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Imidacloprid Poisoning - A Potentially Fatal Chemical Poisoning in Humans?

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Abstract: ***Many pesticides are being introduced into the market to control pests in agricultural lands and farming. Poisoning with pesticides is a public health problem globally and till now mortality rates are still on the rise with these poisonings. Imidacloprid poisoning is one such significant health problem which needs a thorough physical examination and laboratory diagnosing before confirming it. Though ingestion in insignificant amounts is safe, quantity beyond limits ingestion can lead to life-threatening complications and sometimes be fatal. This review mainly focuses on the clinical profile of Imidacloprid poisoning with details of various studies and evidence in the past.***

Keywords: imidacloprid, poisoning, neonicotinoid

1. Introduction

Pesticide poisoning is a significantpublic health problem and an important etiology of intentional self-poisoning in various developing countries. Organophosphorus poisoning accounts for most fatalities among them. Therefore, alternative insecticides are being introduced, which are formulated to be more effective on pests and less harmful to humans. [1]Imidacloprid is one of the newer pesticides belonging tothe neonicotinoid class, which selectively acts on the nervous system of pests.

Other Neonicotinoid groups of drugs include:

a) *First generation Neonicotinoid:* Imidacloprid, Nitenpyram, Acetamiprid, Thiacloprid
b) *Second generation Neonicotinoid:* Thiamethoxam, Clothianidin
c) *Third generation Neonicotinoid:* Dinotefuran, Sulfoxaflor, Cycloxaprid

Imidacloprid is chemically similar to Nicotine and belongs to the chloronicotinyl nitroguanidine neonicotinoid class of compounds.Other members of the neonicotinoid class as already mentioned above include acetamiprid,cycloxaprid, clothianidin, thiacloprid, dinotefuran, nitenpyram, and thiamethoxam. [2]

Imidaclopridis the first insecticide in neonicotinoid class which was developed for commercial use against pesticides and is also the first registered compound for its use as a pesticide in the U.S. in 1994.Due to widespread use, human intoxications due to neonicotinoids and in particular Imidacloprid are being common nowadays.[2] According to WHO and toxicity criteria and animal studies, it is classified as moderately hazardous Class-II and toxicity category-II EPA. [3]

Animal studies revealed that Imidacloprid ingestion accidentally does not cause eye irritation (rabbits) or skin sensitization (guinea pigs). Adverse effects are shown whenthe chemical is absorbed via dermal route, ingestion, or inhalational route. Severe poisoning with life-threatening conditions have been observed with oral ingestion than alternative routes.[1]

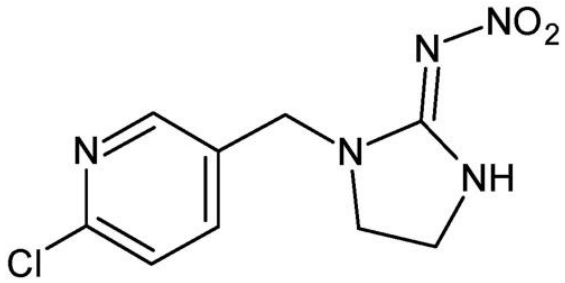

Figure 1: Chemical structure of Imidacloprid

Mechanism of action:

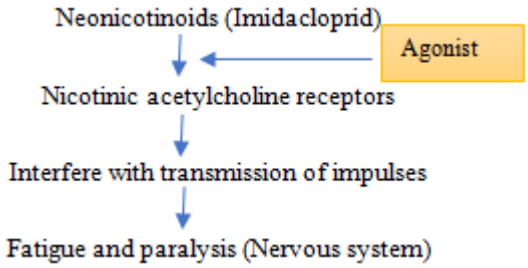

Figure 2: Action of Imidacloprid

Neonicotinoids are agonists at nicotinic acetylcholine receptors and interfere with the transmission of impulses leading to fatigue and paralysisby increased activation.[4] Imidacloprid selectively acts on the nervous system of pests via nicotinic acetylcholine receptors (specifically a4b2 subtype), resulting in their favorable toxicological profile in case of human exposures.[1]

Selective toxicity to insects as compared to mammals is because of different structures and compositions of receptor subunits.

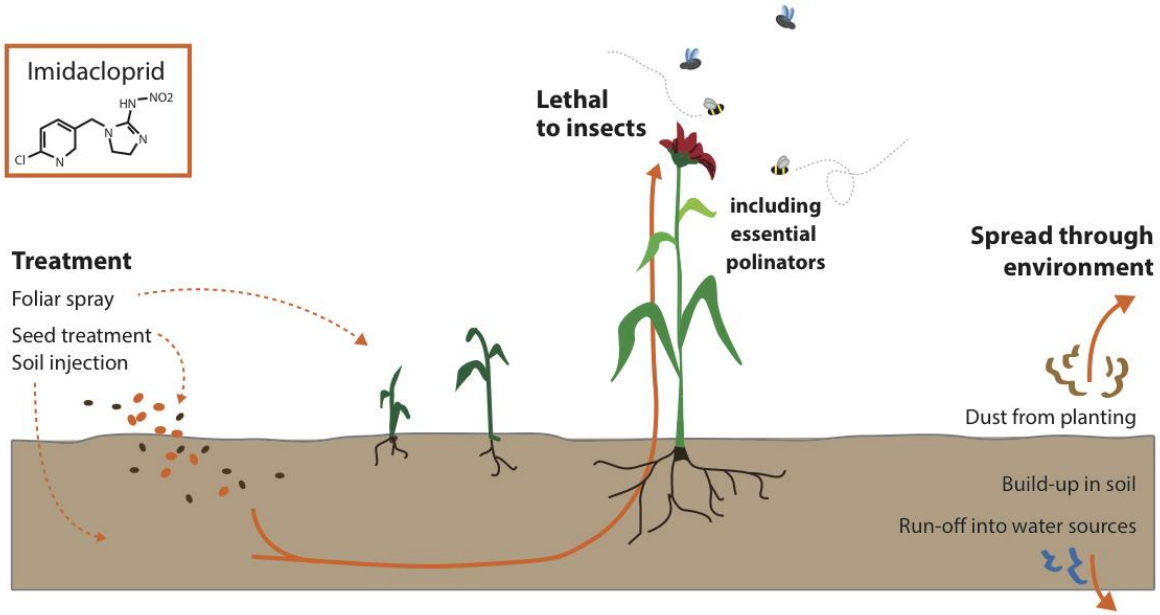

Figure 3: Poisoning of Imidacloprid through AirTransmission

The literature on imidacloprid poisoning in humans is scarce and mainly includes case reports and a few studies from which few data on the clinical profile has been collected and displayed here.[2]

Uses of Imidacloprid:

1) Pesticide on cotton and vegetable crops, turfgrass, and ornamental plant products
2) In indoor and outdoor cockroach control products and termite control products.
3) Pet pest control, home lawns, and garden use, including some, like potting soil, which may not consistently be easily recognized as pesticides.

Clinical presentation of Imidacloprid poisoning:

A case report published by Mundhe et al.in 2017 reported a patient with imidacloprid poisoning with suicidal intention who developed various manifestations such as hypokalemia, paroxysmal atrial fibrillation,central nervous system (CNS) depression, and life threatening situation i.e., respiratory arrest which required mechanical ventilation and recovered subsequently with supportive care.

Receptor stimulation affects CNS as well as autonomic nervous systems. The patient presented with gastrointestinal symptoms followed by transient atrial fibrillation with raised cardiac enzymes and developed CNS depression with respiratory arrest. [6]

CNS stimulation can also occur and can be manifested as dizziness, drowsiness, disorientation, and coma. In contrast, autonomic nervous system (ANS) stimulation causes sweating, dilated pupils, tachycardia, and hypertension, leading to cardiac ischemia and coronary spasm,therefore,increasing the risk of arrhythmia, Hypotension, and bradycardia.[7]

Mohamed et al conducted a multicentric study with Sri Lanka, Portugal, and Australiaandrevealed thatdyspnea, apnea, coma, and mydriasis indicated severe imidacloprid poisoning. He also concluded that investigating plasma concentration of imidacloprid was not helpful in the clinical/pharmacological management of imidacloprid poisoning. [8]

Todani*et al*. in a case report reported that paroxysmal atrial fibrillation was lasting for11 h with first generation neonicotinoids poisoning, and additionally, the patient in their case had CNS depression (GCS-8), hypotension, nausea, hyperglycemia, and vomiting which was improved with supportive care.[9]

Huang *et al*. in his case report presented a patient who had ventricular fibrillation within two hours following oral ingestion of imidacloprid, and this patient presented with altered sensorium with vomiting, diaphoresis, tachycardia, and later symptoms developed were apnea, cyanosis, and ventricular fibrillation and died.[10]

Another case report by Agha *et al*presented that imidacloprid poisoninghad severeleukocytoclastic vasculitis with hepatic and renal dysfunction. Healso stated that imidacloprid toxicity should be considered in the differential diagnosis when multiorgan failure occurs following unknown chemical poisoning.[11]

Taiwan National Poison Center found out a mortalityof 2.85% (2/70) in their retrospective analysis of neonicotinoid exposures. The etiology behind mortality was aspiration of the Imidaclopridleading to asphyxia, respiratory failure, and confirmed mechanicalventilation as the most vital tool in clinical management.[12]

In another case report, Panigrahi*et al*. reported a successful outcome of a patient with respiratory arrest being treated with ventilatory support and found out that the prognosis was better. In contrast, Agarwal and Srinivas reported imidaclopridpoisoning caused neuropsychiatric manifestations and rhabdomyolysis,which were improved with supportive clinical management. [13,14]

Viradiya and Mishra reported severeneuropsychiatric symptoms along with respiratory arrest following imidacloprid ingestion andwere recovered withsymptomatic management. [15] Karatas reported a case of imidacloprid ingestion who were treated with supportive management. They were initially manifested withCNS and ANS symptoms such as disorientation, hypersalivation.[16] In contrast to previous studies, Shadnia and Moghaddam reported imidacloprid poisoning leading to death despite adequate supportive care. [6,17]

Proenca et al reported seizures in two patients who had suicidal ingestion of Imidacloprid. Deaths were reported in the patient and the post-mortem blood concentrations revealed a concentration of 12.5 and 2.05 ng/L[18]

Admire SL 200® (200 g/L), an imidacloprid-containing product in Sri Lanka may induce gastro intestinal toxicity as it contains dimethylsulfoxide and N-methylpyrolidone as solvents which act asirritants. [19]

Few studies have found out that median admission imidacloprid concentration was 10.58 ng/L with a range between 0.02–51.25 ng/L.[5,8,10]

A brief review of the above literature indicates that imidacloprid poisoning can involve the following symptoms:

1) **Gastrointestinal symptoms:** Nausea, vomiting
2) **Cardiorespiratory symptoms:** Respiratory arrest, coronary spasm, and cardiac ischemia, ventricular fibrillation, paroxysmal atrial fibrillation, Hypotension
3) **Central Nervous systems:** Dyspnea, Apnea, coma, Mydriasis, Disorientation, increased salivation, CNS depression, neuropsychiatric manifestations, and rhabdomyolysis
4) **Autonomous nervous systems:** stimulation causes sweating, dilated pupils, tachycardia, and hypertension
5) **Multi-system and life-threatening conditions**:Leukocytoclastic vasculitis with hepatic and kidney dysfunction, multiorgan failure, and hyperglycemia

Laboratory findings:

1) Mild leukocytosis with normal hemoglobin level, RBC, and platelet count.
2) Metabolic acidosis may develop due to acidic metabolites such as 6-chloronicotinic acid and other metabolites.

Treatment:

Management of imidacloprid poisoning remainsonly supportive in the absence of an effective antidote.[3] As neonicotinoids are considered relatively less toxic than other chemical compounds, these patients should be managed with supportive careand regular medications.Somepatients may require mechanical ventilation when respiratory arrest occurs.

2. Conclusion

Available research points towards the significant health risk posed by imidacloprid poisoning and other organophosphate pesticide poisoning. Our review highlights the current available research as well as presents the clinical profile of imidacloprid poisoning and treatment based on current available research evidence.

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