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CASE REPORT

A novel and fatal method of copper sulphate poisoning

Un nouveau mode d'empoisonnement, mortel, par le sulfate de cuivre

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Introduction: Copper sulphate is widely used around the world as a pesticide and seed fungicide. Many cases of accidental intoxication with this substance have been reported among farm workers who have absorbed large amounts of the substance through the skin. It has also been used for self-harm, generally by oral ingestion. Toxic levels of the substance can lead to methaemoglobinaemia and death.
Case report: The case of a 29 year old woman who diluted and inserted copper sulphate vaginally in order to terminate an unwanted pregnancy is reported.
Conclusion: This article is a review of the presentation, diagnosis and treatment of copper-sulphate-induced methaemoglobinaemia, including the challenges of treating this condition in clinical settings that are unprepared for this complication.

Introduction: Le sulfate de cuivre est largement utilisé dans le monde entier comme pesticide et fongicide pour les semences. Nombre de cas d'intoxications accidentelles par cette substance ont été signalés chez des ouvriers agricoles ayant absorbé d'importantes quantités de cette substance par voie cutanée. Ce composé a également été utilisé à des fins d'automutilation, généralement par ingestion orale. Les niveaux toxiques de la substance peuvent entraîner une méthémoglobinémie et la mort.
Etude de cas: Le cas d'une femme âgée de 29 ans ayant dilué et inséré du sulfate de cuivre par voie vaginale afin de mettre un terme à une grossesse non désirée est présenté.
Conclusion: Une étude des symptômes, du diagnostic et du traitement de la méthémoglobinémie induite par le sulfate de cuivre, ainsi que les difficultés liées au traitement de cette affection dans des structures médicales qui ne sont pas préparées à de telles complications.

African relevance

- Many people in rural Africa may be exposed to copper sulphate and its toxicities, often through exposure while farming. Thus, it is important for health care providers to be able to identify and treat copper sulphate poisoning.
- The ease with which copper sulphate can be obtained in Botswana, and perhaps in other African countries, coupled with the high prevalence of HIV/AIDS and unwanted pregnancies may lead to attempted terminations of pregnancy with use of copper sulphate. Should this be the case, this article may serve as a guide for emergency care physicians in our setting.
- The article also highlights the diagnosis and treatment of methaemoglobinaemia regardless of its cause and it is important for physicians in the African setting to be able to manage this condition.
- The unavailability of the required antidote in this case, which contributed ultimately to the patients death, may help to spark discussion about the possible creation of toxicology plans and centres in African health care systems. Through planning ahead for these incidents, rarely used antidotes and clinical guidance may be accessed when needed. This is especially important in the African setting where access to toxicology information, antidotes, or chelators may be limited.

Introduction

Copper sulphate ($CuSO_4$) is widely used around the world as a pesticide and seed fungicide.[1–3] Many cases of accidental intoxication with this substance have been reported among

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farm workers who absorbed large amounts of the substance through the skin.[1] It has also been used for self-harm, generally by oral ingestion.[2] Toxic levels of copper sulphate can lead to methaemoglobinaemia and death.[3,4] A case of poisoning due to copper sulphate inserted vaginally in order to terminate an unwanted pregnancy is described. No other reports on copper sulphate poisoning in Southern Africa or Botswana were found; most reports in the literature are from Asia.[3,4]

Case report

A 29-year-old female, 15 weeks pregnant and recently diagnosed with HIV infection (CD4 count unknown) presented to the Mahalapye District Hospital emergency centre, a village hospital with no specialist physicians and no intensive care unit, with a history of excessive vomiting, extreme weakness, and lower abdominal pains without vaginal bleeding. Eventually, she admitted inserting an unstated amount of copper sulphate powder diluted in water vaginally approximately 2 h before presentation; her intent had been to abort an unplanned pregnancy as her partner was unsupportive. On examination she was conscious and alert, not pale, jaundiced, or cyanosed, and not in respiratory distress, with a respiratory rate of 18 breaths per minute and an oxygen saturation of 96% on room air. Her blood pressure was 128/75 mmHg with a regular pulse of 99 beats per minute. She had mild tenderness in the suprapubic area.

Her underwear had bluish staining and a mucoid blue substance was observed at the cervical os. The cervix was closed and there was no bleeding. Initial laboratory results were a white cell count of 6.81×10^3/mL, haemoglobin of 14.2 g/dL with a haematocrit of 40.5%, serum creatinine 83 μmol/L, AST 22.5 U/L and an ALT of 3.7 U/L. An obstetric ultrasound scan done at admission showed a viable 15 week old foetus. The patient was started on 1 L ringers lactate and oxygen by face mask, then admitted to the ward on 1 g IV Cefotaxime and 500 mg IV metronidazole 8 h, for suspected septic abortion.

Approximately 12 h after admission the patient was cyanotic with a decreased level of consciousness, responding only to pain, and with amniotic liquor draining per vagina. Her blood pressure had dropped to 90/60 mmHg, pulse was 120 beats per minute, and temperature was 37 ° C. She had signs of peripheral vasoconstriction and an initial random blood glucose of 1.5 mmol/L. Oxygen saturations were unknown due to the lack of a monitor, but she was kept on high flow oxygen per face mask and given a 50% dextrose 50 mL bolus followed by 1 L 5% dextrose with simultaneous 1 L ringers lactate bolus. Her blood sugar was 4.4 mmol/L when rechecked. Oxygen saturations were finally obtained and found to be 74% on oxygen by facemask. The patient developed a bluish discolouration of her palms and feet, and her blood was a chocolate brown colour, consistent with methaemoglobinaemia. Her serum creatinine had risen to 289 μmol/L, AST to 564 U/L and ALT to 57 U/L. Her white cell count was 55.89×10^3/mL and her haemoglobin was 15.7 g/dL whilst the haematocrit was 49.3%. There was no blood for transfusion available at the time.

The recommended antidote for methaemoglobinaemia, methylene blue, was not available in the hospital or in any other hospitals contacted. Approximately 22 h after admission, having received 2 doses of antibiotics and a total of 4 L intravenous fluid, the patient died. The cause of death was thought to be tissue hypoxia and multi-organ failure.

Discussion

Ingestion of 15–20 mg of copper sulphate is reported to cause mainly gastrointestinal symptoms, with higher doses resulting in multi-organ damage. Lethal doses of copper sulphate ingestion are 10–20 g.[1,2]

Gastrointestinal symptoms predominate in copper sulphate toxicity include: vomiting, haematemesis, melaena, and diarrhoea. These symptoms seem to be unrelated to the mode of poisoning, whether oral or parenteral.[1,3,5]

Acute liver failure may occur due to direct toxicity of copper sulphate and usually occurs in severe poisoning. Liver failure may present as hepatomegaly, icterus, or an increase in transaminases and prothrombin time.[2,3] Renal injury may be a result of (1) pre-renal failure resulting from the volume depletion secondary to excessive vomiting and or diarrhoea, (2) sepsis, (3) rhabdomyolysis, (4) intravascular haemolysis (haemoglobinuria leading to acute tubular necrosis), or (5) direct copper toxicity on the proximal tubules.[1–4] Sepsis and infection may further aggravate copper sulphate poisoning and antibiotics may be indicated.[3]

The two main haematological complications of copper sulphate poisoning are intravascular haemolysis (due to inhibition of glucose-6-phosphate dehydrogenase or a direct effect on the red blood cell membrane) and methaemoglobinaemia.[1–4]

In the red blood cell, copper oxidizes the iron in the haeme complex from the ferrous Fe^{2+} to the ferric Fe^{3+}.[2,3] This ferric form has a diminished oxygen binding capacity and also increases the oxygen affinity of the remaining ferrous haeme in the haemoglobin tetramer. This results in a shift of the oxygen curve to the left; thus, oxygen is not readily released to the cells.[6] At high levels of methaemoglobinaemia, the patient may have tissue hypoxia despite adequate oxygenation and haemoglobin levels, essentially a functional anaemia.[6,7] The presence of normal arterial partial pressure of oxygen but a low SpO_2 is called a saturation gap and is an indication of methaemoglobinaemia.[6,7] Symptoms of methaemoglobinaemia are not usually seen when blood methaemoglobin levels are below 3%; cyanosis is usually noted at levels above 15% and the chocolate brown colour of blood (as seen in our patient) is usually indicative of levels between 15% and 30%.[8] Methaemoglobin levels above 50% may result in central nervous system depression, cardiac arrhythmias, and death.[8]

Copper sulphate poisoning can be managed in four steps: (1) resuscitative/supportive measures, (2) decreasing absorption, (3) chelation, and (4) management of complications. This article focuses on the management of methaemoglobinaemia, a complication of copper sulphate poisoning, as it was the most immediate cause of the patient's death.

In case of ingestion of the toxin, after initiating resuscitative measures (ABCs) as necessary, milk, water, or activated charcoal may be given to decrease absorption if the patient presents within 4 h of ingestion, although there is no specific evidence to support these measures.[2] Induction of vomiting is not recommended since copper sulphate is highly emetic; for this reason gastric lavage is also not mandatory.[1,2]

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When the methaemoglobin levels are greater than 30% of the total haemoglobin levels, treatment with methylene blue is imperative.[2,6,8] Methylene blue acts by transferring an electron from NADPH to the ferric haemoglobin, thus reducing it to the ferrous form. This dependence of methylene blue on the availability of NADPH renders methylene blue ineffective in people with glucose-6-phosphate dehydrogenase deficiency, as this enzyme is required for NADPH production in the red cell.[2,8,9] For these patients, as well as those with markedly elevated methaemoglobinaemia and/or haemolysis, blood transfusion or exchange transfusion is more beneficial.[1,8,9]

The recommended dose of methylene blue is 1–2 mg/kg given intravenously over 5 min. This dose can be repeated every hour to a maximum of 7 mg/kg if cyanosis persists.[6,8] Methylene blue given at doses greater than 4 mg/kg can result in haemolysis and caution is therefore necessary, as copper can also cause haemolysis.[6,9] Rebound methaemoglobinaemia may also occur if high doses are administered; therefore, where possible, serial measurements of methaemoglobin levels are recommended as additional doses of methylene blue may be necessary.[2,9]

Conclusion

Clinicians in resource-limited settings must be aware of the possibility of methaemoglobinaemia in patients who present with hypoxia not responsive to oxygen therapy and with a saturation gap. They must also be aware of the ease with which patients can come into contact with copper sulphate and its potential toxicity. The powder can be bought at approximately USD$1 over the counter at local chemists.

Some clinical and logistical questions raised by this case include the following: (1) Is per vaginal application of copper sulphate more toxic than oral or parenteral administration? (2) Did the pregnancy and/or the HIV status of the patient contribute to her rapid deterioration? (3) Even though copper sulphate poisoning is rarely reported in our region, should methylene blue be made available in our hospitals? Further discussion of this case with the relevant authorities is ongoing.

Conflict of interest

All authors declare that there are no conflicts of interest to disclose. None of the authors have any financial or personal relationships with other people or organizations that could influence their work.

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