



The Pharmacotherapy of Blood Intoxication (Methemoglobinemia) Induced by Exposure to Ortho-Chlorobenzylidenemalononitrile (CS) in Public Protests

Muhi N. Salman^{1*}

¹*Department of Toxicology, Baghdad College of Medical Sciences, Baghdad, Iraq.*

Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Case Report

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ABSTRACT

Background: Acquired Methemoglobinemia (MetHb) is a rare, but potentially serious and unfamiliarity with this complication may delay diagnosis and appropriate therapy.

Presentation: A case of methemoglobinemia occurring in male teenage demonstrator as a complication of re-current exposure to ortho-chlorobenzylidenemalononitrile (CS) in public protests, the patient became cyanotic with a decrease in his level of consciousness, by the effect of hydrogen cyanide as by-product of (CS), resulting in a toxic methemoglobinemia level in his blood. Methemoglobin is incapable of carrying oxygen and is formed when the ferrous iron in the heme molecule is oxidized to the ferric state. The diagnosis should be entertained when cyanosis, unresponsive to 100% oxygen therapy, appears suddenly, especially when exposure to an oxidant agent is established.

Treatment: The patient received a 1 mg/kg dose of methylene blue intravenously. A coximetry done 1 hour later showed a methemoglobin level of 43%. A second 1 mg/kg dose of methylene blue was given and another hour later the methemoglobin level had dropped to 13%. The patient also showed clinical improvement with resolution of the cyanosis and return of his mental status to baseline.

Conclusion: Methylene blue is the specific antidote, but should be reserved for more severe cases or if co-morbid conditions make mild hypoxia unadvisable.

*Corresponding author: E-mail: muhi_spharm@yahoo.com;

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ABBREVIATIONS

Ortho-Chlorobenzylidenemalononitrile (CS);

Methemoglobinemia (MetHb).

1. INTRODUCTION

Acquired methemoglobinemia is a significant safety risk signed with several common drugs as blue lips and nail beds. e.g., Lidocaine Metoclopramide, Prilocaine, Amyl nitrite, Nitroglycerin, Nitroprusside, sulfamethoxazole [1,2]. Studies of the metabolism of CS have been conducted on the compound itself and not in the form in which it would be used as an incapacitating agent by police officers. It is readily hydrolysed in aqueous mixtures [3,4] and reacts readily with plasma proteins and glutathione in vitro and *in vivo* [5,6]. It undergoes rapid metabolism and chemical breakdown in vitro and in vivo, initially to 2-chlorobenzaldehyde and malononitrile, each of these then undergo further rapid reactions. The half lives ($t_{1/2}$) of CS and the metabolites, 2-chlorobenzaldehyde and 2-chlorobenzylmalononitrile in one in vivo experiment involving the administration of compounds by intra-arterial injection into cats were 5.4, 4.5 and 9.5 seconds respectively [7]. Acute studies in rodents and guinea pigs using pyrotechnically-generated CS smokes indicated that short term exposure (10 to 20 minutes) to concentrations of CS of around 4 grams/metre³ (g/m³), or longer exposure (several hours) to levels of around 30 to 40 mg/m³, resulted in deaths [8]. Lethal cases have usually had levels above 1 µg/ml blood [9]. The stimulated hyperpnea can result in more of the poisonous CS atmosphere being inhaled. The dictation of urinary excretion of thiocyanate is related to endogenous release of HCN with compromising oxygen transfer from the lung to the blood capillaries [10].

2. CASE REPORT

Male teenage demonstrator, was ambulated to emergency tent to tharir

square –Baghdad after exposure to CS gas suffering from typical sign and symptoms (respiratory and ocular) and treated/dischage safely within 45 minutes by supportive measurements ,but after 9 hours the same patient was brought back by public crowd to emergency unit complaining of dyspnea, headache, dizziness, pale and grayish skin, perioral cyanosis , feeling of suffocation, a toxic pulmonary edema accompanied by gastric upset symptoms . His intravenous blood had drawn, was an abnormal chocolate –brown appearance (Fig. 1).



Fig. 1. Blood chocolate –brown appearance

Physical examination is mildly distressed, cyanotic-appearing status. His vital signs revealed a temperature of 99.7F, heart rate of 74beats per minute, blood pressure of 150/70 mmHg, respirations at 18 breaths per minute ,and an oxygen saturation (SpO₂) of 85% saturated oxygen via nasal cannula. The cooximetry of blood measured pH, as 7.34 (7.35–7.45); pCO₂, 44 mmHg (35–48); pO₂, 179.0 mmHg (83–108); HCO₃⁻, 25.3mEq/L (21–28); SaO₂, 97% (95–98); The hemoglobin levels were recorded as , 16.3 g/dL; oxyhemoglobin, 72.9% (95.0–98.0); carboxyhemoglobin, 0.0% (0.5–1–5); methemoglobin, 27.4% (<3.0) with an oxygen content of 19.8 mL/dL (15.0–33.0), his blood

cyanide level was 0.3 ug/ml. The acquired methemoglobinemia treated by 2mg/kg intravenous methylene blue was administered, patient's status was improved gradually with 25 minutes up to one hour. Chocolate-brown blood and oxyhemoglobin at 94.5% and methemoglobin at 0.9%.After a six-hour stay in the emergency department and complete resolution of his signs and symptoms.

3. DISCUSSION

The CS exposure-related symptoms include irritation sensory organ tissues, eye's lacrimation, blepharospasm, nose's burning sensation , excessive salivation ,feeling of suffocation, sneezing and coughing . *In higher concentrations, the* Hydrogen cyanide (HCN) , as the un-dissociated acid major metabolite from malonitrile , it blocks cell respiration or oxidative metabolism even if the partial pressure of oxygen in the tissue is normal. Cells of the brain, especially the brain stem, are very sensitive to the effects of HCN and a dysfunction in this area of the brain may lead to respiratory arrest. A synergistic lethal effect induced by the combination of carbon monoxide and cyanide was reported [11]. Lethal blood cyanide levels are usually greater than 1 mg/l and levels greater than 0.2 - 0.25 mg/l are considered toxic and dangerous [12]. However, it is well known that cyanide can be produced and degraded in blood and tissue, especially dependent on the surrounding temperature, making interpretation of blood levels rather difficult and uncertain [13]. Cyanide is detoxified in the liver by the mitochondrial enzyme rhodanese,which catalyzes the transfer of sulfur from a sulfate donor to cyanide, forming less toxic thiocyanate. Thiocyanate is readily excreted in urine. It is concluded that CS in vivo is hydrolyzed mainly to 2-chlorobenzaldehyde which is then either oxidized to 2-chlorobenzoic acid for subsequent glycine conjugation, or reduced to 2-chlorobenzyl alcohol for ultimate excretion as 2-chlorobenzyl acetyl cysteine or O-(2-chlorobenzyl) glucuronic acid. Malonitrile is converted to thiocyanate via

the formation of cyanide [12]. The significant generation of cyanide blood level after CS exposure is controversial [14,15]. The pharyngeal deposition of incompletely dispersed CS compound can occur with swallowing of respiratory secretions.

4. CONCLUSION

CS is a potent sensory irritant, particularly to the skin and the eyes. It is rapidly hydrolyzed and therefore tissue exposure to CS itself is transient. The toxicity of CS is characterized by transient local irritant effects and central nervous system (CNS) effects (particularly headache, nausea) resulting from occupational exposures of about Severe ----traumatic injuries from exploding tear gas bombs, as well as lethal toxic injuries, have been documented. As chemical gases are easily accessible and the risk of their being used threatens people, the proposed approach is necessary to control all gases. Furthermore, the proper administration route of these tools should be taught to people. Tear gas has gained widespread acceptance as a means of controlling civilian crowds and subduing barricaded criminals. However, demonstrates that exposure to the weapon is difficult to control and indiscriminate, and the weapon is often not used correctly. Severe traumatic injury from exploding tear gas bombs as well as lethal toxic injury had been documented . We believe a thiocyanate assay should be considered in cases of ingestion or extremely high exposure OF CS gas.

CONSENT

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ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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