate these water sources through run off from agricultural lands, from practices related to control of aquatic weeds, insects and effluent from industries involved in chemical and pesticide manufacture [28].

Okaniyia et al. [9] reported high levels of organochlorine and polychlorinated residue in some rivers in the northern part of Nigeria due to the extensive use of Lindane in fishing and Aldrin in cultivated farmland close to these water sources. Osibanjo has also documented the occurrence of organochlorine pesticides in major rivers in Nigeria which serve as drinking water source to the vast majority in the country for domestic and industrial purposes [25]. There are other reports that documented high levels of DDT and heptachlor in ground water sources in Ibadan [29].

South Africa is one the major importers of pesticides in Africa and has more than 500 registered pesticides [30]. In 2006 alone, 170 million dollars worth of insecticides, fungicides and herbicides were retailed in the country [31]. There are no reported data on pesticide production in South Africa. In 2002 about 10,000 kl of liquid insecticides and 28,000 tonnes of solid insecticides were produced in South Africa [31]. Hospital diagnosis and reports are rare in Africa, but there are reported cases of misuse of pesticides resulting in poisoning and hospitalisation in 455 and 736 cases in Kenya and Tanzania, respectively [32].

The levels of dichlorvos have been found to exceed MRL levels in small- and large-scale vegetable farms in Zambia [33]. In Ghana, there have been reports of pesticides exceeding EU MRLs in both raw agricultural products and processed foods [34–37]. In Uganda, each farmer has been estimated to loose 24.6 days per year due to pesticide poisoning, 9.4 days due to respiratory illnesses and 15.2 days due to skin infections [38]. The potential cost of pesticide poisoning in sub-Saharan Africa between 2005 and 2020 is enormous with an estimate of 90 billion dollars with 4.4 billion dollars expected to be the cost of pesticide-related poisoning due to lost work, medical treatment and hospitalisations [39].

Why is pesticide misuse, abuse and poisoning so prevalent in Africa? It has been reported that developing countries use only 25% of the world's pesticides but unfortunately are rewarded with 99% of deaths associated with pesticide poisoning [40]. There are numerous reports of pesticide misuse in African countries [41–43].

Health Effects of Pesticides

Bioconcentration and bio-magnification are two of the most common ecotoxicological effects almost all pesticides exhibit. Bioconcentration occurs when a compound has a higher concentration in the tissues of an organism, than in its surrounding environment. But biomagnifications is concerned with rise in concentration of pesticides longitudinally along the food web. This leads to the highest levels occurring in predators and these levels are much higher, than levels initially applied to land, crops or a water body. Persistence is the single most important reason for bioconcentration and bioaccumulation [44].

The common routes of intoxication with pesticides are through the skin and inhalation as a result of application of pesticides associated with agricultural practices. The eyes and the mouth are also sources of contamination (Box 3) [44]. Foodstuffs which are sprayed with chemicals as part of farming practice and to secure storage and keep away pests are very important source of pesticide contamination. Poisoning also occurs through surface and underground water which are domestic sources of water.

Box 3: [44]

Pesticides enter the body through the

- Skin (dermal)
- Mouth (oral)
- Lungs (respiratory)
- Eyes (ocular)

Pesticide poisoning can present acutely or chronically. Acute presentation will depend on the type of pesticide but mostly will be neurological symptoms as well as respiratory and gastrointestinal symptoms. However, acute cardiac complications such as atrial fibrillation has been documented for organophosphorous pesticides [45].

Chronic effects of pesticides include neurological, developmental, carcinogenic, reproductive, immunological and cardiovascular.

Box 4: Acute Effects of Pesticide Poisoning [44]

CNS: Neuropathy, Headache, dizziness and weakness, Tremors, sweating, blurring and tearing of eyes, Numbness of hands and feet, Convulsions.

GIT, Nausea and vomiting,

Lungs, Difficulty in breathing, Cough Asthma.

Skin, Rashes.

Eyes, Eye irritations.

Box 5: Chronic Effects of Pesticide Exposure [44]

- Allergies and/or asthma
- Cancer (e.g. leukaemia, brain tumours)
- Effects on the immune system
- Birth defects
- Infertility
- Developmental problems in children
- Neurological diseases
- Lung, liver and kidney impairment
- Cardiovascular diseases

Cardiotoxicity and Clinical Management of Pesticide Poisoning

The pharmacological basis of the action of pesticides is indispensable in the management of poisoning. Clinical toxicology is not developed in Africa and this has not helped research and patient care in relation to chemical and pesticide poisons. This section describes the basic pharmacology of some of the most common and most hazardous pesticide poisons and provides the background data on patient management.

Chronic cardiac presentations include bradycardia, hypotension, ST–T changes, prolonged QT interval, polymorphic ventricular tachycardia that can result in sudden death [46].

Organophosphorous Pesticides

Organophosphorous pesticides inhibit acetylcholinesterase through phosphorylation of the esteratic site. This leads to excessive accumulation of acetylcholine which acts via muscarinic, nicotinic and central system receptors. The dominant initial symptoms include miosis, salivation, sweating, bronchial constriction, vomiting and diarrhoea. Central nervous system toxicity presents as cognitive disturbances, convulsions and coma. Often there is peripheral nicotinic effects particularly depolarising neuromuscular blockade.

Organophosphate-induced cardiotoxicity usually starts with a brief period of heightened sympathetic activity which is caused by a combined nicotinic and anxiety effects presenting as tachycardia and hypertension. This is followed by cholinergic-induced parasympathetic activity: bradycardia, hypotension, arrhythmias including atrial fibrillation. A later phase of life-threatening arrhythmias preceded by prolonged QT interval and polymorphic ventricular tachycardia may ensure [47].

The three most common ECG presentations are prolonged QT prolongation, sinus tachycardia and sinus bradycardia. Atrial fibrillation and ventricular premature complexes were the least finding.

Organophosphorous pesticides poisoning is responsible for about 80% of pesticide-associated hospital admissions. The mortality rate ranges from 2 to 30% and cardiotoxicity is a significant predictor of death [45].

Treatment of cardiotoxicity includes

i. maintenance of vital signs which may include mechanical ventilation;
ii. decontamination to prevent further absorption which includes gastric lavage, removal of clothing and washing of skin;
iii. anti-nicotinic and muscarinic agents normally should reverse the effect of organophosphates. However, both nicotinic agonists and antagonists cause blockage of transmission and so effective treatment of nicotinic effect is available. Antimuscarinics, particularly atropine, have been administered intravenously to treat organophosphate poisoning. 1–2 mg in 5–15 min may be required for up to 24–48 h and sometimes therapy may continue for weeks before the muscarinic effects are contained;
iv. some compounds such as pralidoxime are capable of regenerating active enzymes from the organophosphorous and cholinesterase complex and so intravenous infusion can be used, 1–2 g given 15–30 min;
v. prophylactic treatment with pyridostigmine is reserved for cases where possible lethal poisoning is anticipated like in chemical warfare [48].

Carbamate Pesticides

Carbamates are non-persistent pesticides that inhibit acetylcholinesterase by carbamoylation of the esteratic site. These compounds thus have similar toxic properties such as organophosphates. But the binding is weak relatively, and dissociation occurs after minutes to hours and the clinical effects are therefore shorter in duration when compared with organophosphates. There is usually spontaneous reactivation of cholinesterase [15].

The clinical management of carbamate poisoning is also similar to that of organophosphates but it should be noted that pralidoxime is not recommended.

Organochlorine Pesticides

These compounds are divided into four groups: DDT and its analogues, benzene hexachlorides, cyclodienes and toxaphenes. They all contain chlorine substituents. They are usually absorbed through the skin as well as by inhalation or oral ingestion. These chemicals are known as persistent pesticides because of their bioaccumulation in aquatic, animal, plant and human tissues. In humans, they inhibit calcium transport as well as interfere with inactivation of the sodium channels in excitable membranes and cause repetitive firing in most neurons causing tremor and convulsions.

Organochlorine is highly lipophilic and is incorporated into biological membranes and resistant to degradation. The membrane effects of organochlorine may explain some of their pathophysiology. Lindane has been known to cause myocardial degeneration, necrosis, contracture, hypertrophy and electrocardiogram abnormalities. Endosulfan is another organochlorine chemical that has been shown to cause cardiotoxicity in animal studies. Myocardial haemorrhage, single-cell necrosis, inflammatory reactions and fibrotic changes were observed in this study [29, 38].

There is no specific treatment for the acute intoxicated state, and management is symptomatic.

Glyphosate Herbicide

Glyphosate (*N*-[phosphonomethyl]) glycine is the most widely used herbicide in the world and acute intoxication has been known to cause eye and skin irritation, respiratory, haematological, hepatic, gastrointestinal, renal failure, metabolic, ophthalmological, neurological, cardiovascular and when ingested causes esophageal erosion [49–54].

Given the widespread use of glyphosate, both acute and chronic exposure data are important. Acute intoxication of glyphosate has been associated with QT interval prolongation and life-threatening arrhythmias. Chronic exposure to glyphosate has been associated with higher incidences of hypertension, abnormal ECG findings, coronary artery disease and hyperlipemia in a cohort of workers exposed to glyphosate in pesticide chemical industry in China.

The mechanism of toxicity of glyphosate is thought to be uncoupling of oxidative phosphorylation and glyphosate-or polyethoxy ethyleneamine (POEA)-mediated direct cardiotoxicity [55].

There is no known antidote to glyphosate poisoning. Management of glyphosate poisoning is decontamination, and aggressive symptomatic and supportive treatment as no specific protocol is indicated. Gastric lavage or activated charcoal can be administered in patients who present < 1 h after ingestion and who have no evidence of buccal irritation or burns. Hemodialysis has been used in cases of renal failure. Management in intensive care units may be required for patients with hemodynamic instability [56, 57].

Bipyridyl Herbicides

Paraquat is the most important agent of this class and is a non-selective highly toxic herbicide that can damage the lung, kidney, central nervous system, gastrointestinal system as well as the heart. It probably inhibits superoxide dismutase, resulting in intracellular free-radical oxygen toxicity.

Paraquat is usually localised in the lung tissue, with its concentration in the lung found to be 10 times greater than that of plasma. The resulting lung injury leads to respiratory failure which is the most common cause of death. Cardiotoxicity, though not common can present as ECG abnormalities. There are reports of myocardial edema, congestion, haemorrhage and necrosis after ingestion of paraquat [58].

No effective treatment for this highly toxic chemical but symptomatic treatment is advised [59].

i. immediate gastric lavage or whole bowel irrigation;
ii. respiratory failure diuretics, glucocorticoids, cyclophosphamide may be effective in preventing respiratory failure and reducing mortality;
iii. hemoperfusion is very effective for paraquat elimination [60].

Botanical Pesticides

Botanical pesticides are derived from natural sources and include nicotine, rotenone and pyrethrum.

Nicotine is obtained from dried leaves of *Nictiana tabacum* and *N. rustica*. Nicotine reacts with a*cetylcholine receptor of the postsynaptic membra*ne (sympathetic and para sympathetic ganglia, neuromuscular junction) resulting in depolarisation of the membrane. Toxic doses cause stimulation rapidly followed by blockade of transmission. Treatment is symptomatic and may involve suppression of convulsions [61].

Rotenone is derived from *Derris elliptica, D. mallaccensis, Lonchocarpus utilis and L. urucu*. Oral ingestion produces gastrointestinal irritation, conjunctivitis, rhinitis, pharyngitis and dermatitis. Treatment is symptomatic [61].

Pyrethrum is the largest and most notable and most effective class of botanical pesticides. They alter the function of voltage-gated sodium channels, calcium and chloride channels as well as peripheral-type benzodiazepine receptors, causing excitation, convulsions and titanic paralysis. Treatment is symptomatic [61].

Box 6: Safety Precautions [62]

- To read and to follow all label instructions.
- Store all pesticides in safe places out of reach of unauthorised persons
- To wear appropriate protective gear when working with pesticides. Use appropriate PPE for any particular pesticide. For example, a red colour code on a label will require a respirator, not a dust mask to prevent getting sick
- Never to reuse a pesticide container for any purpose. Triple-rinse all pesticide containers after use
- Take the container back to where you bought it or discard the cellophane package appropriately.
- Mixing, loading and rinsing sites should be at least 150 feet away from all water sources.

The lack of awareness and paucity of documented data on cardiotoxicity of pesticide in Africa calls for more work in this area. Research tools that are available and affordable to a large extent include electrocardiography, echocardiography, cardiac enzyme assays and histopathological examination. The establishment of toxicology clinics will train the team that will be equipped scientifically to deliver care and document pesticide and other toxicant-induced cardiotoxicity.

Epidemiological and cause-and-effect studies among exposed subjects will be useful in bringing scientific rigour to this increasing cause of cardiovascular disease. Animal model studies will enable researchers unravel organ-based poisoning since it is easy to obtain pathological specimen. However, animal research comes with some complexities and costs. It is now possible to do in vitro cardiotoxicity assessment of pesticides using an organotypic human-induced pluripotent stem cell-derived model [63]. This has made the study of cardiomyocyte function, cell viability, nuclear morphology and mitochondrial toxicity possible in a dissociated manner by excluding other confounding variables [64].

Conclusion

The exposed group in pesticide poisoning in Africa include workers in pesticide industries, transporters of these chemicals, farmers, farm workers who apply these pesticides, vendors and sellers of farm produce and consumers of foodstuffs that are treated with pesticides as well as persons who consume water and inhale air filled with pesticide. Clearly, there is a widening population of people poisoned by pesticides in

Africa. The severity of any effect from exposure to pesticide depends on the dose, the route of exposure, how easily the pesticide is absorbed, the type of effect of the pesticides and its metabolites, the accumulation and persistence in the body and lastly, the health status of the individual [55].

The WHO and UN Environmental program estimated that each year, 3 million workers in agriculture in the developing world experience severe poisoning from pesticides, about 18,000 of who die. According to one study, as many as 25 million workers in developing countries may suffer mild pesticide poisoning yearly [65]. It is unlikely that Africans will escape from the known organ toxicity of pesticides.

It is true that evidence of pesticide cardiotoxicity in man had come from mainly case reports and epidemiological studies but there are many animal studies that demonstrate cardiac pathology associated with exposure to pesticides. These animal studies have demonstrated histological findings which includes myocardial haemorrhage, vacuolisation, signs of apoptosis and degeneration and remodelling as well as electrocardiographic and echocardiographic findings [66].

Taken together with the ignorance, indiscriminate sale, unguarded use, lack of adequate legislation, inadequate enforcement of legal institutes associated with pesticides poisoning in Africa, there is no doubt that the increasing prevalence and incidence of cardiovascular diseases may partly be due to acute and chronic exposure to these chemicals. More studies will be required to document the pesticide-induced cardiotoxicity in Africa. The poorly developed clinical toxicology specialty may explain the low index of suspicion of cardiovascular diseases resulting from acute and chronic pesticide poisoning in Africa. Many countries have strong laws and enforcement on environmental matters and it is time that Africa takes the right direction to achieve wholesome cardiovascular health.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interests.

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