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Case Report

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Beyond Surgical Site Bleeding: A Case of Life-Threatening Gastrointestinal Bleed With Nonsteroidal Anti-Inflammatory Use After Autologous Breast Reconstruction

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Abstract

We report the case of a 66-year-old female who underwent autologous breast reconstruction and sustained a massive upper gastrointestinal bleed secondary to a duodenal ulcer after using nonsteroidal anti-inflammatory drugs (NSAIDs) consistently for 2 weeks. She required resuscitation with a massive blood transfusion protocol and definitive hemorrhage control with interventional coiling of the gastroduodenal artery. We discuss the importance of thinking beyond surgical site bleeding with NSAIDs as well as risk stratification and prevention of NSAID-induced complications.

Keywords

gastrointestinal bleed, breast reconstruction, post-operative bleeding, nonsteroidal anti-inflammatory drug

Introduction

With the increasing prevalence of opiate overprescription, addiction, and overdose, it is important to consider non-opioid analgesics for post-operative pain control.[1] Nonsteroidal anti-inflammatory drugs (NSAIDs) are a potent alternative and are being adopted more frequently in contemporary plastic surgery and other surgical specialties.[2,3]

Surgeons are particularly cautious with NSAID prescription after breast surgery due to the risk of surgical site bleeding related to NSAIDs, which may necessitate re-operation to evacuate a hematoma. However, there is an increasing body of literature supporting the safety of ibuprofen and ketorolac with regards to surgical site bleeding.[4,5]

When prescribing an NSAID, it is critical to prevent tunnel vision by considering all potential complications rather than shifting all attention to the risk of surgical site bleeding. We present the case of a 66-year-old female who sustained life-threatening upper gastrointestinal (GI) bleed after taking NSAIDs consistently post autologous breast reconstruction. We emphasize looking beyond surgical site complications and remembering the general complications of NSAIDs, including GI, cardiovascular (CV), and renal complications. Risk stratification and preventative measures for NSAID complications are discussed.

Case Report

A 66-year-old female underwent delayed breast reconstruction with deep inferior epigastric artery perforator free flaps, 2 years after bilateral mastectomy for breast cancer. Her past medical history was significant for type 2 diabetes, hyperlipidemia, and hypertension but otherwise had no GI or cardiac history, coagulopathy, and was not taking anticoagulant medications. The procedure was uncomplicated and she was discharged home on post-operative day 4 with flaps in excellent condition, adequate pain control, ambulation, and generally feeling well.

Eighteen days post-operatively, she re-presented with a syncopal episode, diarrhea, melena stool, and a hemoglobin level

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of 66 g/L. She had been taking ibuprofen 600 mg every 6 hours for pain control. She was admitted to hospital, and an upper endoscopy revealed a duodenal ulcer with adherent clot. There was no active bleeding, and thus no intervention was performed. Later in the day, her melanotic stool evolved to contain bright red blood, and her oxygen saturation dropped into the 50s. She was stabilized with 10 units of packed red blood cells, 6 units of fresh frozen plasma, and transferred to a tertiary care centre for definitive management.

Repeat upper endoscopy confirmed the duodenal ulcer, which was now actively bleeding. The hemorrhage was unresponsive to clipping, epinephrine injection, and electrocautery. The patient was taken urgently to the interventional radiology suite where the gastroduodenal artery was successfully coiled to stop the bleed. During this process, a massive transfusion protocol was initiated and she received an additional 14 units of packed red blood cells.

Her abdominal incision dehisced and this was managed with local wound care. She was discharged home 12 days later in stable condition. She has had no other complications. Repeat upper endoscopy 4 months after the bleed showed complete healing of the ulcer.

Discussion

Nonsteroidal anti-inflammatory drugs exert their analgesic effects through cyclooxygenase (COX) inhibition, which slows the production of pro-inflammatory mediators such as prostaglandins, thromboxane A2, and prostacyclin.[4] Although inflammation is inhibited, the protective effects of these mediators are also lost, which may lead to complications within the GI tract, cardiac, and renal systems.

The GI complications of NSAIDs range from dyspepsia to ulceration and life-threatening exsanguination and have been described since the 1980s.[5] Patients taking NSAIDs have a 3-fold increase in the relative risk of a GI complication compared to non-users, and the risk is even higher in elderly patients (over the age of 60), those taking concomitant corticosteroids, and NSAID use within the first 3 months of onset.[6] Disturbingly, the first sign of an NSAID-induced ulcer was a life-threatening bleed in 58.2% of patients in one cohort.[7] In patients with active *Helicobacter pylori* infection who take an NSAID, the odds ratio of developing a peptic ulcer triples compared to non-*H pylori* infected NSAID users.[8]

Renal side effects develop from ischemia due to the decreased levels of circulating prostaglandins causing vasoconstriction of the glomeruli. Acute renal failure results, along with all of its associated complications such as electrolyte and fluid imbalances.[9] Dysregulation of distal tubular reabsorption causes sodium retention, hypertension, and may exacerbate pre-existing congestive heart failure.[9-11] Hyperkalemia can be seen in patients with risk factors such as congestive heart failure, diabetes, or those taking potassium supplements or potassium sparing diuretics.[9] Rarely, NSAIDs can also cause nephrotic syndrome and interstitial nephritis in patients with no risk factors, often presenting with edema, oliguria, and foamy urine. In healthy individuals, NSAID-induced renal complications are dose and duration dependent and often reversible. However, patients with underlying renal risk factors can develop chronic renal failure and become dialysis dependent.[10,11]

Table 1. Patient Factors Associated With Increased Risk of Complications Associated With NSAID Use.[14,15]

Factors Related to GI Complications	Factors Related to CV Complications	Factors Related to Renal Complications
Old age (>65)	Cardiac risk per Framingham risk calculator	History of acute renal failure
Pre-existing peptic ulcer disease		Chronic renal failure
Helicobacter pylori infection		Congestive heart failure
Higher dose, or longer duration of NSAID use		Diabetes
Concomitant use with anticoagulant or corticosteroid		Potassium supplements
		Potassium sparing diuretics

Abbreviations: CI, cardiovascular; CV, cardiovascular; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drugs.

The CV complications of NSAIDs were discovered more recently. Coxibs are a newer type of NSAID which selectively block COX-2 and were developed to satisfy the demand for an NSAID with fewer GI side effects in patients who required prolonged NSAID therapy, such as in rheumatic or arthritic diseases. In 2000, a randomized controlled trial showed that patients who received rofecoxib (a selective COX-2 inhibitor) were half as likely to develop a GI complication compared to those randomized to naproxen (a non-selective COX inhibitor).[12] However, 5 years later, a second randomized controlled trial examining the chemopreventative properties of rofecoxib for adenomatous polyps was prematurely ended because patients receiving rofecoxib were almost twice as likely to develop a cardiac event (hypertension and myocardial infarction).[13] Interestingly, it was later discovered that some authors in the VIOXX™ Gastrointestinal Outcomes Research Trial (VIGOR) in 2000 knowingly withheld reporting of CV complications among patients taking rofecoxib.[14]

When prescribing an NSAID, patient factors related to potential GI, CV, and renal complications need to be assessed[15] (Table 1). There are 3 modifiable risk factors which can be optimized in patients at high risk of a GI complication: (1) add a gastroprotective agent concurrently with NSAID use[16]; (2) use of coxibs, (selective COX-2 inhibitors), which reduce the incidence of GI complications at the expense of higher risk of cardiac events[12]; and (3) test for and completely treat *H pylori* infection.[8] The category and dosage of GI prophylactic medication varies on the patient's risk stratification for GI or CV complications (Table 2). The most commonly used agents are proton pump inhibitors (PPIs) and such as oral esomeprazole 20 or 40 mg daily and oral lansoprazole 15 or 30 mg daily. Misoprostol is no longer routinely used due to the higher frequency of administration and thus lower compliance, and side effects, including cramping diarrhea. Therefore, it is more common to prescribe a PPI for prophylactic GI therapy.

For patients with high CV risk as determined by the Framingham risk stratification, a selective COX-1 inhibitor

Table 2. Recommendations for GI Prophylaxis for Patients Administered NSAIDs for Post-Operative Pain Based on GI and CV Risk.[a]

GI and CV Risk Stratefication	Low CV Risk	High CV Risk
High GI risk	Alternative therapy if possible or NSAID + COX-2 inhibitor + PPI (high dose)/ misoprostol	Alternative therapy—avoid NSAIDs or COX-2 inhibitors if possible
Moderate GI risk	NSAID + PPI/ misoprostol	Naproxen + PPI/ misoprostol
Low GI risk	NSAID at lowest dose	Naproxen + PPI/ misoprostol

Abbreviations: CI, cardiovascular; COX, cyclooxygenase; CV, cardiovascular; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drugs; PPI, proton-pump inhibitor.
[a]Adapted From American Journal of Gastroenterology.[17]

may reduce the risk of a cardiac event at the expense of higher risk of GI events[15] (Table 2). Patients with renal risk factors should be restricted in the dose and duration of NSAID use, and it would be prudent to monitor the renal function in these at-risk patients.

Our patient had a history of diabetes, hypertension, and hyperlipidemia, which put her at risk of renal and cardiac complications, but otherwise no GI risk factors. Nonsteroidal anti-inflammatories were not explicitly prescribed while the patient was admitted post-operatively; however, we routinely verbally recommend trialing NSAIDs and acetaminophen before escalating to narcotics. Our patient used high-dose ibuprofen consistently at home because it provided adequate analgesia without inducing drowsiness.

Ultimately, an informed discussion on the purpose, benefits, risks, and alternatives of NSAID use is paramount before initiating therapy. The side effects of NSAIDs are not benign and should not be taken lightly. Physicians need to elicit risk factors for GI, CV, and renal side effects among their patients and adopt a preventative strategy. Furthermore, when NSAIDs are prescribed, patients need to be monitored closely for these potentially life-threatening side effects, by eliciting changes in GI discomfort, hematemesis, change in stool colour and consistency, chest pain, and decreased urine output.

Statement of Human and Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study.

Statement of Informed Consent

Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identified.

Declaration of Conflicting Interests

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