Clinical Toxicology

Severe metabolic acidosis complicating massive ibuprofen overdose

Andrew Downie, Amza Ali and Derek Bell

Department of Thoracic Medicine, Central Middlesex Hospital, London NW10 7NS, UK

Summary: We report the progress of a patient who presented following the ingestion of ibuprofen in overdose. He survived despite developing an extremely severe metabolic acidosis.

Introduction

Ibuprofen is a widely prescribed non-steroidal anti-inflammatory drug that is now also available for over-the-counter sales. It has low toxicity in overdose, and serious effects are rare. Significant acidosis has been described only occasionally.

We describe a case of severe ibuprofen overdose in which metabolic acidosis developed to a degree previously unreported, but in which the patient ultimately made a full recovery.

Case report

A 33 year old unemployed man presented in casualty with a history of heavy alcohol consumption the previous night, and the ingestion of approximately 60 g of ibuprofen (Motrin 600 mg) and 0.25 g of diclofenac (Voltarol 25 mg) tablets against a background of chronic social problems. At least 9 hours had elapsed from the time of ingestion to being seen in hospital.

He was unconscious and shocked with a blood pressure of 54/34 mmHg and a tachycardia of 122 beats/minute. There was spontaneous respiration but deep coma with small reactive pupils, no spontaneous eye movements and negative doll’s eye reflex. There were no spontaneous limb movements, no response to painful stimuli, and absent reflexes and plantar responses. He appeared well nourished with no stigmata of chronic liver disease.

Arterial blood gases performed on admission demonstrated a severe metabolic acidosis (pH 7.0, P CO\textsubscript{2} 4.0 kPa, P O\textsubscript{2} 17.8 kPa, HCO\textsubscript{3}⁻ 9.3 mmol/l, base excess -22.6 mmol/l). Blood chemistry demonstrated renal impairment (Na 139 mmol/l, K 5.7 mmol/l, bicarbonate 5 mmol/l, urea 6.3 mmol/l, creatinine 226 μmol/l, glucose 4.3 mmol/l). The electrocardiogram showed sinus tachycardia and the initial chest X-ray was unremarkable. Urinalysis was negative for blood, protein and ketones. Samples taken for toxicology approximately 9 hours after ingestion demonstrated 1,000 mg/l of ibuprofen and 1.1 g/l of ethanol. No diclofenac, salicylate, paracetamol, ethylene glycol or methanol were detected.

He required intubation to protect his airway. Activated charcoal was given via a nasogastric tube. Initial resuscitation was with a combination of crystalloid and colloid, to a total of 7.5 litres and 3.5 litres, respectively, in the first 12 hours after admission. This resulted in a prompt restoration of blood pressure and urinary flow, but despite adequate volume expansion, as judged by central venous pressure recording, his acidosis worsened (pH 6.88, P CO\textsubscript{2} 4.2 kPa, HCO\textsubscript{3}⁻ 5.9 mmol/l, base excess -26.2 mmol/l) and he remained cardiovascularly unstable, with a brief profound bradycardia (30 beats/minute) and brief, intermittent episodes of hypotension. In view of this 200 mmol of sodium bicarbonate was infused slowly, with a gradual improvement in his acidosis. He regained consciousness and was extubated 24 hours after the initial insult, but a significant acidosis persisted for a further 12 hours. He ultimately made a full recovery and his renal function returned to normal, although he developed a progressive bilateral perihilar pulmonary infiltrate on the chest X-ray during the first 3 days after admission, which had resolved at follow-up 3 weeks later.

Discussion

Ibuprofen, in common with most non-steroidal anti-inflammatory drugs, is considered to be of low toxicity in overdose. Minor symptoms such as
gastrointestinal disturbance and central nervous system depression are common in doses exceeding 100 mg/kg. Serious effects are rare but have been reported in cases where over 400 mg/kg has been taken.\textsuperscript{1,2} These include coma, respiratory depression, acute renal failure and hypotension.\textsuperscript{3-5} However, both minor and major effects are poorly correlated to serum levels.\textsuperscript{2} Reported fatalities are rare; of seven reported cases, three involved significant co-ingestion of salicylates, and three died of septic complications rather than direct toxic effects.\textsuperscript{1,2,6} In contrast Court and Volans reported a level of 704 mg/l in a symptom-free adult,\textsuperscript{7} and McElwee et al. related a case of coma and mild metabolic acidosis with recovery, with a serum level of 1,034 mg/l, the highest reported.\textsuperscript{1} By comparison, the peak serum ibuprofen level after a single 400 mg dose is of the order of 37 mg/l.\textsuperscript{7}

Although metabolic acidosis is uncommon, Linden and Townsend, and Primos et al., reported three young children who each developed uncompensated increased anion gap metabolic acidosis after taking 500–600 mg/kg of ibuprofen. Each child recovered fully in 12–24 hours.\textsuperscript{8,9} Lee and Finkler reported a 48 year old man who took over 20 g of ibuprofen and developed severe metabolic acidosis (pH 7.06) associated with renal impairment, acute liver cell injury, thrombocytopenia, adult respiratory distress syndrome and probable sepsis. His serum ibuprofen level was 185 mg/l 10 hours after ingestion. Eventually he recovered with supportive therapy.\textsuperscript{4}

The patient we describe took a massive overdose of approximately 800 mg/kg of ibuprofen and developed several complications (coma, hypotension, acute renal impairment), and developed a severe metabolic acidosis to a degree not previously reported. Despite this he made a full recovery with supportive therapy, including aggressive fluid replacement and the judicious use of sodium bicarbonate.

Interestingly he also developed delayed interstitial changes on his chest X-ray at a time when he was not clinically fluid overloaded. Lung involvement has only been described once before, when similar changes were associated with respiratory failure, not a feature in our patient.\textsuperscript{10}

There are a number of possible causes for this degree of acidosis. There were no unusual fluid losses to cause hyperchloraemic acidosis. His initial hypovolaemia would predispose to lactic acidosis, but this cannot be the major factor given that following the prompt restoration of his circulating volume and blood pressure his acidosis actually worsened and persisted for a further 24 hours. While a lactate level was not available, in another reported case of acidosis, lactate was found to be only marginally elevated.\textsuperscript{9}

Although alcohol was also taken in considerable quantity, significant alcohol-induced ketoacidosis seems very unlikely, given that it usually occurs in the undernourished chronic alcohol abuser, causes ketonuria and is almost invariably associated with hypoglycaemia. None of these factors was present in this case. However, the alcohol probably contributed to his initial hypovolaemia. Poisoning by salicylates causes metabolic acidosis by uncoupling oxidative phosphorylation, but this has not been shown with other classes of non-steroidal anti-inflammatory drug.

Ibuprofen and its two main metabolites (2-carboxyibuprofen and 2-hydroxyibuprofen) are themselves acidic. We believe this, and the large quantity ingested, are the main factors causing this patient’s acidosis. The slow resolution is in keeping with the gradual elimination of the drug. However, the extreme degree of acidosis may be due to other exacerbating factors, namely his hypotension and impaired respiratory compensation (both are recognized effects of ibuprofen overdose) and the co-ingestion of alcohol, itself a frequent association with drug overdose.\textsuperscript{11} We conclude that ibuprofen can produce severe metabolic acidosis following significant overdose and recommend arterial blood gas analysis in monitoring such cases to allow detection of this uncommon but potentially life-threatening complication. However, this case also emphasizes that even in cases of severe toxicity due to ibuprofen, full recovery is possible with supportive measures.

Acknowledgement

We thank the National Poisons Unit, New Cross Hospital, for their assistance and analysis of samples.

References


Severe metabolic acidosis complicating massive ibuprofen overdose.
A. Downie, A. Ali and D. Bell

doi: 10.1136/pgmj.69.813.575

Updated information and services can be found at:
http://pmj.bmj.com/content/69/813/575

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/