Is potassium thiosulfate a poison? Is it safe? A case series
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Abstract
Potassium Thiosulfate is a liquid substance used for producing fertilizers. In this case series, we present five patients who have been exposed to potassium thiosulfate inhalation. Three of them were intubated in the scene by paramedics because of confusion and respiratory depression. They had refractory status epilepticus. The other two were exposed during trying to help the others for getting out, they presented to ED with nausea, vomiting and headache. One of the intubated patients died on the 4th day of his follow-up at ICU. Others were sent home after few days with no complication. Potassium thiosulfate is not a substance documented for poisoning and it is assumed to be a safe and stable solution. Although, it was assumed to be a safe substance there are risks of metabolic acidosis, resistant generalized seizures, and death due to disturbance of oxidative reactions with potassium thiosulfate.

Keywords: Potassium thiosulfate, Poisoning, Metabolic acidosis, H2S, Case series.

Introduction
Potassium Thiosulfate is a liquid substance used for producing fertilizers in many countries for agriculture. It contains 17% sulfur and 25% potassium in weight and these two major components are responsible for the mechanisms of action. The sulfur contained in the molecule aids the utilization of nitrogen by plants and living cells, and has a role in interacting with oxidative cycles. The PH of this non-irritant solution is neutral; however at basic PH the solution may be irritant to the mucosa. Furthermore; at acidic PH due to the decomposition of sulfur to sulfite and sulfur dioxide, the substance may be extremely corrosive.

The aim of this article is to present a series of five potassium thiosulfate poisoning cases referred to our Emergency Medicine Department (ED) after they have been exposed to potassium thiosulfate inhalation while cleaning the container tank in industry. The mechanism of action and poisoning of this substance will also be discussed.

Case-1
A 22 years-old male was brought to ED with loss of consciousness and cardiac arrest, after he collapsed while cleaning an empty potassium thiosulfate tank. He was immediately intubated and resuscitated for five minutes by paramedics. On arrival, GCS: 5 (E2V1M2), BP: 140/90 mmHg, pulse rate: 82 beats/min. He was transferred to decontamination room. His physical examination and ECG after decontamination was unremarkable. During follow-up at ED, he suffered a seizure which was treated with parenteral benzodiazepine. No sign of cardiovascular instability was detected on follow-up. His laboratory findings are listed on Table.

He was then referred to intensive care unit, where he was treated with midazolam infusion because of repeated seizures. His diffusion-weighted MRI showed bilateral diffuse impairment. On the 4th day of his follow-up at ICU, patient succumbed due to cardiopulmonary arrest.

Case-2
A 36 years-old man was admitted to ED. His GCS: 4 (E1V1M2), BP: 140/90 mmHg, pulse rate: 128 beats/min,
temperature: 36.7 °C. He was intubated by paramedics before admission to the hospital. He was decontaminated according to standard procedures. His laboratory findings are listed on Table. For his seizures, IV benzodiazepine was started. The patient’s vital signs were stable during ED follow-up. He was transferred to the ward after 3 days of ICU follow-up.

Case-3
A 32 years-old male patient was brought to the emergency room by paramedics following syncope while cleaning the potassium thiosulfate tank. His GCS: 3 and he was intubated by paramedics. On admission his GCS: 4 (E1V1M2), BP: 125/87 mmHg, pulse rate: 112 beats/min (sinus tachycardia), temperature: 36.5°C and spO2: 97% at 100 % O2 support. His physical examination was normal. He was decontaminated with soap and water. IV hydration was started after central catheter placement. On the follow up, he had generalized seizures and was treated with IV midazolam. He was transferred to the intensive care unit. His laboratory findings are listed on Table. He was transferred to the ward after 4 days of ICU follow-up.

Case 4 and 5
Two patients who were 42 and 43 years old presented to the ED with nausea, vomiting and headache after trying to rescue their friends from potassium thiosulfate tank. Their GCS scores, vital signs and systemic physical examination were normal on admission. After decontamination, IV hydration was started and patients were observed for 24 hours. Their laboratory findings are listed on Table. As they had no complaints after observation, they were discharged.

Discussion
Potassium thiosulfate is produced by certain chemical processes and is actually a very stable substance just like other thiosulfate compounds. Thiosulfate is an intermediate compound in oxidative hydrogen sulfide (H2S) metabolism. This pathway is in close relationship with oxidative stress and ATP production in aerobic and aerobic conditions. In the cellular level, interaction between oxygen and sulfur molecules determine the way the organism adapt to many stressful conditions such as ischaemic stroke, myocardial infarction, infections, etc.1 Thiosulfate is supposed to mediate protective effects of H2S in stroke.

H2S is produced by several enzymes in different various tissues. H2S has significant roles in neuronal signal transmission, vasorelaxation, and either pro- or anti-inflammation. H2S has been proved to have protective effects in ischaemia induced or reperfusion induced injuries; and this effect may be observed regardless of the administration of H2S exogenously or produced endogenously.1,2

These cases, show that in people exposed to the major biochemical effect of potassium thiosulfate, the major problem was metabolic acidosis. Three of the five cases were in need for ICU for the seriousness of the clinical conditions. These three patients had metabolic acidosis with seizures. Although it must be considered respiratory acidosis in most of the inhalational poisonings, the situation that came up with our patients was quite the contrary. These three patients also had very resistant seizures not responding to antiepileptic therapy. There was no anion gap in these patients unlike the previously reported individuals.2

Potassium thiosulfate is not a substance documented for poisoning and it is assumed to be a safe and stable solution. The change in the PH of the solution may have triggered the adverse effects we observed in the patients. Most probably these people used a chemical compound to clean the tank which started the chain of reactions. The change in PH starts the irritating and destructive processes, but does not account for the metabolic acidosis. It may be assumed that the continuum of the clinical condition is due to H2S mediated interaction of the oxidative pathways.3,4 In the tissues that are susceptible to this disturbance such as neurons in the central nervous system, or myocytes in the heart degenerative processes start, and they get even worse after reperfusion because of the ischaemia-reperfusion injury.

A number of studies suggest that whether given exogenously or produced endogenously H2S molecule attenuates ischaemia-reperfusion (I/R) injury. H2S is produced from thiosulfate in many living tissues. In the very early stages of life on the earth, when there was no abundant oxygen for the organisms to survive, H2S was a means of keeping many chemical reactions going so that the primitive organisms produced energy to sustain life. Living cells still have the same capability of utilizing H2S in their genetic codes.5 In the poisoning situation, mobilization of H2S from thiosulfate is faster than H2S production from organic thiol compounds, and the degradation process of sulfur may slow down.5,6 This may be due to the blockage of calcium channels. The aerobic pathways are disturbed and an ischaemic injury or ischaemia- reperfusion injury may occur. In Case 1, the cranial MRI of the patient indicating neurological disorder may be a clue to what happened to the patient. In addition, the fact that in four of the five cases there was a
rise in the troponin I (high sensitive) may support the interference with the oxidative pathways.

Our case reports aren't highly identifiable patient information/characteristics or cases of child abuse, elder abuse, or those involving criminal investigation. The consents of three cases are unobtainable (not refused), because they were intubated and unconscious in admission with no relatives, the others sent home with no important findings.

Conclusion
In conclusion, we would like to point out that this is the first report presenting five cases of potassium thiosulfate poisoning. Although, it was assumed to be a safe substance there are risks of metabolic acidosis, resistant generalized seizures, and death due to disturbance of oxidative reactions.

References