ASIA PACIFIC JOURNAL of MEDICAL TOXICOLOGY
APJMT 14;1 http://apjmt.mums.ac.ir March 2025

CASE REPORT

A Rare Case of Emamectin Benzoate Poisoning Causing Methemoglobinemia

A R MOHAMMED UMAR*, JACINTH PREETHI

Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India

Abstract

Introduction: Emamectin Benzoate (4'-deoxy-4'-epi-methyl-amino Benzoate), widely used as a broad-spectrum insecticide has a significant human safety margin. Methemoglobinemia from toxin exposure is a rare presentation of its poisoning. Due to their easy accessibility globally, agricultural insecticides have been utilized for self-poisoning on a regular basis. However, methemoglobinemia resulting from its toxic exposure is a rare occurrence.

Case presentation: A 49-year-old farmer presented with altered mental status and difficulty in breathing 6 hours after ingesting an unknown substance which was later identified as Emamectin Benzoate at Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India, in September 2024. On admission the patient presented with hypoxemia, cyanosis and a "saturation gap", with a co-oximetric methemoglobin level of 48%. The patient was treated with 0.1% methylene blue intravenously (IV) at a dose of 1 mg/kg body weight (total 50 mg) diluted in 50 mL of 5% dextrose over five minutes and also received 1 g intravenous vitamin C three times daily and N-acetylcysteine 1.2 gm for the methemoglobinemia. Despite the initial methylene blue treatment, his clinical status remained unchanged, so a second dose of methylene blue (50 mg) was administered an hour later. His clinical condition improved within 48 hours of treatment and was discharged on the fifth day.

Discussion: Acquired methemoglobinemia can be due to substances like local anesthetic, dapsone, amyl nitrate, quinones, sulphonamides and rarely due to insecticides. In this context, Emamectin Benzoate compound caused methemoglobinemia after ingestion.

Conclusion: Although rare, methemoglobinemia following pesticide ingestion can be fatal. It should be considered in cases of refractory hypoxemia and a "saturation gap." High clinical suspicion and appropriate management are key to improving patient outcomes.

Keywords: Emamectin Benzoate, Insecticide, Methemoglobinemia, Methylene blue

How to cite this article: Umar ARM, Preethi J. A rare case of Emamectin Benzoate poisoning causing methemoglobinemia. Asia Pac J Med Toxicol 2025; 14(1):

INTRODUCTION

Agricultural insecticides are frequently used for self-poisoning due to their easy accessibility. Emamectin Benzoate (4'-deoxy-4'-epi-methyl-amino Benzoate), a semisynthetic avermectin derived from Streptomyces avermitilis, is widely used as a broad-spectrum insecticide, nematicide, and acaricide for vegetables. Emamectin Benzoate functions by stimulating high-affinity GABA receptors. While, it has a significant safety margin for humans, particularly due to its restricted ability to penetrate the blood–brain barrier, high doses can overcome this limitation, potentially leading to severe complications such as methemoglobinemia. This case report discusses the clinical presentation, management, and outcome of a patient with Emamectin Benzoate -induced methemoglobinemia.

CASE REPORT

A 49-year-old male farmer, with no significant medical history, presented to the emergency department, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India, in September 2024, claiming to have consumed unknown substance mixed with alcohol with suicidal intent. He arrived six hours post ingestion to our hospital with symptoms of altered mental status, difficulty in breathing, and two episodes of vomiting. On admission to the Toxicology ICU, the patient was drowsy and under the influence of alcohol. His vital signs were as follows: Blood pressure 100/60 mm Hg in right upper limb in supine position, Pulse rate 96/minute, regular rhythm, normal volume, no special character, felt equally in all the peripheral vessels, and Respiratory rate was 18/minute, abdominothoracic type and Oxygen saturation of 78% on room air, which did not improve with oxygen supplementation. Physical examination revealed cyanosis, including bluish discoloration of the tongue, lips, and fingernails, but his cardiovascular and respiratory examinations were normal. Both pupils were equal and reactive. He also had dark-coloured urine (Figure

*Correspondence to: Dr. A R Mohammed Umar, MD. Government Stanley Medical College, Chennai, Tamil Nadu, India.
Email: mohammedumar.a.r@gmail.com. Tel: +91 9677075096

1) and chocolate brown-coloured blood (Figure 2), all suggestive of methemoglobinemia. Gastric lavage was done and activated charcoal, intravenous hydration and oxygen supplementation was administered.

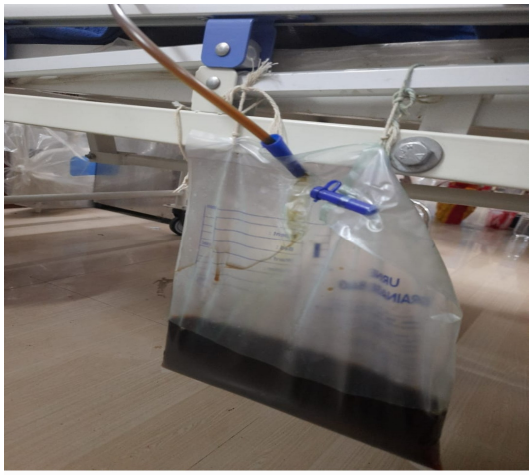

Figure 1. Dark coloured urine of the patient

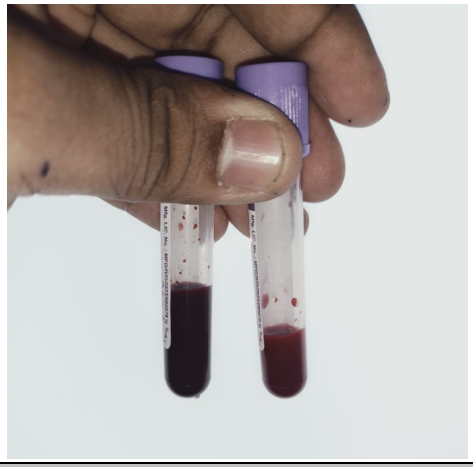

Figure 2. Chocolate brown-coloured blood of the patient on the left side vs blood of a normal person on the right

Diagnostic Workup

Arterial blood gas (ABG) analysis of the patient while he was on non-rebreathing mask with FiO2 of 90% revealed a pH of 7.297, PaO2 of 108 mmHg, SaO2 of 97.55%, CO2 of 48.28mmHg and HCO3− of 22.70mmol/L. The significant saturation gap (approximately 20%) between SpO2 and SaO2 raised suspicion for methemoglobinemia. which was confirmed by a co-oximetric measurement of methaemoglobin (MetHb) levels at 48%. The glucose-6-phosphate dehydrogenase (G6PD) level was within normal limits.

Management

The patient was treated with methylene blue 1 mg/kg in dextrose solution or 0.2 mL/kg of a 1% solution (i.e., 50 mg), which reduces the 3+ ferric state back to the 2+ ferrous state in erythrocytes within 30 minutes of his arrival. Serial arterial blood gas (ABG) (Table 1) was performed. Routine investigations showed leucocytosis, Electrocardiogram (ECG) revealed normal sinus rhythm and Chest X-ray showed no particular abnormality. Despite the initial methylene blue treatment, his clinical status remained unchanged, so a second dose of methylene blue (50 mg) was administered an hour later. He also received 1 g intravenous vitamin C three times daily and N-acetylcysteine 1.2 gm intravenously twice daily to help reduce oxidative stress, repeat methaemoglobin level later that day decreased to 19.2%, and the toxic agent was identified as Emamectin Benzoate from the container brought by the patient's attendants.

Outcome

The patient's consciousness gradually improved, though cyanosis persisted (Figure 3). After 24 hours, the patient's oxygen saturation increased to 95% on room air, cyanosis subsided, and his urine turned green. Repeat methaemoglobin levels decreased to 4.2%. The patient was transferred to the ward on Day 4 and discharged on Day 5 fully recovered.

Table 1. Serial arterial blood gas (ABG) analysis

ABG ANALYSIS	At admission	1 hr	24 hrs
pH	7.297	7.365	7.431
PCO2	48.28	52.64	45.50
PaO2	103	108	109
SaO2	97.55	99.68	98.38
Hb	13.02	13.72	12
Lac	1.45	2.26	0.5
HCO3	22.70	29	29.01
SpO2	78%	84%	95%

Figure 3. Persistent cyanosis even oxygen therapy without severe cardiopulmonary disease

DISCUSSION

Emamectin Benzoate a widely used broad-spectrum insecticide acts by stimulation of high-affinity GABA receptors leading to an increase in chloride ion permeability across cell membranes. Despite its relatively safe profile in humans, due to its restricted ability to penetrate the blood–brain barrier and the mammalian species being much less sensitive due to their lower GABA receptor affinities, high doses might overcome this limitation and a rare case fatality has also been reported [1].

Methaemoglobin occurs when the iron atom in haemoglobin is oxidised from its ferrous (Fe 2+) state into the ferric (Fe 3+) state following exposure to an oxidizing chemical or drug thus impairing oxygen transport and causing tissue hypoxia with a leftward shift of the oxyhaemoglobin dissociation curve. Methemoglobinemia is defined as an abnormal elevation of the methaemoglobin level above 1% [2]. This condition is characterized by cyanosis, dizziness, and altered mental status, potentially leading to coma and death. Whether the initial central nervous system (CNS) manifestations were due to Emamectin alone, or in conjunction with ethanol in our case is unclear.

Methemoglobinemia should be considered when there is a significant difference between SpO2 (measured by pulse oximeter) and SaO2 (measured by ABG), with a saturation gap greater than 5% [2]. In our case, the gap was around 20%, which warranted the suspicion of methemoglobinemia. Treatment is recommended at MetHb levels of 20% in symptomatic individuals and 30% in asymptomatic [3]. MetHb levels exceeding 70% are considered potentially lethal. Treatment involves methylene blue, which acts as a reducing agent for methaemoglobin. The recommended dose of methylene blue is 1–2 mg/kg. It is reasonable to theorize that because the effects of methemoglobinemia occur in the blood compartment, each dose of methylene blue should be limited to a maximum dose of 100 mg regardless of a patient's weight [2]. The maximum dose is 5 to 7 mg/kg/ day. Excessive dose > 7 mg/kg – causes methemoglobinemia by directly oxidizing Hb [4]. Although cases of Emamectin Benzoate poisoning with various presentations have been reported [5,6] only few cases have been reported with methemoglobinemia [7,8].

In our patient, additional therapies including vitamin C and N-acetylcysteine were administered to mitigate oxidative stress. Ascorbic acid can directly reduce MetHb and also reduces excessive oxidative stress, but is very slowly effective when used alone and requires multiple doses to lower MetHb levels. Dosing is not standardized. Doses in adults have ranged from 0.5 gm every 12 hr × 16 doses, 1 g every 12 hr × 14 doses, 1.5-2 g iv × 3–4 infusions, 5 g every 6 hr × 6 doses, or even 10 g × one dose [4]. Ascorbic acid is the treatment of choice in cases of G6PD deficiency or when methylene blue is unavailable. N-acetylcysteine acts as a cofactor in the reduction process, and the benefits are shown in recent research, but it is not yet an approved treatment for methemoglobinemia. Refractory cases of methemoglobinemia can be treated with therapeutic whole blood exchange (TWBE), haemodialysis, and hyperbaric oxygen [4]. The limitation of our study is that we were not able to follow-up the patient.

CONCLUSION

Methemoglobinemia is a potentially life-threatening complication of Emamectin Benzoate poisoning. Early diagnosis, based on clinical suspicion and laboratory findings such as a "saturation gap" and characteristic blood coloration, is crucial. Prompt treatment with methylene blue, along with supportive care, can lead to favourable outcomes. Clinicians should maintain a high index of suspicion for methemoglobinemia in cases of pesticide poisoning, especially when conventional oxygen therapy fails to improve oxygen saturation.

Conflict of Interest: The authors declare no conflict of interest.

Funding and Support: None.

REFERENCES

1. Godhiwala P, Nirmal A, Bakre A, Wanjari A, Kumar S. Acute Emamectin Benzoate Poisoning-A Fatal Case Report. J Evol Med Dent Sci. 2020; 9. 10.14260/jemds/2020/38.
2. Price D. Methemoglobin inducers. Goldfrank's Toxicologic Emergencies, 11th edition. 2019; 1703–1706, 1715.
3. Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia: a retrospective series of 138 cases at 2 teaching hospitals. Medicine (Bal- timore) 2004; 83(5):265–73. DOI: 10.1097/01.md.0000141096.00377.3f
4. Lolascon A, Bianchi P, Andolfo I, Russo R, Barcellini W, Fermo E, et al. Recommendations for diagnosis and treatment of methemoglobinemia. Am J Hematol. 2021 Dec 1;96(12):1666-78. doi: 10.1002/ajh.26340. Epub 2021 Sep 23. PMID: 34467556; PMCID: PMC9291883.
5. Yen TH, Lin JL. Acute poisoning with emamectin Benzoate. J Toxicol Clin Toxicol. 2004;42(5):657-61. doi: 10.1081/clt-200026968. PMID: 15462160.
6. Lalmalsawmi R, Ravikumar YS, Mahesh M, Mariyam Shihuna PM, Ramesh M, Chalasani SH. Management and prognosis of acute Emamectin Benzoate poisoning in a human. Toxicol Rep, 2024; 13:101744, ISSN 2214-7500, https://doi.org/10.1016/j.toxrep.2024.101744.
7. Thuluvath SR, Das RP, Dutta N, Sarma DK. Acute Methemoglobinemia after Emamectin Benzoate Ingestion. Indian Journal of Critical Care Case Report. 2024; 3 (5): 142-44.DOI: 10.5005/jp-journals-11006-0124.
8. Liang C, Cui S, Geng L. Hemoperfusion combined with methylene blue in treating methemoglobinemia caused by emamectin Benzoate + indoxacarb poisoning: A case report and literature review. Asian J Surg. 2023 Dec;46(12):5899-900. doi: 10.1016/j.asjsur.2023.08.235. Epub 2023 Sep 19. PMID: 37730503.