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EC PAEDIATRICS
Case Report

A Low Dose of Ibuprofen May Result in Considerable Gastrointestinal Bleeding in Paediatrics

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Abstract

Upper gastrointestinal (GI) bleeding includes blood loss within the GI system, proximal to the ligament of Treitz, which includes the oesophagus, stomach, and duodenum. GI bleeding can occur due to multiple causes and can be a presenting symptom for paediatrics patients. Patients may present with specific symptoms of haematemesis (vomiting blood), melaena (tarry, black stools), and coffee-ground type vomitus. Patients may also have associated systemic symptoms such as abdominal pain, fatigue, pallor, shortness of breath, light-headedness, and dizziness. Common causes of upper GI bleeding include gastric and duodenal ulcers, esophagitis, gastritis, bleeding disorders, coagulopathies, and necrotizing enterocolitis. Management is often a multifactorial approach, including fluid resuscitation, blood transfusion, endoscopy, drug intervention, and/or surgical intervention. If there is a large amount of blood loss, emergency resuscitation and stabilization of the patient may be necessary. Non-steroidal anti-inflammatory drug (NSAID)-induced haematemesis is a notable cause of upper GI bleeding in paediatrics patients. In our case, we have observed a severe case of upper GI bleeding, likely associated with NSAID administration.

Keywords: *Low Dose; Ibuprofen; Gastrointestinal Bleeding; Paediatrics*

Case Report

In our case, we describe a 7-year-old boy with no significant medical history apart from left-sided hydronephrosis, no family history of gastrointestinal illnesses, and no regular medications. This patient had been feeling generally unwell at home for 2.5 weeks, with a sore throat and cough. For symptom control, antihistamines were given by his parents at home. The illness progressed, and he became febrile with a temperature of 39.9°C associated with intermittent vomiting of food contents and lethargy. The General Practitioner (GP) prescribed amoxicillin and ibuprofen; however, following 4 age-appropriate doses of ibuprofen, he developed abdominal pain and haematemesis. The GP advised emergency department (ED) attendance, where he was stabilized and transferred to the acute paediatrics ward.

Due to 5 further observed episodes of frank haematemesis during the admission, the following were prescribed:

1. Intravenous (IV) fluid bolus
2. 40 mg of omeprazole (Proton pump inhibitor, PPI)
3. Ondansetron (Antiemetic)
4. Tranexamic acid IV, 15 mg/kg x 2 (Antifibrinolytic)
5. IV Vitamin K, 250 micrograms/kg (Clotting cascade co-factor).

A nasogastric tube placed in ED revealed aspirates of fresh blood, estimated at a total of 55 mL. The investigations showed a drop of his haemoglobin from 109 g/L to 100 g/L and his platelets from 157 to 117 within a few hours, so 1 unit of packed red blood cells (PRBC) was transfused, followed by a second unit after re-evaluation.

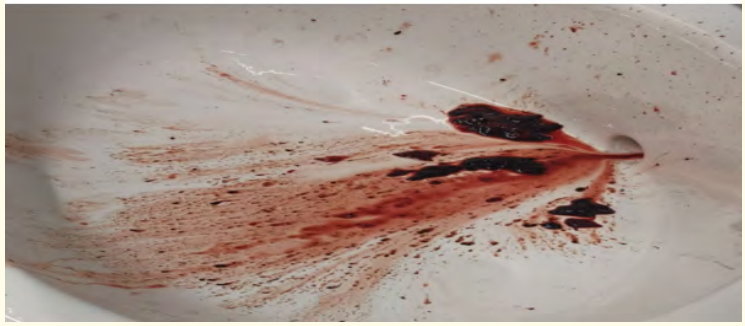

Figure 1: *Haematemesis on admission to the acute paediatrics unit.*

PATHOLOGY RESULTS

Group: COVID ICU bloods profile | VIEW RESULTS:
Start: 01/01/2025
End: 30/03/2026

	10/01/25 13:11 CC222520G	10/01/25 13:11 HH222520W	02/01/25 22:26 CC053063Z	02/01/25 22:26 HH053063P	02/01/25 19:03 CC054211B	02/01/25 19:03 HH054211Z	02/01/25 16:57 CC048774M	02/01/25 16:57 HH048774L	Ref Range
Serum Sodium	136		138		136		133		133 - 146
Serum Potassium	4.5		4.4		3.7		4.0		3.5 - 5.3
Serum Urea	4.2		6.2		6.9 *		4.3		2.5 - 6.5
Serum Creatinine	30		31		35		42		30 - 47
Serum Bilirubin	4						6		0 - 21
Serum Alkaline Phosphatase	145						116		60 - 425
Serum Alanine transaminase	30						17		10 - 50
Serum Total Protein							66		60 - 80
Serum Albumin	43						36		35 - 50
Serum Calcium							2.11		-
Corrected Calcium							2.28		2.22 - 2.51
Serum Inorganic Phosphate							1.20		0.9 - 1.8
Serum CRP					33 *		38 *		- 5
Serum Ferritin							514 *		6 - 110
Serum vitamin B12							1255 *		197 - 771
Serum Folate							9.3		2.4 - 17.5
Haemoglobin		106 *		100 *		106 *		109 *	115 - 155
White Cell Count		9.21		4.95		7.98		5.84	4.5 - 14.5
Platelet Count		475 *		117 *		154		157	150 - 400
Haematocrit		0.305 *		0.300 *		0.316 *		0.326 *	0.35 - 0.45
Mean Cell Volume		84.5		84.0		82.9		82.5	77 - 91
Red Cell Count		3.61 *		3.57 *		3.81 *		3.95 *	4 - 5.2
Mean Cell Haemoglobin		29.4		28.0		27.8		27.6	24 - 30
Red Cell Distribution Width		14.9 *		14.6		15.6 *		15.6 *	11.8 - 14.8
Nucleated RBC		0.07 *		0.01		0.01		0.01	0 - 0.01
Neutrophils		4.35		2.79		4.59		3.77	1.5 - 8
Lymphocytes		4.06		1.82		2.82		1.70	1.50 - 7.00
Monocytes		0.69		0.33		0.55		0.36	0.2 - 1
Eosinophils		0.08		0.00		0.00		0.00	0 - 0.4
Basophils		0.03		0.01		0.02		0.01	0 - 0.1
International Normalised Ratio								1.1	0.8 - 1.2
Prothrombin Time								11.7	10.0 - 11.7
APT Ratio								1.13 *	0.85 - 1.10

Figure 2: *Laboratory results before and after transfusion and prior to the transfer to the tertiary gastrointestinal unit and after discharge.*

The patient was transferred to a tertiary specialized gastrointestinal unit, where he was observed. Intravenous Proton Pump Inhibitor was prescribed as he experienced ongoing melaena. Observations continued to improve, and haemoglobin continued to rise during the admission. After the vomiting turned clear and haematemesis resolved, he was planned for discharge, at which point he was prescribed Omeprazole 30 mg for 2 weeks, to then be reduced to 20 mg for 4 further weeks. Referral for repeat blood investigations and gastrointestinal specialist follow-up, which showed normal investigations and no further GIT bleeding.

Discussion

Acute upper gastrointestinal bleeding is an uncommon but potentially serious problem in children. It usually presents as haematemesis and/or melaena. Large-volume upper GI bleeding may be encountered in non-steroidal anti-inflammatory drug (NSAID)-induced gastritis but is more frequently seen in variceal bleeding, both in young children and adolescents [1].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely prescribed worldwide and commonly prescribed for paediatric patients with fever. The use of NSAIDs has been correlated to gastrointestinal bleeding, and it is recognized that NSAID dose is one of the main indicators for upper gastrointestinal bleeding risk [2].

NSAID correlated gastrointestinal bleeding is hypothesised to include the dual injury hypothesis. This mechanism includes NSAIDs causing direct toxic effects on gastrointestinal mucosa paralleled with indirect effects of producing mucosal-damaging hepatic metabolites and reducing protective mucosal prostaglandins [3].

GIT-associated NSAID damage is specifically based on the blockade of the cyclooxygenase enzyme (COX), which regulates the synthesis of prostaglandins from arachidonic acid. Effects of this blockade include anti-inflammatory, analgesic and antipyretic properties while inducing a systemic decrease in the synthesis of prostaglandins (PGs), known to have cytoprotective effects [3]. Subsequent effects of this mechanism include:

1. Increase in the formation of hydrogen (H^+) ions and pepsinogen in the stomach [4]
2. Decreased production of mucus and bicarbonates [4]
3. Reduction of gastric mucosal blood flow [4]
4. Inflammation and ischemia of the gastric mucosa [4].

Overall, these effects can lead to inflammation, erosion and ulcers within the GIT system4 inducing possible upper GIT bleeding as seen in our case.

Ibuprofen, a widely used NSAID, can lead to gastrointestinal (GI) bleeding and, in rare cases, thrombocytopenia. Understanding the mechanisms behind these adverse effects is crucial for their prevention and management. Ibuprofen contributes to GI bleeding through both topical and systemic mechanisms.

Ibuprofen's weakly acidic nature allows it to remain nonionized in the stomach's acidic environment, facilitating its diffusion into the epithelial cells of the GI mucosa. Inside these cells, the higher pH causes the drug to ionize, leading to cellular damage, erosion, and potential bleeding. Additionally, ibuprofen can disrupt the gastric mucosal barrier by interacting with phospholipids, diminishing the stomach's defence against acid-induced injury [5].

Thrombocytopenia, a condition characterized by abnormally low platelet counts, is a rare but serious reported side effect of ibuprofen. The proposed mechanisms include:

1. Immune-mediated response as ibuprofen or its metabolites may act as haptens, binding to platelet surfaces and forming complexes that the immune system recognizes as foreign. This triggers the production of antibodies against these complexes, leading to platelet destruction and a decrease in platelet count [6].
2. Thrombotic thrombocytopenic purpura (TTP): Although extremely rare, ibuprofen has been associated with TTP, a condition characterized by the formation of small clots within blood vessels, leading to platelet consumption and subsequent thrombocytopenia. The exact mechanism is not fully understood but may involve an immune response or direct toxicity to the vascular endothelium [7].

Several studies suggested the link between NSAIDs and upper GIT bleeding. One study suggested chronic NSAID therapy for patients diagnosed with juvenile rheumatoid arthritis could lead to upper GIT consequences. They found that > 75% of patients with abdominal pain had associated gastritis, antral erosions, or ulcers [3]. On the other hand, reports from the United States described patients between the ages of 16 months- 36 months developing haematemesis within 24hr of receiving weight-appropriate doses of ibuprofen with confirmed antral gastric ulceration confirmed on endoscopy [3].

A national case-crossover study conducted in France identified 177 children with upper GIT bleeding. They reported that one-third of these cases were associated with NSAID use at doses used for analgesic or antipyretic purposes, further suggesting the link between NSAID and upper GI bleeding 8. Notably, the observed risk was over 4X higher (OR = 14.1) in patient age groups of children 0-7 years old when compared to patient age group of 8-16 years old (OR 3.4) [8].

Analysing the use of ibuprofen specifically, a UK cohort study involving 54,830 patients (19.5% of patients aged 15-29) observed patients using ibuprofen (≤ 1200 mg) for more than 3 months. They reported an incidence rate (95% CI) of upper GIT bleeding/10,000 people using ibuprofen was 0.4 (0.04 - 1.3). Although low, the incidence of gastrointestinal toxicity remains the main serious adverse event for ibuprofen [2].

It is important to note that the child's investigations demonstrated a positive adenovirus result, which can contribute to gastrointestinal bleeding through the following mechanisms [9]:

- Direct mucosal damage: Adenoviruses, particularly enteric types such as HAdV-F40 and HAdV-F41, can infect and replicate within the epithelial cells of the gastrointestinal tract. This replication may cause mucosal inflammation and ulceration, compromising the integrity of the gastrointestinal lining and leading to bleeding.
- Vascular involvement and coagulopathy: Disseminated adenoviral infections can result in vascular injury and coagulopathies. The virus may directly damage blood vessels or trigger inflammatory responses that disrupt normal coagulation processes, thereby increasing the risk of bleeding.

Despite this possibility, the liver team at the tertiary hospital believes that ibuprofen is more likely to be the primary cause of the gastrointestinal bleeding than an adenovirus infection.

Conclusion

NSAID-induced upper GIT bleeding is a serious, adverse effect that should be considered when prescribing this medication to paediatric patients. Through a multifactorial mechanism, NSAIDs can induce severe inflammation within the GIT leading to upper GIT bleeding. It is essential to inform carers/patients of this risk and encourage immediate medical support if the child has any associated signs of haematemesis and melaena. While ibuprofen is effective for pain and inflammation management, awareness of these potential adverse effects is essential. Patients should use the lowest effective dose for the shortest duration possible and consult healthcare providers if they have concerns or experience symptoms indicative of GI bleeding (such as black or tarry stools, vomiting blood) or thrombocytopenia (such as unusual bruising or bleeding).

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