The Mysterious Story of Brown Blood and High Saturation Gap

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Dear editor,

The high saturation gap could be a useful diagnostic tool in the absence of co-oximetry or multi-wavelength pulse for the diagnosis of the methemoglobinemia after poisoning with unknown substance. We report a case of methemoglobinemia after ingestion of nitrobenzene 20 % v/v (used as a flowering stimulant). He had high saturation gap, and deep cyanosis and successfully managed with oral methylene blue and ascorbic acid. Here we emphasize on the importance of the high saturation gap and use of oral preparation of the methylene blue and ascorbic acid as prime treatment modality.

An 18-year-old previously healthy male brought in emergency department because of vomiting, seizures, and unconsciousness 2 h after ingestion of 20–30 mL of unknown substance for suicidal attempt. On examination he was unconscious, not responding to command, deeply cyanosed and afebrile. The blood pressure was 110/78 mmHg, pulse rate was 100/min, respiratory rate was 16/min and oxygen saturation (SpO₂) was 81 % by pulse oximetry. His pupils were bilaterally semi dilated and reactive to light. The blood drawn for sampling was chocolate brown colour which did not change colour after oxygen supplementation. The arterial blood gas analysis (ABG) showed a pH of 7.3, PO₂—95.6 mmHg, SaO₂—97.5 %, PCO₂—41 mmHg, and MetHb levels—66.7 %. The saturation gap was 16.5.

He was intubated and put on ventilator. His haemoglobin was 12.5 g/dL, leukocyte count 22,750/mm³ with

normal differential and platelets count. The liver functions, electrolytes, renal function, chest X-ray, echocardiogram and urinalysis were within normal limit. ECG showed sinus tachycardia. The unknown substance was identified as nitrobenzene used as flowering stimulant in the farms. He was treated with four dosages of 50 mg oral methylene blue by naso-gastric tube in a total dose of 4 mg/kg body weight and with oral 1000 mg ascorbic acid 8 hourly for 2 days. After 24 h his MetHb level, oxygen saturation and saturation gap returned to normal level and weaned off from ventilator. The serial ABG findings, saturation gap are mentioned in Table 1. On the 5th day he was discharged in stable hemodynamic condition.

Discussion

The methemoglobinemia is a medical emergency and potentially fatal. Methemoglobinemia commonly occurs after ingestion or inhalation of oxidizing agents such as sodium nitrates or nitrites, aniline dye, nitrobenzene, benzocaine, naphthalene and dapsone. Nitro benzene oxidises ferrous iron (Fe²⁺) of haemoglobin to ferric iron (Fe³⁺) and form MetHb. This molecule impairs the ability of hemoglobin to transport oxygen leading to tissue hypoxia [1, 2]. These patients have characteristically “Chocolate brown” colour of arterial blood which does not change colour after oxygen supplementation. The symptoms and signs of nitrobenzene poisoning depend on the concentration of MetHb. Cyanosis and chocolate brown blood develops when MetHb level reaches 15–20 %, these patients are usually asymptomatic. The severe complications start developing when concentration crosses over 50 % and includes coma, seizures, dyspnoea, heart failure, shock, cardiac arrhythmias, metabolic acidosis and even

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Table 1 Serial arterial blood gas (ABG) analysis

Time/parameters	0 h	6 h	12 h	16 h	24 h	36 h
pH	7.3	7.3	7.38	7.39	7.41	7.4
PaO ₂ (mmHg)	95.6	86.9	145	124	187	165
PaCO ₂ (mmHg)	41	35.7	38	34.2	38	37
Methemoglobin%	66.7	34.5	13.9	4.3	2.3	1.0
HCO ₃ (mmol/L)	20.7	19.8	22.8	20.4	24	22
SaO ₂ %	97.5	98.4	99.1	99.6	99.6	99.5
SpO ₂ % (pulse oximetry)	81	84	88	94	95	98
Saturation gap	16.5	14.4	11.1	5.6	4.6	1.5

death. The concentration of MetHb above 70 % is associated with high mortality. Other common presenting symptoms are headache, fatigue, dizziness, exercise intolerance, syncope, tachycardia, and CNS depression [3, 4].

These patients have falsely low value of oxygen saturation (SaO₂) by conventional pulse oximetry. The ABG usually have inappropriately high or normal value of SaO₂, this difference of SaO₂ measured by conventional pulse oximetry and ABG is called, “Saturation Gap”. The pulse oximetry only measures the relative absorbance of 2 wavelengths of light (660 and 940 nm) to differentiate oxyhemoglobin from deoxyhemoglobin. MetHb increases absorption of light at both wavelengths (more at 940 nm) and therefore offers optical interference to pulse oximetry by falsely absorbing light, hence measure incorrectly. The “saturation gap” of more than 5 % is a possible clue for methemoglobinemia and can be used as fifth vital sign in patients of unexplained cyanosis. The co-oximetry or multiwavelength pulse is diagnostic tool of choice [3–5].

The specific treatment of methemoglobinemia includes use of methylene blue and ascorbic acid. Methylene blue is the antidote for MethHb, it reduces Fe³⁺ ion in haemoglobin to Fe²⁺ ion in the presence of cytochrome-b5-MetHb reductase or NADPH MetHb reductase enzyme, and makes hemoglobin capable to transport oxygen. Methylene blue is indicated in symptomatic patients having MetHb levels greater than 20 % [3]. The initial dosage is 1–2 mg/kg or 0.1–0.2 mL/kg of a 1 % solution, administered intravenously over 5–10 min. This dose can be repeated when response is not achieved after 1–2 h of infusing prior dose. The cumulative dose of methylene blue can be increased up to 7 mg/kg only, because above this dose it can act as an oxidant and can cause methemoglobinemia and hemolysis [1,3]. The methylene blue is contraindicated in candidates with congenital NADPH MetHb reductase deficiency, human red cells deficient in glucose-6-phosphate dehydrogenase and patients with renal

dysfunction. The patients with above mentioned enzyme deficiencies can develop hemolysis after treating with methylene blue [1, 3]. Dextrose solution should be given to provide NADPH through HMP shunt which is necessary for methylene blue to be effective. The laboratory preparation (1 % solution) can be given by oral route successfully in the unavailability of IV preparation of methylene blue [6]. Ascorbic acid also reduces the oxidised haemoglobin but effect is delayed. Other modalities of treatment are hyperbaric oxygen, exchange transfusion and *N*-acetyl cysteine which can be tried when methylene blue is contraindicated [3].

To conclude, in a patient presenting with—unexplained cyanosis, chocolate brown arterial blood and high saturation gap—methemoglobinemia should be suspected. The responsible culprit for methemoglobinemia should be checked. If curable, these patients should be treated with methylene blue and ascorbic acid. Oral preparations of these compounds can also be tried which are equally effective as intravenous preparations. Unavailability of methylene blue should not be an excuse for treatment as it is widely available reagent in hospital laboratories for staining purposes.

Compliance with Ethical Standards

Conflict of interest Author have no conflict of interest and this article is not funded by any source.

Human and Animal Rights Statement This is a single case report; it does not involve human participants and/or animals.

Informed Consent Informed consent has been taken from the patient.

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