

Methemoglobinemia: Rare Presentation of Biofungicide Poisoning

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Abstract: Biofungicides are a viable alternative to chemical fungicides that decrease the risk of pathogens developing resistance in agriculture. Fungicide ingestion vary enormously in their potential for causing adverse effects in livestock but no data is available on human ingestion/poisoning. We report a case of Biofungicide poisoning containing plant alkaloids in a student following suicidal consumption manifested as pale peripheries, cyanosis, bluish discoloration of blood (ABG sample) and saturation gap. Methemoglobinemia was suspected which was successfully managed with Oxygen Supplementation, Inj. Methylene blue and other symptomatic management.

We describe unusual presentation and effective management of Methemoglobinemia secondary to ingestion of Biofungicide which contains plant alkaloids.

Keywords: Biofungicides, Methemoglobinemia, Methylene Blue

I. Introduction:

Diseases in greenhouse vegetables and floriculture crops can be managed effectively with biological fungicides (biofungicides). These specialized fungi and bacteria are microorganisms that normally inhabit most soils. Biofungicides can be a viable alternative to chemical fungicides and can be used as part of an integrated disease management program to reduce the risk of pathogens developing resistance to traditional chemical based fungicides. They act by Direct competition, Antibiosis, Predation and Induced resistance to host plant [1]

In our patient methemoglobinemia occurred following ingestion of Biofungicide (Plant Alkaloids) in a suicidal attempt. This case report highlights the importance of considering the possibility of methemoglobinemia in cases of exposure to Biofungicides and its early recognition and management.

II. Case Report

A 24 year old female student came to the emergency department, with a history of consumption of Biofungicide approximately 20-50ml. The contents of it are – Botanical extract, Plant Alkaloids isolated from Adhatodavastica and Lantana Camara and surface active carbonates. Following ingestion there were 4 episodes of vomitings. On examination Patient was conscious and coherent. Peripheries were pale and there was bluish discoloration of palms, lips and tongue. Her vitals are:-

Pulse rate – 105 bpm and BP – 120/80 mmHg. Systemic examination was normal. SpO₂ was 71% in room air. Oxygen supplementation was given with Non Rebreathing Mask @ 10L/min and Gastric lavage was done. Activated Charcoal was given through Rylestube. Even after supplementation of Oxygen SpO₂ was 72% only.



Pictures showing bluish discoloration of lips and pale arms (below)



Blood investigations were ordered and in an attempt to withdraw blood for ABG, it revealed bluish discoloration of blood.

The **Blood reports** were as follows:-

Hb-11.5gm/dl , TLC-13800 cells/cumm , Neutrophils – 90% , ESR – 35 mm/1hr.

RFT {Urea – 19.3 mg/dl ,Creatinine – 0.72 mg/dl }

Serum electrolytes { Na – 132, K – 4.1, Cl – 94, Mg – 1.9 }

LFT { Total bilirubin 1.09 mg/dl, AST – 24, ALT – 11,ALP – 188 U/L }

S.LDH – 588 IU/L (90-200 IU/L)

ECG and Chest X-ray were normal.

ABG (with 10 L O₂ and SpO₂ – 74%)

Ph – 7.39

pCo₂ – 26 mmHg pO₂ - 198 mmHg

Lactate – 1.7 mmol/L HCO₃-

15.7mmol/L

ABG (Co-Oximetry)

Ph – 7.424

pO₂ – 191mmHg

FMetHb – 48.1%

Saturation gap–117% (which was more than 5%)

So, based on the report with Methemoglobin level being 48.1% and saturation gap more than 5% Methemoglobinemia was considered. Immediately sterile Inj. Methylene blue 1-2mg/kg in 100 ml normal saline was administered intravenously (i.e. 100mg iv bolus over 1 hour)[2] Inj. Vitamin-C 1g IV along with dextrose containing fluids.

Repeat ABG (After 100mg of Methylene Blue)

Ph – 7.3 mmHg

pCO₂ – 25.9 mmHg

pO₂ – 143 mmHg

FMetHb – 2.5%

The patient gradually started showing signs of improvement and her SpO₂ gradually improved to 92 - 95% within four hours.

Patient recovered well symptomatically. Inj. Methylene blue 60 mg IV BD and Inj. Vitamin - C 1 g IV were continued for 2 more days along with Oxygen supplementation. On day 3 Methemoglobin level is 2.8% and patient was discharged on Day 6.

Thus our patient was managed successfully with methylene blue and other supportive treatment for Methemoglobinemia which was probably secondary to BIOFUNGICIDE poisoning.

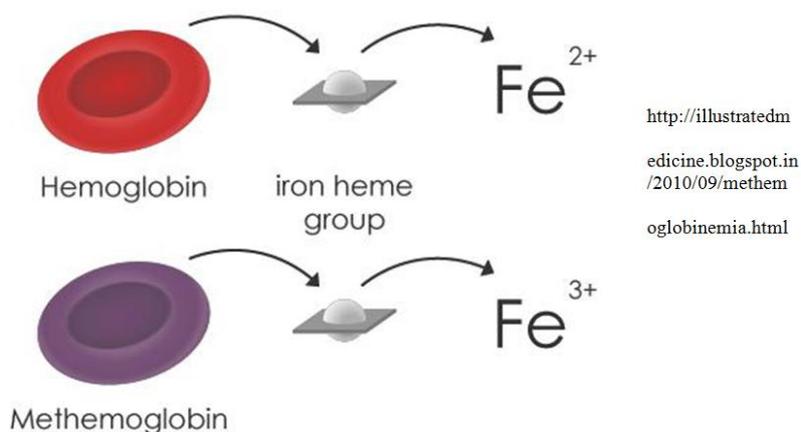
III. Discussion

Biofungicides can be a viable alternative to chemical fungicides and can be used as part of an integrated disease management program to reduce the risk of pathogens developing resistance to traditional chemical based fungicides. They usually contain microorganisms and naturally available substances like plant alkaloids.[1]. In our case this biofungicide contains plant alkaloids of *Adhatodavastica* and *Lantana camara*. *Adhatodavastica* has got many medicinal values like Bronchodilation, Hypotensive agent, Antibiotic properties etc.[3]. So far no adverse effects of *A. vasica* were noted. *Lantana camara* is used in construction purposes [4]. Studies conducted in India proved antimicrobial, fungicidal and insecticidal properties of *L. camara*. It has also been used in traditional herbal medicines for treating a variety of ailments, including cancer, skin itches, leprosy, rabies, chickenpox, measles, asthma and ulcers.[5][6]. In livestock it is known to cause generalized weakness, diarrhea, vomitings and notorious to cause photosensitivity and hepatotoxicity.[7][8][9]. The toxicity of *L. camara* to humans is undetermined, with several studies suggesting that ingesting berries can be toxic to humans, such as a study by O P Sharma which states "Green unripe fruits of the plant are toxic to humans"[10]. However other studies have found evidence which suggests that ingestion of *L. camara* fruit poses no risk to humans and are in fact edible when ripe.[11][12]. In our patient none of the toxicity features of *L. camara* were observed.



Actual Biofungicide agent consumed by the patient

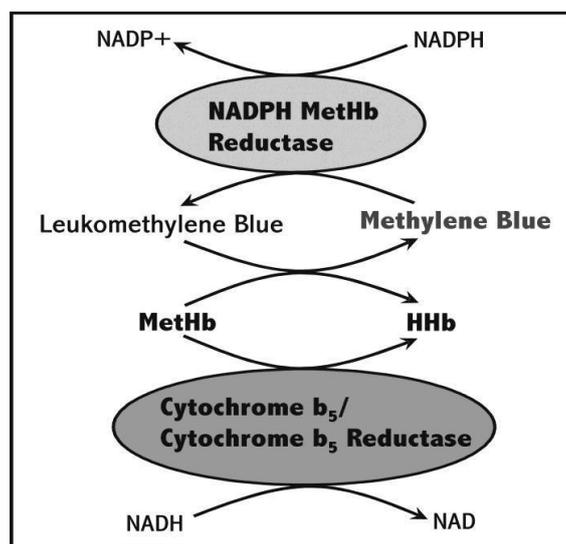
Our patient had consumed Biofungicide which contains plant alkaloids in a suicidal attempt. In the above mentioned case, our patient had developed pale peripheries and had bluish discoloration of blood. With an index of suspicion, after ruling out other poisonings, methemoglobinemia was diagnosed and treated. Methemoglobin is generated by oxidation of the heme iron moieties to ferric state, causes bluish-brown muddy color resembling cyanosis. It has got very high affinity to oxygen and oxygen is not delivered to the tissues (oxygen dissociation curve shifted to the left). It is suspected in patients with hypoxic symptoms who appear cyanotic but have a sufficiently high PaO₂. Muddy appearance of freshly drawn blood is a critical clue for diagnosis.[2] Normal Meth-Hb levels are <1%. The physiologic reduction of MethHb Fe³⁺ to Hb Fe²⁺ is mainly accomplished by red cell NADH-cytochrome b5 reductase.



It is manifested by Muddy or Chocolate brown colored fresh blood, Bluish discoloration of skin and mucosa (at 1.5g% or 10% of meth-hb), irritability, seizures. Cerebral ischemia occurs at >15% and >60% are lethal.[2]

It can be congenital or acquired due to drugs/chemicals. It can be diagnosed by co-oximetry,[13] methemoglobin levels,[13] ABG, SpO₂. In our patient methemoglobin was 48.1% and had signs of bluish discoloration of blood and cyanosis.

Treatment includes ceasing the offending agent, correcting the metabolic abnormalities, administering methylene blue at a dose of 1-2 mg/kg loading dose q 30-60 min, to a maximum of 7 mg/kg, followed by 50-100 mg twice or thrice daily[13] and other supportive measures as required. In our patient, we instituted treatment with 1 mg/kg of methylene blue as a loading dose, followed by 60 mg twice daily. Methylene blue gets reduced to leucomethylene blue which in turn reduces methemoglobin by NADPH reductase. Methylene blue reduces half-life of methemoglobin from 15-20 hours to 40-90 minutes.



We also administered Vitamin C 1gm/day and dextrose containing fluids for supplementing NADH/NADPH which is needed for reduction of methemoglobin by NADPH reductase enzyme. She made an uneventful recovery and was discharged home after six days.

In our patient, methemoglobinemia had occurred following ingestion of Biofungicide containing plant alkaloids (*Adhatodavasica* and *Lantana camara*) and treated early with methylene blue. Literature search for methemoglobinemia secondary to Biofungicide poisoning did not retrieve any articles. Toxic effects of Biofungicides or plant alkaloids in humans are not described.[11][12] Hence, this case report of Methemoglobinemia secondary to Biofungicide poisoning.

Footnotes:-

Source of Support: Nil

Conflict of Interest: None declared.

References

- [1]. Managing Plant Diseases With Biofungicides. Cathy Thomas, Integrated Pest Management Program, Pennsylvania Department of Agriculture <https://pubs.ext.vt.edu/2906/2906-1298/2906-1298.html>
- [2]. Edward J. Benz, Jr. Disorders Of Hemoglobin. In: Kasper DL, Loscalzo, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Harrison's principles of internal medicine. 18th ed. McGraw-Hill; 2012. pp. 857–858.
- [3]. The Ayurvedic Pharmacopodia of India. Indian medicine plants a compendium of 600 species - PK Warier et al. c. Indian medicinal plants CP Ghare et al. <http://www.medicinalplantdatabase.com/index.php/item/adhatoda-vasica>
- [4]. Khanna L. S.; Prakash R. (1983). Theory and Practice of silvicultural Systems. International Book Distributions.
- [5]. "Global Invasive Species Database". Retrieved 2014-03-22 issg.org.uk.
- [6]. Chavan and Nikam (1982). "Investigation of *Lantana camara* Linn (Verbenaceae) leaves for larvicidal activity"
- [7]. Ross, Ivan. A. (1999). Medicinal plants of the world (PDF). Humana Press. p. 187.
- [8]. Burns, D. (2001). Storey's Horse-Lover's Encyclopedia: an English & Western A-to-Z Guide. Storey Publishing. p. 302. ISBN 978-1-58017-317-9.
- [9]. Barceloux, D. G. (2008). Medical Toxicology of Natural Substances: Foods, Fungi, Medicinal Herbs, Plants, and Venomous Animals. Wiley. pp. 867–8. ISBN 978-0-471-72761-3.
- [10]. Sharma O. P. (2007). "A review of the hepatotoxic plant *Lantana camara*". *Critical Reviews in Toxicology* 37: 313–
doi:10.1080/10408440601177863.
- [11]. Herzog et al. (1996), Coppens d'Eeckenbrugge & Libreros Ferla (2000), TAMREC (2000)
- [12]. Carstairs, S. D. et al. (December 2010). "Ingestion of *Lantana camara* is not associated with significant effects in children". *Pediatrics* 126 (6): e1585–8. doi:10.1542/peds.2010-1669. PMID 21041281.
- [13]. Verive M, Kumar M. Methemoglobinemia. In eMedicine Specialties > Pediatrics: Hematology > Hematology