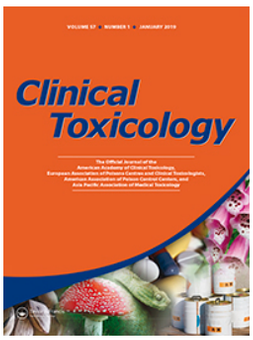

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Severe hemolytic anemia due to transient acquired G6PD deficiency after ingestion of sodium chlorite

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Disclosure statement

No potential conflict of interest was reported by the authors.

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Severe hemolytic anemia due to transient acquired G6PD deficiency after ingestion of sodium chlorite

Dear Editor,

Sodium chlorite is an oxidative compound used as household detergent or bleaching agent. After ingestion, the reactive radical chlorine dioxide is formed which may cause massive oxidation of hemoglobin leading to methemoglobinemia and intravascular hemolysis.

A 40-year old female presented with vomiting and diarrhea after ingesting 30ml of 28% sodium chlorite solution. Arterial blood gas analysis: pH 7.19, p_aCO_2 32 mmHg, p_aO_2 154 mmHg, bicarbonate 11.7 mmol/l, methemoglobin 5.2%, and lactate 6.3 mmol/l. Hemoglobin was 17.6 g/dl and creatinine 143 μmol/l. Urinalysis showed hemoglobinuria and proteinuria.

Renal function normalized after fluid resuscitation. Methemoglobin level decreased to 3.0% without treatment. Severe hemolytic anemia developed (Hb from 17.6 to 6.5 g/dl in 9 d). Haptoglobin was decreased and the Coombs test was negative. G6PD activity was decreased: 8 d after ingestion 3.4 IE/g (normal 3.8–5.9 IE/g) and normalized (5.2 IE/g) 4 months later. DNA sequencing of the gene coding for G6PD revealed no mutations. Besides two blood transfusions, patient received no treatment and was dismissed 9 d after admission in good condition.

In earlier case reports, patients presented with renal insufficiency, gastrointestinal symptoms, methemoglobinemia, and hemolysis (Table 1). Methemoglobinemia develops when the oxygen carrying ferrous ion (Fe^{2+}) of the heme groups in the hemoglobin molecule is oxidized into the ferric state (Fe^{3+}). The effects of this conversion of hemoglobin to methemoglobin are (1) inability to bind oxygen to the (Fe^{3+}) site in the lungs and (2) increased affinity of the other heme groups for oxygen, preventing the release of oxygen in tissues. Although erythrocytes possess potent mechanisms to maintain a reduced intracellular environment under normal circumstances, severe oxidative stress can lead to methemoglobinemia and massive intracellular damage resulting in hemolysis. Glucose-6-phosphate dehydrogenase (G6PD) is a key enzyme generating reducing equivalents that can be used by different enzyme systems to prevent oxidative damage. The harmful effect of oxidative stress on G6PD

Table 1. Case reports.

	Lin (1993)	Romanovsky (2013)	Gebhardtova (2014)	Hulshof (2018)
Amount $NaClO_2$	100 ml 10%	Mouthful 28%	<100 ml 28%	30 ml 28%
Time between ingestion and presentation	30 min	4 h	Unknown	8 h
Methemoglobin (time of presentation)	59.0%	6.7%	40.1%	5.2%
Hemoglobin (time of presentation)	17.6 g/dl	18.4 g/dl	17.9 g/dl	17.6 g/dl
Hemoglobin (lowest point)	7.1 g/dl	8.3 g/dl	5.9 g/dl	6.3 g/dl
G6PD activity	–	Decreased	–	Decreased
Gastroscopy	–	–	Erosions	–
Dialysis/CVVH	+	–	+	–
Methylene blue	+	–	+	–
Red cell exchange	–	+	–	–
N-Acetylcystein	–	+	–	–

activity and the synchronous increase of erythrocyte fragility have been demonstrated *in vitro* [1].

Patients with an inherited G6PD deficiency are vulnerable for oxidative stress. Theoretically, an acquired transient G6PD deficiency causes similar effects. G6PD activity in our patient was decreased during hemolysis and normalized after recovery, suggesting that decreased G6PD activity was the result of oxidative damage to the enzyme itself or to exhaustion of the anti-oxidative mechanisms in the erythrocytes.

It is unclear whether patients benefit from treatment with methylene blue. In the cases reported, it had either no beneficial effect [2] or slowly decreased methemoglobin levels without preventing the development of haemolytic anemia [3]. In another case, methylene blue was not administered because of the low methemoglobin level and decreased G6PD activity [4]. With reduced G6PD activity and consequent low reducing power, treating methemoglobinemia with methylene blue may be counterproductive and even enhance hemolysis [5].

In conclusion, intoxications with sodium chlorite can cause severe hemolysis. Besides methemoglobinemia, transient G6PD deficiency appears to be a key component in the pathophysiology. Administration of methylene blue to reduce methemoglobinemia should only be considered with significant G6PD activity in red blood cells.

Disclosure statement

No potential conflict of interest was reported by the authors.

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A case of massive metoprolol and amlodipine overdose with blood concentrations and survival following extracorporeal corporeal membrane oxygenation (ECMO)

Dear Editor,

Calcium channel inhibitor and beta blocker overdoses may cause life-threatening circulatory failure that can be challenging to manage. We present a massive overdose of amlodipine and metoprolol where pharmacological treatment alone was insufficient to reverse the hemodynamic shock, but where the use of ECMO was ultimately successful. Blood levels of both agents were followed daily from seven hours until 168 h (7 d) after the ingestion (Figure 1).

A 28-year old woman presented at the emergency department in deep circulatory shock, two hours after ingesting 10 g of metoprolol succinate (extended-release) and 1 g of amlodipine in a suicide attempt.

Resuscitation, including infusions of noradrenaline (0.8 μg/kg/min), high-dose insulin (titrated to 10 U/kg/h), dobutamine (5 μg/kg/min) was futile and 5 h after arriving at the hospital she was cannulated for venoarterial ECMO. Six days after the overdose she was successfully weaned off the ECMO system and rapidly made a complete recovery.

The ingested doses in this case were large enough to be potentially lethal even if taken separately. Lethal doses of metoprolol and amlodipine have been described from 7.5 g and 70 mg, respectively [1,2].

Fatal cases of amlodipine intoxication have occurred with blood concentrations from 185 μg/l [3], almost an order of magnitude lower than the 1200 μg/l in this case. Amlodipine has a long elimination half-life (about 30–55 h) and substantial overdoses may cause severe symptoms persisting for days, consistent with this case. The patient's blood level was still within the potentially lethal range 7 d after the overdose.