

# Pharmacovigilance in Gastrointestinal Surgeries: Ensuring Patient Safety and Optimal Outcomes

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## ABSTRACT

Gastrointestinal surgeries encompass a diverse range of procedures aimed at treating conditions affecting the digestive system. While these surgeries offer the potential for improved patient outcomes, they also carry inherent risks, including adverse drug reactions (ADRs) related to the medications used throughout the perioperative period. Pharmacovigilance, the science, and activities aimed at detecting, assessing, understanding, and preventing ADRs, is critical in ensuring patient safety during gastrointestinal surgeries. This review explores the principles of pharmacovigilance in the context of gastrointestinal surgeries, including the identification and management of ADRs, challenges encountered, and strategies for optimizing medication safety and patient outcomes.

**Keywords:** Pharmacovigilance, Gastrointestinal Surgeries, Patient Safety

## INTRODUCTION

Gastrointestinal surgeries are performed to treat a wide range of conditions affecting the digestive system, including gastrointestinal cancers, inflammatory bowel disease, and gastrointestinal bleeding. These surgeries may involve various procedures such as resections, bypasses, and reconstructions, each with its own set of risks and complications. Throughout the perioperative period, patients undergoing gastrointestinal surgeries receive a variety of medications to manage pain, prevent infection, support gastrointestinal function, and address comorbid conditions. While these medications are essential for optimizing surgical outcomes and promoting patient recovery, they also carry the potential for adverse drug reactions (ADRs), which can compromise patient safety and result in significant morbidity and mortality. Pharmacovigilance, therefore, plays a crucial role in monitoring and mitigating the risks associated with medication use in gastrointestinal surgeries.

## Pharmacovigilance: Principles and Framework

Pharmacovigilance encompasses the systematic monitoring, detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. The primary objectives of pharmacovigilance are to ensure the safety of medications throughout their lifecycle and to minimize the risks associated with their use [1]. Pharmacovigilance activities involve collecting and analyzing data from various sources, including spontaneous reports, clinical trials, epidemiological studies, and regulatory agencies, to identify potential safety signals and take appropriate regulatory action when necessary. The pharmacovigilance framework includes key components such as adverse event reporting systems, signal detection and evaluation, risk management strategies, and communication of safety information to healthcare professionals and patients [2,3].

### Medication Use in Gastrointestinal Surgeries

Patients undergoing gastrointestinal surgeries receive a variety of medications throughout the perioperative period to address their medical needs and support their recovery.

**Preoperative Medications:** Before gastrointestinal surgery, patients may receive medications for various purposes, such as prophylaxis against infection, bowel preparation, and management of comorbid conditions. Common preoperative medications include antibiotics, laxatives, proton pump inhibitors (PPIs), and medications for chronic conditions like diabetes or hypertension. Preoperative medications can lead to adverse reactions such as allergic reactions to antibiotics [4], electrolyte imbalances from laxatives [5], and gastrointestinal disturbances from PPIs [6]. Additionally, interactions between medications used to manage chronic conditions and those administered for surgical preparation must be carefully monitored to avoid complications.

**Intraoperative Medications:** During gastrointestinal surgery, anesthesiologists and surgical teams administer a variety of medications to induce anesthesia, maintain hemodynamic stability, control pain, and prevent complications such as nausea and vomiting [7]. Intraoperative medications carry the risk of adverse reactions such as allergic reactions to anesthesia agents, respiratory depression from opioids used for pain management, and adverse cardiovascular effects from vasopressors or inotropes [8,9]. Special attention must be paid to patients with preexisting cardiovascular or respiratory conditions to minimize the risk of intraoperative

complications [10].

**Postoperative Medications:** After gastrointestinal surgery, patients often require medications to manage pain, prevent infection, promote wound healing, and support gastrointestinal function. Common postoperative medications include analgesics, antibiotics, antiemetics, and medications to facilitate bowel recovery [11]. Postoperative medications can lead to adverse effects such as opioid-related respiratory depression, surgical site infections due to antibiotic-resistant bacteria, and gastrointestinal complications such as nausea, vomiting, or ileus [12]. Additionally, medications used to manage postoperative pain may interact with other drugs or exacerbate underlying medical conditions, necessitating close monitoring and adjustment of treatment regimens.

### ADRs in Gastrointestinal Surgeries

ADRs are common in patients undergoing gastrointestinal surgeries due to the complex interplay between surgical interventions, patient factors, and medication use. ADRs may manifest as allergic reactions, medication side effects, drug interactions, or complications related to underlying medical conditions.

Medication risks during gastrointestinal surgeries encompass a spectrum of potential adverse events and complications related to the use of medications in the perioperative period. These risks arise from various factors including the complexity of surgical procedures, the physiological changes induced by anesthesia, and interactions between medications used for pain management, infection prevention, and other therapeutic purposes. Understanding and mitigating these risks is essential for ensuring patient safety and optimizing surgical outcomes. Some common risks include:

### Polypharmacy and Drug Interactions

Patients undergoing gastrointestinal surgeries often receive multiple medications for pain management, prophylaxis against infection, and management of comorbid conditions such as hypertension and diabetes. The concurrent use of multiple medications increases the risk of drug interactions, potentially leading to adverse outcomes such as:

**Reduced efficacy of medications:** Drug interactions may diminish the therapeutic effects of medications, compromising their ability to manage pain, prevent infection, or control underlying medical conditions [13].

Increased toxicity: Certain drug combinations can potentiate the adverse effects of medications, leading to toxicity or exacerbation of preexisting medical conditions [14].

Altered pharmacokinetics: Drug interactions may affect the absorption, distribution, metabolism, and excretion of medications, resulting in unpredictable pharmacokinetic profiles and suboptimal drug concentrations [15].

### **Anesthesia-related Complications**

Anesthesia is an integral component of gastrointestinal surgeries, but it also carries inherent risks, including medication-related complications such as:

Allergic reactions: Anesthesia agents, particularly muscle relaxants and antibiotics, can trigger allergic reactions ranging from mild rashes to life-threatening anaphylaxis [16].

Respiratory depression: Opioids and sedative agents used for anesthesia and pain management can depress respiratory function, leading to hypoventilation, hypoxemia, and respiratory failure [8].

Hemodynamic instability: Vasopressors and inotropes administered during anesthesia may cause adverse cardiovascular effects such as hypertension, tachycardia, or arrhythmias [17].

### **Gastrointestinal Complications**

Gastrointestinal surgeries inherently disrupt normal digestive processes and can predispose patients to medication-related gastrointestinal complications, including:

Nausea and vomiting: Anesthesia, opioid analgesics, and surgical manipulation can trigger postoperative nausea and vomiting (PONV), which can delay recovery, increase the risk of aspiration, and compromise patient comfort. [18] Studies have explored different approaches to prevent and manage PONV, including the use of antiemetic medications and regional anesthesia techniques. PONV is affected by various factors associated with the patient, the surgical procedure, and anesthesia administered before, during, and after surgery. Evaluating the likelihood of PONV can be achieved through tools like the Apfel simplified scoring system [19], which relies on four distinct risk factors. Patients identified as having medium to high risks according to this scoring system are typically given preventive measures against PONV.

Delayed gastric emptying: Opioids and certain anesthetic agents can impair gastric motility, leading to delayed gastric emptying (ileus) and postoperative ileus, which can prolong hospital stays and increase the risk of complications such as aspiration pneumonia and surgical site infections [20].

Gastrointestinal bleeding: Nonsteroidal anti-inflammatory drugs (NSAIDs) and antiplatelet agents used for pain management can increase the risk of gastrointestinal bleeding, particularly in patients with preexisting gastrointestinal ulcers or coagulopathies [21]. A study conducted in Beijing [21] stated that familial background of gastrointestinal bleeding, a past medical record of peptic ulcers, cardiovascular and cerebrovascular conditions, diabetes mellitus, the use of antiplatelet medications, presence of *Helicobacter pylori* infection, low levels of cholesterol, and the consumption of NSAIDs were independent risk factors for gastrointestinal bleeding in older population.

### **Surgical Site Infections**

Prophylactic antibiotics are commonly administered before gastrointestinal surgeries to reduce the risk of surgical site infections. However, inappropriate antibiotic selection, timing, or duration can contribute to antibiotic resistance and increase the risk of adverse outcomes such as:

Surgical site infections: Inadequate antibiotic prophylaxis or prolonged antibiotic exposure can lead to surgical site infections (SSI) caused by multidrug-resistant bacteria, resulting in prolonged hospitalization, increased healthcare costs, and poorer patient outcomes [22]. Addressing allergic responses to antibiotics poses a complex obstacle in preventing SSI. These reactions can vary widely, spanning from minor skin irritations and itching to critical and potentially fatal anaphylactic shock [23].

*Clostridium difficile* infection: Broad-spectrum antibiotics disrupt the normal gut microbiota, predisposing patients to *Clostridium difficile* infection (CDI), a potentially life-threatening condition characterized by diarrhea, pseudomembranous colitis, and systemic complications. The correlation between CDI and prophylactic antibiotics underscores the delicate balancing act inherent in surgical procedures. While antibiotics are prescribed to forestall SSI, they may inadvertently foster an environment conducive to CDI emergence. Healthcare professionals must judiciously select and administer antibiotics, considering their potential impact on CDI development [24].

## Medication-related Hepatotoxicity

Some medications used in gastrointestinal surgeries, such as acetaminophen (paracetamol) and certain antibiotics, can cause hepatotoxicity, particularly in patients with underlying liver disease or impaired hepatic function. Hepatotoxic medications can lead to drug-induced liver injury. Hepatotoxic medications may cause liver enzyme elevation, hepatocellular necrosis, cholestatic injury, or fulminant hepatic failure, necessitating discontinuation of the offending agent and close monitoring of liver function tests [25].

## Electrolyte imbalances:

Bowel preparations, such as those taken before colonoscopies or other gastrointestinal procedures, often involve the use of laxatives or other medications to empty the bowels. These preparations can lead to electrolyte imbalances, particularly disturbances in sodium, potassium, and magnesium levels, due to the loss of fluids and electrolytes through diarrhea induced by the laxatives. Bowel preparations may cause electrolyte disturbances which remain asymptomatic and unrecognized in the majority of cases [26].

The occurrence of these ADRs can prolong hospital stays, increase healthcare costs, and negatively impact patient outcomes, highlighting the importance of pharmacovigilance in identifying and mitigating these risks.

## Challenges in Pharmacovigilance in Gastrointestinal Surgeries

Pharmacovigilance in gastrointestinal surgeries faces several challenges that must be addressed to ensure effective monitoring and management of ADRs:

- **Underreporting of ADRs:** Healthcare professionals may fail to recognize or report ADRs due to a lack of awareness, time constraints, or perceived insignificance of the event.
- **Polypharmacy:** Patients undergoing gastrointestinal surgeries often receive multiple medications, increasing the risk of ADRs and drug interactions.
- **Limited data:** There may be insufficient data on the safety and efficacy of medications used in gastrointestinal surgeries, particularly in specific patient populations such as children, pregnant women, and the elderly.
- **Variability in practice:** Surgical techniques, anaesthesia

protocols, and medication regimens may vary among healthcare institutions, making it challenging to standardize pharmacovigilance practices and compare outcomes.

## Strategies for Optimizing Pharmacovigilance in Gastrointestinal Surgeries

To address the challenges associated with pharmacovigilance in gastrointestinal surgeries, several strategies can be implemented:

- **Enhance ADR reporting:** Healthcare professionals should be educated about the importance of reporting ADRs and provided with easy-to-use reporting systems to facilitate timely and accurate reporting.
- **Implement standardized protocols:** Standardized protocols for medication use, anaesthesia management, and surgical techniques can help minimize variability in practice and improve patient safety.
- **Multidisciplinary collaboration:** Collaboration among surgeons, anaesthesiologists, pharmacists, and other healthcare professionals is essential for optimizing medication management and identifying and addressing ADRs promptly.
- **Pharmacovigilance training:** Healthcare professionals should receive training in pharmacovigilance principles and practices to enhance their awareness and skills in detecting and managing ADRs.
- **Utilize technology:** Electronic health records, medication reconciliation tools, and decision support systems can facilitate the monitoring and managing of medications and ADRs in gastrointestinal surgeries.
- **Patient education:** Patients should be educated about the medications they are prescribed, potential side effects, and the importance of reporting ADRs to their healthcare providers.

## CONCLUSION

Pharmacovigilance is critical in ensuring patient safety and optimizing outcomes in gastrointestinal surgeries. By systematically monitoring and managing medication use throughout the perioperative period, healthcare professionals can minimize the risk of adverse drug reactions and enhance

patient care. Addressing the challenges associated with pharmacovigilance in gastrointestinal surgeries requires a multidisciplinary approach, standardized protocols, enhanced reporting systems, and ongoing education and training. By implementing these strategies, healthcare providers can mitigate the risks associated with medication use and improve the quality and safety of care for patients undergoing gastrointestinal surgeries.

## REFERENCES

- Hamid AAA, Rahim R, Teo SP. (2022). Pharmacovigilance and Its Importance for Primary Health Care Professionals. *Korean J Fam Med.* 43(5):290-295.
- Jose J, Al Rubaie MH, Al Ramimmy H, Varughese SS. (2021). Pharmacovigilance: Basic concepts and an overview of the system in Oman. *Sultan Qaboos Univ Med J.* 21(2):e161-e163.
- Jeetu G, Anusha G. (2010). Pharmacovigilance: a worldwide master key for drug safety monitoring. *J Young Pharm.* 2(3):315-320.
- Golembiewski JA. (2002). Allergic reactions to drugs: implications for perioperative care. *J Perianesth Nurs.* 17(6):393-398.
- Chu T, Wu Z, Xu A. (2022). Association between preoperative hypokalemia and postoperative complications in elderly patients: a retrospective study. *BMC Geriatr.* 22(1):743.
- Vaezi MF, Yang YX, Howden CW. (2017). Complications of proton pump inhibitor therapy. *Gastroenterology.* 153(1):35-48.
- Tippireddy S, Ghatol D. (). Anesthetic Management for Enhanced Recovery After Major Surgery (ERAS) [Updated 2023 Jan 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
- Karcz M, Papadakos PJ. (2013). Respiratory complications in the postanesthesia care unit: A review of pathophysiological mechanisms. *Can J Respir Ther.* 49(4):21-29.
- Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, et al. (2019). Guidelines for Perioperative Care in Cardiac Surgery: Enhanced Recovery After Surgery Society Recommendations. *JAMA Surg.* 154(8):755-766.
- Ganesh R, Kebede E, Mueller M, Gilman E, Mauck KF. (2021). Perioperative Cardiac Risk Reduction in Noncardiac Surgery. *Mayo Clin Proc.* 96(8):2260-2276.
- Mazzotta E, Villalobos-Hernandez EC, Fiorda-Diaz J, Harzman A, Christofi FL. (2021). Postoperative Ileus and Postoperative Gastrointestinal Tract Dysfunction: Pathogenic Mechanisms and Novel Treatment Strategies Beyond Colorectal Enhanced Recovery After Surgery Protocols. *Front. Pharmacol.* 11:583422.
- Khansari M, Sohrabi M, Zamani F. (2013). The Useage of Opioids and their Adverse Effects in Gastrointestinal Practice: A Review. *Middle East J Dig Dis.* 5(1):5-16.
- Zhao Q, Chen Y, Huang W, Zhou H, Zhang W. (2023). Drug-microbiota interactions: an emerging priority for precision medicine. *Sig Transduct Target Ther.* 8: 386
- Guengerich FP. (2011). Mechanisms of drug toxicity and relevance to pharmaceutical development. *Drug Metab Pharmacokinet.* 26(1):3-14.
- Teo YL, Ho HK, Chan A. (2015). Metabolism-related pharmacokinetic drug-drug interactions with tyrosine kinase inhibitors: current understanding, challenges and recommendations. *Br J Clin Pharmacol.* 79(2):241-53.
- Harper NJ, Dixon T, Dugué P, Edgar DM, Fay A, Gooi HC, et al. (2009). Working Party of the Association of Anaesthetists of Great Britain and Ireland. Suspected anaphylactic reactions associated with anaesthesia. *Anaesthesia.* 64(2):199-211.
- Bangash MN, Kong ML, Pearse RM. (2012). Use of inotropes and vasopressor agents in critically ill patients. *Br J Pharmacol.* 165(7):2015-2033.
- Shaikh SI, Nagarekha D, Hegade G, Marutheesh M. (2016). Postoperative nausea and vomiting: A simple yet complex problem. *Anesth Essays Res.* 10(3):388-396.
- Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. (1999). A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. *Anesthesiology.* 91:693-700.
- Melnyk M, Casey RG, Black P, Koupparis AJ. (2011). Enhanced recovery after surgery (ERAS) protocols: Time to change practice? *Can Urol Assoc J.* 5(5):342-348.
- Chi TY, Zhu HM, Zhang M. (2018). Risk factors associated with nonsteroidal anti-inflammatory drugs (NSAIDs)-

- induced gastrointestinal bleeding resulting on people over 60 years old in Beijing. *Medicine (Baltimore)*. 97(18):e0665.
22. Dhole S, Mahakalkar C, Kshirsagar S, Bhargava A. (2023). Antibiotic Prophylaxis in Surgery: Current Insights and Future Directions for Surgical Site Infection Prevention. *Cureus*. 15(10):e47858.
23. Sastic C. (2014). Appropriate assessment of patient medication allergies. *Hosp Pharm*. 49:322–323.
24. Mullish BH, Williams HR. (2018). Clostridium difficile infection and antibiotic-associated diarrhoea. *Clin Med (Lond)*. 18(3):237-241.
25. Rotundo L, Pysopoulos N. (2020). Liver injury induced by paracetamol and challenges associated with intentional and unintentional use. *World J Hepatol*. 12(4):125-136.
26. Reumkens A, van der Zander Q, Winkens B, Bogie R, Bakker CM, Sanduleanu S, et al. (2022). Electrolyte disturbances after bowel preparation for colonoscopy: Systematic review and meta-analysis. *Dig Endosc*. 34(5):913-926.