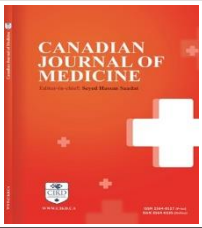
ISSN 2564-0127 (Print)
ISSN 2564-0135 (Online)

Canadian Journal of Medicine 6(2024) 82-87



Canadian Journal of Medicine

WWW.CIKD.CA

journal homepage: https://www.cjm.cikd.ca

A Case of Severe Copper Sulphate Poisoning

Sumaiya Lahir[1*], Peumini Rajapakse[2], Deepa Amarasekara[3], Pubudu Jayasekara[4]

[1,2]Colombo North Teaching Hospital, Ragama, Sri Lanka
[3,4]Consultant Physician in Internal Medicine, Colombo North Teaching Hospital, Ragama, Sri Lanka

Keywords:
Copper sulphate, Hemolysis, Acute liver injury, Methemoglobinemia, Rhabdomyolysis, Penicillamine

Received
29 July 2024
Received in revised form
21 August 2024
Accepted
25 August 2024

***Correspondence:**
sumaiyanufais@gmail.com

ABSTRACT

Copper sulphate poisoning is a serious medical concern, particularly in regions where its use is prevalent in various industries and where accidental or intentional ingestion poses risks, such as in Sri Lanka. We present the case of an 18-year-old female who ingested a substantial amount of copper sulphate, leading to severe toxicity and multiple complications. Despite initial management with gastric lavage and activated charcoal, the patient developed intravascular hemolysis, methemoglobinemia, rhabdomyolysis, acute liver injury, and aspiration pneumonia. Treatment involved supportive measures, including fluid resuscitation, blood transfusions, and antibiotics, along with chelation therapy using penicillamine. Notably, our patient exhibited favorable clinical progress and recovery within a week of admission. This case underscores the importance of prompt recognition and management of copper sulphate poisoning, emphasizing the potential for severe complications and the need for further research to establish standardized treatment protocols. Restricting access to copper sulphate in its powdered form may serve as a preventive measure against intentional ingestion, thereby reducing the incidence of poisoning cases.

Copper sulphate is widely used in various industries in Sri Lanka, such as agriculture, textiles, timber, and leather. It finds its applications in photography, veterinary, and human medicine. Additionally, it was previously utilised in copper-plated tubing for hemodialysis [1, 2]. The blue colour of hydrated copper sulphate crystals is attractive to children, increasing the risk of accidental poisoning. Most cases of copper sulphate poisoning in adults are due to intentional self-harm [3].

Copper is essential for humans, animals, and plants, serving as a cofactor in numerous enzymatic activities within the human body [2]. Rich sources of copper in our diets include shellfish, seeds and nuts, organ meats, wheat-bran cereals, whole-grain products, and chocolate. The recommended daily allowance for copper varies by age, but on average, an adult needs around 900 micrograms of copper per day [4]. Homeostasis is maintained by regulated consumption and excretion [2]. Ingesting more than 1 gram of copper sulphate can cause toxic symptoms, and an untreated dose of 10-20 grams can be lethal [1].

Following ingestion, copper can cause a metallic taste, salivation, nausea, vomiting, abdominal pain, and bloody diarrhoea due to irritation and erosion of the stomach lining [5]. It may also result in hemolysis, which can cause hemoglobinuria, hematuria, and hemolytic anaemia. In addition, liver and kidney failure may occur. If a shock syndrome occurs, it could lead to profound hypotension, coma, and even death. Early death is usually caused by shock, while delayed mortality is linked to renal and hepatic failure [2].

It is crucial to administer chelating agents early along with resuscitation measures to prevent the fatal consequences of severe copper poisoning. Out of various chelating agents like dimercaprol, penicillamine, edetate calcium disodium, and 2,3-dimercaptopropane-1-sulphonate (DMPS), DMPS has proven to be a promising treatment based on animal studies and some human case reports [1, 2, 6].

We report a successful case of managing severe poisoning from copper sulphate benzaldehyde through general supportive measures and penicillamine.

Case Presentation

An 18-year-old girl was admitted to the hospital after ingesting about 15 to 20 grams of copper sulphate 2 hours before admission. Initially, she received gastric lavage and activated charcoal at the local hospital and was transferred to a tertiary care hospital due to persistent hypoxia. Upon admission, she experienced generalised body aches, right hypochondria pain, nausea, vomiting, and shortness of breath without any bleeding manifestation on admission. However, within 24 hours of ingestion, he developed dark-coloured urine and reduced urine output.

During the examination, the patient appeared drowsy, not pale, not cyanosed. Her pulse rate was 110 /minute and BP 90/60mmhg. Her respiratory examination revealed an RR of 20 bpm, with equal chest expansion and crackles in the right lower zone of the lung; saturation on room air was 84% on admission. Epigastric and right hypochondriac tenderness was noted, but other abdominal examinations were normal. There were no neurological deficits.

The patient developed several complications from copper sulphate poisoning throughout the hospital stay, including intravascular hemolysis, methemoglobinemia, rhabdomyolysis, acute liver, and myocardial injury. The other complication includes aspiration pneumonia. The aspiration pneumonia was treated with IV antibiotics, including co-amoxiclav and Flagyl, as well as oxygen for hypoxia.

The intravascular hemolysis developed within 24 hours of the illness was suggested by increased total and indirect bilirubin, high LDH, high Retic count, and hemoglobinuria (negative Urine full report and no supernatant on urine centrifuging), with the blood picture showing evidence of hemolysis, along with the drop in haemoglobin. It was managed symptomatically with 4 pints of blood transfusion. Additionally, IV omeprazole was given with the suspicion of erosive gastropathy.

The hepatitis, which developed progressively over 2-3 days, was managed symptomatically, and the liver enzymes were improved. The chelation therapy with penicillamine was initiated at 500 mg every six hours and continued for seven days.

Aggressive fluid resuscitation was carried out to manage rhabdomyolysis with good recovery without developing renal injury. Myocardial injury was managed symptomatically, and UOP improved with hydration.

Although biochemical confirmation of methemoglobinemia is not possible with the clinical evidence of peripheral oxygen saturation and arterial oxygen saturation difference and positive bedside blotting paper test, methemoglobinemia was confirmed but managed without giving methylene blue as the estimated percentage of methemoglobinemia was less than 20 %.

Luckily, the patient exhibited favourable progress in her clinical condition on the 7th day of illness and was discharged. Upon a subsequent examination on the 14th day, all the clinical parameters were within normal limits. The investigation summary is presented in Table 1.

Table 1. Investigation summary.

Investigations	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
FBC-WBC(10^3/microlitre)	25	33	26	32	25	29	4.1
HB(g/dl)	9.8	7.9	6.6	5.6	9	10	11
PLT (10^3/micro liter)	279	152	112	94	167	194	370
Blood picture 1. Appearances are in favour of oxidative stress-induced hemolytic process (bite cells, blister cells, Heinz bodies, spherocytes, few polychromasia seen) 2. Later appearances are in favor of Micro angiopathic hemolytic anaemia, No evidence of oxidative hemolysis. 3. On discharge-NO Microangiopathic hemolytic anaemia, NO hemolysis							
Retic count (%)			4.7				
LDH(U/L)	1000	2142	4591	5310	4104	1688	986
LFT-							
Ast(U/L)	155	128	242	198	65	27	
Alt(U/L)	7	10	23	23	18	18	
T.protein(g/dl)	6.5	5.3	5.1	4.9	5	5.2	
S.Albumin(g/dl)	3.7	3.2	3.3	3.3	3.1	3.3	
S.Globulin(g/dl)	2.8	2.1	1.8	1.6	1.9	1.9	
T.bil(micromole/l)	22	37	42	47	28	15	
D.bil(micromole/l)	9	16	13	16	9	6	
I.bil(micromole/l)	13	21	29	31	19	9	
S.GGT(U/L)							
S. Alp(U/L)	42	47	51	65	40	37	
PT/INR		1.02	1.1	0.97	0.98	1.07	1
APTT		26.8	28	30	27	25	28
Coombs test - Negative							
CRP (mg/l)	83	121	77	70	37	8.2	< 6
S.creatinine (micromole/l)	98	67	59	56	42	45	70
Blood urea(mg/dl)			38				
Serum Electrolytes (mmol/l)							
Sodium	133	137		141	135	137	142
Potassium	5.7	4.2		3.5	3	3.5	4.7
Calcium				1.9			
Magnesium				0.7			
CPK			800	736	500		50
ECG - T inversions in leads 3, aVF, V4-V6							
Troponin I(ng/l)	57.6	95.5	384	84	20		
ABG-							
PH	7.2	7.4					
Pco29(mmhg)	31	32					
Po2(mmhg)	85	80					

Hco_3^-(mmol/l)	14	18					
Sao2 (%)	95	95					
Lactate (mmol/l)	6.3	1					
Anion gap	23	12					
p/f ratio (mmhg)	405	381					
CXR- PA -	Right side lower zone consolidation						
UFR -	No red cells, no pus cells, no protein, HB 3+						
U.Culture -	No growth						
Blood culture -	No growth						
Uss abdomen -	Normal						
2D ECHO -	No evidence of myocarditis, normal						

Discussion

Consuming more than 1 gram of copper sulphate can lead to symptoms of toxicity. However, the toxicity threshold varies by individual factors. In cases of severe poisoning, mortality rates are high, and the lethal dose of copper sulphate ingestion is between 10-20 grams [1, 2, 3].

Copper exposure can lead to local and systemic effects due to its ability to induce cellular toxicity. Various mechanisms have been proposed to explain this, including forming reactive oxygen species that cause DNA strand breaks and other oxidative damage. Additionally, lipid peroxidation can occur, which alters cell membrane fluidity and permeability or denatures intracellular proteins, resulting in cellular damage [1].

The clinical manifestations of copper sulphate poisoning include erosive gastropathy, intravascular hemolysis, methemoglobinemia, hepatitis, acute kidney injury, and rhabdomyolysis. Arrhythmias and seizures may also occur, likely due to the involvement of other organ systems [3]. Our patient's systemic toxicity resulted in GI, liver, renal, and muscle injury and haematological manifestations.

Intravascular hemolysis can begin within 24 hours of consumption and is caused by direct oxidative damage to red blood cell membranes. Hemolysis can occur rapidly and severely, leading to significant decreases in the haemoglobin level. Copper ion Cu2+ oxidises iron ion Fe2+ in haemoglobin to Fe3+, leading to the formation of methemoglobin. This leads to cyanosis and reduced blood oxygen-carrying capacity [2, 3, 5].

Our patient experienced signs and biochemical features of intravascular hemolysis within 24 hours of ingestion. However, anaemia developed after the first day, likely due to intravascular hemolysis and gastrointestinal blood loss due to gastropathy. It was managed with blood transfusions.

Methemoglobinemia was suspected due to Pao2- Sao2 mismatch and supported by the positive blotting paper test. If Methemoglobinemia is severe, it should be treated with an intravenous injection of methylene blue at 1-2 mg/kg, which can be repeated if cyanosis persists beyond one hour. Methylene blue is contraindicated in individuals with G6PD deficiency due to its potential to cause hemolysis. Hyperbaric oxygen or ascorbic acid (a weaker reducing agent) may be considered as alternatives [7]. In our case, the antidote methylene blue was not administered as the percentage of methemoglobin was less than 20%.

After ingestion, some people may experience elevated levels of liver enzymes 2-3 days after exposure, jaundice, and tenderness due to the accumulation of copper in hepatocytes. Still, these symptoms typically subside within a week. Acute liver failure following necrosis of hepatocytes occurs due to direct toxic effects [1, 2, 3]. Our patient showed clinical features of liver injury

with rising liver enzymes and normal PT/INR on the following day of admission. However, the liver enzymes returned to normal within a week without residual damage, as mentioned above. The incidence of acute kidney injury because of toxicity is quite common, with some case reports indicating rates as high as 40-60% [1, 3]. The possible causes of kidney damage may include dehydration-related pre-renal failure (due to vomiting, diarrhoea, or reduced fluid intake), hemoglobinuria, sepsis, rhabdomyolysis, direct copper toxicity on proximal tubules, and secondary effects of multi-organ dysfunction. It has been observed that recovery of renal function after copper sulphate ingestion is slow and incomplete [1, 3, 5]. Dialysis is not successful in removing copper from the body, but it is necessary to support life in cases of acute renal injury. Peritoneal dialysis is ineffective in sustaining the prolonged need for dialysis until renal function improves [3].

Our patient experienced an initial episode of Acute kidney injury with reduced urine output, possibly due to the causes mentioned above; however, it resolved early without an increase in serum creatinine levels with good hydration. Various copper chelators are available, and there needs to be a consensus on the most effective one. Options include D-Penicillamine, dimercaprol, and edetic acid (EDTA)[6].

Chelating agents are recommended for severe toxicity. One of the chelating agents, penicillamine, at a dose of 1-1.5 g/d, taken in 2-4 divided doses, was widely used [1]. Our patient received a high amount of oral penicillamine without ill effects. Our patient experienced severe epigastric pain likely caused by copper sulphate ingestion, which was treated with a proton pump inhibitor. However, upper GI confirmation is unavailable. Our patient exhibited mild rhabdomyolysis, with slight increases in serum creatine kinase levels, and successfully treated with aggressive hydration. Copper can damage skeletal muscle cells and cause rhabdomyolysis, although it is rare in cases of acute copper intoxication.

Conclusion

Although rare, copper sulphate poisoning can have severe complications and high mortality rates, making it crucial for clinicians to be knowledgeable in managing affected patients. Poisoning can damage the upper digestive tract, kidneys, liver, and blood, causing intravascular hemolysis and methemoglobinemia, as in our case.

Treatment includes fluid and electrolyte resuscitation, blood transfusion for anaemias, methylene blue for severe methemoglobinemia, and the early use of copper chelating agents such as D-penicillamine, dimercaprol or EDTA in removing excess copper; however, the optimal chelator has not been determined. This case was managed successfully through a multidisciplinary approach, including haematology, toxicology, nephrology, and medicine.

Further research and clinical studies are warranted to establish standardised guidelines for best chelating agents and other treatment modalities. To prevent intentional self-harm from ingesting copper sulphate, restricting the availability of the pulverised powdered form of the compound in the open market can be an effective measure.

Declarations

Acknowledgements
Not applicable.

Disclosure Statement
The authors reported no potential conflict of interest.

Ethics Approval
Not applicable.

Funding Acknowledgements
Not applicable.

Citation to this article
Sumaiya LF, Rajapakse RPDP, Amarasekara D, Jayasekara P. (2024). A case of severe copper sulphate poisoning. Canadian Journal of Medicine. 2024 Aug 25;6(2):82-87. doi: 10.33844/cjm.2024.6040

Rights and Permissions


References

[1] Oon S, Yap CH, Ihle BU. Acute copper toxicity following copper glycinate injection. Internal Medicine Journal. 2006 Nov;36(11):741-3. https://doi.org/10.1111/j.1445-5994.2006.01195.x

[2] Sinkovič A, Strdin A, Svenšek F. Težka akutna zastrupitev z bakrovim sulfatom-prikaz primera [Severe Acute Copper Sulphate Poisoning: A Case Report]. Arhiv za higijenu rada i toksikologiju [*Archives of Industrial Hygiene and Toxicology*]. 2008 Mar 21;59(1):31-5. https://doi.org/10.2478/10004-1254-59-2008-1847

[3] Gamakaranage CS, Rodrigo C, Weerasinghe S, Gnanathasan A, Puvanaraj V, Fernando H. Complications and management of acute copper sulphate poisoning; a case discussion. Journal of Occupational Medicine And Toxicology. 2011 Dec;6:1-5. https://doi.org/10.1186/1745-6673-6-34

[4] Office of Dietary Supplements Copper. (n.d.). https://ods.od.nih.gov/factsheets/Copper-HealthProfessional/

[5] Park KS, Kwon JH, Park SH, Ha W, Lee J, An HC, Kim Y. Acute copper sulfate poisoning resulting from dermal absorption. American Journal of Industrial Medicine. 2018 Sep;61(9):783-8. https://doi.org/10.1002/ajim.22892

[6] Franchitto N, Gandia-Mailly P, Georges B, Galinier A, Telmon N, Ducassé JL, Rougé D. Acute copper sulphate poisoning: a case report and literature review. Resuscitation. 2008 Jul 1;78(1):92-6. https://doi.org/10.1016/j.resuscitation.2008.02.017

[7] Fernando R (Ed). Management of poisoning. 3rd edition. Colombo National Poisons Information Centre, National Hospital of Sri Lanka; 2007.