BRIEF RESEARCH COMMUNICATION

Clinical Profile and Predictors of Intensive Care Admission in Neonicotinoid Poisoning in a Tertiary Care Hospital in South India

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Abstract

Background and objectives: Neonicotinoids are a newer class of pesticides that are believed to cause predominantly mild toxicity in humans. This study aimed to describe the clinical features of neonicotinoid poisoning and identify predictors of severe toxicity.

Materials and methods: This retrospective study included all patients with neonicotinoid poisoning admitted to a Tertiary Care Center in India over an 18-year period. Clinical and laboratory features were compared against outcomes to identify predictors of the need for intensive care admission.

Results: Twenty-eight patients were included in the study of which 28.6% had severe disease requiring ICU admission. A higher respiratory rate, blood lactate level, SOFA, and qSOFA scores as well as a lower Glasgow coma score at presentation predicted ICU admission. First-generation compounds and imidacloprid consumption were associated with longer ICU stays and a longer duration of invasive ventilation.

Conclusion: Neonicotinoid compounds can cause significant toxicity with oral ingestion. Imidacloprid and other first-generation compounds were associated with more severe toxicity requiring intensive care. Simple clinical parameters assessed at presentation can be used to predict severe disease and the need for ICU care. Larger, prospective studies are required to confirm these findings.

Keywords: Intensive care, Neonicotinoid, Outcomes, Pesticide poisoning.

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Highlights

Neonicotinoid pesticides can cause severe toxicity requiring ICU care in a minority of cases. Simple clinical parameters can predict the need for ICU admission at presentation. First-generation neonicotinoid compounds were associated with longer ICU stays.

Introduction

Background and Rationale

Neonicotinoids are a relatively new class of pesticides that are now widely used across the world.[1] These compounds act via an agonistic effect at the postsynaptic nicotinic acetylcholine receptors (nAChRs). They are believed to cause mild toxicity in humans because of low affinity for human nAChRs and limited penetration of the blood-brain barrier.[1] However, with wider use, reports of toxicity from intentional or accidental ingestion via the skin or GI tract have increased.[1,2] Ingestion of a significant volume of the insecticide can result in severe, even fatal poisoning. This is especially relevant in India where pesticide poisoning is a common form of deliberate self-harm. Manifestations of neonicotinoid toxicity are usually mild, including gastrointestinal symptoms and local irritation but more severe neurological and cardiovascular manifestations also occur in a minority of cases. The treatment is primarily supportive. Neonicotinoids are classified into four generations of compounds based on their chemical structure.[3]

Objectives

This study aimed to describe the clinical profile of patients presenting with neonicotinoid insecticide poisoning to a Tertiary Care Hospital in South India and identify predictors of severe toxicity as defined by the need for intensive care admission.

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Materials and Methods

Study Design and Setting

This study is a retrospective cohort study conducted in a Tertiary Care Hospital and Medical College in South India. It was approved by the Institutional Review Board of the Hospital (IRB min number 14356 dated 24.11.2021).

Participants

All patients presenting to the Emergency Department with an alleged history of neonicotinoid poisoning during the study period (2005–2022) were included.

Variables and Data Sources

Data was retrieved from the Emergency Department, in-patient, and discharge records. Demographic data, details of the type and

quantity of poison consumed, clinical presentation, laboratory reports, treatment received, and outcomes at hospital discharge were retrieved. Data was entered in to a specially-designed proforma. Severe disease was defined as patients requiring intensive care admission.

Bias

All patients presenting in the study period were included. Patient data was entered into a specially designed proforma.

Statistical Methods

Variables were described using frequencies and percentages for categorical variables and mean and standard deviation for continuous variables. Risk factors for ICU admission were assessed using the Chi-square test or Fisher's exact test for categorical variables and the independent student *t*-test for continuous variables. Binary logistic regression was used for multivariate analysis.

Results

A total of 28 patients were included in the study. Clinical details of the cohort are described in Table 1. The study subjects were predominantly male (60.7%) and had a mean age of 31.4 years (SD 12.4 years). The majority had taken the compound Imidacloprid and a minority had ingested multiple toxins. All patients had ingested the poison orally and intentionally. All patients presented with nausea or vomiting with nervous system involvement such as altered consciousness (32.1%) or muscle weakness (21.4%) being the next most common manifestation of toxicity. A minority of patients required invasive care (28.6%) or invasive ventilation (25.0%). Patients required admission for a mean of 4.6 days. There were no deaths in this cohort.

Table 2 describes predictors of severe disease. A higher lactate level, higher respiratory rate, lower Glasgow Coma Score (GCS), and higher SOFA and qSOFA scores at admission predicted severe disease and the need for ICU admission in this cohort. These associations remained significant when adjusted for age and sex on multivariate analysis. When lactate and SOFA scores were entered into the multivariate model, the SOFA score remained an independent predictor for ICU admission (OR = 5.35; 95% CI = 1.04–27.41, *p*-value = 0.044).

The neonicotinoid compounds consumed were Imidacloprid, Acetamiprid, Thiacloprid (first-generation compounds, *n* = 22), and thiamethoxam (second-generation compound, *n* = 6). The variation in severity of disease between compounds is described in Table 3. Forty percent of patients who consumed imidacloprid required ICU admission compared to 0% of patients who consumed other compounds but this association fell short of statistical significance (*p*-value = 0.063) in this small cohort. Both imidacloprid and all first-generation neonicotinoid compounds resulted in longer ICU stays and days of ventilation. Imidacloprid consumption was also associated with longer hospital stays and first-generation compounds with a lower GCS. The quantity of insecticide consumed was only available for a minority of patients and did not correlate with clinical outcomes.

Table 1: Patient characteristics (*N* = 28)

Characteristic	*N (%) Mean (SD)*
Sex (Male)	17 (60.7)
Age (years)	31.36 (12.39)
Residence in Vellore district	16 (57.1)
Compound taken	
First generation compound	22 (78.6)
Imidacloprid	20 (71.4)
Multiple substance poisoning	7 (25.0)
Quantity (mL)	
Treatment received	
Atropine	14 (50.0)
GI decontamination	9 (32.1)
Organ involvement	
Gastrointestinal	28 (100.0)
Altered consciousness/seizures	9 (32.1)
Muscle weakness	6 (21.4)
Cardiovascular	3 (10.7)
Respiratory	2 (7.1)
Vital signs at presentation	
Heart rate (/min)	96.57 (19.09)
Respiratory rate (/min)	22.46 (2.90)
Glasgow Come Scale	13.32 (3.47)
Systolic blood pressure (mm Hg)	107.71 (17.96)
SOFA score at presentation	1.11 (1.70)
Laboratory investigations	
Hemoglobin (gm/dL)	13.48 (3.01)
Total WBC count (/cumm)	12200 (6713.89)
Creatinine (mg%)	0.81 (0.18)
Bicarbonate (mmol/L)	18.76 (3.21)
Lactate (mmol/L)	2.01 (1.32)
Cholinesterase (U/L)	6020.1 (2800.44)
Outcomes	
ICU admission	8 (28.6)
Invasive ventilation	7 (25.0)
Duration of admission (days)	4.61 (2.90)
Days in ICU	1.30 (2.03)

Discussion

Pesticide poisoning is a common problem in India. While newer compounds such as neonicotinoids may be less toxic than older insecticides, intentional ingestion of larger amounts can result in significant morbidity. Between 2017 and 2018, 5 cases of neonicotinoid poisoning constituted only 0.28% of all deliberate self-poisoning cases presented to the emergency department in our center.[4] In this study, more than a quarter of patients admitted with neonicotinoid poisoning required ICU care and invasive ventilation. This was similar to rates of severe disease documented elsewhere.[1] Mortality was absent in this cohort and low in other studies suggesting that with supportive care in an ICU, most patients with severe disease recover.[1] Patients in this cohort appeared to have a higher rate of gastrointestinal symptoms and but similar rates of other systemic symptoms compared to a study from Taiwan. This may be due to the fact that all patients consumed the pesticide orally.

Table 2: Predictors of ICU admission*

	Intensive care not required	*Intensive care required*	*Bivariate statistics t-value, p-value*	*Multivariate statistics** OR (95% CI), p-value
Lactate	1.75 (1.19)	3.18 (1.20)	–2.33, 0.031	2.98 (1.01–8.78), 0.048
Respiratory rate	21.58 (2.36)	24.86 (3.02)	–2.91, 0.008	2.25 (1.07–4.74), 0.033
Glasgow Coma Scale	14.35 (2.68)	10.75 (4.06)	2.76, 0.01	0.71 (0.52–0.98), 0.036
SOFA score	0.29 (0.73)	3.4 (1.51)	–6.15, 0.00	5.89 (1.21–28.59), 0.028
qSOFA score	0.89 (0.68)	1.86 (0.69)	–3.20, 0.004	15.02 (1.52–148.28), 0.02

*Factors that did not show a significant association with severe disease: Age, sex, residence, compound, quantity consumed, time to presentation, gastrointestinal decontamination, gastrointestinal symptoms, cardiovascular involvement, respiratory involvement, hemoglobin, platelet count, total leukocyte count, creatinine, liver function tests, electrolytes, pH, pO2, pCO2, cholinesterase levels, heart rate, systolic and diastolic blood pressures
**Adjusted for age and sex

Table 3: Imidacloprid and first-generation neonicotinoids compared to other compounds

Characteristic	*First generation compound mean (SD)*	*Second generation compound mean (SD)*	*Bivariate statistics t-value, p-value*
Glasgow Coma Scale	12.91	14.83 (0.41)	2.31, 0.030
Days of ventilation	1.04 (1.73)	0.00 (0.00)	–2.83, 0.01
Days in ICU	1.67 (2.18)	0.00 (0.00)	–3.51, 0.002
	Imidacloprid mean (SD)	*Other mean (SD)*	*Statistics t-value, p-value*
Duration of stay	7.75 (3.28)	3.35 (1.46)	–1.61, 0.006
Days of ventilation	1.15 (1.79)	0.00 (0.00)	–2.88, 0.01
Days in ICU	1.74 (2.26)	0.25 (0.71)	–2.59, 0.016

Gastrointestinal symptoms are sometimes attributed to the corrosive effect of the solvents mixed with the neonicotinoid pesticides.[1]

Simple clinical parameters (GCS, respiratory rate), commonly-used clinical scores (SOFA, qSOFA), and elevated blood lactate at presentation predicted severe disease requiring ICU admission in these patients and can be used to prognosticate at the time of admission. Among these only CNS involvement and coma have been previously documented. Factors that were associated with severe disease elsewhere that were not noted in our cohort included age, respiratory failure, gastrointestinal bleeding, cardiovascular involvement, and hypotension.[1]

Imidacloprid is the most widely used neonicotinoid and this was reflected in our study. The association of severe disease with imidacloprid and first-generation compounds has not been previously documented however in the only other study that examined predictors of severe disease, all the patients with fatal or severe disease had oral exposure to imidacloprid and most had suicidal intent, similar to the patients in this cohort.[1] First-generation compounds appear to have significantly worse toxicity than second generation compounds despite both being classified as class II compounds (moderately hazardous) according to the WHO classification.

The quantity of insecticide consumed, though available for only a small number of patients, did not correlate well with outcomes. This is similar to a study from Sri Lanka which showed that blood concentrations did not correlate well with toxicity.[5] Individual variations in cytochrome P450 isoenzymes may account for this variable toxicity.[6]

Limitations

This study is limited by being a small, retrospective cohort. It includes only intentional, oral ingestion of neonicotinoids in patients presenting to a Tertiary Care Center which is likely to be more severe than accidental and dermal or inhalational exposure to the insecticides and those presenting to primary or secondary care hospitals.

Conclusion

Neonicotinoid compounds can cause significant toxicity in oral ingestion. Imidacloprid and other first-generation compounds are associated with more severe toxicity. Simple clinical parameters assessed at presentation can be used to predict severe disease and the need for ICU care. Larger, prospective studies are required to confirm these findings.

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References

1. Phua DH, Lin CC, Wu ML, Deng JF, Yang CC. Neonicotinoid insecticides: An emerging cause of acute pesticide poisoning. Clin Toxicol (Phila) 2009;47(4):336–341. DOI: 10.1080/15563650802644533.
2. 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(4):282–286. DOI: 10.1111/bcpt.12027.
3. Lawrence J Cheskin, Manuel Franco, Daniel J Hoffman. Encyclopedia of Human Nutrition, 4th edition. ScienceDirect 2023. Available from: http://www.sciencedirect.com:5070/referencework/9780323908160/encyclopedia-of-human-nutrition.
4. Abhilash KPP, Murugan S, Rabbi NAS, Pradeeptha S, Kumar S, Selvaraj B, et al. Deliberate self-poisoning and harm: A meticulous quest of

methods in vogue. J Fam Med Prim Care 2022;11(1):233–239. DOI: 10.4103/jfmpc.jfmpc_1184_21.
5. 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(4):e5127. DOI: 10.1371/journal.pone.0005127.
6. Tomizawa M, Casida JE. Neonicotinoid insecticide toxicology: Mechanisms of selective action. Annu Rev Pharmacol Toxicol 2005;45(1):247–268. DOI: 10.1146/annurev.pharmtox.45.120403.095930.