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Peptic Ulcers and Aspirin: Uncovering the Cause, Diagnostic Techniques, Prevalence Insights, and Alternative Treatment Approaches

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Abstract: ***Peptic ulcers represent a significant global health burden, with aspirin emerging as a prominent contributing factor. This comprehensive review article aims to elucidate the intricate relationship between peptic ulcers and aspirin by exploring the underlying causes, diagnostic techniques, prevalence patterns, and alternative treatment approaches. Extensive analysis of pertinent literature and research studies was conducted to provide an evidence - based synthesis of the topic. The findings underscore the importance of comprehending the role of aspirin in peptic ulcer pathogenesis and shed light on novel avenues for diagnosis and therapeutic intervention.***

Keywords: peptic ulcers, aspirin, etiology, diagnostic techniques, prevalence, alternative treatment approaches

1. Introduction

Peptic ulcers, characterized by the formation of erosions in the mucosal lining of the gastrointestinal tract, have long been recognized as a significant global health issue. These ulcers can occur in various regions of the gastrointestinal tract, including the stomach (gastric ulcers) and the upper part of the small intestine (duodenal ulcers). Peptic ulcers can lead to complications such as bleeding, perforation, and obstruction, causing substantial morbidity and mortality.

The association between aspirin use and peptic ulcers has been extensively studied and established. Aspirin, a widely used medication known for its broad therapeutic actions, has been linked to an increased risk of developing peptic ulcers. Originally developed as a nonsteroidal anti - inflammatory drug (NSAID) to alleviate pain and inflammation, aspirin also exhibits antiplatelet effects, making it an essential medication for the prevention and treatment of cardiovascular diseases. As a result, aspirin is available over the counter (OTC) and is widely used by individuals around the world.

While the beneficial effects of aspirin in cardiovascular disease management are well - documented, its use is not without adverse consequences. Aspirin can cause gastrointestinal side effects, particularly in the upper gastrointestinal tract. Dyspepsia, gastric irritation, and peptic ulcer disease (PUD) are among the common adverse effects associated with aspirin use. The risk of gastrointestinal bleeding, including potentially life - threatening hemorrhage, is also increased in individuals taking aspirin.

Understanding the etiology of peptic ulcers, particularly in relation to aspirin use, is crucial for effective management and prevention. Aspirin - induced ulcers are primarily attributed to its inhibitory effect on prostaglandin synthesis, which disrupts the protective mechanisms of the gastrointestinal mucosa. By inhibiting cyclooxygenase (COX) enzymes, including COX - 1, aspirin interferes with the production of prostaglandins that help maintain the integrity of the gastric mucosal lining. This disruption leads to increased susceptibility to acid damage and impaired mucosal repair processes, resulting in the development of peptic ulcers.

Accurate diagnosis of peptic ulcers is essential for appropriate treatment and management. Various diagnostic techniques are employed to identify and assess the extent of ulceration. Endoscopy, including esophago gastroduodenoscopy (EGD), is considered the gold standard for visualizing and confirming the presence of ulcers. It allows direct visualization of the gastric and duodenal mucosa and facilitates tissue sampling for histological examination. Additionally, radiographic imaging techniques such as barium contrast studies and computed tomography (CT) scans can aid in the detection and evaluation of peptic ulcers. Laboratory tests, including Helicobacter pylori testing and assessment of blood parameters, are also employed to identify underlying causes and evaluate the severity of ulceration.

The prevalence of peptic ulcers, especially those associated with aspirin use, varies across different populations and regions. The widespread availability and use of aspirin contribute to the increasing incidence of aspirin - induced ulcers. Epidemiological studies have reported varying prevalence rates, with a higher incidence observed in older age groups and individuals with concurrent risk factors, such as Helicobacter pylori infection and concomitant NSAID use. Understanding the prevalence patterns of peptic ulcers can aid in implementing preventive strategies and tailoring appropriate management approaches.

Considering the adverse effects of aspirin and the increasing incidence of aspirin - induced ulcers, alternative treatment approaches have been explored to mitigate ulcer development and promote healing. Pharmacological interventions include the use of proton pump inhibitors (PPIs) to reduce gastric acid secretion and enhance ulcer

healing. Cytoprotective agents, such as sucralfate and misoprostol, can also be employed to enhance mucosal defense mechanisms. Additionally, eradication of Helicobacter pylori infection, when present, is crucial in managing and preventing peptic ulcers. Lifestyle modifications, including dietary changes and stress reduction, can complement pharmacological approaches in ulcer management.

In conclusion, peptic ulcers represent a significant health concern, with aspirin identified as a common contributing factor. The etiology of aspirin - induced ulcers involves the disruption of protective mechanisms in the gastrointestinal mucosa, leading to ulceration. Accurate diagnosis and evaluation of peptic ulcers are crucial for effective management and prevention of complications. Prevalence patterns vary across different populations, necessitating tailored preventive strategies. Alternative treatment approaches, including pharmacological interventions and lifestyle modifications, can aid in managing aspirin - induced ulcers. A comprehensive understanding of the relationship between aspirin and peptic ulcers is essential to guide clinical practice and promote optimal patient care.

Aspirin and its Properties:
Aspirin is one of the most commonly used medication all around the world because of its broader therapeutic actions [1]. This drug is rapidly available as OTC (over the counter) medications [2]. Aspirin was first originated as NSAID for its activity pain and inflammation, lately it was found that it has a very good antiplatelet activity and hence now it is one of the common drugs which is used in case of treating variety of cardiovascular diseases which turns out to be a lifesaving medication. Standard dose for aspirin for the purpose of treating pain and inflammation ranges from 500 to 1000 mg daily whereas in treating cardiovascular diseases the dosage lies between 75 to 325 mg per day [3, 4]. Most common side effects from aspirin are most probably related to upper gastro intestinal tract, some of the mild side effects including dyspepsia to some serious side effects including Peptic ulcer disease (PUD) as well as severe GI bleeding [3].

Peptic Ulcer and its Types
Peptic ulcer has become one of the commonest diseases which causes both morbidity as well as mortality [5]. It is also said that the widespread of ulcers maybe because of overuse or misuse of Nonsteroidal anti - inflammatory drugs (NSAIDs) and aspirin which are the common source for inducing ulcers [6]. Ulcer can be classified into different types based on the location it is present (FIGURE 1) [5].

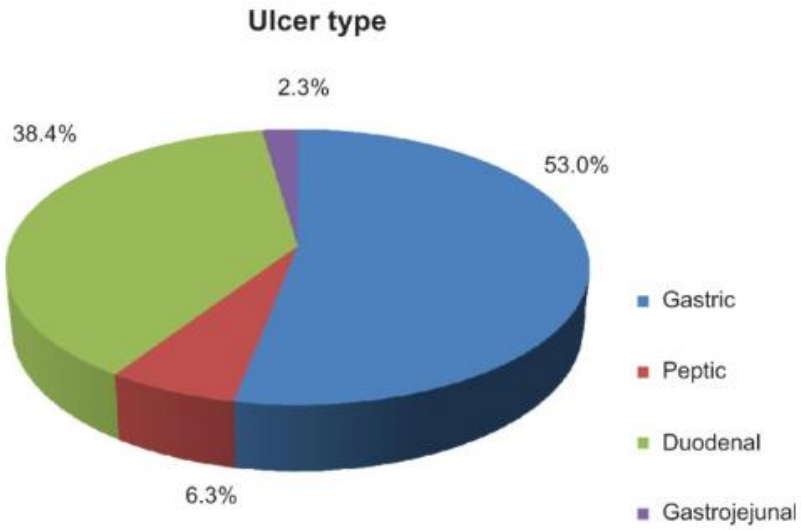

Figure 1: Demonstrating the different types of ulcers and its prevelance

Diagnosis of peptic ulcers:
There are few set of symptoms which are common in the case of ulcers which includes epigastric pain, fullness, bloating, premature satiety, weight loss and even nausea [6]. In some cases, the other set of symptoms include the following gastroesophageal reflux disease, general dyspepsia whereas asymptomatic ulcers may only be detected after the clinical presentation of GI bleed.

Awareness of PUD risk factors must be created among both physicians as well as the patients in order to identify and save people from high risk for ulcer formation and initiate appropriate gastric protection therapy.

Every patient with an infection who is taking aspirin or not taking aspirin should be tested for *H. Pylori* infection to determine the best treatment regimen for the patient [7]. Helicobacter pylori was first discovered in the year 1982. After its growth the causes and pathogenesis of ulcers are understood and treatment protocols have been evolved. Since then, ulcer treatment was focused on eradication of *H. Pylori*using antibiotics. It is noted that aspirin as well as *H. Pylori* are both important contributors for causing ulcers. It is observed that more than 50% of the world population has *H. Pylori* infection.

Treatment, Management and Prevention of Ulcers:
If the patient develops an ulcer while on NSAIDs or Aspirin, they should be stopped if possible and started on ulcer therapy either with a Proton pump inhibitor (preferred due to its superior ulcer healing properties) or an H2 antagonist [8]. The discontinuation of aspirin in the setting of acute ulcer

bleeding must be decided based upon cardiac risk and GI risk assessment of an individual with the concern on thrombotic and hemorrhagic complications [4]. If the patient has been taking low dose aspirin for cardiovascular prophylaxis, the ulcer severity and Aspirin indications are considered. If still indicated, Low dose of aspirin should be restarted approximately 3 to 5 days after initiating Proton Pump Inhibitor (PPI) therapy. The patient's status on *H. pylori* infection should be assessed; if positive, appropriate therapy should be initiated [8].

The central mechanism for NSAID - ulcer development is Prostaglandin depletion, so therapy involving the replacement with synthetic prostaglandin – Misoprostol reduces the ulcerogenic effects of low dose Aspirin [4]. Misoprostol has been evidenced to significantly reduce the development of erosions in patients taking Aspirin (300 mg/day) [9]. In addition among patients with a history of gastric ulcer who were receiving Low dose Aspirin and other NSAIDs, Misoprostol (200 mcg QID) has been showed to prevent recurrence of Gastric ulcers [10]. However, Misoprostol is often associated with side effects, particularly diarrhoea, which led to discontinuation of treatment.

Sucralfate (2 g BD) has been shown to be effective in the treatment of NSAIDs associated duodenal ulcers, as they form an ulcer - adherent complex at duodenal ulcer sites, protecting the ulcer and promoting healing, particularly when the NSAID is stopped, but it is not effective in the treatment of NSAIDs related gastric ulcers [4].

The traditional dose of H2 Receptor Antagonists (H2RA) does not prevent most NSAIDs related gastric ulcers due to their level of acid suppression. The H2RA Ranitidine (150 mg/day) reduced the amount of gastric bleeding in patients taking Aspirin 300 mg/day, by significantly increasing the intragastric pH [11]. But there are very few data available on H2RA in conjunction with Aspirin.

The Ulcer in patients taking low dose Aspirin, NSAIDs therapy or both are rapidly healed with a PPI than an H2RA, Misoprostol or Sucralfate [8]. PPIs have been proven superior to both Misoprostol and Ranitidine in preventing NSAID ulcer recurrence and overall symptom control, related to their ability to reduce ulcers and improve NSAID - associated dyspepsia [4]. Among the Antisecretory agents or Nitrate treatment, PPI therapy was found to be associated with marked consistent risk reduction of ulcers in patients receiving all types of agents including non - Aspirin antiplatelet agents [12].

PPIs works by inhibiting the parietal proton pump which exerts suppressive effect on gastric acid. The concomitant use of PPI along with Aspirin did not increase the risk of cardiovascular events [13]. Aspirin along with Clopidogrel as Antiplatelet dual therapy is widely prescribed with PPI frequently, to prevent GI bleeding [14].

Among the patients who take low dose Aspirin with *H. pylori* infection and history of upper GI bleeding, the eradication of *H. pylori* is equivalent to the treatment with PPI - Omeprazole (20 mg) in preventing recurrent bleeding, even in patients taking other NSAIDs - Naproxen [15]. In long term users of NSAIDs, Esomeprazole (20 mg) is effective in prevention of ulcers, including patients who use COX - 2 inhibitors [16]. The recurrence of ulcer complications is less in patients taking Lansoprazole (15 or 30 mg OD), suggesting that PPI therapy along with *H. Pylori* Eradication is effective than *H. pylori* Eradication alone [17].

Depending on the location, size and severity of ulcer in initial assessment, the treatment with PPI is generally continued for 4 to 6 weeks. For ulcers <1 cm (duodenal ulcers) is treated with a PPI therapy (20 to 40 mg daily) for 4 to 6 weeks whereas for ulcers ≥1 cm (gastric ulcers), PPI therapy is for 6 to 8 weeks. Maintenance PPI therapy is indicated in patients who restart the treatment with low dose aspirin or NSAIDs [8].

H. pylori infection and NSAIDs use are the two etiological factors mostly associated with peptic ulcer and its complications. However, there is no association between *H. pylori* infection and Aspirin induced NSAIDs and there is no effect between increasing *H. pylori* infection or decreasing the risk of NSAID induced ulcers [18]. *H. pylori* eradication protects against aspirin induced peptic ulcer bleeding, but this is not sustained for the long term [19].

H. pylori Eradication is recommended as preventive care for Peptic ulcer recurrence. Eradication involves first line and second line therapy. First line therapy includes Triple therapy - PPI (Lansoprazole 30 mg BD, Omeprazole 20 mg BD, Rabeprazole 20 mg BD or Esomeprazole 20 mg BD) + Amoxicillin (750 mg BD) + Clarithromycin (200 mg BD). A high dose of PPI increases the efficacy of triple therapy. For second line eradication, Triple therapy with Moxifloxacin is suggested. Sequential therapy and Concomitant Quadruple therapy are also equally effective for *H. pylori* Eradication [20].

In elderly, the risk factors of ulcers have been clearly identified of which some factors such as age or comorbidities are not modifiable, but NSAIDs use, *H. pylori* infections and some habits like smoking and alcohol can be managed appropriately.

NSAIDs are most common cause of ulcer in elderly, so they are started when necessary, considering the presence of risk factors. In addition, use of gastroprotective drug is considered. Among the many gastroduodenal protective agents, PPI or misoprostol are the most effective.

Misoprostol therapy is slightly cheaper than PPI therapy, but it is administered four times a day and may cause abdominal cramps and diarrhoea, so PPI therapy is considered. Moreover, PPI therapy appears to be more effective in duodenal ulcers prevention than Misoprostol. Among the PPI therapy, Omeprazole, Pantoprazole and Lansoprazole are effective. As these drugs interfere with CYP2C19, there is a risk of possible interactions with other drugs used by elderly patients. So Rabeprazole and Esomeprazole are preferred which are more rapid in onset than the above drugs and have better pharmacokinetic and pharmacodynamic profiles.

H pylori infection in elderly are treated with 10 days sequential regimen – 5 days of dual therapy (PPI + Amoxicillin) followed by 5 days of triple therapy (PPI + Clarithromycin + Tinidazole), which are associated with high eradication rate [21].

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