



Methemoglobinemia Following Acute Novaluron–Emamectin Benzoate Ingestion: A Rare Case Report

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KEYWORDS

Methemoglobinemia.

ABSTRACT:

Background: Novaluron and emamectin benzoate are insecticides widely used in agricultural regions of India. Human toxicity is uncommon, and methemoglobinemia is rarely reported.

Case Presentation: A 26-year-old male presented 3 hours after deliberate ingestion of approximately 500 mL of Barazide® (Novaluron 5.25% + Emamectin benzoate 0.9%). He had multiple episodes of vomiting. On admission, SpO₂ was 80% on room air, 86% on 6 L/min O₂, with normal hemodynamics. ABG showed falsely normal SO₂ & PaO₂ with elevated methemoglobin levels up to 14.8%. Chest X-ray and ECG were normal. Gastric lavage was performed, and methylene blue was administered. Serial ABGs showed gradual normalization of methemoglobin levels.

Outcome: The patient improved clinically and was discharged stable on day 3.

Conclusion: This case highlights a rare presentation of methemoglobinemia due to novaluron–emamectin ingestion, emphasizing the need for early recognition and antidotal therapy.

INTRODUCTION

Pesticide poisoning continues to be a major public-health concern worldwide, particularly in low- and middle-income countries where agricultural chemicals are widely accessible, often without adequate regulatory control. The World Health Organization has estimated that nearly 3 million cases of pesticide poisoning and over 300,000 deaths occur annually, the majority in South and Southeast Asia.¹ In India, intentional self-poisoning with agrochemicals remains one of the most common modes of suicide, especially in rural farming communities where occupational exposure and easy availability contribute significantly to the burden.² The introduction of newer insecticides, such as novaluron and emamectin benzoate, has increased the complexity of toxicological presentations because their human toxicity profiles are not as well-characterized as those of traditional organophosphates.

Novaluron is a benzoylurea insect growth regulator that inhibits chitin synthesis in insects, and is generally considered to have low acute toxicity in mammals.³ However, accidental or intentional ingestion of concentrated commercial formulations may lead to unexpected systemic effects due to solvents and

synergistic agents used in these products. Emamectin benzoate, a semisynthetic avermectin analogue, acts by stimulating glutamate-gated chloride channels in insects, causing neuronal hyperpolarization; in humans, reported toxicity includes nausea, neurotoxicity and, rarely, respiratory symptoms.⁴ Although neither chemical is classically associated with oxidative stress, emerging evidence suggests that certain insecticides—either through their metabolites or solvent carriers—can induce methemoglobinemia, a rare but potentially life-threatening condition characterized by oxidation of ferrous (Fe²⁺) hemoglobin to ferric (Fe³⁺) form.⁵

Methemoglobinemia reduces the oxygen-carrying capacity of blood and impairs tissue oxygen delivery, leading to cyanosis, dyspnea, neurological dysfunction, and, in severe cases, cardiovascular collapse. The condition is typically associated with exposure to oxidizing agents such as nitrates, aniline dyes, benzocaine and dapson, but insecticide-induced methemoglobinemia has been documented in a few isolated case reports.⁶ Diagnosis is often challenging because pulse oximetry readings remain low despite normal arterial oxygen tensions, creating a characteristic “saturation gap.” Early recognition and treatment with



methylene blue, the antidote of choice, is essential for preventing complications.

Given the growing use of novel insecticides in India and the scarcity of published data regarding their systemic toxicity, especially methemoglobinemia, documentation of such cases becomes crucial and paramount. The present case describes acute ingestion of a combined formulation of novaluron and emamectin benzoate leading to clinically significant methemoglobinemia, highlighting the need for heightened awareness, prompt diagnosis, and appropriate management strategies among clinicians practicing in agricultural regions.

CASE PRESENTATION

A 26-year-old male agricultural worker from Belagavi district, Karnataka, was brought to the Emergency Department approximately three hours after intentional ingestion of nearly 500 mL (two bottles) of a commercial insecticide formulation Barazide® containing Novaluron 5.25% and Emamectin benzoate 0.9%. The ingestion occurred at his residence following a psychosocial stressor. Within 20–30 minutes of ingestion, he developed three episodes of non-bilious vomiting but did not experience seizures, loss of consciousness, or chest pain. Family members immediately transported him to the nearest tertiary care hospital.

Initial Assessment

On arrival, the patient was conscious, alert, and oriented to time, place, and person. He was moderately built and nourished. Vital parameters were as follows:

- Blood Pressure: 110/70 mmHg
- Heart Rate: 90 beats/min
- Respiratory Rate: 20 breaths/min

Serial Arterial Blood Gases and Pulse oximeter readings

Date/Time	pH	pCO ₂ mmHg	PaO ₂	SpO ₂ (ABG)	MetHb (%)	Interpretation	SpO ₂ (Pulse oximeter)
04-12-2025, 19:36 (Venous sample)	7.389	35.3	—	74.4%	10.1%	Moderate methemoglobinemia	80% at room air 86% with 6L O ₂ /min.

- Temperature: 37°C
- SpO₂: 80% at room air, 86% on 6 L/min oxygen via face mask (Refractory hypoxemia)

He had hypoxia on pulse oximeter despite supplemental oxygen. There were no signs of pallor, icterus, cyanosis, clubbing, or lymphadenopathy.

Systemic Examination

Cardiovascular system:

- Precordium was normal with no visible pulsations.
- Apical impulse located in the 5th intercostal space, 1.25 cm medial to the mid-clavicular line.
- S1 and S2 were heard normally; no murmurs or gallops.

Respiratory system:

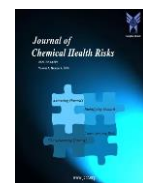
- Chest symmetrical, with bilaterally equal air entry.
- No crepitations, wheeze or bronchospasm.

Abdomen:

- Soft, non-tender, with normal bowel sounds.
- No distension or organomegaly.

Central Nervous System:

- Higher mental functions intact.
- Cranial nerves normal.
- Motor and sensory systems normal.
- Plantar reflex flexor bilaterally.



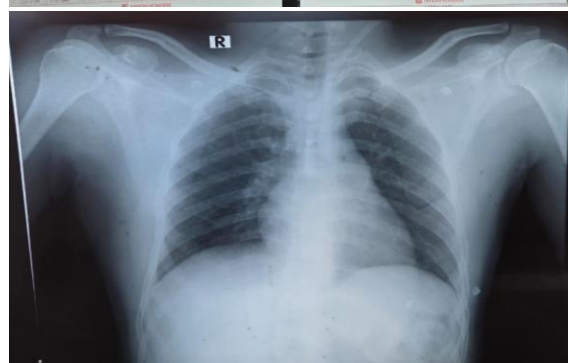
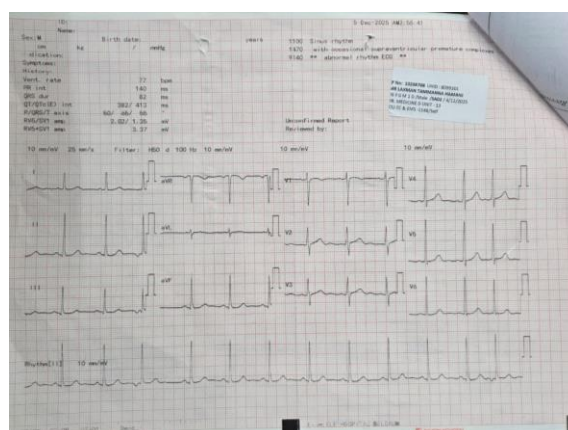
04-12-2025, 20:33	7.378	31.5	145 mmHg	99.1%	14.8%	“Saturation gap” noted which is more than 5%.	80% at room air 86% with 6L O2/min
04-12-2025 10pm							94% with 6L O2/min
05-12-2025							95% at room air.
06-12-2025, 10:33	7.397	35.5	—	95.6%	1.5%	Post-treatment improvement	95% at room air

The discordance between pulse oximetry (86%) and arterial oxygen saturation (~99%) was strongly suggestive of methemoglobinemia.

Electrolytes were normal (Na⁺- 139, K⁺- 4.44, Bicarbonate- 19.2, Chloride- 104). Lactate levels were mildly elevated initially (2.02–3.66 mmol/L), normalizing with supportive care.

Other Investigations

- Complete blood count: Neutrophilic leukocytosis (WBC 11,100/mm³, neutrophils 80%).
- Renal and liver function tests: Within normal limits.
- Coagulation profile: PT/INR within normal limits.
- G6PD level: 5.2 U/gHb (adequate; no contraindication for methylene blue).
- Chest X-ray: Clear lung fields, normal cardiac silhouette, no infiltrates or aspiration.
- ECG: Sinus rhythm, normal axis, no ischemic changes.
- 2D Echocardiography: Normal LV function, LVEF 60%.
- Toxicology: Gastric lavage sample was negative for chlorpyrifos and permethrin via thin-layer chromatography, supporting exposure to non-OP insecticide (novaluron + emamectin).



Treatment

Emergency management started immediately and included:

- Gastric lavage upon arrival.
- High bowel wash to reduce systemic absorption.
- Intravenous fluids (NS/DNS) at 75 mL/hr.



- Oxygen therapy via face mask.
- Inj. Pantoprazole 40 mg IV once daily.
- Inj. Ceftriaxone 1 g IV twice daily for 3 days.
- Psychiatric evaluation for suicide attempt.

Because of worsening hypoxemia and rising methemoglobin levels (14.8%), the team administered:

- Inj. Methylene Blue (1mg/kg body weight (total 60mg) after dilution in 5 % Dextrose, infused over 30 minutes) as per poisoning guidelines and after confirming adequate G6PD activity.

Clinical Course

Following methylene blue administration, the patient showed dramatic improvement within 1–2 hours

- SpO₂ improved to >94% on oxygen, and subsequently >95% on room air.
- Repeat ABG over the next 36 hours demonstrated reduction of MetHb to 1.5%.
- No neurological deficits or arrhythmias developed.

The patient remained hemodynamically stable, tolerated oral intake, and maintained normal urine output.

He was discharged on day 3, clinically stable, advised on psychiatric follow-up, and scheduled for outpatient review in 15 days.

DISCUSSION

Pesticide poisoning continues to represent a significant toxicological and public-health challenge in developing countries, especially in agrarian regions of India where agrochemicals are widely accessible and frequently used without strict regulation.⁷ In recent years, there has been a shift from classical organophosphate poisoning toward newer insecticides such as benzoylurea derivatives and avermectin analogues. Although these agents are often labeled as having “low mammalian toxicity,” emerging evidence suggests that co-formulated chemicals, surfactants, and solvents in commercial preparations can produce unexpected systemic effects.⁸

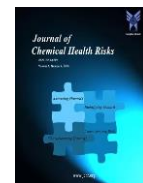
Novaluron, a benzoylurea insect growth regulator, primarily inhibits chitin synthesis in insects and has been classified as a low-toxicity (WHO Class III) compound

in mammals based on experimental studies.³ Emamectin benzoate, a macrocyclic lactone derived from avermectins, exerts neurotoxic effects in insects but generally demonstrates limited systemic toxicity in humans at routine exposure levels.⁴ However, ingestion of concentrated agricultural formulations may lead to toxic manifestations not attributable solely to their active ingredients. This is particularly relevant for self-poisoning cases in India, where ingestion volumes tend to be large and solvents may contribute significantly to toxicity.²

In the present case, the patient developed significant methemoglobinemia, a rare complication for this class of insecticides. Methemoglobinemia occurs when oxidative stress converts ferrous (Fe²⁺) hemoglobin to ferric (Fe³⁺) methemoglobin, which is incapable of binding oxygen. Although endogenous enzyme systems—including NADH-cytochrome b5 reductase—normally keep methemoglobin levels below 1%, exposure to exogenous oxidants can overwhelm this capacity.⁹ Classical etiologies include nitrates, nitrobenzene, aniline dyes, benzocaine, dapsone, and certain antimalarials; however, pesticide-induced methemoglobinemia has been reported in only a handful of cases worldwide.⁶

The mechanism by which novaluron–emamectin formulations induce methemoglobinemia remains unclear. Commercial pesticide preparations often contain aromatic hydrocarbons, emulsifiers, and oxidative stabilizers that can generate reactive oxygen species (ROS), leading to hemoglobin oxidation.¹⁰ Some benzoylurea insecticides have been shown experimentally to activate oxidative stress pathways, increasing susceptibility to red blood cell injury under certain conditions.¹¹ It is plausible that solvent interactions or synergistic toxicity from emamectin’s benzoate moiety contributed to the oxidative stress observed in this patient.

Clinically, the patient demonstrated the typical “saturation gap”—persistent low peripheral oxygen saturation despite normal SO₂ & PaO₂ on ABG analysis. This discrepancy between SpO₂ and arterial oxygenation is a hallmark diagnostic clue for methemoglobinemia.¹² Arterial blood gas confirmed elevated methemoglobin levels. Prompt treatment with methylene blue, the standard antidote, resulted in rapid clinical and biochemical improvement. The absence of G6PD



deficiency ensured safe use of methylene blue without risk of hemolysis. This patient improved with single dose of methylene blue without need for additional doses of methylene blue or adjuvant Vit C or N acetyl cysteine or hemodialysis or hyperbaric oxygen.

Overall, this case highlights the importance of recognizing non-classical manifestations of poisoning with newer insecticides. As agricultural patterns evolve and pesticide formulations diversify, clinicians must maintain a broad differential diagnosis and consider oxidizing toxicity even with compounds traditionally deemed low-risk. Documentation of such cases expands the evidence base for managing emerging agricultural poisonings.

CONCLUSION

This case highlights a rare presentation of methemoglobinemia following ingestion of a combined novaluron–emamectin benzoate insecticide formulation, underscoring that even pesticides considered relatively safe can produce life-threatening oxidative effects. Early recognition of the “saturation gap,” by ABG & pulse oximeter clinically helps diagnosis, and timely administration of methylene blue were critical to the patient's rapid recovery. As the use of newer insecticides increases in India, clinicians should remain vigilant for atypical toxic presentations and ensure appropriate toxicological evaluation. Documentation of such cases is essential to expanding the clinical understanding of emerging pesticide toxicities.

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