

Gastrointestinal Tract Disorder as a Side Effect of Non-steroidal Anti Inflammatory Drugs (NSAIDs)

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Non-steroidal anti inflammatory drugs (NSAIDs) are extremely essential for patients with osteoarthritis (OA), rheumatoid arthritis (RA), and other rheumatoid diseases, especially to alleviate complaints. NSAIDs are commonly prescribed by physicians all over the world, making an estimated 4.5% of all prescriptions, aside from accounting for a great number of over-the-counter (OTC) drugs.¹

It is known that NSAIDs cause damage of gastroduodenal, intestinal, and colonic mucosa.^{2,3,4} The possible side-effects of NSAIDs on the gaster and duodenum are bleeding, erosion, or ulceration/ulcer.^{5,6}

During endoscopy of the upper gastrointestinal tract, approximately half of patients who regularly consume NSAIDs suffer from gastric erosion, and 15-30% suffer from ulcer. However, the incidence rate of upper gastrointestinal tract incidents due to NSAIDs ranges around 3 to 4.5% of patients who consume NSAIDs, and severe complication is found in approximately 1.5%.² In general, at least 10-20% of patients complain of dyspepsia when consuming NSAIDs.³ What is most important to know for clinical purposes is that 40-60% of patients with mucosal lesion do not present with any symptom or complaint.⁵ The reported side effect of NSAIDs on the small intestines were ulceration, chronic diarrhea, stricture, and even perforation.^{2,7,8} NSAIDs could also affect the colon in the form of diaphragmatic stricture, colon ulceration, etc.⁷ These gastrointestinal side-effects of NSAIDs are more common in high-risk patients, which are those with previous history of gastrointestinal ulcer, age over 60 years, concurrent use of NSAIDs with corticosteroids, use of high dose of NSAIDs, duration of rheumatoid arthritis, heart disease

and other illnesses, use of NSAIDs in the first month, previous history of dyspepsia, and *Helicobacter pylori* infection.²

There are two main pathogenic mechanisms caused by NSAIDs, the first one being a topical effect that involves “uncoupling of mitochondrial oxidative phosphorylation” with increased intestinal permeability resulting in gastric/intestinal inflammation, and the second one being a systemic effect that inhibits cyclo-oxygenase-1 (COX-1).⁹ NSAIDs could increase the formation of free radicals that aggravates gastrointestinal mucosal damage by damaging cell membranes, causing gene signal changes, and causing damage to the DNA.¹⁰

As we know, in humans, prostaglandin is formed through COX-1 and COX-2 pathways. The prostaglandin formed through the COX-2 pathway acts by means of the inflammatory mechanism. The prostaglandin formed via the COX-1 pathway plays a greater role in normalizing physiological conditions. NSAIDs mostly inhibit COX-1 and COX-2 pathways, resulting in gastrointestinal complications. The recent COX-2 selective inhibitor NSAIDs only inhibit the COX-2 pathway, and thus theoretically does not cause gastrointestinal disorders, or only minimally does so.¹¹

The study by Girawan D et al, a difference in NSAID gastropathy endoscopic score was found to be 78% in patients receiving pyroxicam and 40% in patients receiving meloxicam. The increase in endoscopic score in the group receiving meloxicam is less than that of the pyroxicam group ($p < 0.05$). This is in line with references that state that both COX-1/COX-2 non-selective inhibitors as well as COX-2 selective inhibitor NSAIDs could cause mucosal damage in the gaster, small intestines, and colon. However, the damage in gastrointestinal mucosa among patients receiving COX-2 selective inhibitor is much less.² Cytoprotective agents, H2 receptor antagonists (H2RA), and proton pump inhibitors (PPI) could be used to prevent and treat

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gastrointestinal side-effects of NSAIDs.^{6,12}

Most patients suffer from dyspeptic syndrome due to *Helicobacter pylori* infection, NSAIDs and stress. The management of patients with dyspepsia due to NSAID-gastropathy and *Helicobacter pylori* infection is still controversial. Some researchers recommend the eradication of *Helicobacter pylori*, while a number of others disagree because in several studies no correlation was found between the severity of gastric mucosal damage due to NSAIDs and *Helicobacter pylori* infection. The cellular pathogenesis of ulcer due to NSAIDs and *Helicobacter pylori* have been demonstrated to be independent of each other, *Helicobacter pylori* does not increase the risk of NSAID-induced toxicity.¹

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