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A fatal case of acute copper sulphate poisoning presenting with methaemoglobinemia and intravascular haemolysis: a case report

Ranasinghe KMIU[1], **Thirumavalavan K**[1]

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Abstract

Copper sulphate is a common industrial chemical that is rarely used for suicide. Ingestion of more than one gram of copper sulphate causes features of toxicity, mainly severe gastrointestinal tract erosions, methaemoglobinemia, acute kidney injury, intravascular haemolysis, and acute hepatitis. A dose of more than 10g is lethal. The management is mainly supportive. Copper chelation with penicillamine, edetate calcium disodium (EDTA) and British anti-Lewisite (BAL) can be used to minimize the toxicity. Exchange transfusion for severe methemoglobinemia has been attempted with variable success.

We report a lethal case of poisoning with 75g of copper sulphate resulting in severe methaemoglobinemia, intravascular haemolysis, gastrointestinal bleeding and multi-organ failure. Exchange transfusion was carried out without success and the patient succumbed to death on the third day of the poisoning. Though it is rare, the fatality of copper sulphate poisoning necessitates proper knowledge about manifestations and management options.

Key words: acute severe copper sulphate poisoning, methaemoglobinemia, intravascular haemolysis

Introduction

Copper containing salts are commonly used in the leather industry and as a pesticide in agriculture. Out of various copper salts, copper sulphate is easily available in Sri Lanka.[1] However, it remains a less reported cause of suicide compared to other chemicals like organophosphate, and carbamate.[2] Ingestion of more than 1g of copper sulphate leads to features of toxicity.[3] The main clinical manifestations are due to gastrointestinal tract erosions, methaemoglobinemia, intravascular haemolysis, acute kidney injury and acute hepatitis. Circulatory collapse also supervenes and ultimately multi-organ failure sets in. This can be severe enough to cause death within a short period of time, depending on the ingested dose. Unfortunately, despite all the therapeutic advances, there is no effective method of removing free copper as it is not effectively dialysable. There are several case reports in medical literature where copper chelators have been successfully used in management.[1,4,5] But in cases with ingestions of substantial amounts, the fatality rate has been significantly high.[1]

Thorough knowledge of possible mechanisms of toxicity, clinical manifestations and management options will lead to better clinical outcomes. We share our experience with a patient who presented following ingestion of 75g of copper sulphate.

Case presentation

A 54-year-old farmer was transferred from a local hospital following ingestion of 75g of copper sulphate (Palmanikkam - Sinhala and Tamil term). He was found semiconscious after 12 hours of ingestion. On admission to the Emergency Treatment Unit, he was conscious, rational, and complained of a severe burning sensation in the throat and epigastrium. He was

[1]*National Hospital of Sri Lanka, Colombo, Sri Lanka.*

Correspondence: KMIUR, e-mail: indrachaparanasinghe@gmail.com

https://orcid.org/0000-0002-6179-0734

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dyspnoeic with mild central and peripheral cyanosis. Blood pressure was 110/70 mmHg with a pulse rate of 108 beats per minute. Pulse oximeter saturation on air was 72% and improved only up to 80-82% with 15 L/min of oxygen. Coarse crepitations were heard in the lower zones of bilateral lungs most probably due to aspiration. After catheterization, dark brown colour urine was drained.

Arterial blood gas (ABG) on admission revealed partially compensated metabolic acidosis with a pH of 7.31, PaO_2 198mmHg, oxygen saturation 99.9%, $PaCO_2$ 22mmHg, HCO_3 17 mmol/L, lactate 1.8 mmol/L and haemoglobin 10.4 g/dL. As he was cyanosed and ABG was suggestive of the presence of methaemoglobinemia, he was given methylene blue 2mg/kg intravenously over 10 minutes. We did not have the facilities to directly assess serum methaemoglobin levels. Instead, the methaemoglobin colour chart was accessed through the web.

Repeat ABG one hour later showed pH of 7.29, PaO_2 232 mmHg, oxygen saturation 99.9%, HCO_3 15 mmol/L, lactate 5.2mmol/L and haemoglobin 7.9g/dL. He was haemodynamically stable and oxygen saturation on high-flow oxygen was 82%. Intravenous methylene blue was repeated. A blood transfusion was arranged after sending an urgent blood picture. Results of serum investigations done 24 hours after were creatinine 4.1mg/dL, creatine phosphokinase (CPK) 860 U/L (55-100), amylase 834 U/L (30-100), CRP 40 mg/dL, AST 127 U/L, ALT 38 U/L, total bilirubin 3.1mg/dL (direct fraction 0.4 mg/dL). WBC 15,800/mm^3, and hemoglobin 7.8g/dL. The blood picture showed evidence of haemolysis. Urine for haemoglobin was positive. Initial ECG showed sinus tachycardia with no ischemic changes.

There was no improvement in oxygen saturation with repeated doses of methylene blue. Oral penicillamine 500 mg 6 hourly was started as a copper chelator. Intravenous infusion of omeprazole was started suspecting gastric erosions. Intravenous metronidazole and co-amoxiclav were given for possible aspiration pneumonia.

During the illness his serum creatinine rose, and he became oliguric. Haemoglobin further dropped to 5.1g/dL with ongoing haemolysis. An exchange transfusion was arranged, however, methaemoglobinemia did not improve despite the exchange transfusion. He required inotropic support to maintain blood pressure and severe aspiration pneumonia required mechanical ventilation. Unfortunately, on the third day of admission, he developed melena which deteriorated the condition further and he succumbed to death.

Discussion

Though poisoning with copper sulphate is not a frequent encounter in clinical settings, it is potentially fatal which mandates prompt and proper management to save the life. As it is rare, limited evidence exists about the condition, mainly case reports or case series are the sources of knowledge. We believe our case will contribute to the limited medical literature on copper sulphate poisoning.

Copper plays an important role in the human body as a co-factor for oxidative enzymes including peroxidase, catalase, glucose 6 phosphate dehydrogenase, glutathione reductase and cytochrome oxidase.[6] This explains its vital role in protecting cells against oxidative stress. In the serum, copper exists in two forms; bound to ceruloplasmin (93%) and bound to albumin (7%).[7] Liver is the main organ that stores copper. The main mechanism of excretion is via fecal route, whereas only about 4% is excreted via urine.[8]

Ingestion of more than 1g of copper sulphate leads to features of toxicity.[3] Doses of more than 10g have been associated with high mortality rates and are considered to be lethal.[9] In situations where the ingestion of copper is not certain, serum copper estimation can be done at an early stage. However, the serum copper level and clinical severity are not closely related.[10]

Copper sulphate elicits its toxic effects predominantly via oxidative damage as it is a powerful oxidant. Oral ingestion leads to immediate effects on the gastrointestinal epithelium due to its corrosiveness. Metallic taste, burning pain in the throat and epigastrium, nausea, vomiting, and haemorrhagic gastroenteritis are reported. Our patient also experienced those symptoms on presentation itself and developed melena by the third day which we thought was due to gastric and upper small intestinal erosions.

Methaemoglobinemia seen in copper sulphate poisoning is due to the oxidization of ferrous ions to ferric ions in haemoglobin molecules. This causes tissue ischemia and pulse oximeter shows low oxygen saturation despite elevated partial pressure of oxygen in arterial blood gas analysis.[11] Intravascular haemolysis reported in two previously published case series of copper toxicity ranged from 47% to 65%.[12,13] Haemolysis can be a result of direct cell membrane toxicity and oxidative damage due to glutathione reductase inhibition. In our patient haemolysis was severe enough by day 3 to drop haemoglobin to 5.1g/dL. Gastrointestinal bleeding also contributed to this rapid drop of haemoglobin.

Acute kidney injury occurs in 20-40% of patients and the severity depends on the dose of copper sulphate. It is usually observed after 48 hours.[14] Haemoglobinuria causes acute tubular necrosis. This is compounded by myoglobinuria due to rhabdomyolysis, and pre-ischemic injury due to cardiovascular collapse.[15] In addition, acute liver injury due to oxidative damage to mitochondria is known to occur as evidenced by mild to moderate transaminase elevation and jaundice. Both hepatocellular and cholestatic patterns of injury are documented.[16] Our patient had a lethal dose ingested and he developed gastrointestinal erosions, methaemoglobinemia, intravascular haemolysis, acute kidney injury, acute liver injury and circulatory collapse finally succumbing to death.

Management of copper sulphate poisoning is mainly supportive. Immediate dilution of gastric content with water or milk can be done if the patient is seen within 4-6 hours. This is to be done only if the patient is conscious and cooperative and it is advisable in pre-hospital setting as well.[17] Activated charcoal may be given within 1-2 hours of ingestion, however, it is of unproven benefit.[18] As copper is corrosive, emesis and gastric lavage should be avoided. Sucralfate will help in alleviating pain due to gastro-esophageal erosions; proton pump inhibitors can be given for gastric protection. Methylene blue is effective in managing methaemoglobinemia and repeated doses will be required in severe cases.[18] When administering methylene blue, full blood count needs to be monitored as methylene blue can cause intravascular hemolysis in patients with G6PD deficiency. Ascorbic acid and hyperbaric oxygen are alternatives that can be used in methaemoglobinemia, but less effective than methylene blue.[18] In cases of severe anemia due to haemolysis or gastrointestinal bleeding blood transfusion should be given. There are few case reports where exchange transfusion was done with some success in cases of severe methaemoglobinemia.[19,20]

Severe renal failure will require haemodialysis and cardiovascular collapse necessitate ionotropic support. Copper chelators are used to remove excess copper from the body though the efficacy is not proven.[1] Penicillamine 1-1.5g/day in 2-4 divided doses is commonly used. Penicillamine is nephrotoxic and needs to be used with caution in patients with acute kidney injury. Other potential copper chelators that can be used in acute poisoning are edetate calcium disodium (EDTA) and British anti-Lewisite (BAL). BAL is administered intramuscularly and will be useful in cases of severe gastrointestinal mucosal erosions where penicillamine cannot be safely administered. However, its efficacy compared to penicillamine is questionable. EDTA has the potential to cause acute tubular necrosis.[21] There is no good enough evidence as to how long the chelation should be continued, however, it is recommended to continue until serum copper level normalizes.[4] Haemodialysis or haemofiltration is ineffective in removing copper[5] due to early binding to plasma protein and rapid storage in liver, muscles and erythrocytes.[22]

Conclusions

Though acute copper poisoning is very rare, it has a high mortality rate. The management is mainly supportive. Chelation therapy does not have a high success rate. Lack of facilities to monitor serum methaemoglobin levels is a limitation in managing such patients in resource poor settings. Although evidence is limited, exchange transfusion is a newer therapeutic option to treat severe methaemoglobinemia,

Author declaration

Consent for publication

Informed written consent was taken from the spouse of the patient to publish details relevant to the disease and management.

Competing interests

None.

Authors' contributions

All authors were involved in the management of the patient. IR did the initial literature review and wrote the first draft. KT reviewed the first draft and did the final corrections before submission. All authors have read and approved the final manuscript.

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