A rare case of amino nitrogen poisoning with methemoglobinemia and severe metabolic acidosis

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Abstract
Methemoglobinemia can be managed medically with methylene blue but in severe methemoglobinemia sometimes extracorporeal therapy may be required, here we report a rare case of Amino nitrogen poisoning who presented with severe metabolic acidosis, shock and had severe methemoglobinemia that was treated with methylene blue and haemo dialysis.

Keywords: Amino, Methemoglobinemia.

Introduction
Amino nitrogen poisoning is rare and methemoglobinemia due to this compound is not yet reported, the nitrogen compound is converted into nitritesby bacteria in our saliva, stomach, and intestines, and it is primarily the nitrites that cause toxicity. Nitrites oxidize the iron component of red blood cells (haemoglobin), rendering them unable to carry oxygen. The resulting condition is called methemoglobinemia, and the lack of oxygen is the reason behind the characteristic pale to blue-gray color of the skin. The severity of methemoglobinemia is directly proportional to the percentage of red blood cells affected. The higher the percentage, the more serious the symptoms, and the bluer the patient appears.

Ferrous iron can be converted to ferric iron by oxidative stress which results in the formation of methe-moglobin.[1] The iron moiety in hemoglobin exists in the "ferrous" state and undergoes oxidization to the "ferric" state forming methemoglobinat a rate of ~3% per day.[2] The initial sign of methemoglobinemia is cyanosis[3] and the diagnosis should be considered in all patients who present with cyanosis, particularly if it does not improve with supplemental oxygen. Methemoglobin levels of >70% are generally lethal, although survival has been reported with a level of 94%.[4] Methylene blue is indicated as the first-line antidote therapy for patients with severe methemoglobinemia.[5] Patients with methemoglobinemia typically present withskin discoloration ("chocolate cyanosis"), especially of the nails, lips, and ears, whereas the color is more often brown rather than blue. Even at low levels of MetHb, this discoloration can be striking.[6] Methylene blue should be used with caution in individuals with severe renal insufficiency and in young patients with G6PD deficiency. This group of patients can develophemolyticanemia characterized by formation of Heinz bodies without any reduction in MetHb levels.[6-8] Methemoglobin forms when the ferrous (Fe2+) form of heme in hemoglobin is oxidized to the ferric (Fe3+) state. Ferric heme is unable to bind oxygen, and the remaining ferrous heme develops increased oxygen affinity and causes impaired oxygen delivery to tissues, resulting in a "left shift" in the oxygen dissociation curve.[9]

Which results in hypoxic ischemia to the tissues and causes severe lactic acidosis, now we report a case of amino nitrogen poisoning with severe methemoglobinemia and severe metabolic acidosis.

Case Report
A previously healthy, 34-year male came with the chief complaints of self-ingestion of Amino nitrogen of 350ml, at his residence at 6:30pm. Gastric lavage was performed at the local hospital and came to SRMC at 8:30 pm for further management. On his arrival the patient was in gasping state and CPR was done for cardiac arrest. Patient was intubated in the emergency ward. Later the patient was on mechanical ventilation. On examination, he was afebrile(98.6^0F), with heart

rate 120/min, regular BP 116/72,respiratory rate was 20/min and the oxygen saturation is 80% of room air latter he was becoming hypotensive and inotropes were initiated.

Presenting symptoms of the patient were

1. Bluish skin due to lack of oxygen (noticed around mouth/lips first)
2. Shortness of breath
3. Nausea, vomiting
4. Dehydration (from loss of bodily fluids)
5. Tachycardia

Fig. 1:

Patient was shifted to critical care medicine (CCM) for further management and observation. In CCM, he received inotropes like Noradrenaline and Vasopressin to maintain his vitals which was shown in the Table 1. The patient was cyanosed had both central and peripheral cyanosis with hypoxia and had metabolic acidosis with PH of 7.052, so diagnosis of Amino nitrogen ingestion with severe central and peripheral cyanosis, (Fig.1) methemoglobinemia was suspected and Methylene blue was initiated, the patient hadsevere metabolic acidosis, so dialysis (Hemo diafiltration)was initiated with blood flow of 150,dialysate flow of 300, heparin free, Ultra filtration nil and Methylene blue injection @ 1mg/kg (100mg) IV was given over 20 minutes. After initiation of methylene blue and Hemodialysis, inotropic support was decreased and was stopped after 24hrs. His haemoglobin levels were 15.2g/dl and methaemoglobin levels were 60%. After 2 days the methaemoglobin levels were decreased to 58%.

Initial Renal function tests, Arterial Blood Gas were enclosed in tables. The patient was maintained on high Po2 (hyper baric oxygen) to improve oxygenation initially by increasing the dissolved oxygen and oxygen saturations in pulse oximeter was not considered because after giving Methylene blue they were not significant, we were depending on lactates in ABG(Arterial Blood Gas analysis) shown in the (table 2), to know the perfusion of tissues and oxygenationdaily depending on them we were maintaining the pa02 by altering the FI02 and ventilator modes, the ventilator parameters were shown in the Table 4.

The molecular weight of amino nitrogen is 29 g/mol and it is water soluble excreted through kidneys even then we have dialysed him 3 times as his methemoglobin levels were high for first 4days inorder to decrease the poison load from the body though his metabolic parameters were corrected and Renal Function Tests (RFTs) were normal, and he was extubated on 7th day, he had DVT due to femoral catheter and started on 5000u heparin twice a day. He was discharged on 14th day of his admission after subsidence of DVT.

Table 1:

On arrival at ER	Pulse	BP	Spo2	Inotropics	
				Noradrenaline	Adrenaline
6 hrs	132	118/77	79	10ml	0.5ml
12 hrs	128	139/73	99	4ml	0.5ml
1st day	132	118/77	79	NO	NO
2nd day	100	168/75	76	NO	NO
3rd day	113	130/81	83	NO	NO

4th day	103	140/86	78	NO	NO
5th day	183	154/88	100	NO	NO
6th day	132	118/78	100	NO	NO
7th day	118	141/65	67	NO	NO

Table 2: ABG values

Date& Time	Blood Gas values			Electrolyte & Metabolite values					Oximetry values	Calculated values	
	pH	pCO_2	pO_2	cK^+	cNa^+	cCa^{2+}	cCl^-	cLac	ctHb	sO_2	Hct_c
11/10&3:51AM	7.052	30.2	366	3.9	149	1.03	114	19	16.3	-	49.9
11/9&8:28AM	7.465	29.1	107	2.5	16	0.60	128	0.9	4.5	98.2	14.4
11/10&7:31AM	7.267	38.2	188	4.0	147	1.07	114	8.2	17.2	97.1	52.6
11/10&6:31PM	7.423	39.4	233	3.6	139	1.07	111	10.4	14.7	97.0	45.1
11/10&7:30PM	7.374	39.1	480	3.4	141	1.06	111	11.5	14.8	97.6	45.3
11/11&6:42AM	7.468	37.7	491	3.5	141	1.06	112	10.8	13.3	96.8	40.9
	7.533	28.6	465	3.4	140	1.09	111	12.4	13.0	96.8	39.8
11/12&6:38AM	7.492	31.5	332	3.3	139	1.08	112	10.4	12.5	96.0	38.4

Table 3: Dialysis chart

S. No	Day from admission	QB	QD	Heparin	Ultra filtration	Duration	Pulse rate	Blood Pressure	sPO_2	HCO_3^-
1	Day 1	150	300	free	Nil	3hrs	86	107/70	80	8.4
2	Day 3	150	300	free	Nil	6hrs	82	120/80	76	26.3
3	Day 4	150	300	free	Nil	6hrs	114	145/82	98	27.3

Table 4: Ventilator settings

Date	Mode of ventilation	FiO2	Respiratory Rate	Tidal Volume	PEEP
10/11/2020	AC/PC	110	20	599	8
11/11/2020	AC/PC	90	20	372	10
12/11/2020	ADL/PCV	80	25	301	10
13/11/2020	ADL/PCV	75	21	550	10
14/11/2020	PCV/CPAP	100	27	553	10
15/11/2020	CPAP	35	37	480	9.8

Table 5: Renal function tests

Date	Urea	Creatinine	Uric Acid
10/11/2020	20	1.35	8.2
11/11/2020	38	0.60	5.6
12/11/2020	43	0.84	3.2
13/11/2020	42	0.82	5.9
14/11/2020	39	0.70	3.4
15/11/2020	39	0.55	3.5

Discussion

Methylene blue is used to help make oxygen available to the body by reversing what nitrates have done to the molecules that carry oxygen in the body. His haemoglobin levels were 15.2g/dl and methaemoglobin levels were 60%. After 2 days the methaemoglobin levels were decreased to 58%. Methemoglobin levels of >70% aregenerally lethal, although survival has been reported with a level of 94%.[10] In 1959, aniline poisoning has been first described in a case series of marking-ink poisoning causing methemoglobinemia in babies.[11] Later,more cases have been published, most often in correlation with dye or herbicides exposure.[12-15] Hyperbaric oxygen, either alone or in combination withmethylene blue, has been successfully used for management of methemoglobinemia.[16-18] A case of methemoglobinemia occurred after the application of silver nitrate solution to burns; the production of nitrite was shown to be due to Aerobacter cloacae present on the skin.[19] Three patients who were burned with molten sodium and potassium nitrate in an explosion developed methemoglobinemia and one patient died.[20] However, eight cases of severe methemoglobinemia were reported in patients with some degree of renal impairment or gastrointestinal dysfunction, following the ingestion of therapeutic doses of ammonium nitrate over periods ranging from 2 to 46 days.[21-23] Methylene blue should be used with caution in individuals with severe renal insufficiency and in young patients with G6PD deficiency. This group of patients can develop hemolytic anemia characterized by formation of Heinz bodies without any reduction in MetHb levels.[6-8] Alternative therapies include exchange transfusion, hyperbaric oxygen and ascorbic acid.[24]

Conclusion

The patient had Central and peripheral cyanosis and severe metabolic acidosis, due to amino nitrogen poisoning, which is not yet reported, he required not only medical management for poisoning with methylene blue but also Haemo dialysis in view of severe metabolic acidosis and after to support the kidneys in excretion of residual poison in view of severe methemoglobinemia, till the crisis period the person was maintained on hyperbaric oxygen to improve oxygenation of the tissues and regular lactates were monitored for clinical decisions.

Aniline

Conflict of Interest

None.

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