The Impact of Nonsteroidal Anti-Inflammatory Drugs on Ulcer Development

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Abstract—**Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for their analgesic, anti-inflammatory, and antipyretic properties. However, their use is associated with an increased risk of gastrointestinal complications, particularly peptic ulcer disease. This review article examines the mechanisms by which NSAIDs contribute to ulcer development, the associated risk factors, and potential strategies for prevention and management.**

I. INTRODUCTION

A peptic ulcer is a digestive tract injury caused by acid reflux that breaks down the mucosa and reaches the submucosa [1]. Peptic ulcers can occur in the oesophagus or Meckel's diverticulum, but they are most commonly found in the stomach or proximal duodenum [2]. Peptic ulcers in the duodenum or stomach are referred to as peptic ulcer disease. The majority of peptic ulcer diseases were previously believed to be caused by an acidic environment with hypersecretion, stress, and food factors [3]. However, the identification of Helicobacter pylori infection and the extensive use of nonsteroidal anti-inflammatory drugs (NSAIDs) during the second half of the 20th century have altered this belief.

NSAIDs are among the most commonly prescribed medications worldwide, used to treat a variety of conditions ranging from minor aches and pains to chronic inflammatory diseases [4]. Despite their therapeutic benefits, the gastrointestinal side effects of NSAIDs, particularly their role in ulcer development, remain a significant concern for both patients and healthcare providers [5].

A. Pathophysiology of ulcer

Under normal circumstances, the mucus-bicarbonate barrier, the neutral pH, and ongoing epithelial cell renewal preserve the integrity of the duodenum and gastric mucosa [6]. PGE2 stimulates mucus production, cell division, and H3 CO3 secretion, supporting a crucial function in mucosa preservation [7]. An important distinguishing characteristic of gastric homeostasis is adequate blood flow [8]. The gastric mucosa's proper perfusion is maintained by the NO and PGs, who also ensure that nutrients and oxygen are delivered to the area and that harmful metabolites are removed, preventing tissue damage [9].

Helicobacter pylori infection and the use of NSAIDs are common risk factors that precede PUD and gastritis [10]. Less common risk factors include Crohn's disease, radiation therapy, severe illness, autoimmune issues, alcohol, smoking, cocaine, and other unique situations [11].

Helicobacter pylori: The duodenal side of the stomach is better understood to have mechanisms through which the Hp promotes the growth of PU [12]. H. pylori cause the mucosal layer to become inflamed, attracting neutrophils, lymphocytes, plasma cells, and macrophages. It also causes epithelial cell deterioration and damage [13]. With little to no inflammation in the corpus, gastritis frequently gets worse in the antrum. H. pylori testing should be done on all patients who develop peptic ulcer. An H pylori infection-related inflammation can result in either hypochlorhydria [14].

A. Mechanisms of Ulceration Caused by NSAIDs

1.The suppression of prostaglandin synthesis

NSAIDs primarily function by inhibiting the cyclooxygenase (COX) enzymes, which are responsible for the production of prostaglandins [15]. The integrity of the gastric mucosa is maintained by prostaglandins, which increase mucosal blood flow, stimulate mucus and bicarbonate secretion, and promote epithelial cell proliferation and repair [16].

NSAIDs undermine these defences by preventing the production of prostaglandins, which leaves the stomach mucosa open to harm from gastric acid and other dangerous substances [17].

2.Topical Irritation Directly

Many NSAIDs are weak acids that, when they come into contact with the stomach epithelium, can cause direct irritation. This local effect may result in erosions and the development of ulcers. [18].

3. Impaired Platelet Function

NSAIDs inhibit platelet aggregation, which can prolong bleeding time and potentially exacerbate mucosal injury [19].

B. Risk Factors for Ulcers Caused by NSAIDs

The following variables raise the chance of NSAID-inducedulcers:

1.Age(over65)

2. Peptic ulcer disease's history

3. Concurrent use of anticoagulants or corticosteroids

4. Long-term or high-dose NSAID use

5. Infection with Helicobacter pylori

6. Drinking alcohol and smoking

7. Comorbidities (such as renal impairment and cardiovascular disease) [20].

C. Epidemiology and Clinical Impact Research has indicated that:

Endoscopically detectable ulcers occur in 15–30% of frequent NSAID users [21].

NSAID use raises the risk of upper gastrointestinal bleeding by four to five times, an 1-2 percent of users experience major gastrointestinal problems each year [22].

These issues have a major impact on healthcare expenses, morbidity, and mortality.

D. Prevention and Management Strategies

1. Risk Assessment

Careful evaluation of individual patient risk factors is crucial before initiating NSAID therapy [23].

2. Gastroprotective Agents

- Proton Pump Inhibitors (PPIs): Highly effective in reducing the risk of NSAID-associated ulcers [24]
- Misoprostol: A prostaglandin analog that can replace the protective effects lost due to COX inhibition [25]
- H2 Receptor Antagonists: Offer some protection, particularly at high doses [26]

3. COX-2 Selective Inhibitors

These drugs were developed to provide anti-inflammatory effects with reduced gastrointestinal toxicity. However, concerns about cardiovascular risks have limited their use [27].

4. H. pylori Eradication

Testing for and treating H. pylori infection in high-risk patients before initiating long-term NSAID therapy can reduce ulcer risk [28].

5. Alternative Pain Management Strategies

Considering non-NSAID pain management options for high-risk patients, such as acetaminophen or topical analgesics [29].

II. REPAIR OF ULCER

NSAIDs not only cause ulcers to form, but they can also accelerate the bleeding and slow the healing of pre-existing ulcers [30]. Once more, the effects on ulcer healing are likely linked to NSAIDs' capacity to inhibit prostaglandin synthesis. The primary mechanism for prostaglandin synthesis in the normal gastric mucosa is the cyclo-oxygenase-1 isoform [31]. However, it seems that cyclo-oxygenase-2 is the main factor influencing prostaglandin synthesis at an ulceration site, especially in the vicinity of the ulcer margin [32]. Given these findings and reports of selective cyclo-oxygenase-2 inhibitors aggravating intestinal inflammation and ulceration, care should be taken when assuming that the novel cyclooxygenase-2 inhibitors are safe for the gastrointestinal tract [33]. SAIDs' capacity to accelerate bleeding from pre-existing ulcers is most likely due to their inhibition of platelet aggregation. The inhibition of thromboxane synthesis is the result of NSAIDs' suppression of platelet aggregation [34]. It should be mentioned that aspirin causes an irreversible inhibition of platelet thromboxane synthesis, in contrast to other NSAIDs [35]. Therefore, the risk of gastrointestinal bleeding can be significantly increased by even small doses of aspirin used to prevent myocardial infarction and stroke [36]. NSAIDs' capacity to accelerate bleeding from pre-existing ulcers is most likely due to their inhibition of platelet aggregation NSAIDs' capacity to accelerate bleeding from pre-existing ulcers is most likely due to their inhibition of platelet aggregation [37].

III. CONCLUSION

The relationship between NSAID use and ulcer development is well-established and multifaceted. While NSAIDs remain invaluable therapeutic agents, their use must be carefully balanced against the risk of gastrointestinal complications. Proper patient

assessment, judicious use of gastroprotective strategies, and ongoing monitoring are essential to minimize the risk of NSAID-induced ulcers while maintaining effective pain and inflammation management.

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