

Hemoadsorption to treat severe iatrogenic intoxication to Patent Blue: A Case Report

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This case reports on a 27-year-old woman (body weight 45 kgs), who was admitted to the Emergency Department of a peripheral hospital in Brussels due to intoxication of unknown origin.

Case presentation

- The patient had no previous medical history, was on no chronic medication prior to this intoxication, did not smoke and rarely consumed alcohol. Also, no particular medical history from her family was reported
- On the day of admission, she had been in a nightclub and was found on the floor with rigor, tachycardia, hypertension (190/100 mmHg), hyperthermia (41.6°C), agitation and altered consciousness
- Direct intubation was performed while blood and urine drug screening proved positive for 3,4-methylenedioxy-N-methylamphetamine (MDMA) without concomitant alcohol intake
- Upon admission to the Emergency Department at the peripheral hospital, she was sedated and paralyzed and had dilated pupils; no abnormalities on lung, abdominal, cutaneous and joint examination were found and no other focal neurological signs were observed (i.e. asymmetric reflexes, pyramidal syndrome)
- Heart rate was 130 bpm, blood pressure dropped to 75/35 mmHg and body temperature increased to 41.8°C
- She showed no signs of cyanosis or hypoperfusion
- Initial echocardiography showed a left ventricular ejection fraction of 50%; chest X-ray revealed bilateral infiltrates (probably due to aspiration), while electrocardiogram showed sinus tachycardia
- Initial blood gas indicated the following: pH 7.28, PaCO₂ 32 mmHg, PaO₂ 182 mmHg (on FiO₂ 100%), lactate 3.0 mmol/L, base excess -10.9 mmol/L and metHb 1.1%
- Laboratory tests showed: creatinine 1.6 mg/dL, glucose 55 mg/dL, C-Reactive Protein (CRP) 4.9 mg/L, Creatinine kinase (CK) 3800 IU/L
- Over the next 2 hours she developed a severe shock state necessitating the initiation of a norepinephrine infusion
- Meanwhile, serum lactate levels increased to 8.5 mmol/L and the patient exhibited diffuse bleeding in the throat, on puncture sites, the bladder probe but also from her rectum
- Initial therapy consisted of fluid administration (i.e. 6000 mL crystalloids within 3 hours), intravenous glucose and norepinephrine at 0.4 µg/kg/min; also fresh frozen plasma, prothrombin complex concentrates, tranexamic acid and fibrinogen were given
- At that point, the patient had hepatic failure, distributive shock, hypoglycemia, acute kidney injury, rhabdomyolysis and severe acute respiratory distress syndrome (ARDS)
- Due to the option for potential liver transplantation, the patient was transferred to the Department of Intensive Care at Erasme Hospital, Brussels

- On admission, she exhibited severe ARDS (pH 7.19, PaCO₂ 33 mmHg, PaO₂ 72 mmHg on FiO₂ 100%, lactate 5.5 mmol/L and metHb 1.2%), hemodynamic instability (i.e. profound vasopressor requirement) and persistent capillary leakage
- Ongoing therapies included: propofol (2.0 mg/kg/h via continuous intravenous infusion), sufentanil (0.2 µg/kg/h), norepinephrine (1.3 µg/kg/min), pantoprazole (20 mg iv q24h), cisatracurium (0.03 mg/kg), N-acetylcysteine (100 mg/kg/day)
- Antibiotic therapy with amoxicillin/clavulanic acid (2g q8h) and continuous renal replacement therapy (CRRT) were started
- Additionally, administration of IV methylene blue (2 mg/kg one dose) was prescribed to reduce the vasoplegia and to reduce the norepinephrine requirement
- However, immediately after the dye injection, the skin of the patient became green/blue, oxygen saturation (SpO₂) fell to 75% and blood analysis revealed metHb of 21% and a lactate of 8.1 mmol/L, indicating severe tissue hypoxia
- While the patient was rapidly treated with a veno-venous extracorporeal membrane oxygenation (ECMO) device, it was discovered that Patent Blue V had been erroneously administered instead of methylene blue (both drugs being beside one another in the pharmacy), resulting in life-threatening methemoglobinemia
- As no significant improvement was observed on SpO₂ and persistent metHb > 15% was observed after a few hours of ECMO and CRRT therapy, a CytoSorb adsorber was installed into the CRRT circuit

Treatment

- Two consecutive CytoSorb treatments were performed for a total of 35 hours (1st treatment 15 hours, 2nd treatment for 20 hours)
- CRRT was performed in hemodiafiltration mode
- Blood flow rate: 160 ml/min
- Cumulative ultrafiltration and dialysate flows: 55 mL/Kg/h
- Citrate was administered for anticoagulation
- CytoSorb was integrated in pre-hemofilter position

Measurements

- Hemodynamics
- Plasma metHb levels and toxic Patent Blue V plasma levels
- Lactate levels

Results

- CytoSorb therapy was associated with an improvement in hemodynamic parameters and the norepinephrine dose could be significantly reduced
- Treatment further resulted in a progressive and significant reduction in plasma metHb levels and the efficient removal of toxic Patent Blue V from the blood
- Therapy further resulted in a decrease in lactate plasma levels and later normalization

Patient Follow-Up

- Analysis of urine (i.e. blood, proteins, sediment), different serological tests (i.e. herpes virus, different hepatitis viruses, human immunodeficiency virus, Borrelia burgdorferi, Treponema pallidum, Coxiella burnetii, and Rickettsia spp) and microbiological samples (i.e. blood cultures, tracheal aspirates, broncho-alveolar lavage, were all negative
- Weaning from ECMO and from CRRT was possible on day 5 and day 7, respectively
- Tracheostomy was performed on day 19 and weaning from mechanical ventilation on day 26
- The patient was transferred to the normal ward on day 30 and was successfully weaned from her tracheostomy on day 41, before being discharged to a rehabilitation facility on day 56 and finally back home on day 75
- Two years after ICU admission, the patient had made full physical recovery and is dialysis-independent
- Since this event, methylene blue has been placed in the ICU pharmacy while Patent Blue V has been moved to the general hospital pharmacy

Conclusion

- In this woman exhibiting severe intoxication with methamphetamine and iatrogenic intoxication to Patent Blue associated with multiple organ failure, treatment with a combination of VV ECMO, CVVHD and CytoSorb hemoadsorption resulted in a rapid and significant reduction in plasma methHb and circulating Patent Blue V, accompanied by improved hemodynamics and normalization in serum lactate levels
- Neither MDMA or Patent Blue have any known antidotes. Therefore, their rapid and effective removal by the CytoSorb cartridge based on clinical parameters offers a unique opportunity in such cases of acute intoxication
- Consequently, there is a potential role for CytoSorb in wider drug intoxications, however this needs to be verified on a wider scale