Heart & Lung xxx (2016) 1–4

Contents lists available at ScienceDirect

Heart & Lung

journal homepage: www.heartandlung.org

Use of continuous renal replacement therapy in salicylate toxicity: A case report and review of the literature

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ARTICLE INFO

Article history:
Received 18 February 2016
Received in revised form
13 May 2016
Accepted 4 July 2016
Available online xxx

Keywords:
Salicylate
Intoxication
Aspirin
Overdose
Hemofiltration
Hemodiafiltration
Continuous renal replacement therapy

ABSTRACT

Objective: To report a case of salicylate toxicity treated with continuous venovenous hemodiafiltration (CVVHDF) and review the literature regarding the use of continuous renal replacement therapy (CRRT) for salicylate toxicity.
Case: A 16-year-old male presented after ingesting 1901 mg/kg of enteric coated aspirin. Salicylate level was 92 mg/dl 4 h after ingestion. Sequele included seizure, acute kidney injury, pulmonary edema, and prolonged QTc. He received 5.5 h of hemodialysis followed by CVVHDF to continue to augment clearance. His aspirin level fell to 37.4 mg/dl after HD and then to 11.3 mg/dl after nearly 10 h of CVVHDF.
Discussion: Cited reasons for the use of CRRT for salicylate toxicity primarily have been hypotension or desire for ongoing augmentation of salicylate clearance in the setting of multiorgan toxicity. CVVHDF may have a role in severe salicylate toxicity to enhance ongoing clearance after an initial round of HD in order to prevent significant rebound.

Published by Elsevier Inc.

Introduction

According to the national poison database, in 2013 about 33,000 acetylsalicylic acid (ASA) and non-ASA salicylate exposures were reported with over 7000 cases requiring treatment in a health care facility and 29 deaths.[1] The primary toxic effects of salicylate occur at the cellular level where it uncouples oxidative phosphorylation, inhibits enzymes involved in the Krebs cycle, stimulates glycolysis and gluconeogenesis, and stimulates fatty acid oxidation.[2,3] In the central nervous system (CNS) it causes cerebral edema, tinnitus, and direct respiratory stimulation leading to hyperpnea and tachypnea.[4–6] In the respiratory system it can cause non-cardiogenic pulmonary edema leading to hypoxemia.[7] Arrhythmias also can occur.[8] The most common abnormal rhythm associated with salicylate toxicity is sinus tachycardia, however, cases of sinus bradycardia, atrial fibrillation, as well as monomorphic and polymorphic ventricular tachycardia have been reported.[8] Treatment includes supportive measures aimed at optimizing electrolytes and fluid status, enhancing drug elimination, and in certain circumstances preventing further drug absorption. In less severe intoxications drug elimination can be enhanced non-invasively with volume expansion and urine alkalization, however, in severe intoxications hemodialysis (HD) is indicated to achieve rapid toxin clearance. In a published review of California poison control records, over a 10 year period salicylates were the most common toxin for which HD was performed (29 of 88 cases).[9]

In 2015 evidence-based guidelines for the use of extracorporeal treatment of salicylate poisoning were published by the Extracorporeal Treatments in Poisoning (EXTRIP) Workgroup, a multidisciplinary international group focused on providing evidence-based guidelines for use of extracorporeal treatments in poisoning. The EXTRIP guidelines recommended indications for extracorporeal salicylate removal as presence of altered mental status, acute respiratory distress syndrome requiring supplemental oxygen, or if

Financial support: none.
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0147-9563/$ – see front matter Published by Elsevier Inc.
http://dx.doi.org/10.1016/j.hrtlng.2016.07.003

standard therapy is deemed to be failing regardless of salicylate level.[6] Additionally, the guidelines suggested indications for dialysis based on salicylate levels regardless of signs or symptoms as salicylate level >90–100 mg/dl if there is no renal dysfunction and levels >80–90 mg/dl if renal function is impaired.[6] Severe academia with pH < 7.2 in the absence of other indications was also suggested as an indication although the authors of the guidelines gave this as a weaker recommendation.[6] HD is the preferred first line method of salicylate removal because it achieves more rapid drug clearance compared to other modalities.[6] Despite this there are some practical advantages to continuous renal replacement therapy (CRRT) that make its use attractive.[10] Two key advantages are that it can be set up and run in the ICU with staff and equipment that is readily available, and it can be run 24 h a day.[10] Currently published data on the use of CRRT for salicylate toxicity is extremely limited. In this report, we will discuss the use of continuous venovenous hemodiafiltration (CVVHDF) after initial HD in the treatment of an adolescent with multiorgan toxicity from aspirin overdose and will summarize the current available data on CRRT and salicylate toxicity including mode, timing and duration or CRRT as well as the reason for CRRT use.

Case

A 16-year-old male with depression and type 1 diabetes mellitus presented with altered mental status after ingesting 135 g (1901 mg/kg) of enteric coated aspirin. He had a generalized tonic clonic seizure that resolved with treatment with benzodiazepines. Initial salicylate level was 90.6 mg/dl, 4 h after ingestion and EKG revealed a QTc of 550. Sodium bicarbonate infusion was started, and he was transferred to the intensive care unit (ICU).

On arrival to the ICU the patient was sleepy but arousable, would answer a few questions and then fall back asleep and would only intermittently follow commands. He was afebrile with heart rate 94, blood pressure 124/57 mm Hg, respiratory rate 27, and oxygen saturation 99% on 2 L nasal canula. The nasal canula was discontinued several hours after arrival to the ICU and the patient remained breathing room air throughout the duration of his hospitalization. Physical examination was notable for kussmaul respirations and he complained of tinnitus, chills, headache, changes in vision described as “bright lights and black spots.” His chest radiograph showed prominence of his pulmonary vasculature, however, lungs were clear to auscultation. Admission labs showed a salicylate level of 92.2 mg/dl 8.5 h after ingestion, venous blood gas: pH 7.48 pCO_2 21 mm Hg, bicarbonate 14 meq/l, ionized calcium of 0.96 mmol/l (1.12–1.32 mmol/l), creatinine of 1.3 mg/dl normal liver enzymes, lactate 4.3 mmol/l, and urine pH of 6.

A femoral vascular catheter was placed and HD was started using an optiflux 180 filter with a prescribed blood flow rate of 300 ml/min and dialysate flow rate of 800 ml/min and no fluid removal. Salicylate levels were followed hourly through the first day of hospital admission. Blood flow rates varied through the course of HD (100–250 ml/min). This was because the catheter was in the femoral vein and the patient repeatedly moved the leg despite directions to keep the leg straight causing kinking in the catheter leading to difficulty achieving consistent flow rates. Duration of HD was 5.5 h. At the end of HD and prior to initiation of CRRT the salicylate level had decreased from 87.7 mg/dl to 37.4 mg/dl (Fig. 1), and his arterial blood gas was: pH 7.55, pCO_2 24 mm Hg, bicarbonate 21 meq/l. The patient was then transitioned to CVVHDF with a Prismaflex CRRT machine, HF 1000 filter, ultrafiltrate rate of 2.7–3.7 ml/min, blood flow rate of 150 ml/min, dialysate flow rate of 1000 ml/h, and a target net even fluid balance. The salicylate level decreased from 30.5 mg/dl to 11.3 mg/dl after 9 h and 53 min if CVVHDF (Fig. 1). A follow up level about 2.5 h later was 25.9 mg/dl signifying a rise while still on CVVHDF, however, as the patient’s symptoms had resolved, and QTc had normalized the decision was made to stop CVVHDF at that time. The total duration of CVVHDF was 12.5 h. His arterial blood gas at the end of CVVHDF was: pH 7.51, pCO_2 30 mm Hg, bicarbonate 24 meq/l. The salicylate level peaked at 32.8 mg/dl 3 h after CVVHDF was stopped (Fig. 1) without further signs or symptoms and then subsequently fell to undetectable levels. His respiratory alkalosis had nearly resolved by 30 h after cessation of CVVHDF with arterial blood gas of pH 7.44, pCO_2 35 mm Hg, bicarbonate 24 meq/l.

Discussion

Extracorporeal removal of salicylate has been achieved with HD, hemoperfusion, CRRT, peritoneal dialysis (PD), and exchange transfusion.[6] To date 9 cases of salicylate intoxication treated with CRRT have been reported in the literature, (8 in acute overdose and

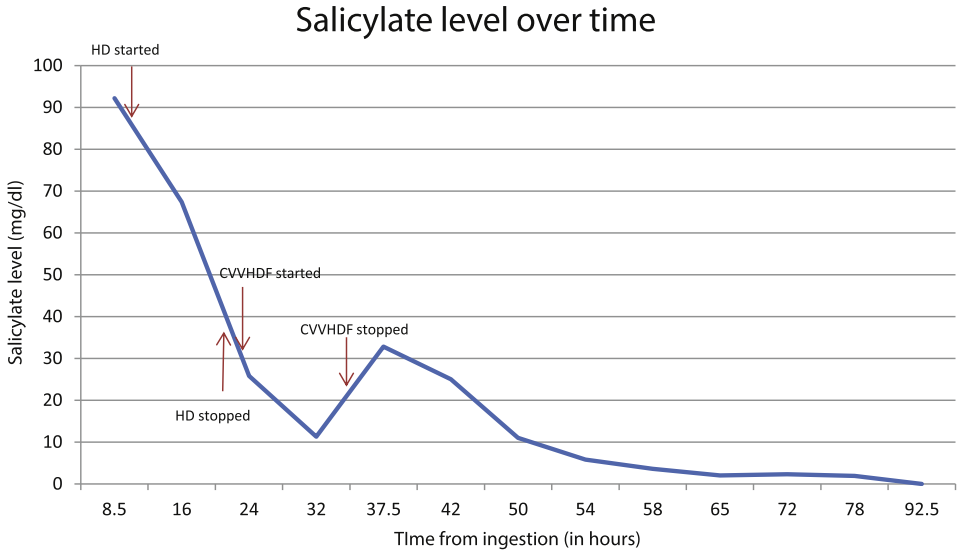

Fig. 1. Graph of salicylate as a function of time.