

CAUSES OF PUD: MEDICATIONS

FLAME LECTURE: 75

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LEARNING OBJECTIVES

- ▶ To know the most common medications causing peptic ulcer disease (PUD)
- ▶ To describe the pathophysiology of how non-steroidal anti-inflammatory drugs (NSAIDs) can cause PUD & how to lower this risk
- ▶ Prerequisites:
 - ▶ NONE
- ▶ See also – for closely related topics
 - ▶ FLAME LECTURE: Management & Treatment of PUD
 - ▶ FLAME LECTURE: Causes of Peptic Ulcer Disease: H. Pylori

NSAIDs & PUD

- ▶ NSAIDs are the most common pharmacologic cause of PUD
 - ▶ Increases risk of PUD from 8% in non-NSAID users → 36% in NSAID users¹
 - ▶ Relative risk (RR) varies between meds in this class²:
 - ▶ Lowest with ibuprofen & celecoxib (RR <2)
 - ▶ Intermediate with diclofenac & meloxicam (RR 2-4)
 - ▶ Higher with naproxen & indomethacin (RR 4-5)
 - ▶ Highest with ketorolac (RR 11.5)

1. Huang, J. Lancet 2002.
2. Drinl, M. Aust Prescr 2017.

PATHOPHYSIOLOGY

- ▶ Gastric mucosal damage inflicted via multiple mechanisms¹:
 - ▶ NSAIDs decrease protective prostaglandin synthesis via inhibition of COX-1
 - ▶ Cause topical irritation of the epithelium
 - ▶ Decrease gastric mucosal blood flow
 - ▶ Impairs mucosal barrier properties

RISK FACTORS FOR GI TOXICITY FROM NSAIDs

- ▶ Age >65 years
- ▶ Chronic use of high-dose NSAIDs
- ▶ Aspirin, anticoagulant or corticosteroid use
- ▶ History of previous ulcer
- ▶ H. pylori positive

PREVENTION OF NSAID GI TOXICITY

- ▶ If risk factors for toxicity are present, adjunctive therapies may help protect the mucosa:
 - ▶ Proton pump inhibitors
 - ▶ Misoprostol (prostaglandin analogue)
 - ▶ Histamine H2 receptor antagonists
 - ▶ Switching to COX-2 inhibitor (i.e. celecoxib) instead of a standard NSAID
 - ▶ *But use with caution given FDA warning for possible increased cardiovascular risk*

OTHER PHARMACOLOGIC CAUSES OF PUD

- ▶ Bisphosphonates, clopidogrel, corticosteroids
 - ▶ Generally only a risk when combined with NSAIDs
- ▶ Spironolactone (at high doses)
- ▶ Selective serotonin reuptake inhibitors (SSRIs) and venlafaxine
 - ▶ Particularly when combined with NSAIDs; further research needed
- ▶ Sirolimus

REFERENCES / IMPORTANT LINKS

1. Castellsague, Jordi, et al. "Individual NSAIDs and Upper Gastrointestinal Complications." *Drug Safety*, vol. 35, no. 12, 2012, pp. 1127–1146., doi:10.1007/bf03261999.
2. Drina, Musa. "Peptic Ulcer Disease and Non-Steroidal Anti-Inflammatory Drugs." *Australian Prescriber*, vol. 40, no. 3, 2017, pp. 91–93., doi:10.18773/austprescr.2017.037.
3. Fashner, Julia, et al. "Diagnosis and Treatment of Peptic Ulcer Disease and H. pylori Infection." *Am Fam Physician*. 2015; 91 (4): 236-242.
4. Huang, Jia-Qing, et al. "Role of Helicobacter Pylori Infection and Non-Steroidal Anti-Inflammatory Drugs in Peptic-Ulcer Disease: a Meta-Analysis." *The Lancet*, vol. 359, no. 9300, 2002, pp. 14–22., doi:10.1016/s0140-6736(02)07273-2.
5. Vakil, Nimish, et al. "Unusual causes of peptic ulcer disease." *UpToDate*. Accessed 12/2/2019.
6. Wallace, John L. "How Do NSAIDs Cause Ulcer Disease?" *Best Practice & Research Clinical Gastroenterology*, vol. 14, no. 1, 2000, pp. 147–159., doi:10.1053/bega.1999.0065.