

IMIDACLOPRID POISONING- A POTENTIALLY FATAL CHEMICAL POISONING IN HUMANS?

Public Health

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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

INTRODUCTION:

Pesticide poisoning is a significant public 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 to the 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]

Imidacloprid is 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 when the 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]

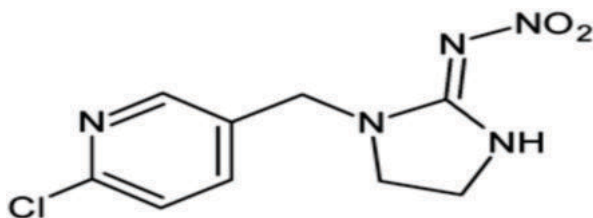


Figure 1: Chemical structure of Imidacloprid

Mechanism of action:

Neonicotinoids are agonists at nicotinic acetylcholine receptors and interfere with the transmission of impulses leading to fatigue and paralysis by increased activation. [4] Imidacloprid selectively acts on the nervous system of pests via nicotinic acetylcholine receptors (specifically $\alpha 4\beta 2$ 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.

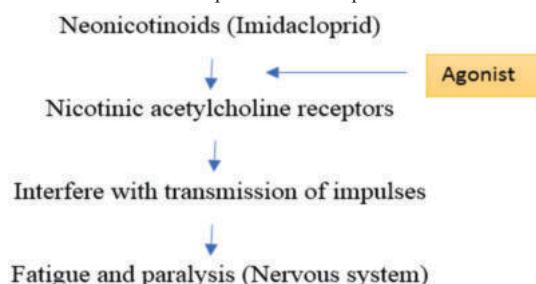


Figure 2: Action of Imidacloprid

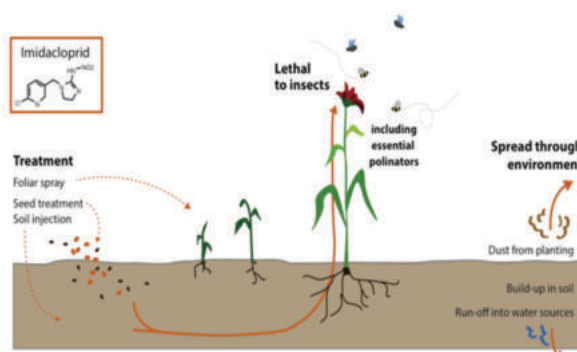


Figure 3: Poisoning of Imidacloprid through Air Transmission

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 Australia and revealed that dyspnea, 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]

Todaniet al. in a case report reported that paroxysmal atrial fibrillation was lasting for 11 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 poisoning had severe leukocytoclastic vasculitis with hepatic and renal dysfunction. He also 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 mortality of 2.85% (2/70) in their retrospective analysis of neonicotinoid exposures. The etiology behind mortality was aspiration of the Imidacloprid leading to asphyxia, respiratory failure, and confirmed mechanical ventilation 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 imidacloprid poisoning caused neuropsychiatric manifestations and rhabdomyolysis, which were improved with supportive clinical management. [13,14]

Viradiya and Mishra reported severe neuropsychiatric symptoms along with respiratory arrest following imidacloprid ingestion and were recovered with symptomatic management. [15] Karatas reported a case of imidacloprid ingestion who were treated with supportive management. They were initially manifested with CNS 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 dimethyl sulfoxide and N-methyl pyrrolidone as solvents which act as irritants. [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 remains only 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 care and regular medications. Some patients may require mechanical ventilation when respiratory arrest occurs.

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.

REFERENCES:

1. Tomizawa M, Casida JE. Neonicotinoid insecticide toxicology: Mechanisms of selective action. *Annu Rev Pharmacol Toxicol*. 2005; 45:247–68.
2. Cimino AM, Boyles AL, Thayer KA, Perry MJ. Effects of neonicotinoid pesticide exposure on human health: A systematic review. *Environ Health Perspect*. 2017; 125:155–62.
3. U.S. EPA Office of Pesticide programs. Pesticide fact sheet: Imidacloprid 1994; 18:1.
4. Zwart, Ruud, Marga, Oortgiesen, and Henk PM. Nitromethylene heterocycles: selective agonists of nicotinic receptors in locust neurons compared to mouse NIE-115 and BC3H1 cells. *Pest. Biochem. Physiol* 1994; 48:202-213.
5. Doull J, CD Klassen, and MO Amdur (eds.). Toxic effect of pesticides. In Cassarett and Doull's Toxicology: The Basic Science of Poisons. 4th ed. NY: Pergamon Press. 1991;889-893.
6. Mundhe, Sanjay A., et al. "Imidacloprid poisoning: An emerging cause of potentially fatal poisoning." *Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine* 21.11 (2017): 786.
7. Lin PC, Lin HJ, Liao YY, Guo HR, Chen KT. Acute poisoning with neonicotinoid insecticides: A case report and literature review. *Basic Clin Pharmacol Toxicol*. 2013; 112:282–6.
8. Mohamed F, Gawarammana I, Robertson TA, Roberts MS, Palangasinghe C, Zawahir S, et al. Acute human self-poisoning with imidacloprid compound: A neonicotinoid insecticide. *PLoS One*. 2009;4: e5127.
9. Todani M, Kaneko T, Hayashida H, Kaneda K, Tsuruta R, Kasaoka S, et al. Acute poisoning with neonicotinoid insecticide acetamiprid. *Chudoku Kenkyu*. 2008; 21:387–90.
10. Huang NC, Lin SL, Chou CH, Hung YM, Chung HM, Huang ST, et al. Fatal ventricular fibrillation in a patient with acute imidacloprid poisoning. *Am J Emerg Med*. 2006; 24:883–5.
11. Agha A, Bella A, Aldasary B, Kazzi ZN, Alhumaidi MA. Imidacloprid poisoning presenting as leukoclastic vasculitis with renal and hepatic dysfunction. *Saudi J Kidney Dis Transpl*. 2012; 23:1300–3.
12. Phua DH, Lin CC, Wu ML, Deng JF, Yang CC. Neonicotinoid insecticides: An emerging cause of acute pesticide poisoning. *Clin Toxicol (Phila)* 2009; 47:336–41.
13. Panigrahi AK, Subrahmanyam DK, Mukku KK. Imidacloprid poisoning: A case report. *Am J Emerg Med*. 2009; 27:256. e5–6.
14. Agarwal R, Srinivas R. severe neuropsychiatric manifestations and rhabdomyolysis in a patient with imidacloprid poisoning. *Am J Emerg Med* 2007; 25:844-845.
15. Viradiya K, Mishra A. Imidacloprid poisoning. *J Assoc Physicians India*. 2011; 59:594–5.
16. Karatas AD. Severe central nervous system depression in a patient with acute imidacloprid poisoning. *Am J Emerg Med*. 2009; 27:1171. e5–7.
17. Shadnia S, Moghaddam HH. Fatal intoxication with imidacloprid insecticide. *Am J Emerg Med* 2008; 26:634.
18. Proenca P, Teixeira H, Castanheira F, Pinheiro J, Monsanto PV, et al. Two fatal intoxication cases with imidacloprid: LC/MS analysis. *Forensic Sci Int*. 2005; 153:75–80.
19. Mohamed F, Gawarammana I, Robertson TA, et al. Acute human self-poisoning with imidacloprid compound: a neonicotinoid insecticide. *PLoS One*. 2009;4(4):e5127. doi:10.1371/journal.pone.0005127