

## INGESTION OF NSAIDS A SERIOUS PROBLEM IN YOUNG CHILDREN

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### Aims

The authors would like to highlight some severe clinical consequences of the empirical use of NSAIDs and the necessity of educating parents and caregivers.

### Case reports

Four children (two boys and two girls, median age  $26 \pm 0.9$  months) have been hospitalized in our unit for upper digestive hemorrhage after receiving NSAIDs. Two patients received aspirin (500 mg) and the other two received ibuprofen (50-100 mg). In three cases, aspirin and ibuprofen were given for fever control, while the 4<sup>th</sup> child accidentally ingested two half-tablets of aspirin, which were used as a preservative agent in home-made stewed fruits. Within the first 24-48 hours after receiving NSAIDs, all patients were brought to our unit, with hematemesis (two cases), melena (one case) and both hematemesis and melena (one case). History for gastrointestinal problems, chronic drugs usage or over dosage of NSAIDs was negative. Hemoglobin values ranged from 5.5 to 10.5 mg/dl and the coagulation tests were normal. Within 24-48 hours of admission, an upper digestive endoscopy was performed in two children; for the other two cases we could not obtain an informed consent from the parents. In both patients who underwent endoscopy we found double gastric ulcers in the antral region. No evidence of *Helicobacter pylori* infection was obtained. In one case, lack of early endoscopy due to parental refusal was followed by progressive worsening vomiting and acute dehydration; a barium meal revealed a decompensated pyloric stenosis that imposed an antrectomy. Two children were treated with intravenous PPI and one with H<sub>2</sub>-blockers. The patients were discharged after 7-10 days with a recommendation for oral PPI/H<sub>2</sub>-blockers. The endoscopic reevaluation after two months showed a complete healing of the gastric lesions in three children.

### Results

Improving parental education about the risks of self medication and severe side effects of NSAIDs and using acetaminophen as a first choice medication for fever control in young patients seems to be

a reasonable attitude of general practitioners and pediatricians.

NSAIDs is a group of medication largely prescribed in pediatric pathology in antithermic purposes. Ibuprofen is the most frequently used, while aspirin is contraindicated due to potential risk of Reye syndrome and gastrointestinal bleeding. While many persons are treated with NSAIDs every day, some severe adverse side effects may occur in a small percentage of subjects. Acute gastrointestinal bleeding is one major side effect, and it may occur either with oral or parenteral administration. This suggests that many mechanisms are involved and it looks like that interindividual variability in drug metabolism plays a major role. There are at least two mechanisms that NSAIDs trigger: a direct, toxic effect on gastrointestinal mucosa and an indirect one through active hepatic metabolites excreted into the bile and subsequently into the duodenum; these metabolites cause mucosal damage to the stomach during the duodenogastric reflux and to the small bowel by antegrade passage through the gastrointestinal tract.

Clinical manifestations such as dyspepsia and GI discomfort occur in at least 10 to 20 percent of persons taking NSAIDs; however, dyspeptic symptoms do not correlate well with clinically significant ulcerations. There are studies who report a close relationship between the patient's age, comorbidities, the dose of NSAIDs and the complications rate. It has been demonstrated that comorbid illnesses such as rheumatoid arthritis, concomitant corticosteroid or anticoagulant use, infection with *Helicobacter pylori* and prolonged continuous administration increase the risk of gastrointestinal hemorrhage. In children NSAIDs are largely prescribed for many reasons, the most common one being fever, followed by musculoskeletal pains, arthritis, headache and pain due to tooth eruption. Pediatric rheumatologists also prescribe selective COX-2 NSAIDs after failure of one or more traditional NSAIDs. Traditional and selective COX-2 NSAIDs are perceived as safe by pediatric specialists. There are large randomized trials of ibuprofen (versus acetaminophen) safety in pediatric patients and the observed risk of gastrointestinal bleeding in the ibuprofen group was 7.2 per 100,000; authors also report a dose-response relationship between ibuprofen and adverse gastrointestinal reactions. However, gastric ulcers due to NSAIDs are infrequent in the pediatric population, the most common adverse reactions being abdominal pain, nausea and anorexia.

In Romania, administration of NSAIDs by the parents without medical advice and ignorance of their contraindications or side effects represent a

large scale phenomenon. In our small number of patients three of four families did not call a doctor to report the child's fever and two of them did not know that aspirin was not indicated in children for fever control; in one case, the parents reported that they had not even read the prospectus of ibuprofen which clearly stated it was not suitable for children under 3 months. Analyzing our reports, we noticed the following aspects: the median age at presentation was  $26 \pm 0.9$  months, NSAIDs were given for fever control in three cases, the history for gastrointestinal problems, chronic drugs usage or over dosage of NSAIDs was negative for all patients. The symptoms appeared within 24-48 hours following ingestion, in three of four children gastrointestinal bleeding was due to an endoscopically proven double gastric and/or pyloric ulcer produced by a single dose of 50-100mg ibuprofen or 500 mg of aspirin. Additionally, we recorded one rapid and unusual evolution to pyloric stenosis and acute posthemorrhagic anemia in three children (median hemoglobin values  $9.3 \pm 0.7$  mg/dl, but no evidence of *Helicobacter pylori*. A favorable evolution has been noticed after treatment with PPI/H2-blockers with negative endoscopy at two-month follow-up.

### Conclusions

Chronic use of NSAIDs has been associated with gastroduodenal injuries, including ulcers and bleedings. As aspirin intake decreased in children, involvement of ibuprofen has been described. This paper reports unusual complications such as multiple hemorrhagic ulcer lesions or rapid evolution to pyloric stenosis after receiving only single dose of aspirin or ibuprofen. As in Romania self-medication is not rare, general practitioners and pediatricians should be more concerned about informing the parents about the severe side-effects of these drugs. We therefore agree with other authors who consider acetaminophen safer when used as a first choice medication for fever control in young patients.