Case report

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STOMACH PERFORATION FROM PIROXICAM POISONING

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An 8-year-old girl presented with stomach perforation one week after piroxicam poisoning. Six hours before hospitalization, the girl had accidentally taken piroxicam capsules in a total dose of 280 mg. At admission the child did not present signs and symptoms of intoxication of piroxicam. In spite of the late time of presentation from piroxicam exposure, we performed gastric lavage, and administered activated charcoal and laxatives. The patient was discharged after 24 hours, in good clinical condition, but without gastro protective medication. After a period of seven days the patient was readmitted to the PICU, with signs and symptoms of acute abdomen: severe epigastric pain whose intensity increased with the change of position, nausea, vomiting, fever and chills. On physical examination, abdominal rigidity of the muscles was noticed. On the abdominal X-ray free air in the abdomen was visualized. The child underwent emergency surgery. Stomach perforation was identified and corrected. Ten days after the surgery, the child was discharged, fully recovered. **Conclusion -** We present this rare case to alert physicians to the necessity of monitoring abdominal signs and symptoms and consideration of use of gastro protective agents after piroxicam overdose in a child.

Key words: Piroxicam overdose ▪ Gastrointestinal ulceration delayed onset ▪ Gastro protective agents ▪ Child

Introduction

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) commonly used for analgesia, following day care surgery. It is not often used in children and should not be prescribed below 6 years of age (1, 2). NSAID use

is associated with an increased risk of serious adverse gastrointestinal events including bleeding, ulceration, and perforation of the stomach or intestines (2). These serious adverse events may occur in patients treated with NSAIDs at any time, with or without warning symptoms. Only one in five patients who develop serious adverse upper gastrointestinal (GI) events on NSAID therapy is symptomatic (3). Due to the increasing use of anti-inflammatory agents, it seems important to draw attention to the potential serious effects of accidental over-dosage (4). The long plasma half-life should be considered when treating an overdose with them.

We present a case of stomach perforation one week after piroxicam poisoning. Through this case we seek to underline to doctors that in piroxicam poisoning, immediate treatment is important, as well as the ongoing reassessment of patient because of long plasma half-life.

Case report

An 8-year-old girl was admitted to our Pediatric Intensive Care Unit (PICU), intoxicated with piroxicam (Feldene®). Six hours before hospitalization, the patient had accidentally taken 14 piroxicam capsules (20 mg/capsule, total 280 mg). On admission the child did not present signs and symptoms of GI bleeding/or ulcers (epigastric pain, dyspepsia, melena and hematemesis). The laboratory tests (complete blood count, serum electrolytes, renal and liver function) were normal. No history of gastritis or ulcer, medical treatment with NSAID or corticosteroids was present in the anamnesis vitae. In spite of the late time of presentation from piroxicam exposure, we performed gastric lavage, and administered activated charcoal and laxatives. The patient was discharged after 24 hours, in good clinical condition, but without gastro protective medication.

After a period of seven days the patient was readmitted to the PICU, with signs and symptoms of acute abdomen: severe epigastric pain, whose intensity increased with the change of position, nausea, vomiting, fever and chills. On physical examination, abdominal rigidity of the muscles („wooden belly“) was noticed. On the abdominal X-ray, free air was visualized in the abdomen (Fig. 1). The child underwent emergency surgery. Stomach perforation was identified and corrected (Fig. 2). Ten days after the surgery, the child was discharged fully recovered.

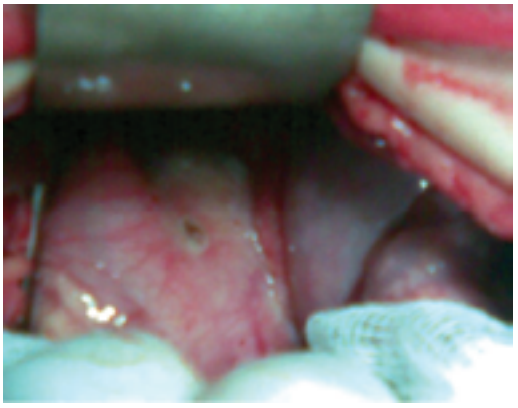

Fig. 1 *The stomach perforation.*

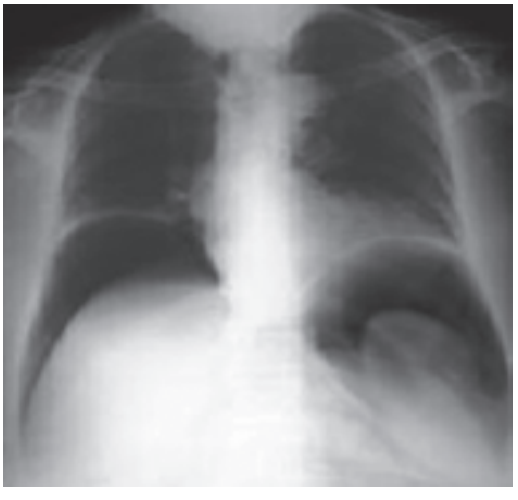

Fig. 2 *Upright chest radiograph shows a large pneumoperitoneum outlining the spleen and the superior surface of the liver.*

Discussion

NSAID exposure of both short and long duration causes an increased risk of serious gastrointestinal events, including bleeding, ulceration, and perforation of the stomach or intestines (1, 2, 5, 6). Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3 to 6 months, and in about 2 to 4% of patients treated for one year (3). Evidence from observational studies suggests that piroxicam may represent a high risk of serious gastrointestinal toxicity relative to other NSAIDs (5). Approximately 20% of patients experience side effects with piroxicam, and about 5% of patients discontinue its use because of such effects (7).

Data published so far about overdoses of piroxicam in children are insufficient. We found only a case report with piroxicam poisoning in a 2 –year old child, who had taken 5 piroxicam capsules (≈ 8 mg/kg) and developed severe multisystem toxicity (5). From one post – marketing study of poisoning among people who took piroxicam, presented by eHealthMe, based on 6 reports from FDA and the user community (May 2012), 2362 patients reported having side effects after taking piroxicam. Among them, 6 patients (0.25%) experienced poisoning. None of them was a child (8).

In children, the maximum daily dose of piroxicam is 0.4 mg/kg once daily (1, 2). It should not be used below 6 years of age (1, 5). Our patient received 14 piroxicam capsules of 20 mg (≈ 10 mg/kg), approximately 25 times more than the therapeutic dose. According the protocols for poisoning treatment (5, 6, 7) our patient was treated by gastric lavage, activated charcoal and laxative, but with no favourable effect. This was probably due to the quick oral absorption of piroxicam at acid pH, achieving thus high concentrations in plasma within 2-3 hours (7, 9, 10).

A single piroxicam dose of 20 mg generally peaks with plasma levels of 1.5 to 2 mcg/ml (2, 5, 6, 7). The patient had taken 14 capsules of 20 mg. We did not measure the plasma level, but theoretically plasma levels could have been 28 mcg/ml, approximately 14 times higher than expected for the therapeutic dose. There are not sufficient data to determine the correlation between the drug amount and plasma concentration, and clinical toxic effects. Analyzing piroxicam pharmacokinetics, it appeared that the plasma half-life ($t^{1}/_{2}$) for piroxicam is approximately 45-50 hours (5, 7), thus explaining why the perforation ensued a week after piroxicam exposure.

On the other hand, no gastroprotective agent was used by our doctor with the argument that the results of two separate studies indicate a slight but significant increase in absorption of piroxicam (5) following cimetidine administration. Absorption time in our case had elapsed, and from the results of the same studies, no significant changes have been seen in elimination rate constants or half-life (5). H2-antagonists and proton pump inhibitors (PPIs) may prevent GI irritation, but their usefulness in this situation is unproven (11, 12).

From the fact that piroxicam has been shown to be associated with an increased risk of gastrointestinal complications, it was necessary to consider carefully the treatment with gastroprotective agents (e.g. histamine H2-receptor antagonists or proton pump inhibitors) (1, 5, 6, 7). On the other hand, a careful reassessment should be undertaken during the first week of piroxicam poisoning, because of its prolonged plasma half-life.

Conclusion

An 8 year old girl who had ingested 280 mg of pirixicam capsules (25 times more than therapeutic dose) previously timely treated, presented seven days later with stomach perforation. This is to alert physicians for signs and symptoms of GI ulceration and/

or bleeding after piroxicam overdose, caused by its long plasma half-life. Patients should be warned to report any new or unusual abdominal symptoms after the use piroxicam. Additional clinical evaluation and the use of gastroprotective agents should be considered in these cases.

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Conflict of interest: The authors declare that they have no conflict of interest. This study was not sponsored by any external organization.

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