Archives of Emergency Medicine and Intensive Care

ISSN: 2638-5007

Volume 3, Issue 1, 2020, PP: 01-05

Evaluation of Pediatric Patients with Gastrointestinal Bleeding Following a Single Dose Ingestion of NSAID

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Abstract

Aim: *The 5 children who were admitted to Düzce University Medical Faculty Pediatric Emergency Clinic and were diagnosed with gastrointestinal bleeding after a single dose of NSAIDs were included in this study. We were analyzed the demographic characteristics of the patients and the healing processes of the disease. We aimed to emphasize that NSAIDs do gastrointestinal bleeding even in single dose use.*

Method: *Children who admitted to Duzce University Pediatric Emergency Department with gastrointestinal bleeding after a single dose of NSAID between January 2015 and March 2019 were retrospectively analyzed. Bloody vomiting was observed in all cases a few hours later after NSAID intake. After exclusion of other causes that may cause these findings, there was gastrointestinal bleeding due to NSAID use.*

Results: *Five children who were two girls and three boys were admitted to the hospital due to gastrointestinal bleeding after the use of NSAIDs. None of them had a known chronic disease and no history of drug use. Bloody vomiting was present in all cases. Two patients had abdominal pain, two cases had black stools and one patient had syncope.*

Conclusion: *Patients presenting with bloody vomiting and bloody saliva after NSAIDs intake should be evaluated for gastrointestinal bleeding. In terms of anemia, serum hemoglobin, urea, blood urea nitrogen and creatinine levels should be investigated in terms of acute renal failure. Treatment should be decided according to the patient's clinical condition.*

Keywords: *NSAID, Gastrointestinal Bleeding, Child.*

İntroduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used as analgesic, antipyretic, and anti-inflammatory agents (1,2). These drugs are known to cause injury throughout the gastrointestinal (GI) tract. It is among the most commonly prescribed drug groups in the world. NSAID use has been associated with cardiovascular, renal and GI complcations and pediatric patients are at increased risk. GI bleeding is common in children due to various causes (3). Severe life-threatening ones are, however, rare, and their incidence is relatively unknown. There is a patient of data on the incidence of complications of NSAID use in the pediatric population. There are few studies in the literature about pediatric patients with gastrointestinal bleeding after NSAID use.

Pediatric patients with gastrointestinal bleeding following a single dose ingestion of NSAID presented. It was aimed to analyze the demographic characteristics of the patients and the healing processes of the disease.

Materials and Methods

In this study, children who admitted to Duzce University Medical Faculty Pediatric Emergency Department with GI bleeding after a single dose of NSAID between January 2015 and March 2019 were retrospectively analyzed. Bloody vomiting was observed in all cases a few hours later after NSAID intake. GI bleeding diagnosis was considered due to NSAID were after exclusion of other causes that may cause these findings, there was GI bleeding due to NSAID use.

Results

After the use of NSAIDs, five children were admitted to the hospital due to GI bleeding, two girls and three boys. None of them had a known chronic disease and no history of drug use. Bloody vomiting was present in all cases. Medical histories showed that, two patients had abdominal pain, two cases had black stools and one patient had syncope in retrospective analysis.

Three patients had ibuprofen, one had diclofenac sodium and one had naproxen intake.

The clinical findings of the 16-year-old patient with severe syncope, bloody vomiting and black stool findings were more severely found. Adrenaline injection was performed by endoscopic examination of Case 5, on the ulcerated lesion. The patient was followed up in the intensive care unit for 1 day and in the inpatient service for 9 days.

Erythrocyte suspension was given in two patients because of anemia findings. Acute renal failure developed in two cases and improvement was achieved after treatment (Table).

Table: *Demographic, examination and laboratory findings of patients*

	Case 1	Case 2	Case 3	Case 4	Case 5
Demographic findings of patients					
Gender	Male	Female	Male	Female	Male
Age (year)	15	9	5	4	16
Complaint	Abdominal pain, Bloody vomiting	Headache, Abdominal pain, Bloody vomiting, Black stools	Bloody vomiting	Bloody vomiting	Syncope, Bloody vomiting, Black stools
Hospitalization Period (day)	2	4	5	4	10
Received NSAID	Diclofenac sodium	Ibuprofen	Ibuprofen	Ibuprofen	Naproksen
Vital signs of patients					
Pulse (beats / min)	86	108	95	113	143
Systolic blood pressure (mmHg)	117	101	113	112	87
Diastolic blood pressure (mmHg)	67	58	61	56	65
Temperature (°C)	36,9	36	37,1	38,7	36,3
Respiratory rate (min)	20	24	28	32	35
Examination findings of patients					
General situation	Good	Good	Good	Good	Good
Consciousness	Ok	Ok	Ok	Ok	Ok
Rebound and defance	No	No	No	No	No
Interventions done to patients					
Was the erythrocyte suspension given?	Yes	Yes	No	No	Yes
The decompression of the stomach by the nasogastric catheter was done.	No	Yes	No	No	Yes
Endoscopy	No	No	No	No	Yes
Treatments given to patients					
IV Antacid	Yes	Yes	Yes	No	Yes
H2 receptor blocker	Yes	No	Yes	Yes	Yes
PPI	No	No	Yes	Yes	Yes
IV fluid therapy	Yes	Yes	Yes	Yes	Yes
Laboratory results					
Hemoglobin(g/dl)	7,5-9,6	7,9-9,9	8,4-8,8	16,2	8,2-6,9-10,4
Leukocyte (/mm3)	N*	N	N	N	N
Platelets (/mm3)	N	N	N	N	N
aPTT (sec)	N	N	N	N	N
INR	N	N	N	N	N
AST (U/L)	N	N	N	N	N
ALT (U/L)	N	N	N	N	N
Urea (mg/dl)	N	N	33	N	100-17
Bun (mg/dl)	N	N	16	N	45-13
Creatinine (mg/dl)	N	N	1,38-0,42	N	0,66-0,60

*:Normal range; ALT: alanine aminotransferase; AST: aspartate aminotransferase

Discussion

Adequate pain management is a widespread clinical concern, and both prescription and over-the-counter (OTC) nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently used for pain relief (4). NSAID use has been associated with cardiovascular (CV), renal, and gastrointestinal (GI) complications, and certain patients are at increased risk. NSAID use results in small but consistent increases in the risk of CV events such as myocardial infarction, affected in part by dose and potency of cyclooxygenase-2 (COX-2) inhibition (5-6). These complications prompted the US Food and Drug Administration (FDA) to release a scientific statement in 2005 emphasizing "the importance of using the lowest effective dose for the shortest duration possible if treatment with an NSAID is warranted for an individual patient."(7-9).

GI complications are generally thought to be mediated primarily through inhibition of mucosal cyclooxygenase-1 (COX-1) and resultant suppression of prostaglandin production (10). Thus, it prevents arachidonic acid from being attached to these regions. The suppression of mucosal prostaglandin synthesis, by the systemic inhibition of cyclooxygenase (COX) enzymes, confers on NSAIDs their ability to injure the GI mucosa (2).Thus, it prevents the conversion of arachidonic acid to prostaglandins which cause calor (heat,), dolor (pain), rubor (redness), and tumor (swelling) (11). Prostaglandins also play a role in sensitizing pain-sensitive nerve fibers that explain the analgesic effect of NSAIDs. Ibuprofen also works on the thermoregulatory center of the hypothalamus to control fever (12).

There is a paucity of data on the incidence of these injuries in the pediatric population. In our environment, NSAID syrups are readily available over the counter drugs that some use as antipyretic or analgesic agents. Our patients had taken medications prescribed in peripheral hospitals before the onset of their GI bleeding.

Different NSAIDs do show different risks for GI ulceration. Studies in Denmark have shown that for Ibuprofen and Naproxen, there was a clear trend in an increasing risk for upper GI bleeding with increasing dose (13,14). Our three patients had ibuprofen, one had diclofenac sodium and one had naproxen intake.

NSAID-induced enteropathy is believed to be more common than gastric and duodenum injuries, which are often seen as hidden blood loss (14). Topical irritation by NSAIDs appear to play a role here, given that enterohepatic recirculation of these drugs prolongs the exposure of the intestinal mucosa to them, with the luminal bile and enterobacteria potentiating the damage after the initial increase in gut permeability induced by the NSAID (2).

The COX-1 enzyme is found in the gastric mucosa and is effective in the production of prostaglandins that regulate blood flow and bicarbonate production in the stomach. A non-selective COX inhibitor, ibuprofen, may impair the mucosal integrity of the gastric mucosa. Intramucosal bleeding may occur several hours after NSAID uptake. Bleeding may progress towards continuing erosions, but is typically reversible. In sensitive individuals, they may progress to peptic ulcers. The severity of GI side effects may range from dyspepsia to life-threatening upper GI bleeding or viscous organ rupture. Symptoms include nausea, vomiting, dyspeptic symptoms, and abdominal pain. GI bleeding has been described in many case reports, especially after large applications. The perforation of the duodenum is described in one patient after a single intake (15-17). In the case report of Anyanwu et al., GI bleeding was seen in two patients after ibuprofen intake (2).

Studies have shown that most GI injuries after NSAID use will occur within the first 30 days after NSAID initiation (18). Our patients were admitted to the hospital within a few hours after NSAID intake.

NSAID enteropathy may produce a higher disease burden in children, given that there are age-related differences in the effectiveness of intestinal blood flow autoregulation (19). Mucosal epithelium is believed to be the primary barrier to bacterial translocation in the intestine, and injury to this barrier may lead to septicemia by allowing for bacterial translocation of the intestine and may also occur as NSAID enteropathy, resulting in occult blood loss (20-21).

NSAIDs are known to have adverse effects on kidney function. Situations with a stimulated renin-angiotensin system such as volume depletion or pre-existing chronic renal failure predispose to acute renal failure via inhibition of prostaglandin synthesis by NSAIDs (22). Two of our patients developed acute renal failure. The clinical and laboratory findings regressed after the treatment and follow-up of cases.

Blood laboratory examination in patients should be performed in patients who were admitted to hospital with complaints such as bloody vomiting and bloody saliva after NSAID intake. Three of our patients had erythrocyte suspension due to low hemoglobin levels.

Endoscopy should be performed in massive and unstoppable bleeding. Endoscopy was performed in a patient who had massive bleeding. During endoscopy, adrenaline injection was performed on the ulcerated lesion. Surgical treatment or medication may be applied to ulcers.

NSAIDs, especially ibuprofen, are frequently used drugs. Patients presenting with bloody vomiting and bloody saliva after NSAIDs intake should be evaluated for GI bleeding. In terms of anemia, serum hemoglobin, urea, blood urea nitrogen and creatinine levels should be considered in terms of acute renal failure. Treatment should be decided according to the patient's clinical situation.

Gastric acid release increases later after food intake. However, a gastric mucosal barrier is formed which prevents the acid from damaging the gastric mucosa. NSAIDs break down the gastric mucosal barrier and damage the gastric mucosa. NSAIDs including a single dose were saw to cause GI bleeding in our patients. When we look at the NSAID prospectus, it does not write a definite instruction for use on an empty stomach or after food.

As a results, we think that the use of NSAIDs on with or after food will reduce gastric bleeding. Future studies on this subject are needed.

Thanks

We would like to thank Emine Dağdelen for her efforts in data entry.

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Citation: **Ramazan Cahit TEMİZKAN, Muhammet Mesut Nezir ENGİN, Betül TÜREN, Kenan KOCABAY.** *Evaluation of Pediatric Patients with Gastrointestinal Bleeding Following a Single Dose Ingestion of NSAID. Archives of Emergency Medicine and Intensive Care. 2020; 3(1): 01-05.*