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Case Series

Gastrointestinal perforations induced by long-term non-steroidal anti-inflammatory drugs use: a case series analysis and discussion

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDS) are used in a wide range but may cause harm to the gastrointestinal mucosa, which leads to various complications. This study shows the impact of long term NSAID use on small and large intestine and presents 2 cases of patients with NSAID induced perforations. The first case involves a 62-year-old male patient with RA on long term Ibuprofen use, presented with abdominal pain, vomiting, and lower limbs pain. Laparotomy revealed a 5 mm perforation in the proximal jejunum. The second case, a male patient of 65 years of age using diclofenac without a prescription, which lead to a 4×4 cm sigmoid colon perforation. The comparison of both the cases presents a difference in examination and laboratory findings. Long-term NSAID use has been associated with various GI complications, including perforations. The case presents the importance of considering NSAID related complications, mainly in older patients and the persons with ulcers. Combining NSAIDS with other drugs, like misoprostol may minimize the risk of the GI complications. NSAIDs are also linked with cardiovascular events, and heart related issues. This study shows the need of careful NSAID prescription, with their association with preventable adverse effects. 30% of hospitalizations for adverse drug reactions are only by the NSAIDs. PPIs and H2 receptor antagonist are commonly used to protect the gastrointestinal mucosa which minimizes the occurrence of ulcers. Healthcare professionals should be careful particularly in case of high risk patients to minimize the NSAID related complications.

Keywords: NSAIDs, GI mucosa, Perforations, Complications, PPIs, Cardiovascular events

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDS) frequently cause harm to the mucosa of small and large bowels. They include ulceration, haemorrhage, strictures, enteropathy, colitis, perforation.[1] NSAIDs are known to induce gastroduodenal ulcers. NSAIDs are linked to adverse effects on both small and large intestine.[2] Although NSAIDs are well-tolerated, their wide use in the community leads to considerable morbidity and mortality of gastrointestinal (GI), renal and other complications.[3] Small intestinal ulcers are less frequent distal to duodenum and seldom may lead to perforation. Differential diagnoses of jejunal or ileal ulcers include neoplasms, trauma, congenital malformations (such as Meckel's diverticula), and chemical irritation. Symptoms may be vascular anomalies, Crohn's disease, drug-related issues, or idiopathic disorders.[1] Approximately 20% of NSAID users experience mild GI problems that would be insignificant. The risk of gastrointestinal problems is based on usage pattern and demographic.

Short-term usage of non-prescription ibuprofen has mild risk of gastrointestinal damage. Long-term usage of non-prescription dosages may raise the risk of GI haemorrhage. Certain subgroups are particularly at risk for gastrointestinal toxicity. Older patients, using low-dose aspirin, and with a history of ulcers are more prone to experience NSAID- induced gastrointestinal bleeding.[4]

CASE SERIES

Case 1

A 62-year-old man who had been vomiting for three days and experiencing lower limb pain appeared with abdominal pain that had been present for four days and was insidious in its onset and progression. He had normal vital signs. He has been taking Ibuprofen (NSAID) for the past 7 years as part of his treatment for rheumatoid arthritis. Diabetes (DM), hypertension (HTN), and asthma have never been diagnosed in him. Social habits are non-significant. On examination patient's abdomen was found to be stiff, swollen, guarding, and to have bowel sounds. The abdominal X-ray revealed air under the diaphragm, and the renal parenchyma was visible on the ultrasound. White blood cell (WBC)- 16,000/ml and serum creatinine was 1.8 mg/dl and blood urea 45 mg/dl, hemoglobin 9 mg/dl, liver function tests were normal. After being diagnosed with an acute intestinal perforation, acute kidney injury (AKI), and 3 cc grade II BPH, the patient underwent an emergency laparotomy with proximal jejuna vesection. A 5 mm puncture in the proximal jejunum was presented by the patient. He received intravenous fluids, antibiotics, pantop, and ondansetron, among other things. The jejunum's final pathology revealed a 5mm perforation in the proximal jejunum 15.2 cm distal to flexion and a purulent collection with intra-bowel films adhesion.

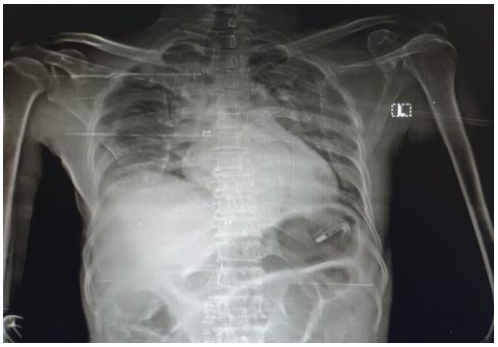

Figure 1: X- ray of patient I with air under diaphragm.

The presence or absence of air under the diaphragm is a crucial finding in abdominal X-rays. In case 1, the presence of air suggests perforation of the intestinal tract, contributing to the diagnosis of acute intestinal perforation. In case 2, the absence of air under the diaphragm indicates a different presentation, and the diagnosis of hollow viscus perforation was made based on other clinical findings and exploration during the laparotomy.

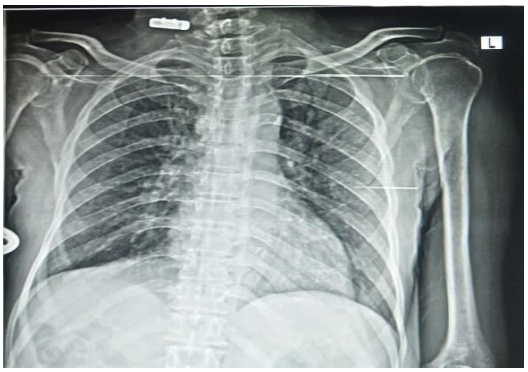

Figure 2: Normal X-ray of patient II.

Case 2

A 65 years old male presented with abdominal pain and vomiting from 2 days. He had no past medical history of hypertension, diabetes mellitus. He had the past medication history of diclofenac tablet 5 mg twice daily for generalized body pains without prescription. The abdominal X-ray shows no air under diaphragm. Laboratory examination reveals that serum creatinine-2.4 mg/dl, blood urea-28 mg/dl, hemoglobin-12.9 g%, total count-5300 cells/cum, platelet count-2.4 lakhs. After the patient diagnosed with hallow viscus perforation, the patient underwent emergency exploratory laparotomy, closure of sigmoid colon and left pelvic sigmoid loop colostomy. He was noted to have perforation around 4×4 cm in the sigmoid colon (descending loop) and he extubated on post-operative day 3 allow oral fluids and eventually step down the floors.

Table 1: Comparison of case 1 and case 2 on different parameters.

Parameter	Case 1	Case 2
Age	72 years old	75 years old
Symptoms	Vomiting for 3 days, lower limb pain, insidious abdominal pain for 4 days	Abdominal pain, vomiting for 2 days
Medication history	Ibuprofen (NSAID) for 7 years for rheumatoid arthritis	Diclofenac 5 mg twice daily without prescription for generalized body pains
Past medical history	Rheumatoid arthritis (no DM, HTN, or asthma)	No known hypertension or diabetes mellitus
Examination findings	Stiff, swollen abdomen with guarding, bowel sounds present, air under diaphragm on X-ray, visible renal parenchyma on ultrasound	No air under diaphragm on X-ray

Continued.

Parameter	Case 1	Case 2
Laboratory investigations	WBC 16,000/µl, creatinine 1.8 mg/dl, BUN 45 mg/dl, Hb 9 mg/dl	Creatinine 2.4 mg/dl, BUN 28 mg/dl, Hb 12.9 g/dl, total count 5300 cells/cu mm, platelet count 2.4 lakhs
Diagnosis	Acute intestinal perforation, AKI, 3 cc grade II BPH	Hollow viscus perforation
Treatment	Emergency laparotomy with proximal jejuna vesection, 5 mm perforation in the proximal jejunum, intravenous fluids, antibiotics, pantop, ondansetron	Emergency exploratory laparotomy, closure of sigmoid colon, left pelvic sigmoid loop colostomy, 4×4 cm perforation in the sigmoid colon
Post-operative course	Not specified	Extubated on postoperative day 3, allowed oral fluids, step down the floors

DISCUSSION

In the above cases the patients were using only the NASIDs for long term which caused them intestinal perforation. Studies indicate that the use of NSAIDs with other drugs might minimize the risk of GI effects. Misoprostol in combination with NSAIDs are known to reduced NSAID induced gastroduodenal lesions.[5] Misoprostol when taken with indomethacin in humans was known to decrease small-intestinal inflammation.[6] NSAID use raises probability of hospitalisation for congestive heart failure (CHF). This may lead to alterations in renal function or vascular resistance. The American Heart Association states that NSAIDs may maximize the risk of cardiovascular events like stroke and myocardial infarction.[4] Apart from advantages of long-term usage, including reduced colorectal cancer risk and polyp regression. NSAIDs have several negative effects on the colon.[2] Patients with perforations were approximately 3 times more likely to use NSAIDs compared to simple perforations. Steroids are known to be linked to increased risk of perforation in diverticular disease.[7] NSAIDs have significant responses against COX-1 and COX-2, which explains the adverse effects of their anti-inflammatory properties. Anti-inflammatory drugs with high COX-2 potency and COX-2/COX-1 activity ratio are more effective and maintains fewer stomach and renal adverse effects.[6]

CONCLUSION

The study highlights the importance of prescribing NSAIDs with utmost care. It is evident that NSAIDs are responsible for 30% of hospitalisations due to preventable adverse medication responses. To protect the gastroduodenal mucosa in NSAID users, proton pump inhibitors (PPIs) and H2 receptor antagonists are routinely used. PPIs' efficacy in decreasing the incidence of gastroduodenal ulcers among long-term users.

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