

# Complicated Peptic Ulcer Disease after Ingestion of Single Dose NSAIDs in Children

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**Abstract** **AIMS:** In our small case series we would like to highlight some severe clinical consequences of the empirical use of NSAIDs and the necessity of educating parents and caregivers. **CASE REPORTS:** Throughout a period of two years, 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 single doses of NSAIDs. Two patients received aspirin (500mg) and the other two received ibuprofen (50-100mg). 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 overdosage of NSAIDs was negative. Hemoglobin values ranged from 5.5 to 10.5mg/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 H2-blockers. The patients were discharged after 7-10 days with a recommendation for oral PPI/H2-blockers. The endoscopic reevaluation after two months showed a complete healing of the gastric lesions in three children. **CONCLUSIONS:** 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.

**Keywords:** Peptic Ulcers, Hemorrhage, NSAIDs, Children

## 1. Introduction

Gastrointestinal hemorrhage is a common problem encountered by pediatric gastroenterologists and those caring for children. Hemorrhage is due to a variety of causes ranging from minor problems to severe life threatening conditions. Parents are often alarmed by any type of unexpected bleeding and will appropriately seek immediate medical attention. Patients who are seriously ill require timely, focused and appropriate assessment and treatment. Adequate management of the situation requires experience, common sense and good coordination from the nursing staff and physicians in charge [1,2]. Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used for fever control and are generally considered to be safe. However, prolonged use and higher doses of NSAIDs are associated with gastrointestinal complications; even a chronic mini dose of aspirin (<100mg/d) may release a gastrointestinal bleeding [3]. Many studies demonstrated that chronic use of NSAIDs can determine gastroduodenal injuries including gastritis, gastric or duodenal ulcer disease and gastrointestinal bleeding. Gastric and duodenal ulcers are detected during

endoscopy in as many as 15% to 30% of adult chronic NSAIDs users. More than 75% of the pediatric patients with juvenile rheumatoid arthritis receiving chronic NSAIDs therapy and suffering from abdominal pain had gastritis, antral erosions or even ulcerations [4]. Throughout a two-year period, four children (two boys and two girls) have been hospitalized in our unit (Gastroenterology Department of “St. Mary” Children’s Emergency Hospital Iasi, Romania) for upper digestive hemorrhage after receiving single dose NSAIDs.

## 2. Case Reports

First case: A 3-year old boy was admitted for hematemesis and melena occurring at 48 hours after administration of aspirin (half-tablet) by his parents for hyperthermia in the context of an acute upper respiratory tract infection. Laboratory investigations revealed severe posthemorrhagic anemia (hemoglobin values ranging between 5.5 and 9.9mg/dl), leukocytosis with neutrophilia, hypoglycemia, hyponatremia, hypokalemia but normal coagulation tests and thoracic-abdominal X-ray. However, an early upper digestive endoscopy was not performed due to parental refusal and technical reasons. The child

received hemostatics, intravenous PPI and transfusions together with broad spectrum antibiotics for the respiratory infection. His general condition improved, with disappearance of vomiting and abdominal pains and the patient was discharged after 9 days of hospitalization with martial therapy recommendations for the correction of anemia. After a week, he returned to the hospital with severe acute dehydration due to progressive worsening vomiting. An upper GI series showed a decompensated pyloric stenosis. Laparotomy confirmed a dilated stomach with thickened walls and cicatricial pylorus of pseudotumoral aspect. An antrectomy with P éan-Bilroth-type gastroduodenostomy was performed. Postsurgical evolution was favorable with normalized bowel transit on the 4th postoperative day, the patient being discharged on the 10th day. He returned for control after 3 weeks, when a new upper GI series was performed, showing a normal aspect and functioning of the operation. Later checks confirmed the favorable evolution, the weight curve and biological parameters being within normal ranges.



**Figure 1.** Barium meal showing pyloric stenosis (first case report)

Second case: A 3-year old girl with a history of cleft velum (operated two years before, at the age of one) was admitted in the Emergency Room for food succeeded by coffee grounds vomiting in the last 48 hours. History revealed that three days earlier the child presented fever and her parents have administered 5ml of ibuprofen. Clinical examination showed impaired general condition, paleness, signs of acute dehydration, intense hypertrophic and congestive tonsils, systolic blast grade 2/6, intense and diffuse abdominal pains. Laboratory data revealed acute posthemorrhagic anemia (hemoglobin values ranging between 8.5 and 10.5mg/dl,) normal coagulation tests; thoracic-abdominal X-ray and abdominal ultrasound were normal and the echocardiography showed ASD type ostium secundum. An esophagogastroduodenoscopy performed within 24 hours after admission showed a double antral ulcer, Forrest 2c; the biopsies for *Helicobacter pylori* were negative. The evolution was favorable under hemostatics and intravenous followed by oral PPI; the patient was discharged after 8 days with recommendation for oral PPI for six weeks. Finally the child recovered with good short and long term evolution.

Third case: A 2-year old boy presented melena 24 hours after an incidental ingestion of two half-tablets of aspirin used as a preservative agent in home-made stewed fruits. History for gastrointestinal problems, chronic drugs usage or overdosage of NSAIDs was negative. The clinical examination showed an influenced general condition and pain in the superior abdomen. Laboratory investigations highlighted acute posthemorrhagic anemia (Hb=8.8mg/dl)

with normal coagulation tests and the upper digestive endoscopy revealed a double antral ulcer. The presence of *Helicobacter pylori* could not be demonstrated. Intravenous fluids, PPI and hemostatics were started; the patient was discharged after 7 days of hospitalization, with the recommendation of oral PPI use for eight weeks. Endoscopic reevaluation after two months showed complete healing of the gastric lesions.



**Figure 2.** Upper digestive endoscopy showing double antral ulcer (2<sup>nd</sup> case report)

Fourth case: A 3-month old girl was admitted for small hematemesis after receiving a half-teaspoon (2.5ml) of ibuprofen given without medical advice by her mother for fever control. Clinical examination and laboratory data were within normal limits, excepting the positive occult stool blood test. Upper gastrointestinal endoscopy was not performed due to the impossibility to obtain an informed consent. Evolution was favorable with intravenous H<sub>2</sub>-blockers, the patient being discharged after 7 days of hospitalization with recommendation for oral H<sub>2</sub>-blockers for two weeks.

### 3. Results and Discussions

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 [5]. 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 [4]. 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 [7]. 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 [6]. 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 [8,9]. However, gastric ulcers due to NSAIDs are infrequent in the pediatric population, the most common adverse reactions being abdominal pain, nausea and anorexia [10,11,12]. 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.

## Authors' Contribution

SD: (turti23@yahoo.com): conceived and wrote the paper.

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MB: (burleamarin@yahoo.ro): critical review and corrections.

NG: (chiti\_nico@yahoo.com): review of existing literature, corresponding author.

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