

## Management of Herbicide Induced Methemoglobinemia

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Received date: April 10, 2018; Accepted date: May 20, 2018; Published date: May 30, 2018

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### Abstract

Methemoglobinemia is an altered state of haemoglobin that leads to impaired oxygen delivery to the body tissues. Deliberate ingestion of certain herbicides may lead to this condition. Modern herbicides are often synthetic mimics of natural plant hormones that interfere with growth of the target plants. These modern herbicides act by various mechanisms some of them being Acetyl co-enzyme A carboxylase inhibition, aceto lactate synthase inhibition, photosystem II inhibition, 4-hydroxy phenyl pyruvate dioxygenase inhibition and so on. We report a case of Methemoglobinemia after deliberate ingestion of an herbicide marketed to be safe and containing only biological extracts and filters. The patient was treated with ascorbic acid successfully. Our paper emphasizes the use of ascorbic acid as an alternative method in the treatment of Methemoglobinemia. Ascorbic acid is the main stay of treatment in patients with G6PD deficiency.

**Keywords:** Methemoglobin; Impaired oxygen; Ascorbic acid; Herbicide; Discoloration of blood; G6PD deficiency

### Introduction

Methemoglobinemia is a disorder in which the oxidised form of haemoglobin (Hb), the ferrous ( $\text{Fe}^{2+}$ ) iron is transformed into ferric ( $\text{Fe}^{3+}$ ) state, which makes it incapable of binding to oxidizing agents, resulting in the shift of oxygen dissociation curve to the left there by leading to impaired oxygen delivery to the tissues. Methemoglobinemia can be congenital, but the most common form is acquired form. The acquired form may be seen after consumption of some foods like refrigerated “dim-sum”, stuffed-pork, Chinese sausages and exposure to certain chemicals and drugs containing nitrites and nitrates [1-3].

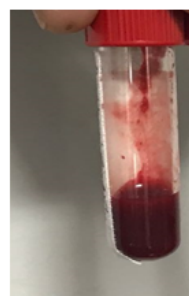
It causes brownish discoloration of blood and urine. It can be potentially fatal if untreated. Ingestion of deliberate amount of herbicides may produce this situation.

### Case Report

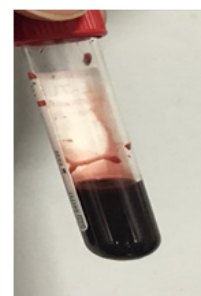
A healthy 23 years old male patient was brought to emergency with alleged history of consumption of herbicide poisoning. There was a history of vomiting, nausea and dizziness.

On examination the patient was found to be normotensive, with no tachycardia and with oxygen saturation of 87% which did not improve with 100% oxygen. The patient was cyanosed. The cardiac evaluation was normal. Blood samples drawn for ABG had a chocolate brown colour, showed compensated metabolic acidosis with  $\text{PaO}_2$  152 mmHg. Urine samples too were chocolate brown in colour. X-ray of chest and ECG were within normal limits, and liver enzymes were markedly raised. Serum creatinine and blood urea were within normal range. Haemoglobin at admission was 13.3g/dl and Methemoglobinemia level was 6.9%. (Normal Methemoglobin level=2%) Blood serology for direct and indirect coombs was found to be negative.

Disparity between  $\text{PaO}_2$  and  $\text{SpO}_2$  and increased level of methemoglobin were suggestive of acquired Methemoglobinemia due to ingestion of herbicide poisoning. The contents of the herbicide namely mononitrobenzene lead to the formation of Methemoglobinemia. A diagnosis of Methemoglobinemia was made clinically (Figure 1).



Normal Blood



Chocolate Brown coloured Blood

**Figure 1:** Normal Blood vs. dark brown colored blood due to Methemoglobinemia.

### Discussion

Normally, Methemoglobin levels are less than 2% of total haemoglobin and have high oxygen affinity to oxygen [2]. Therefore, tissue oxygenation decreases and cyanosis develops with the shift of oxygen dissociation curve to the left. Acquired Methemoglobinemia occurs as a result of many drugs with oxidizing effects and when methemoglobins are more than the reductive capacity of the

erythrocytes. Most other drugs causing this condition are nitroglycerine, dapson, phenytoin, phenacetin and local anaesthetics.

Generally 10%-20% of methemoglobin levels are well tolerated and the symptoms are usually detected when the levels are more than 20%. Methemoglobinemia levels higher than 70% may lead to coma and death [4,5].

The clinical manifestations of Methemoglobinemia are due to impaired oxygen delivery to the tissues and hence correlate with severity of Methemoglobinemia (Table 1).

Methemoglobin %	Signs and symptoms
<15%	Asymptomatic
20-30%	Cyanosis, headache, fatigue, mental status changes, syncope, dizziness and exercise intolerance
30-50%	Shortness of breath and headache
50-70%	Lethargy, stupor, dysrhythmias, seizure, coma
>70%	Death

**Table 1:** Levels of methemoglobin and associated clinical features.

In our patient presence of cyanosis and disparity between measured SPO2 and PaO2 in the absence of cardiac and respiratory disease led us to think of the diagnosis of Methemoglobinemia in our case.

Methylene blue is the treatment of choice for Methemoglobinemia patients other than those with G6PD deficiency. Ascorbic acid is generally used in Methemoglobinemia patients with G6PD deficiency as methylene blue in these patients may lead to hemolysis.

Methylene blue is indicated for asymptomatic patients with methemoglobin levels more than 20% or in symptomatic patients even with methemoglobin levels less than 20%.

Since the methemoglobin levels in our patient is less than 20% and as the patient the patient was asymptomatic we used ascorbic acid to treat our patient. Moreover ascorbic acid is an alternative treatment in Methemoglobinemia as it has got no major side effects [6-8].

### Treatment

Since the patient was asymptomatic with Methemoglobinemia level of <20%, he was treated with supportive measures such as oxygen therapy, PPI, fluids and Vitamin C.

### Result

The patient was extubated on the fourth day. There was rapid fall in methemoglobin levels with improved discoloration and oxygen

saturation. The patient was discharged on the sixth day with ascorbic acid supplements.

### Conclusion

The present study demonstrates that treatment with vitamin C can reduce the level of methemoglobin in blood. Ascorbic acid penetrates the human erythrocyte membrane. It can reduce oxidation induced methemoglobin formation. It also stabilises the RBC membrane preventing them from hemolysis. It acts as a co-factor for NADP reductase required for glutathione metabolism. It has been demonstrated that reduction of the methemoglobin formation occurs at low vitamin C concentration. However, critically increased methemoglobin contents of the blood levels more than 20% make methylene blue the mainstay of the treatment. Ascorbic acid is the treatment of choice in patients of Methemoglobinemia with G6PD deficiency. Recent reports show that a high dose Vitamin C can be used for "quick", "effective" and "safe" treatment of Methemoglobinemia.

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