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REVIEW OF TOXIC CHEMICAL FACTORS INFLUENCE IN GASTRIC AND DUODENAL ULCERS

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ABSTRACT

Peptic ulcer is a lesion most often located in the stomach or the proximal duodenum. The incidence, the hospitalization rate and the associated mortality in the last decades is decreasing due to modern therapy and hygiene measures. Approximately half of the population is colonized by H. Pylori, which is one of the main causes of ulcers. Other contributing factors are diet and stress. Non-steroidal anti-inflammatories cause damage to the gastro-duodenal mucosa by inhibiting cyclooxygenase-1. Concomitant consumption of proton pump inhibitors can be a solution. Natural evolution can lead to healing or complications. Ulcer perforation is one of the loudest and most serious complications of ulcers. Alcohol consumption has been shown to be a strong risk factor. Various studies have shown that smokers have a double risk of developing gastro-duodenal ulcers.

Keywords: ulcer, smoking, alcohol, Helicobacter pylori

Introduction

Peptic ulcer is a lesion in the digestive tract induced by acid hypersecretion, which is frequently located in the stomach or proximal duodenum. It is characterized by a denuded mucosa, whose defect can extend to the level of the submucosa or to the level of the muscularis propria. (1)

The estimated prevalence of peptic ulcer is approximately 5-10% (2), but more recent studies have shown a decrease in the incidence, hospitalization rate, and associated mortality, most likely due to improved therapy and hygienic measures, which have led to a decrease in number of Helicobacter pylori infections. (3)

In addition to the action of the hypersecretory acid environment, dietary factors and stress can contribute to the disruption of mucosal damage. Other risk factors for developing peptic ulcer are: Helicobacter pylori infection, use of nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol consumption, smoking, and Zollinger-Ellison syndrome. (4)

Approximately half of the world's population is colonized by H. pylori, which represents one of the most common causes of peptic ulcer. (5) The mechanism by which it contributes to the appearance of various types of ulcers is not fully elucidated, but this infection

appears to cause hypo- or hyperchlorhydria. (5)

The main mechanism by which NSAIDs cause damage to the gastroduodenal mucosa is represented by the inhibition of cyclooxygenase-1 (COX-1), whose role is the synthesis of prostaglandins, causing a decrease in blood flow in the mucosa, a decrease in the secretion of bicarbonate and mucus, and the inhibition of cell proliferation. NSAIDs inhibit COX-1 reversibly, their action being dependent on the administered concentration. (6)

There are various strategies to prevent the occurrence of gastro-duodenal ulcers associated with the consumption of NSAIDs and aspirin, but also to prevent the occurrence of their complications. One method would be the concomitant use of NSAIDs with a proton pump inhibitor (PPI), histamine-2 (H2) receptor antagonist, or misoprostol. PPIs are the most popular and effective agents used for peptic ulcer prophylaxis. (7)

The mechanism by which they provide protection is the reduction of gastric acid secretion due to the irreversible binding to the hydrogen/potassium ATPase enzyme in the gastric parietal cells. The best protection conferred against the development of complications of gastro-duodenal ulcer is provided by the combination of COX-2-selective NSAIDs and a PPI. (8)

The natural evolution of peptic ulcer varies from healing without the involvement of any intervention to the appearance of various complications, such as: bleeding, perforation or obstruction; complications that have a high morbidity and mortality potential. (9)

Methods

The study was conducted by searching articles in the "Pubmed" database. We made the selection of studies by searching for keywords and the combination between them: peptic ulcer, toxic, chemical factors, alcohol, smoking, nonsteroidal anti-inflammatory drugs. The list of citations was also searched for the selection of articles. The studies were manually reviewed to select and compare 14 of them regarding the toxic chemical factors that influence gastro-duodenal ulcers

Results

Several studies have been used to highlight the different risk factors of gastro-duodenal ulcer:

According to the retrospective study carried out by Stephen Tabiri, Prosper Akanbong and Braimah Baba Abubakari, which included 2035 patients admitted to the Tamale Teaching Hospital in Tamale, Ghana, between the years 2010-2014, the link between different risk factors was highlighted, such as be: smoking, H. pylori infection, alcohol consumption and the occurrence of gastro-duodenal ulcer. Of the 2035 patients, 1812 (89%) consumed alcohol in quantities greater than 5 units/day, and 1344 (66%) consumed NSAIDs. Chi-square values of bivariate analysis were considered statistically suggestive when $P < 0.05$. (10)

Also in the same study, an incidence of peptic ulcer was also observed depending on the age of the patient, thus out of the total of 2035 patients: most patients (680) with ulcers were part of the 31-40 age group, towards unlike the 35 patients who represented the smallest number, aged between 2 and 15 years. (10)

On the other hand, the increased incidence of peptic ulcer among women was highlighted (1037 female patients out of a total of 2035). (10)

Another study conducted by Anand in the United States pointed out that peptic ulcer affects approximately 4.6 million people annually. Anand demonstrated that H. pylori infection is associated in 90% of duodenal ulcer cases and 70-90% of gastric ulcer cases. At the same time, the incidence of peptic ulcer increases with age. (11)

Regarding the prevalence of peptic ulcer depending on the patient's sex, an approximately equal incidence was observed: 11-14% in male patients and 8-11% in female patients. (11)

Smoking as a risk factor for peptic ulcer has not presented enough conclusive evidence, but it has been observed that the association between H. pylori infection and smoking may increase the risk of ulcer recurrence. (11)

According to the article by Nimish Vakil, H. pylori infection and NSAID use are the most common risk factors involved in the development of peptic ulcer. More than 50% of

peptic ulcer cases are associated with excessive use of NSAIDs. In addition to these, smoking has also been shown to be a risk factor for the development of ulcers and their complications, affecting healing and causing an increase in the incidence of recurrence. It seems that alcohol is also a strong promoter of gastric secretion, but there is not enough definitive evidence. (12)

Sang Pyo Lee et al. investigated 12,852 subjects between the years 2010 and 2015, highlighting different risk factors involved in the occurrence of peptic ulcer: advanced age, H. pylori infection, NSAIDs and smoking. Regarding NSAID use, it was an independent risk factor for peptic ulcers. Of the total of 12,852 patients, 7,079 were male. (13)

DH Hull and PJ Beale conducted a study that included 70 male smoking patients. This study aimed to analyze the influence of smoking on the degree of ulcer healing. In this study, patients were advised to quit smoking by receiving a course of cimetidine. At 3 months, most patients (79%) showed ulcer healing. (14)

Another study performed in our clinic included 544 patients, 226 were smokers (40.79%), and 320 were non-smokers (59.2%), noting the high percentage of smokers. (15) (Figure 1)

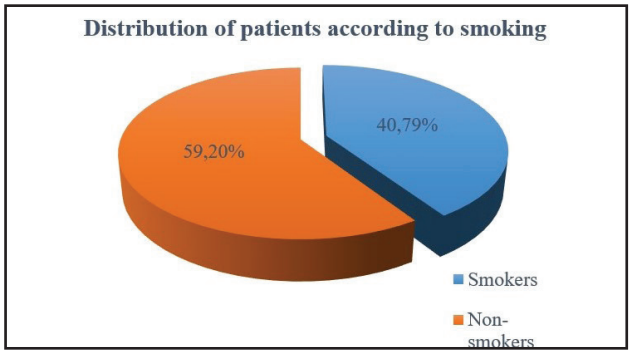


Figura 1 - Distribution of patients according to smoking

As I mentioned before, the consumption of non-steroidal anti-inflammatory drugs is a risk factor for the appearance of ulcers, which was also proven in this study. Out of the total of 554 patients, 68 (12.27%) of them consumed NSAIDs, in contrast to 486 (87.72%) patients who do not consume this type of medication. (15) (Figure 2)

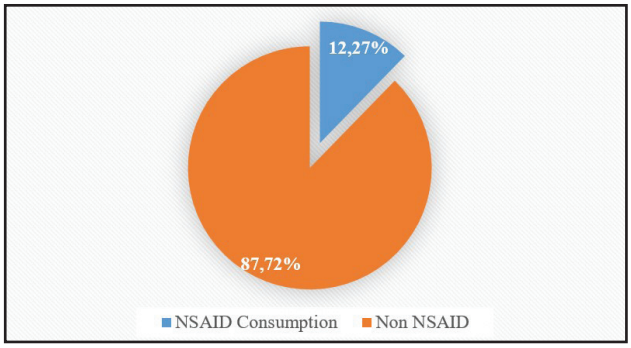


Figure 2 NSAID Consumption

Another risk factor highlighted in the context of this study is alcohol consumption. Thus, 220 patients (39.71%) stated that they consumed alcohol, compared to 334 patients (60.28%) who stated that they did not consume alcohol. Following them, we can point out a fairly high percentage of alcohol consumers. (15) (Figure 3)

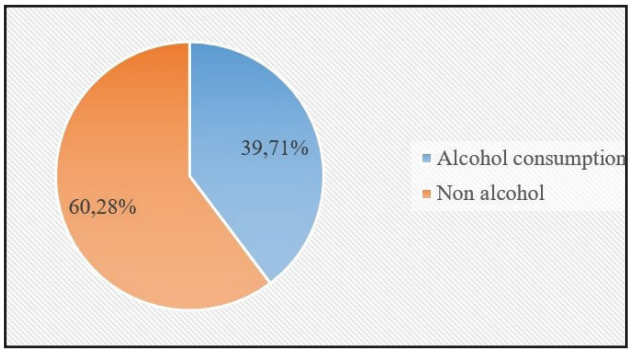


Figure 3 Dsitribution of patients according to alcohol consumption

Table 1– Risk factors in gastroduodenal ulcers

Study	Female/Male	H. pylori infection	NSAID	Smoking	Alcohol consuption
Tabiri, 2016 (10)	1037/998	P=0,01 $\chi2 = 19,9$	P=0,001 $\chi2 = 24,9$ 34%	P=0,001 $\chi2 = 27,3$ 9%%	P = 0,001 $\chi2 = 30,6$ 89%
Anand, 2021 (11)	8-11%/ 11-14%			It increases the risk of recurrence in association with H. pylori infection	
Nimish, 2021 (12)		Frequently	>50%		
Lee,2017 (13)	5773/7079	P<0,001	P=0,040	P<0,001	P=0,005

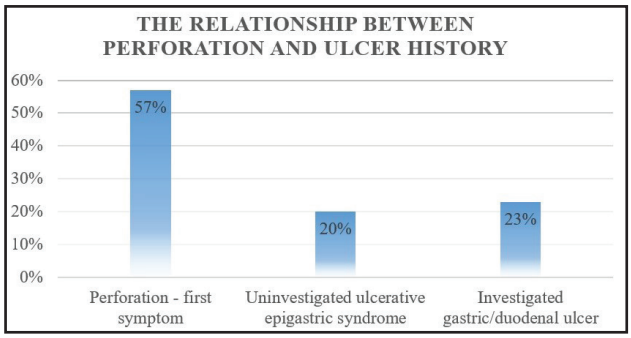


Figure 4 the relationship between perforation and ulcer history

The first symptom of gastro-duodenal ulcer was in most cases perforation (57% of cases). In contrast to these, 20% of the patients presented an uninvestigated "ulcer type" epigastralgic syndrome before the perforation, and 23% had previously been diagnosed with gastric or duodenal ulcer. (15) (Figure 4)

Discussions

Following the study conducted by Stephen Tabiri, the same risk factors for peptic ulcer were identified in patients from northern Ghana as in other geographical regions of the world. (10)

According to the study by Sang Pyo Lee et al. excessive alcohol consumption has been shown to be the strongest risk factor for peptic ulcer development. On the other hand, as I mentioned, advanced age and smoking are risk factors that can contribute to the appearance of ulcers, something also highlighted in this study. (13)

Regarding the incidence of ulcers related to the patient's sex, it has been shown that it is more common among men, but asymptomatic peptic ulcers are more common in them. Unlike them, it seems that the female sex is more prone to the development of a peptic ulcer, but with the presence of functional disorders at the gastrointestinal level. (13)

Ulcer perforation is one of the loudest and most serious complications of ulcers. This was found in 554 patients (34%) from the total of 1601 patients who participated in the study during the years 1991-2000. This is before hemorrhage, which was found in 518 patients, but also before stenosis, which was present in 190 patients. (16)

As mentioned before, smoking is also an independent risk factor for peptic ulcer. According to the study conducted by DH Hull and PJ Beale, it has been shown that smoking affects healing, resulting in a slower rate of healing. (14)

Conclusions

Ulcer incidence increases with age for both gastric and duodenal ulcers. A difference can be seen in the rapidity of ulcer onset: duodenal ulcers show a faster onset by about two decades than gastric ulcers, especially in male patients.

After all the studies, it was highlighted that advanced age, smoking, alcohol consumption, use of non-steroidal anti-inflammatory drugs and Helicobacter pylori infection are independent risk factors for the occurrence of peptic ulcer.

Different epidemiological studies suggest that smokers have twice the risk of developing gastro-duodenal ulcer compared to non-smokers.

In addition to the high risk of peptic ulcer development among smoking patients, it is also observed that it affects its healing.

The primary prevention of NSAID-induced peptic ulcers consists in avoiding their unnecessary use, using the lowest effective doses of NSAIDs, or switching to other NSAIDs with less toxic effects.

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