

Ibuprofen Overdose Requiring Vasopressor Support in a Pediatric PatientAnthony DiPasquale¹, Alexander B. Norinsky^{1*} Natali Snyder¹¹Department of Emergency Medicine, Rowan University SOM, Kennedy University Hospital, Stratford, NJ, USA.**Corresponding Author:** Alexander B. Norinsky, Department of Emergency Medicine, Rowan University SOM, Kennedy University Hospital, Stratford, NJ, USA, **Tel:** 646-241-5695; **Email:** alexnorinsky@gmail.com**Received Date:** 14 Feb 2017**Accepted Date:** 23 Feb 2017**Published Date:** 27 Feb 2017**CASE PRESENTATION**

Here we present the case of a 14-year-old female who presented to our community emergency department after reportedly ingesting about 30 tablets of an unknown medication while at school about 2 hours prior to arrival. She denies suicidal ideation, gestures, plan or attempt (although she admitted a history of suicide attempts); stating she took it for relief of knee pain. The medication was her friend's. She reported malaise, nausea, dry mouth, blurry vision, jitteriness, and dyspnea; denying any other systemic complaints, including vomiting of pill fragment, chest or abdominal pain, diarrhea, headaches, syncope, light-headedness, or diaphoresis.

She had no medical or surgical history, and denied drug or food allergies. She took no medications on a daily basis, and all immunizations were up-to-date. The patient admitted to smoking marijuana once within the past month; no other illicit drug intake, as well as no alcohol or tobacco products.

Given her significant presentation, she was dispositioned as ESI level 1 (emergency severity index, on a scale from 1 to 5, with a lower number representing higher acuity). Initial vital signs were as follows: blood pressure 105/54 mmHg, pulse rate of 130 beats per minute and regular, respirations of 14 breath per minute, saturating 100% on ambient air, and axillary temperature of 98.8 Fahrenheit. On examination, she was somnolent but arousable to loud verbal as well as noxious stimuli; Glasgow Coma Scale 14. On physical examination, she appeared toxic and uncomfortable. Neurologic exam including speech and mentation were intact, aside from her eyes which were 3 mm bilaterally, not reactive to light and exhibited roving movement. Cardiopulmonary exam was insignificant aside from the tachycardia as noted. Skin was not diaphoretic, of normal colour and without piloerection. She weighed 52 kg (BMI: 19).

A work-up was immediately undertaken focusing on suspected overdose, inflammatory and cardiac markers. Lactate was 3.7 mmol/L (reference range: <2.2). Arterial pH 7.34. Remaining

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bloodwork, including electrolytes, blood counts, liver/kidney/pancreas functions, cardiac biomarkers, coagulation studies, osmolality, urinalysis, urine drug screen, alcohol, and salicylate levels were unremarkable. Her urine pregnancy was negative. A portable plain chest film was without an acute process. An electrocardiogram done upon initial presentation and repeated about 3 hours later both revealed sinus tachycardia in the 120-130 beats per minute, with normal axis and intervals (QRS 84 and 110 milliseconds, QTc 457 and 489 milliseconds, respectively), without an acute current of injury.

Intravenous fluids in the form of normal saline were ordered as well as lorazepam for agitation. Naloxone was also attempted for somnolence without a response. Despite a weight-based dose for fluid resuscitation, her blood pressure was 84/57 mmHg; she remained tachycardic in the 120s, vital signs otherwise were stable. A central line was placed and Dopamine initiated.

Anticholinergic overdose was briefly entertained, although her clinical presentation did not completely align with the familiar toxidrome. More information was soon available when the patient's parents arrived: the mother strongly suspected she took Motrin from one of her friends, estimated to be about 18 grams (30 tablets, 600 mg each). It was also discovered she was taking oral contraceptives, valacyclovir, and was on a course of ciprofloxacin for cystitis. Pantoprazole was added intravenously.

Importantly, an initial acetaminophen level of 18 mcg/mL (reference range: <25) was subsequently re-drawn about 5 hours later and was found to be increased to 41. After discussion with the pediatric intensivists, N-acetylcysteine was administered. On further questioning, she adamantly denied ingesting acetaminophen, combination or any other products. She was transferred to a tertiary care center for continued care in the pediatric intensive care unit. Prior to her discharge from the emergency department, her blood pressure had stabilized

to 90/52 mmHg on Dopamine 10mcg/kg/min; her heart rate remained in the 120s.

DISCUSSION

Ibuprofen overdose manifesting clinically as shock and altered mental status is a relatively rare clinical entity encountered in the emergency department. Given the relative ease with which almost anybody can obtain a potentially unlimited amount of NSAIDs and related products (over 30 billion doses of NSAIDs are ingested in America each year), it is important for clinicians to be aware of the potential symptoms of overdose patients. According to a recent study from the American Association of Poison Control Centers National Poison Data System (AAPCC-NPD) [1], the majority of NSAID ingestions occurred in the pediatric population (over 50,000 cases in children 5 years old or younger).

Ever since the mid-1980s, case reports identified a number of potential deleterious effects affecting the nervous system (e.g. seizures, visual complaints, and somnolence), gastrointestinal upset, renal dysfunction, and cardiovascular collapse (hypotension and bradycardia). In one report, the mean ingestion dosage where symptoms became evident in the pediatric population was 440 mg/kg (also noting that ingestions of less than 99 mg/kg generally developed no symptoms) [2]. More recently, in the 2013 AAPCC-NPD study mentioned above, they reported less than 100 major toxicity outcomes (most commonly due to naproxen or ibuprofen; four of the deaths were secondary to ibuprofen). Similarly in Great Britain a decade ago [3], only seven cases of death were attributed to ibuprofen overdose (out of 1033 patients; 0.67%).

A review of the mechanism of action adds little insight into the toxicity patterns. Briefly, nonsteroidal anti-inflammatory drugs work by inhibiting cyclooxygenase (COX) reversibly, which subsequently decreases the formation of prostaglandins and thromboxanes, thus addressing pain and inflammation. In contradistinction, acetaminophen works on COX in the central nervous system, while salicylates bind to the same enzyme irreversibly, effectively inactivating the following pathway. However, the exact connection to the nervous and cardiovascular systems is yet to be determined. It has been well established in multiple sources that available ibuprofen nomograms poorly correlate with severity of disease. As such, it is generally not recommended to check ibuprofen concentration levels.

An excellent review of the literature [4] was recently published reviewing the various biochemical pathways and manifestations of toxicity, however even here there is no discussion of hemodynamic instability as in our case; there is scant literature available for examples and recommendations beyond scattered case reports. One significant case [5] reported a

14-year-old male who ingested about 50 grams of ibuprofen and required extracorporeal membrane oxygenation secondary to refractory hypotension despite multiple vasopressors (norepinephrine, phenylephrine, and vasopressin). He exhibited the other, more common consequences of ibuprofen toxicity as well, including GI and renal issues; nonetheless, he had a full recovery in less than one week with no residual sequelae. Another case [6] reported a 26-year-old female who ingested about 105 grams of ibuprofen: vasopressors (epinephrine and norepinephrine) were initiated secondary to persistent hypotension, however she eventually succumbed. Several other cases have been reviewed as well with similar consequences and outcomes [7-9]. Based on our patient's weight, it may be extrapolated that she ingested a significantly smaller dose than as quoted in these case reports (18 grams), and in fact below the often quoted "440 mg/kg" figure as mentioned earlier when symptoms become evident (she would need to have ingested about 24 grams).

CONCLUSION

Our patient was unfortunately lost in follow-up and the clinical course is unknown at this time. She was seen in our emergency department about 2 years later for suicidal ideation, and as far as can be interpreted from chart review she was in good health and had no subsequent negative sequelae. Ibuprofen overdose must be considered on the differential diagnosis and work-up for all overdose patients; this especially holds true in a scenario when the ingestant is not known, the patient is hemodynamically unstable, and the remaining level-able agents (e.g. salicylates) are negative. The ease with which one may obtain a vast amount of NSAIDs mandates the emergency physician be intimately aware of the presentation and clinical course of this challenging diagnosis, in spite of the fact that the greatest majority of overdoses remain relatively benign. Our case reports is important in emphasizing these points, as well as highlighting an important new finding: life-threatening disease may be evident in ibuprofen toxicity in doses much less than previously quoted.

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