

Nurofen Plus misuse: an emerging cause of perforated gastric ulcer

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Over a 6-month period, two patients presented to a community hospital emergency department with perforated gastric ulcers as the result of recreational misuse of over-the-counter ibuprofen–codeine preparations. Misuse of these medications appears to be an emerging cause of significant morbidity in patients with codeine addiction. (MJA 2008; 188: 56-57)

Clinical records

Patient 1

A 39-year-old woman was referred by her general practitioner to the emergency department (ED) of our community hospital with a 24-hour history of acute epigastric pain. She had a past history of alcohol misuse, codeine misuse and pancreatitis.

While in the ED, she described recreationally taking 16–24 Nurofen Plus tablets (Reckitt Benckiser, Sydney, NSW) (containing ibuprofen and codeine) per day for the previous 3 weeks. Clinical examination revealed pallor, mild diaphoresis, a heart rate of 130 beats/min and blood pressure of 92/60 mmHg. The patient's abdomen was grossly distended and maximally tender on palpation in the epigastrium. Bowel sounds were absent. Intravenous access was established and infusion of 2 L crystalloid fluid was commenced.

An erect chest x-ray confirmed the presence of gas under the diaphragm (Box 1). An urgent laparotomy revealed a perforated anterior gastric antrum ulcer and 2.6 L of green turbid fluid in the peritoneal cavity. The patient was given an additional four units of packed red cells intraoperatively, and her ulcer was oversewn. Postoperatively, she was transferred to an intensive care unit at another hospital.

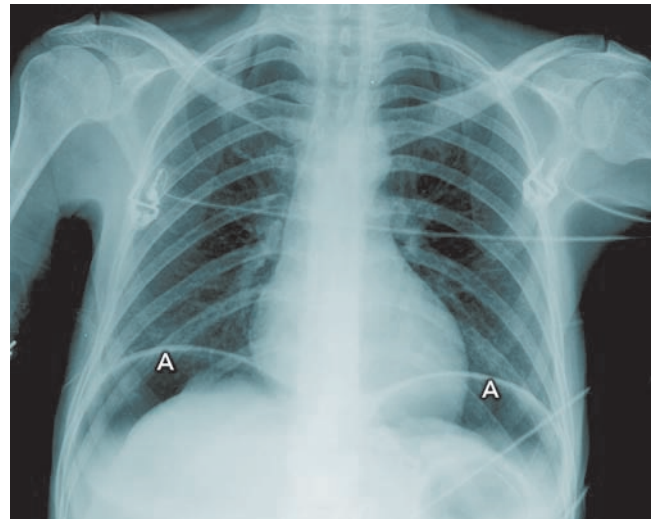
Patient 2

A 41-year-old man presented to our ED with a 12-hour history of progressively worsening severe abdominal pain. The patient had been recreationally taking "a packet" of Nurofen Plus each day for the past year. To ease the abdominal pain, he had already tried a liquid paraffin-based laxative (Parachoc [Paedpharm, Sydney, NSW]) and an osmotic laxative (Microlax [Johnson & Johnson Pacific, Sydney, NSW]) at home, with no relief of his discomfort. Clinical examination revealed generalised abdominal tenderness, with no guarding, and the presence of bowel sounds. He had a heart rate of 93 beats/min and blood pressure of 143/93 mmHg.

The pain initially settled in the ED after the patient had received a total of 10 mg intravenous morphine over a 2-hour period. After admission for observation, he developed a slight fever (37.8°C), his heart rate increased to 120 beats/min, and his abdomen became increasingly distended. Pain recurred on the ward, and was not responsive to 20 mg intravenous morphine given over a 2-hour period.

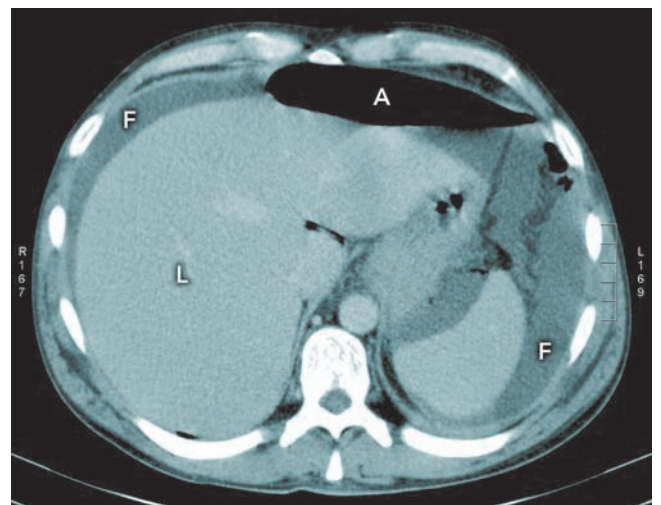
Intravenous contrast computed tomography revealed the presence of free fluid and gas in the peritoneal cavity (Box 2). An urgent laparotomy revealed a 1.5 cm gastric antrum ulcer with gross peritoneal contamination. Postoperatively, the patient was offered care at an inpatient drug and alcohol service, but absconded before transfer could be arranged.

1 Erect portable chest x-ray of a 39-year-old woman with acute abdominal pain



A = free air under the diaphragm. ♦

2 Computed tomography image of the abdomen of a 41-year-old man with acute abdominal pain



A = free air within the peritoneal cavity. F = free fluid within the peritoneal cavity. L = liver. ♦

Discussion

Ibuprofen–codeine preparations first entered the Australian over-the-counter (OTC) market in October 2002. The leading product in the market, Nurofen Plus, contains 200 mg ibuprofen and 12.8 mg codeine phosphate in each tablet,¹ making it the strongest codeine tablet available in Australia without prescription.

Codeine phosphate is a known drug of misuse. Ibuprofen–codeine products are particularly vulnerable to misuse because of the relatively high amount of codeine contained in each preparation and the absence of toxicity in overdose that is associated with paracetamol preparations.

Several cases of severe hypokalaemia secondary to ibuprofen-induced renal tubule acidosis after Nurofen Plus misuse have been reported in the literature.^{2–4} One study showed that patients with acute upper gastrointestinal presentations were 5.2 times more likely to have consumed high-dose OTC non-aspirin non-steroidal anti-inflammatory drugs within the previous week, and the increased risk was dose-dependent.⁵

To our knowledge, the two cases described here are the first reports of perforated gastric ulcers associated with recreational Nurofen Plus misuse.

The database of Australia's Adverse Drug Reactions Advisory Committee (ADRAC) relies on voluntary reporting, and a drug's adverse reaction profile becomes better defined as the market gains experience with it. As at July 2007, there had been 26 cases reported to ADRAC of adverse events in patients taking Nurofen Plus (Dr Patrick Purcell, Medical Officer, Adverse Drug Reactions Unit, Therapeutic Goods Administration, personal communication). ADRAC records show that Nurofen Plus was the sole suspected agent associated with two duodenal ulcer perforations. The first case involved a 28-year-old woman who took eight tablets a day "for a period of months" for back pain, and the second involved a 24-year-old woman for which there was no further clinical information. ADRAC has received no reports of perforated

gastric ulcers associated with Nurofen Plus, and only one report of this condition in a patient taking an ibuprofen-only preparation.

With only two patients presenting to our community hospital with perforated gastric ulcer in the past 6 months, the presentation is unusual. Misuse of ibuprofen–codeine analgesics, associated with both cases, appears to be a new and important aetiology for this condition.

Vigilant reporting of adverse drug reactions to ADRAC, tighter enforcement of legislative requirements for the dispensing of pharmacy-only medicines, or reformulation of this product (as has occurred with OTC pseudoephedrine products) may help to minimise the health sequelae of ibuprofen–codeine misuse.

Competing interests

None identified.

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