The gastrointestinal side effects and toxicity associated with nonsteroidal anti-inflammatory drugs (NSAIDs)

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Abstract

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used to alleviate pain, but unfortunately, they are associated with significant gastrointestinal complications that give rise to considerable clinical and public health challenges. In this literature review, we aim to explore the gastrointestinal side effects and toxicity tied to NSAID use by investigating the underlying mechanisms and examining potential approaches for minimizing these risks. NSAIDs inflict harm by inhibiting cyclooxygenase enzymes, disrupting prostaglandin synthesis, and diminishing gastric mucosal protection. This disruption can result in gastric ulcers, bleeding, or even perforation; however, their severity depends on several factors, including the specific type of NSAID used, the dosage administered, and characteristics unique to each patient. Various risk factors have been identified, such as advanced age, previous history of gastrointestinal complications, concurrent medication usage, and infection with *Helicobacter pylori*. An understanding of these particular mechanisms and an appreciation for associated risk factors serve as a foundation upon which tailored preventive measures can be developed to optimize patient outcomes. With this review acting as a catalyst for further research endeavors, we hope that interventions to promote safer pain management will be realized to address better the prominent clinical implications behind NSAID use within our society.

Background

- Nonsteroidal anti inflammatory drugs (NSAIDs) are commonly used by people to alleviate pain, however they can have negative effects on the gastrointestinal (GI) system. The main way NSAIDs affect the GI tract is by inhibiting enzymes called cyclooxygenases (COX) COX 1 and COX 2.
- COX 1 is always present in the body, it plays a role in maintaining protective substances called prostaglandins, essential lipid compounds that maintain gastrointestinal mucosal integrity. When COX 1 is inhibited fewer prostaglandins are produced, making it harder for the stomach to withstand the effects of gastric acid and pepsin, increasing possibility of GI complications.

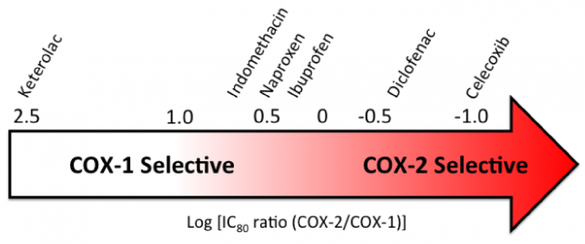

Figure 1: This illustrates the comparative COX-1 and COX-2 selectivity, the preference of one substrate over another, of frequently used non-aspirin NSAIDs. Among these, only Celecoxib stands out as a COX-2 selective NSAID available in the US market. (Danelich et al. in 2015.)

In order to make the use of NSAIDs while also minimizing the risks to the GI system healthcare providers need to take into account specific factors, about each patient. These factors include age, any previous GI problems and any other medications being taken at the time. By identifying these risk factors healthcare professionals can develop strategies and preventive measures that prioritize safety and enhance pain management practices.

Discussion

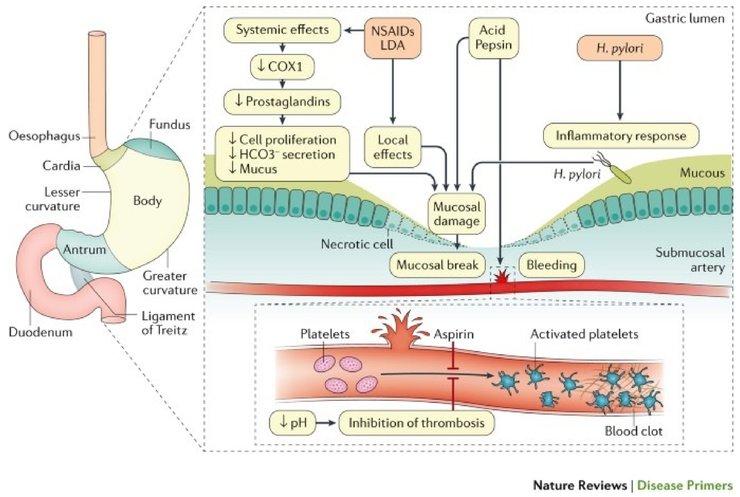

Figure 2: The effect of NSAIDs and other possible contributing factors, such as *H. pylori* and stomach acid, on the mucosal lining of the GI tract. Contributed damage leans to mucosal break and bleeding. Aspirin can further inhibit the healing process by slowing the activation of platelets. (Lanas, Angel, et al 2018)

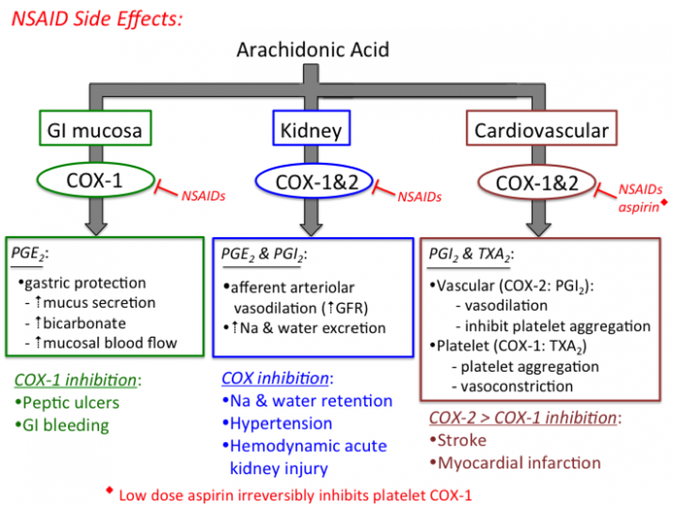

Figure 3: The primary physiological functions of COX-1 and COX-2, and the mechanisms responsible for drug-induced side effects. PGI2 (prostacyclin), TXA2 (thromboxane), PG (prostaglandin)(Tulane University 2017)

- The adverse effects of NSAID usage include gastric ulcers, bleeding, and perforation.
- Certain NSAIDs, like aspirin and indomethacin, are associated with gastric ulcers, which may become chronic and lead to complications such as bleeding or obstruction.
- Gastrointestinal bleeding is a significant complication, in severe cases, gastrointestinal perforation can occur, requiring immediate medical attention.
- Various patient characteristics and preexisting conditions increase vulnerability to NSAID-related gastrointestinal complications, with advanced age being a major risk factor due to impaired gastric mucosal defense mechanisms.
- Previous histories of gastrointestinal ulcers or bleeding also elevate the risk of experiencing NSAID-induced gastrointestinal toxicity.
- Concurrent use of specific medications, including SSRIs (selective serotonin reuptake inhibitors), corticosteroids, and anticoagulants, can further impact the likelihood of gastrointestinal ulcers or bleeding.
- *H. pylori* infection in the stomach exacerbates NSAID effects on the gastrointestinal system.

Future Directions

- Further investigations are crucial to enhance our understanding of NSAID-induced gastrointestinal toxicity and minimize risks.
- Addressing knowledge gaps in specific areas can optimize NSAID use.
- The impact of COX 1 inhibition on cytoprotective prostaglandins versus broader COX activity inhibition remains debated, requiring additional research.
- Comparative studies between COX 1 selective inhibitors and nonselective NSAIDs can clarify contributions to gastrointestinal side effects.
- Novel drug delivery systems and targeted approaches show promise in reducing toxicity while ensuring effective pain management.
- Longitudinal studies in vulnerable populations, like the elderly, can assess chronic complications.
- Identifying risk factors and integrating clinical and genetic data can aid personalized medicine approaches.
- By pursuing these future directions, we can establish evidence-based methods for safer pain management and improved patient outcomes.

Citations