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CASE REPORT

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# Intentional acetylsalicylic acid acute intoxication and its clinical management

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**Abstract**

In the last decade, our knowledge about OTC drug intoxication has been expanded much further relative to previous years, though the absence of antidotes in some cases results in healthcare professionals using symptomatic treatment. This case report reminds the reader of the importance of clinical and toxicology laboratories in the management of acute salicylate intoxication in order to avoid hemodialysis.

**KEYWORDS**

acetylsalicylic acid, aspirin, intoxication, monitoring

## 1 | INTRODUCTION

Salicylate intoxication is one of the most commonly reported over the counter (OTC) drug intoxications. The management of salicylate intoxication has remained relatively unchanged in the past few decades, with a lack of direct antidote making the treatment more challenging. To improve and control the intoxication and to limit organ damage, the 24/7 clinical (toxicology) laboratory appears to be crucial. This is because clinical care given to patients depends on salicylate dosage, monitoring of renal function, plasma metabolic acidosis and/or alkalosis, plasma bicarbonate, and C-reactive protein (CRP).

The report below outlines the case of a 50-year-old man admitted to the emergency department (ED) of our hospital within the context of a "suicidal attempt by taking a considerable amount of aspirin." The use of clinical laboratory tests appeared to be beneficial in managing intoxication and not only improved the treatment but also positively impacted the patient's length of stay at the hospital, avoiding any organ damage.

## 2 | CASE REPORT

Hereby, we report the case of a 50-year-old man that was admitted around 4 PM in the emergency department (ED) of Saint-Luc hospital in the context of a suicide attempt. On the arrival at the ED, the patient was awake, alert, and oriented with a Glasgow Coma Scale of 15/15. During the anamnesis, the patient revealed the ingestion of 120 tablets of aspirin (acetylsalicylic acid or ASA) 500 mg (total drug intake of 60 g) from the early morning to 11 AM on the same day, before he fell asleep. All tablets had been purchased in various

pharmacies by the patient several days before the intake. The patient had taken different types of ASA (regular and enteric coated in unknown distribution) tablets. The patient woke up around 2 PM, at which point he decided to call the emergency services. Based on this information, the patient was subsequently treated with a single dose of activated charcoal (50 g activated charcoal mixed in water) and hyperhydration (2× Baxter Hartmann Viaflo 500 mL and 1× Baxter Hartmann NaCl 0.09% 1000 mL). Gastric lavage did not seem beneficial as it is recommended up to 1-hour postingestion.[1]

At the time of admission, temperature of the patient was recorded as normal (36.1°C; 96.8° F), his heart rate was 76 beats/min, blood pressure at 170/100 mm Hg, and glycemia at 5.05 mmol/L (value for normal glucose metabolism ≤5.55 mmol/L). Sodium was measured at 147 mmol/L (reference range [RR] 133-145 mmol/L) and potassium at 3.4 (RR 3.5-5.0 mmol/L). The renal function was normal (creatinine 84 μmol/L [RR 53-115 μmol/L], eGFR 0.90 mL/s/m$^2$ [value for normal glomerular filtration rate >0.58 mL/s/m$^2$], urea 10.7 mmol/L [RR 5.4-17.9 mmol/L]). The patient was also taking prescribed methotrexate and folic acid for treatment of his present rheumatoid arthritis, but he was not on ASA therapy for the latter condition.

Electrocardiogram, cardiac markers, and hepatic enzymes were within normal ranges as well as platelet count and hemostasis tests (data not shown). Total white blood cells (13.6 × 10$^9$/L, RR: 4.0-10.0 × 10$^9$/L) and CRP were slightly increased (13 mg/L, value for normal CRP < 5 mg/L). Both stabilized 5 days after the patient's admission. Partial pressure of oxygen [pO2] and carbon dioxide [pCO2] were 10.77 kPa (RR: 11.31-12.64 kPa) and 3.72 kPa (RR: 4.66-5.99 kPa), respectively. A pH of 7.47 (RR: 7.35-7.45) and a bicarbonate level of 21 (RR: 22-28 mmol/L) were also indicative of acid-base disturbance.

More than 30 hours after the admission, pH and bicarbonate were regulated (7.39 and 24 mmol/L, respectively; Figure 1). Biochemistry tests, complete blood count tests, and blood gas tests were performed on the Cobas® 8000 (Roche Diagnostics®), Sysmex® XN-9000 (Sysmex Corporation®), and ABL90 FLEX® (Radiometer®) accordingly. The toxicological analysis revealed a particularly high concentration of salicylates 719 μg/mL (or 5.23 mmol/L; limit of quantification (LOQ) <10 μg/mL or 0.07 mmol/L). In our laboratory, salicylates are measured on the Cobas® 8000, c502 module in heparinized plasma.

Briefly, salicylate and NADH are enzymatically transformed into catechol and NAD, in the presence of salicylate hydroxylase. The decrease of absorbance due to this transformation is measured and proportioned to the concentration of salicylates in the sample. The sample was diluted because salicylates plasma level was above assay range (3-700 μg/mL or 0.02-5.09 mmol/L).

Based on the toxicological result, clinicians decided to admit the patient in the intensive care unit (ICU) immediately. During his stay in the ICU, the patient's condition remained hemodynamically stable. The patient's treatment continued by hydration (3.5 L per day of Hartmann NaCl 0.9%) and 50 gr of activated charcoal every 8 hours only for the first 24 hours. The patient was also treated by sodium bicarbonate (100 mL IV) to increase the renal clearance of salicylates and to reduce the blood-brain barrier passage,[2] and by pantoprazole to prevent gastrointestinal damage. This decision was based on the patient's ASA plasma levels (<1000 μg/mL) during his hospitalization and as there was not any significant comorbidities and/or end-organ toxicity, intensivist decided to use activated charcoal, hyperhydration, and sodium bicarbonate to manage the intoxication instead of hemodialysis. Since laboratory results did not show any sign of anemia or internal bleeding, we did not perform an upper gastrointestinal endoscopy in order to avoid any potential risk of vomiting and aspiration.[3]

Twenty-four hours following the first measurement, the level of salicylates decreased and reached a nontoxic level of 2.0 mmol/L (or 275 μg/mL corresponding to an anti-inflammatory coverage; 100-300 μg/mL or 0.73-2.18 mmol/L; Figure 2). A normalization of pH and bicarbonate was also observed (Figure 1).

Finally, the patient was discharged and returned home after 6 days of hospitalization. A psychiatric evaluation was also planned in order to assess his subsequent behavior and mental state. To this date (more than 8 months later), the patient has not been readmitted to our hospital due to complications of ASA intoxication.

## 3 | DISCUSSION

Acetylsalicylic acid (ASA) or aspirin displays analgesic, anti-inflammatory, and antipyretic properties facilitated by the irreversible inhibition of cyclooxygenase enzymes (COX-1; COX-2 isoenzymes). Low-dose ASA is also used as an antiplatelet agent in the prevention of myocardial infarction and stroke.[4,5] The peak concentration of ASA is approximately 2 hours, and the half-life of ASA is short ($t_{1/2}$:15 min) due to its rapid hydrolysis into salicylate. The normal elimination half-life is between 2-3 hours (mainly by conjugation and eliminated in urines); however, this can increase to 20-30 hours in case of high or toxic dose intake.[4,5] The fraction of its conjugated form is inversely proportional to the dose ingested, due to enzyme saturation.[6]

Concentration of salicylate generally ranges from <60 μg/mL (0.44 mmol/L) to 150 μg/mL (1.09 mmol/L) for analgesic or antipyretic effects and ranges from 150 μg/mL (1.09 mmol/L) to 300 μg/mL (2.18 mmol/L) for anti-inflammatory effects.[4] Higher concentrations of salicylate (>300 mg/L, 2.18 mmol/L)

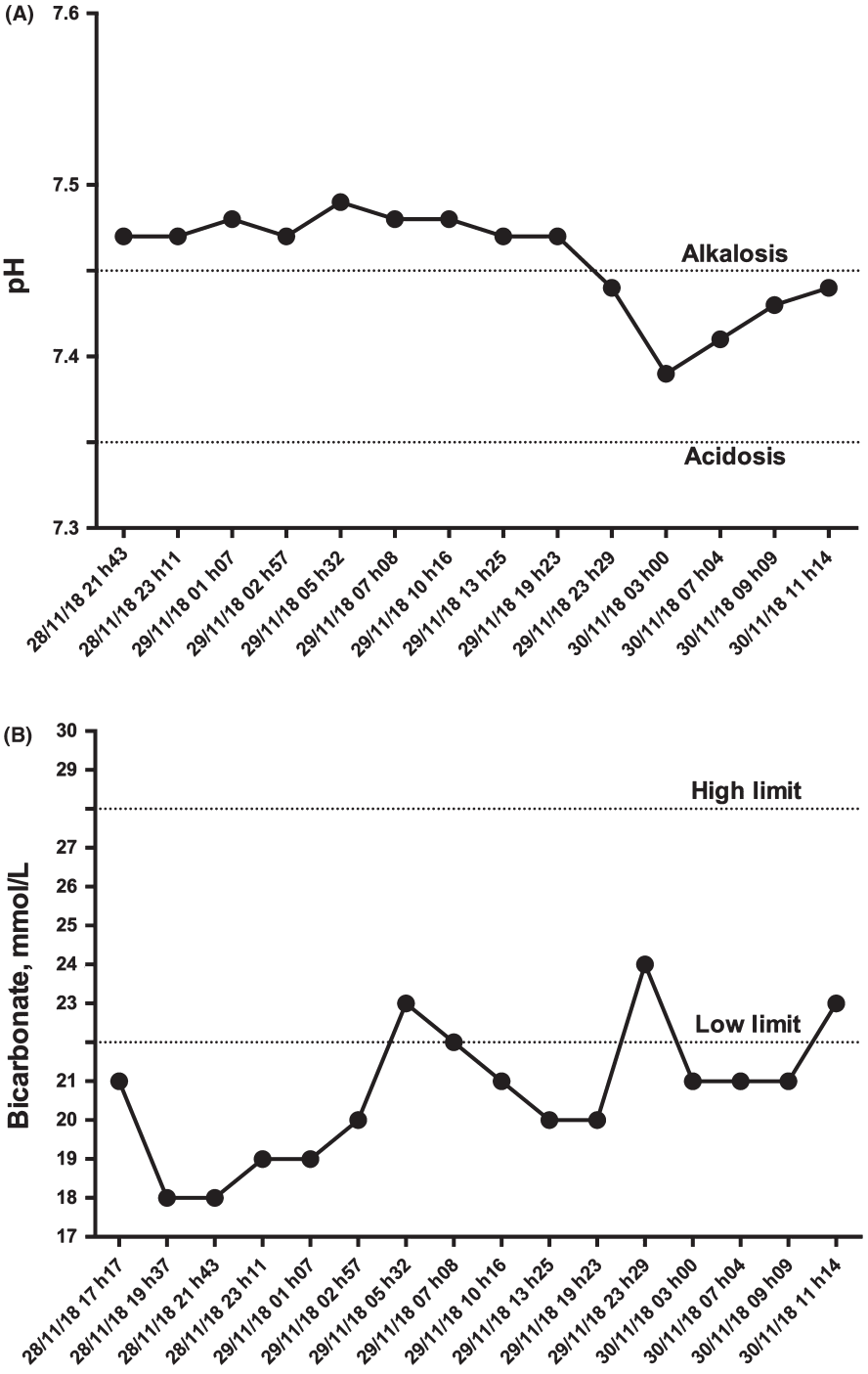


**FIGURE 1** A, Monitoring of pH since the admission of the patient in the ED. B, Monitoring of bicarbonate since the admission of the patient in the ED

are considered toxic, and a concentration >1000 mg/L (7.27 mmol/L) is often chosen as a trigger to hemodialysis.[4,6,7] Hemodialysis is the most effective approach for the treatment of salicylate intoxication[5] and is also considered effective at salicylate concentration <1000 mg/L (7.27 mmol/L) in case of significant comorbidity and end-organ toxicity.[8,9]

To the best of our knowledge, the first published case of ASA poisoning goes back to 1919, outlining the case of a 24-year-old US army sergeant who had taken 200 gr of ASA within 6 hours to treat influenza symptoms.[10] The patient died a day after due to gastrointestinal bleeding.

In a recent study describing 602 acute salicylate fatalities over a 29 year period, the mean peak of salicylate concentration was identified as 991.9 μg/mL (7.21 mmol/L) ± 502.0 μg/mL (3.65 mmol/L).[11] In the cases of intoxication, patients may first be asymptomatic. Thereafter, symptoms including nausea, vomiting, tinnitus, tachypnea, and altered mental status may develop. In adults, respiratory alkalosis is more frequently observed in the case of ASA intoxication, whereas metabolic acidosis occurs more frequently in children.[11]

Although ASA has antiplatelet effects, patients rarely suffer from hemorrhage.[5] In our case, only the respiratory

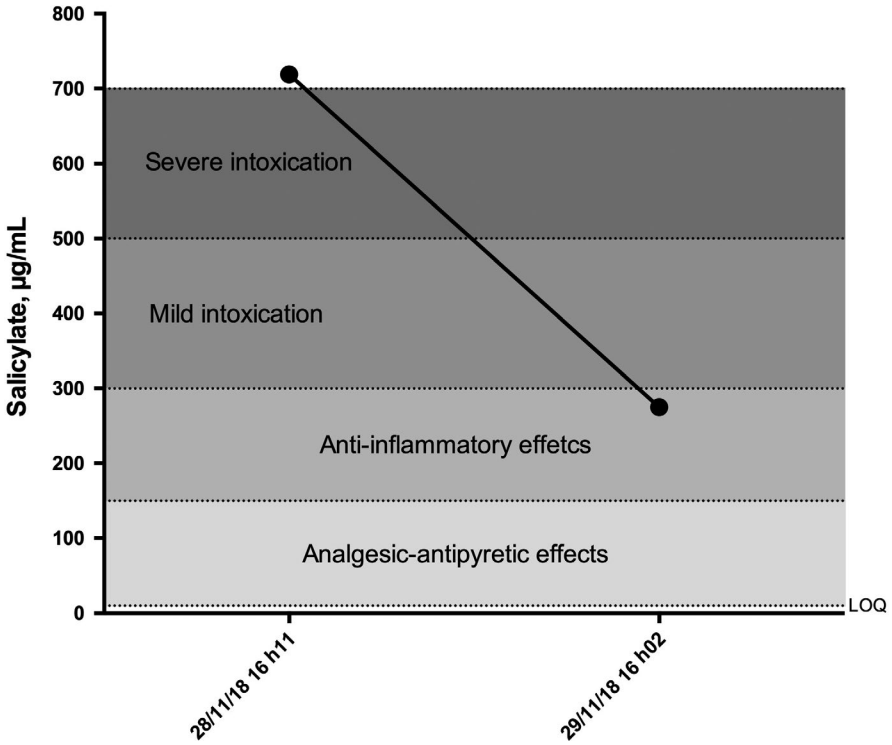


**FIGURE 2** Measurement of salicylate at the admission and 24 h following treatment. References for ranges[4,7].

alkalosis, tinnitus, and irritability were documented. In various case reports, increase in total WBC and CRP was also observed and resolved during the hospitalization.[5]

The measurement of salicylates may also correlate with symptoms. Patients with salicylate concentration <300 µg/mL (2.18 mmol/L) are generally asymptomatic. Concentrations ranging from 300 to 500 µg/mL (2.18-3.64 mmol/L) are related to mild intoxication (nausea, vomiting), and higher concentration between 500 and 700 µg/mL (3.64-5.09 mmol/L) could correspond to severe intoxication (tachypnea, incoordination, respiratory alkalosis, metabolic acidosis). Concentrations above 750 µg/mL (5.45 mmol/L) may well associate with coma, hallucinations, and cardiac or renal failure.[5,12] However, the assessment of salicylate concentrations must always be performed along with a careful evaluation of the patient's clinical status. For example, the maximum concentration of salicylate could be delayed in the case of large dose ASA intake as a result of formation of concretions (especially with sustained release formulations). Clinical manifestations also appear with lower concentrations in case of chronic intoxication.[4,5]

To date, there is no known antidote for ASA intoxication. Current treatments of ASA intoxication include decreasing further absorption (activated charcoal, ipecacuanha syrup, and gastric lavage), increasing elimination by administrating bicarbonate for the alkalization of urine and to accelerate the renal function for cleaning the drug out, correction the electrolytes, and acid-base disturbance and to provide supportive care.[4,5,13-15] Even in the case of very high salicylates plasma levels (>1000 µg/mL), where hemodialysis is considered the most efficient treatment, Dukes et al state that forced alkaline diuresis using hyperhydration (NaCl 0.9%) and sodium bicarbonate solution (2%) was as efficient as hemodialysis in ASA poisoning management.[11,13]

We here reported the efficiency of these low-cost treatments without using hemodialysis in a case of severe ASA intoxication. This could particularly be useful in countries or hospitals with a limited budget and a limited access to hemodialysis.

## 4 | CONCLUSION

In this reported case study, we report the survival of a patient with severe ASA intoxication due to intensive and special care given to him based on his laboratory test results. Even though, there is no antidote for ASA, fast intoxication management based on clinical toxicology laboratory appears to be beneficial in improving the treatment result, ultimately limiting organ damage. Thus, we show that activated charcoal, hyperhydration, and sodium bicarbonate could be used as a treatment in a case of severe ASA intoxication.

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## CONFLICT OF INTEREST

The authors have nothing to disclose and have no conflict of interest.

## AUTHOR CONTRIBUTIONS

Reza Soleimani: conceived of the case report from the laboratory perspective, collected the data, wrote the manuscript in collaboration with Karl Brousmiche and Julien Favresse, reviewed the literature, and responded to the reviewers. Karl Brousmiche and Philippe Hantson: are clinicians involved in the anamnesis, medical description, and supervision of the poisoning management, respectively. Julien Favresse: contributed to a deep literature review and to the manuscript preparation and suggested Clinical case reports as the journal target to publish the case. Vincent Haufroid and Damien Gruson: collaborated to the toxicological and clinical chemistry analytical aspects of the project. Pierre Wallemacq: supervised the whole project: manuscript preparation, responses to reviewers, and covered costs of the work/publication.

## INFORMED CONSENT

An informed consent was signed by the patient for the publication of the case.

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