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NATIONAL UNIVERSITY OF PHARMACY
faculty for foreign citizens' education
department of clinical pharmacology and clinical pharmacy

QUALIFICATION WORK

on the topic: «**THE ROLE OF THE PHARMACIST IN THE PVEVENTION OF PEPTIC ULCER DISEASE AND ITS COMPLICATIONS»**

Prepared by: higher education graduate of group
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educational program Pharmacy
Hajar LAMSAOURI
Supervisor: associate professor of higher education institution of department of clinical pharmacology and clinical pharmacy, PhD, associate professor Inna OTRISHKO
Reviewer: professor of higher education institution of department of pharmacology and pharmacotherapy, DSc,
professor Kateryna SHCOKINA

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ANNOTATION

Hajar Lamsaouri. The role of the pharmacist in the prevention of peptic ulcer disease and its complications. – The manuscript. – National University of Pharmacy of Ministry of Healthcare of Ukraine, Kharkiv, 2024.

The qualification work discusses the role of pharmacists in the prevention of peptic ulcers and their complications, namely, the unique opportunity to provide patients with information and manage risk factors associated with the development and recurrence of peptic ulcers.

Qualification work is presented on 49 pages of typewritten text, consists of summary, introduction, 3 chapters, conclusions, references. The work is illustrated with 5 tables, 10 figures. The list of references contains 85 resources.

Key words: pharmacist, peptic ulcer, complications, prevention, efficacy and safety of therapy, quality of life

АНОТАЦІЯ

Хажар Ламсаурі. Роль фармацевта у профілактиці виразки шлунка та її ускладнень. – На правах рукопису. – Національний фармацевтичний університет МОЗ України, Харків, 2024.

У кваліфікаційній роботі обговорено роль фармацевта у профілактиці виникнення виразки шлунка та розвитку її ускладнень, а саме, висвітлена унікальна можливість надавати пацієнтам інформацію та керувати факторами ризику, пов'язаними з розвитком та рецидивами пептичної виразки.

Кваліфікаційна робота викладена на 49 сторінках машинописного тексту, складається з резюме, вступу, 3 розділів, висновків, списку літератури. Робота проілюстрована 5 таблицями, 10 рисунками. Список літератури містить 85 найменувань.

Ключові слова: фармацевт; виразка шлунка, ускладнення, профілактика, ефективність та безпека терапії, якість життя

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INTRODUCTION

Relevance of the topic. Peptic ulcer disease (PUD) is a common condition that can occur complicate and threaten the patient's vital prognosis. It is a multifactorial disease resulting from an imbalance between the factors of aggression and the factors of defense and repair of the gastroduodenal mucosa in which *Helicobacter pylori* (HP) plays a role primordial. The definition of ulcer is histological: a localized, deep loss of substance, rounded or oval with sharp edges covered with a yellowish false membrane which amputates the muscularis which becomes sclerotic (formerly called Cruveilhier's disease). The true ulcer should be distinguished from abrasions, erosions and ulcerations which are less deep. PUD is a benign condition but its severity is linked to the risk of occurrence of complications. The prognosis depends on the initial treatment, mortality is due to complications, after perforation, it is on average 10%, as well as after hemorrhage digestive. It is linked to age and specially to associated visceral defects. His prognosis has improved thanks to [1, 2, 3].

- the better understanding of the pathophysiology [19, 20, 21] of PUD and the definition of the role of HP, which made it possible to modify the natural history of the disease by eradicating HP;
- the use of proton pump inhibitors (PPI), powerful secretion inhibitors gastric, which made it possible to reduce the forms of the disease requiring non-treatment medicinal. The cost of ulcer disease is not known. In 1987, a study medico-economic estimated in France the annual cost of peptic ulcer disease more than 3.5 billion francs. Currently, the reduction in the direct and indirect cost of ulcer disease is evident (although not quantified) due to the decrease in prevalence. Of HP infection, the effectiveness of HP eradication treatments, which reduced considerably the frequency of ulcer recurrences and their complications. It should be noted also the virtual disappearance of the use of surgery and the reduction in work stoppages. Good care is therefore necessary: early diagnosis, treatment adequate [4], as well as prevention of the occurrence of ulcer or its

complications [5]; from where highlights the interest of an epidemiological study analyzing the profile of this condition, the possible contributing factors, the progression of the disease, the various complications linked to this disease and therapeutic success.

The objective of our work is to determine the epidemiological profile of the disease peptic ulcer disease in our context through a series of patient observations ulcer carriers during my internship period in the pharmacy, study of prescriptions for patients suffering from PU problems [19, 20].

The aim of the study. The aim of the work is to discuss the role of the pharmacist in the prevention of peptic ulcer disease and its complications.

The objectives of study. Objectives of the work encompass various aspects related to the condition, including:

1. To investigate the epidemiology, etiology and pathogenesis of the peptic ulcer disease.

2. To investigate approaches to peptic ulcer disease treatment and prevention of its complications.

3. To study the opinion and beliefs of healthcare providers concerning efficiency and safety criteria of peptic ulcer disease treatment.

4. To study the opinion and beliefs of patients with peptic ulcer disease concerning efficiency and safety criteria of treatment.

5. To develop practical recommendations for healthcare professionals to increase the efficiency safety of peptic ulcer disease treatment and prevention of its complications.

Object of research: pharmacotherapy of peptic ulcers, prevention of their complications.

Subject of research: medication adherence of patients with peptic ulcer disease.

Research methods. Questionnaire for pharmacy visitors and pharmacists; statistical.

By employing a multidisciplinary approach and using a combination of

research methods, scientists and clinicians can advance our understanding of peptic ulcers and improve strategies for prevention, diagnosis, and treatment of the condition.

The practical significance of the work. The results of the research can be used in the process of developing the main directions for solving the problems of pharmaceutical provision of patients with gastric ulcer.

Structure and scope of qualification work. Qualification work consists of an introduction, three chapters and a list of references, which contains 85 sources. The work is illustrated with 5 tables and 10 figures.

CHAPTER 1
MODERN PRESENTATION ABOUT PEPTIC ULCER DISEASE, APPROACHES TO TREATMENT AND PREVENTION (LITERATURE REVIEW)

1.1. Peptic ulcer disease: epidemiology, etiology and pathogenesis

A gastric or duodenal ulcer corresponds to a localized loss of substance from the wall of the stomach or the first part of the small intestine called the duodenum. it does not only concern the internal mucosa, we then rather speak of erosion, but digs and destroys the wall deep down to its muscular outer layer (Fig. 1.1) [6].

The ulcer corresponds to a hollow loss of substance, of variable size, generally oval or rounded in shape with a pseudomembranous base (whitish or yellowish), sometimes necrotic (blackish) with regular, slightly raised and erythematous edges. in the stomach, it is most common at the level of the antrum and the lesser curvature. in the duodenum, the ulcer is most often located in the center of the bulb or at the tip of the bulb. it is most often single, on the other hand the acute ulcer secondary to NSAIDS often causes several lesions [7].

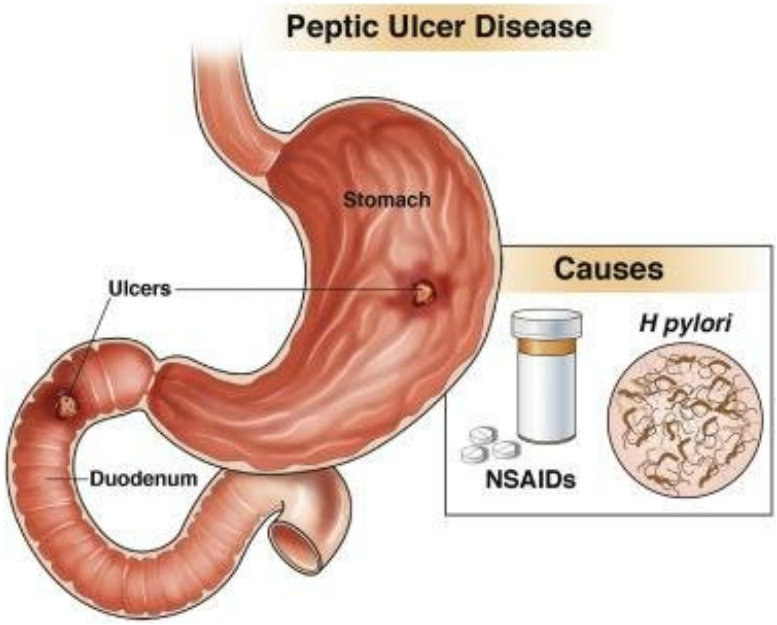


Fig. 1.1. Location of the ulcer at the level of the gastroduodenal wall [6].

PUD is a universal condition with a chronic, relapsing course. The incidence of which gives it the status of public health disease. This disease has undergone an evolution since the description of new pathways physiopathological. Indeed, stress was the main cause of PUD. The healings were therefore rare and the disease affects approximately 10% of the population. But the discovery of *Helicobacter pylori* by two Australian researchers, Marshall and Warren in 1982 overturned this conception and made PUD a disease essentially infectious [8]. In Morocco, the frequency of hospital admissions for ulcers hemorrhagic has been relatively stable for around twenty years and the Mortalities due to hemorrhagic ulcer remained unchanged during this period. It varies from 6 to 10% of cases despite the progress made, both in the diagnosis than in therapy. Among all digestive hemorrhages acute high by gastric or duodenal ulcer, 75 to 80% healed spontaneously, 20% persist or recur, and 5% are considered fatal [9]. Epidemiological data of gastroduodenal ulcer in countries developed are now well known. It is a fairly common disease affecting 8 to 10 people per 100 inhabitants. It affects 1 in 15 women and 1 in man in 10. The age group most affected is between 40 and 60 years old. The hospitalization due to complications of ulcers is approximately 250,000 patients and 25,000 deaths annually [10, 11].

Helicobacter pylori is a bacterium whose main reservoir is the man. It can chronically infect the human gastric mucosa thanks to a powerful urease activity, which allows it to survive the local acidic environment [12].

The other reservoirs of *H. pylori* are poorly known, but the microorganism can be isolated from the stomach of animals including primates, pigs and cat. It can be isolated from dental plaque, saliva, materials feces of children and, rarely, adults. Human-to-human contamination occurs in the fecal-oral or oro-oral mode. Another possible source of human acquisition of *H. pylori* is water and food contaminated with feces. This bacterium is capable of survive in distilled saline water at lower temperatures than in sea water, and becomes uncultivable at room temperature between 1 and 3 days [13].

H. pylori can be acquired from birth. Vomiting mucus achlorhydric can be

used as an transmission vehicle. Studies have reported data on the percentage of *H. pylori* isolation from juice stomach of symptomatic patients: the microbe seems to survive outside the human body in unbuffered gastric juice and often present in large quantities quantity in vomit. These results are in favor of a transmission gastro-oral, especially during childhood, in association with poor hygienic conditions [14].

Saliva is another possible source of *H. pylori*, since the gastric microbiota can reach and colonize the mouth after regurgitation or vomiting. The DNA of *H. pylori* was amplified from saliva, subgingival biofilm and dental plaque. According to these reports, the mouth could be a reservoir of *H. pylori* [15]. Oral transmission mainly involves mother-child transmission: the oral secretions of the mother, who may be contaminated by *H. pylori*, can be directly transmitted to the infant. Oral transmission is not the main modality of transmission of *H. pylori*, at least in adults [16].

The DNA of *H. pylori* was frequently detected in stools, but attempts to cultivate the germ from feces have had a limited success, because the bacteria persist there mainly in a form not cultivable (coccoid) [17, 18].

Environmental contamination must also be considered, despite that the exact way in which *H. pylori* access to the human stomach is unknown. When hygienic conditions are poor, household contamination treated water cannot be excluded, but it is easily controlled by the chlorination [19]. Some authors hypothesize that water plays a role in both as an environmental reservoir of infection and as a support for fecal-oral transmission of *H. pylori* infection.

It has also been shown that children living in homes with external water supply, or those consuming raw vegetables, and which are often irrigated with untreated wastewater, had a higher prevalence of *H. pylori* infection [20, 21]. The association serum antibodies against *H. pylori* and serum antibodies against two agents known waterborne pathogens (hepatitis A virus) [22] and Giardia [19], suggests that the infection can be waterborne or linked to poor hygiene conditions.

Like water, food products can also be contaminated when handled in poor

hygienic conditions. Several studies address the role of food in the transmission of *H. pylori*, the food products analyzed are mainly milk, meat and vegetables. Among these, dairy products are the most studied, probably because the infection is mainly acquired during childhood, and that milk is mainly consumed during this period [23].

The pathophysiology of PUD is an area of knowledge where enough progress has been made over the past three decades. In the conditions normal, there is a physiological balance between the secretion of gastric acid and the gastric and duodenal mucosal defense systems (Fig. 1.2.). The injuries mucous membranes occur when the balance between aggressive factors and protectors is broken [24].

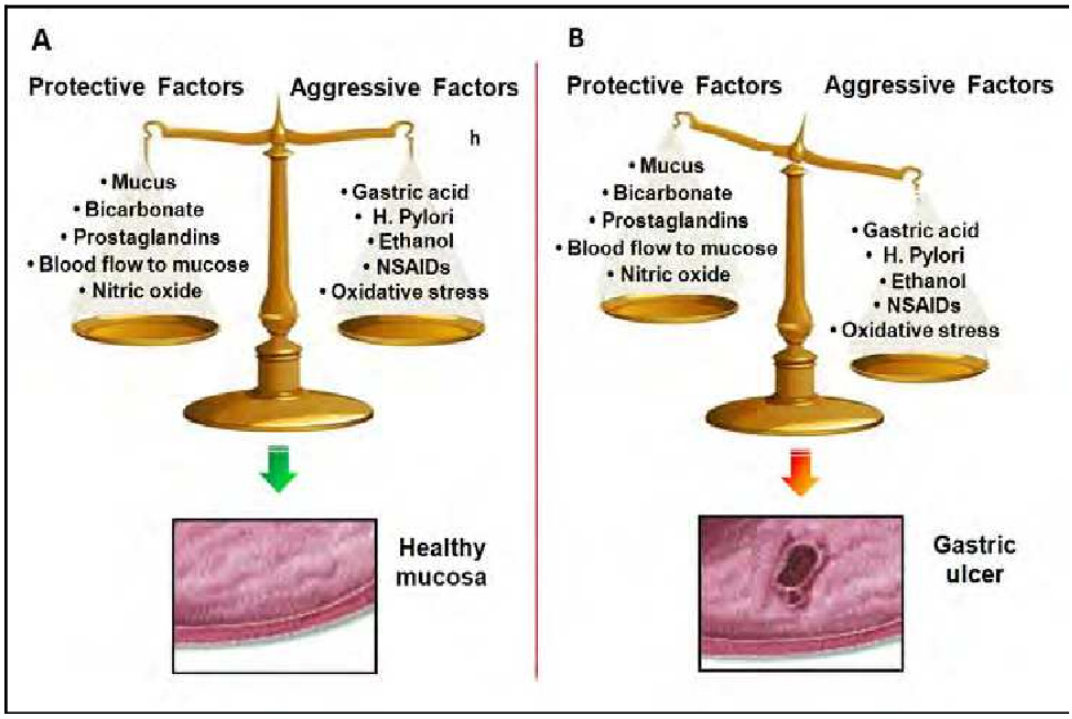


Fig. 1.2. Balance between protective and aggressive factors of the mucosa [24].

Thus, ulcers are defined as defects in the mucosa and the gastric or duodenal submucosa, which extend through the muscularis. Epithelial cells of the stomach and duodenum secrete mucus under the influence of cholinergic stimulation or in response to irritation of the epithelial lining. Foveolar cells produce mucus and

bicarbonate, which form a gel layer impermeable to aggressive factors such as acid, pepsin, etc. This layer is extremely important, because it prevents irritation and degradation of the inner layer of the stomach.

When injured, other mechanisms prevent acid and pepsin from penetrate epithelial cells. For example, increasing the flow blood eliminates the acid that diffuses through the damaged mucosa and provides an adequate level of bicarbonate in the gel layer superficial to the cells epithelial. Additionally, these cells regulate intracellular pH by eliminating excess hydrogen ions from cell membrane ion pumps basolateral. As mentioned previously, damage to the mucosa, or specifically peptic ulcers, occur when the balance between aggressive and defensive factors is broken. Aggressive factors include infection with *H. pylori*, NSAIDs, alcohol, bile salts, acid and pepsin. However, the defensive mechanism includes mucus, bicarbonate, prostaglandins, adequate mucosal blood flow and capacity epithelial renewal [25].

The mucus-bicarbonate barrier is the first line of defense of gastric mucosa. The surface of the gastric mucosa is covered with a layer formed by mucus gel and bicarbonate anions. This layer has the ability to retain bicarbonate ions secreted by epithelial cells and to maintain a pH close to 7 near the mucosa. She is also capable of protecting the epithelium against the proteolytic actions of pepsin, The mucus secreted by the foveolar cells is almost 95% water. And various types of mucin glycoproteins, such as MUC2, MUC5AC, MUC6, and others (26). Gel formation is possible due to the capacity mucin units to polymerize into large mucin multimers. In Besides, various gastrointestinal hormones, such as gastrin, secretin, and prostaglandins, play a role in the regulation of mucus secretion gastric.

The secretion of bicarbonate anions into the mucus layer is essential for maintaining a pH gradient at the epithelial surface, which represents a first line of defense against stomach acid. They are secreted by the apical membrane of surface epithelial cells. The Cl-/HCO3- exchanger, which is responsible for regulating the secretion of bicarbonate, can be stimulated by the action of stomach acid. It is important to note that the mucus-bicarbonate barrier is the only system that

separates the epithelium from the gastric lumen. This barrier protective is broken during pathological events or under the influence injurious agents, or when other protective mechanisms are activated (the intracellular neutralization of acid, rapid renewal of the epithelium) [26].

The gastric mucosa is characterized by constant production of PGs, particularly PGE_2 and PGI_2, which play a crucial role in maintaining mucosal integrity and protection against harmful factors [27]. PGs have been proven to interact with almost all mucosal defense mechanisms. Notably, they have the potential to reduce acid production, stimulate mucus and bicarbonate production, as well as increase mucosal blood flow. In addition, PGs are responsible for accelerating the healing of the mucosa. In addition, they have the ability to inhibit mast cell activation and leukocyte adhesion to vascular endothelium [27].

These cells form a continuous surface layer, closely connected to each other by tight junctions by forming a waterproof barrier, which prevents the retro-injection of gastric acid, carbon dioxide, pepsin and pepsin and therefore protects against the damage of the deep layers of the gastric wall [28]. Epithelial cells, due to the presence of phospholipids on their surface, are hydrophobic and can hunt water -soluble agents and the acids responsible for the mucosa lesions. In addition, epithelial cells produce cathelicidins and beta defensins, which are cationic peptides with antimicrobial properties. These cationic peptides play an important role in the system of innate defense on the surface of the mucosa and prevent the mucosa of the stomach of bacterial colonization [27].

The integrity of the continuous layer of epithelial cells of the stomach is maintained by a constant process of cell renewal using the progenitor cells of the gastroduodenal mucosa. The complete renewal process of the epithelium takes approximately 3 to 7 days, while the Restitution of the epithelium after exposure to a pathogen or injuring agents occurs in a few minutes [28].

The proliferation of progenitor cells is controlled by growth factors, such as the growth factor transforming-α (TGF-α) and the growth factor similar to insulin 1 (IGF-1). These factors activate the principal Receiver of the epidermal growth

factor (EGFR), located at the level of gastric cells [28].

In addition, prostaglandins (PGE_2) and gastrin interacting with EGFR, stimulate cell proliferation and renewal of the mucosa gastric [29].

Maintaining adequate blood flow at the mucous membrane is crucial to deliver the essential substances, such as nutrients and oxygen, and to eliminate toxic metabolites from the gastric mucosa. Endothelial cells located at the level of small gastric vessels produce powerful vasodilators such as NO and prostacycline, which protect the gastric mucosa against the harmful effect of a restriction of blood flow, After exposure to irritating agents, a massive and rapid increase in blood flow from the gastric mucosa. This process allows the elimination of harmful agents and the dilution of gastric acid. An adequate blood flow is essential to prevent lesions of the gastric mucosa And yet the decrease in flow leads to the development of tissue necrosis. Experimental evidence clearly shows that the increase in blood flow of the mucosa is mediated by the NO and that its inhibition exacerbates lesions of the gastroduodenal mucosa [30].

Gastric acid is a liquid formed in the stomach, plays an important role in the digestion of proteins by activating digestive enzymes. The main constituent of gastric acid is hydrochloric acid, produced by parietal cells of the gastric gland, with a pH of 1.5 to 3.5.

Helicobacter pylori is a bacteria that infects about half of the world population. It was first identified at the beginning of the 1980s, as a cause of stomach problems. This discovery allowed researchers to establish a link between the infection by H. pylori and other conditions such as gastritis, ulcers and cancer of the stomach. It even paved the way for the healing of certain ulcers gastroduodenal. Today, scientists continue to discover new clues about these mysterious bacteria.

In 1982, two Australian researchers, Barry Marshall, doctor in internal medicine, and Robin Warren, who holds a bachelor's degree in medicine and of a bachelor's degree in surgery with a specialty in pathology, described the impact of infection by *H. pylori* [31].

1.2. Peptic ulcer disease: approaches to treatment and prevention

The aim of medical treatment is:

• Strengthen the natural defenses of the gastric and duodenal mucosa;

• Ease the pain;

• Heal the ulceration;

• Avoid complications;

• Eradication of *H. pylori* with antibiotics, in order to stop the natural progression of the disease and particularly prevent recurrences.

Since healing *H. pylori* reduces the recurrence of the ulcer and facilitates its healing; Antibiotic therapy is definitely indicated for all patients suffering from ulcers infected by *H. pylori*. Successful treatment requires the simultaneous administration of two or more ATBs [32, 33]. It is also recommended in patients who are infected and suffer from dyspepsia, in patients with a predisposition to gastric cancer and in those who receive prolonged treatment with PPIs for gastroesophageal reflux [34]. The major obstacles encountered during the eradication of *H. pylori* are: side effects associated with antibacterial treatment, the development of bacterial resistance to the ATBs used, as well as problems with compliance with prescribed treatment [35].

H. pylori is very sensitive (in vitro and in vivo) to β-lactams, mainly amoxicillin, which is used in *H. pylori* [35].

It acts by inhibiting the synthesis of bacterial walls, it is stable in an acidic environment, but it is more active at a neutral pH [36]. The CMIs of the *H. pylori* to amoxicillin are very low (MIC=0.03 mg/I). These values increase 10 to 20 times in vitro, when we go from pH 7.5 to pH 5.5. Bacterial resistance to amoxicillin is less common [37].

However, amoxicillin can mainly cause diarrhea, dyspepsia, urticaria, rarely headaches and allergic reactions.

H.pylori is sensitive to macrolides, especially clarithromycin, thanks to its good tissue diffusion. This antibiotic inhibits bacterial protein synthesis. Its

spectrum is similar to that of erythromycin, but it is more stable in an acidic environment, better absorbed and more effective against *H. pylori*.

The MICs of all macrolides are increased by 10 to 100 times, when the pH is 5.5. Bacterial resistance may develop when clarithromycin is given as monotherapy [38].

Clarithromycin is also the most expensive antimicrobial drug, used to treat *H. pylori* infection. It generally causes more severe digestive disorders than amoxicillin, treated by the simultaneous administration of probiotics such as Saccharomyces boulardii and good hydration [39].

Metronidazole is a bactericidal ATB, belonging to the nitroimidazole family. It acts on DNA after reduction of the nitrate group and causes breaks in its strands. It is the key drug in the eradication treatment of *H. pylori*, despite its relatively modest activity in vitro. Indeed, metronidazole is actively secreted into gastric juice and saliva. It is active after absorption, with a half-life of 8 to 12 hours. Its activity is relatively independent of pH variations, unlike the antibiotics mentioned above (MIC = 0.5-8 mg/I) [40].

Resistance rates are very high in parts of the world [41]. Although resistance develops less often when metronidazole is combined with bismuth or a second ATB [39], its occurrence, regardless of the circumstances, is associated with a marked reduction in the eradication rate of *H. pylori* [42].

The side effects of metronidazole in the mouth are the most marked: feeling of dry mouth, metallic taste, discoloration of the tongue. In addition, the combination: alcohol + metronidazole should be avoided to avoid the antabuse effect [43].

H. pylori is also very sensitive to tetracycline, which is a bacteriostatic antibiotic, inhibiting bacterial protein synthesis by preventing RNA aminoaryl transferase from reaching its acceptor site on the ribosome. It is active at low pH [44]. Since 1990, tetracycline has been one of the drugs used in triple therapy for infection and until now no bacterial resistance has been reported [45].

Tetracycline should not be given to pregnant women and children because it

causes permanent discoloration of developing teeth [45].

Rifabutin is a bacteriostatic ATB, belonging to the rifamycin family. It is active against bacilli, including multi-resistant mycobacteria. Its mechanism of action is based on the inhibition of bacterial DNA synthesis. Rifabutin also has good intracellular activity against *H. pylori*, which is why it is used to treat the infection, after treatment failure in cases of resistance to both metronidazole and clarithromycin. Since this ATB is an enzyme inducer, its use must be accompanied by precautions [46].

Helicobacter pylori eradication treatment is based on the combination of anti-secretory drugs and antibiotics [47]. Anti-secretory drugs include H_2-blockers (cimetidine, famotidine, ranitidine, nizatidine) and PPIs (omeprazole, esomeprazole, lansoprazole, pantoprazole). These two classes lead to an inhibition of gastric acid secretion and therefore a significant improvement in the very acidic gastric pH in ulcerative diseases.

In terms of effectiveness, PPIs have a greater anti-secretory capacity than H_2-blockers, when prescribed at the same dose. On the other hand, H_2-blockers are antacids without intrinsic antibacterial activity or specific pharmacokinetic interaction with antibiotics [48].

Tolerance of antisecretory drugs is good, even when administered long term. The side effects described are mild and resolve after reducing the dosage [49].

H_2-antihistamines are histamine H_2-receptor antagonists. They act on gastric parietal cells to reduce their acid secretion. H_2-antihistamines include cimetidine, ranitidine, famotidine and nizatidine.

Cimetidine is an H_2-antihistamine, it has anti-secretory activity, inhibiting the secretion of gastric acid not only caused by histamine, but also by pentagastrin, insulin, food or caffeine. It lowers the flow of pepsin by reducing the volume of gastric juice.

Its administration immediately allows for a greater rise in intragastric pH which lasts for approximately 3 hours. This early elevation with cimetidine alone

increases the speed and duration of action [50]. In clinical trials, its most common side effect is gynecomastia.

Ranitidine is a selective and competitive antagonist of histamine H_2 receptors, acts by blocking their actions. Ranitidine has been approved by the FDA for the short-term treatment of gastric pathologies [51].

It is indicated at a dose of 75 mg, in adults and children (> 15 kg), in the treatment of RGOGGT6, and at a dose of 150 and 300 mg in adults in the treatments: inflammation of esophagus due to GERD, UGD and their relapses, ZES, eradication of Helicobacter pylori in association with specific antibiotic therapy.

Ranitidine is 4 to 10 times more potent than cimetidine in inhibiting stimulated gastric acid secretion. Clinical studies have demonstrated that it is as well tolerated and effective as cimetidine.

Since September 26, 2019, the marketing stoppage on the French market of oral and injectable forms, specialties as well as their generics, following the identification in certain batches of an impurity, called NDMA (N-nitrosodimethylamine), classified probable carcinogen for humans by the WHO [52].

The Directorate of Medicines and Pharmacy (DMP) in Morocco has also decided to withdraw medicines containing this active ingredient: Acidac® – Pep-rani®-Azantac®-Ranimat®-Efitac®-Ranitil®-Zantac®- Normacide® [53].

Famotidine is 20 times more potent than cimetidine, 7.5 times more potent than ranitidine, in terms of inhibiting basal gastric acid secretion in humans [54].

Therapeutic trials have shown that famotidine, at a dose of 20 mg twice daily or 40 mg at bedtime, can be an effective alternative to cimetidine and ranitidine for the healing of gastric and duodenal ulcers.

Some studies obtained in some patients with Zollinger-Ellison syndrome indicate that famotidine, alone or in combination with an anticholinergic agent, allows good control of gastric hyperacidity, without signs of hematological or biochemical toxicity, therefore it seems to be well tolerated. Unlike cimetidine, it

does not have anti-androgenic effects and does not modify the hepatic metabolism of drugs [55].

Studies in humans have confirmed that nizatidine is a potent inhibitor of basal, nocturnal or stimulated gastric acid secretion [56].

A therapeutic dose of 300 mg at bedtime, or 150 mg twice daily, is more effective than standard doses of ranitidine in increasing the healing rate of duodenal and gastric ulcers, and as effective as a standard dose of cimetidine in the treatment of active duodenal ulcer.

Nizatidine is well tolerated, unlike cimetidine, it has no anti-androgenic effect and does not modify the hepatic metabolism of drugs [50.56].

PPIs are molecules that irreversibly inhibit the function of the proton pump (H+/K+ ATPase), which suppresses gastric acid secretion for several hours [57].

Their effect is linked to their ability to increase intragastric pH, which optimizes the antimicrobial action of drugs administered simultaneously, such as amoxicillin [58]. H+/K+ ATPase inhibitors are rapidly inactivated at acidic pH and are therefore administered in an enteric form, which is released into the small intestine rather than the stomach. These drugs are also expensive

Currently, several studies confirm that PPIs are more effective than H_2 blockers and other medications in acid-related disorders. In addition, they have a certain direct action against *H. pylor*i in vitro.

Omeprazole is the leading proton pump inhibitor. It has greater antisecretory activity than type 2 histamine receptor antagonists

Omeprazole is administered to adults at a dose of 20 to 40 mg/day, for the short-term treatment of duodenal or gastric ulcer, ZES and GERD. It is also a first-line treatment for children suffering from ulcerations [58].

The use of omeprazole in patients with peptic ulcer disease associated with H. pylori, allows an increase in intragastric pH, which leads to self-destruction of the host (the urease activity of *H. pylori* does not protect the bacteria at neutral pH) and therefore [59], increases the effectiveness of antibiotics against *H. pylori* (amoxicillin or clarithromycin).

Adverse effects, which are uncommon, are of a gastrointestinal nature similar to those of histamine H_2-receptor antagonists.

The results of short-term clinical trials (8 weeks) showed that the effectiveness of lansoprazole is significantly superior to ranitidine and famotidine in the treatment of duodenal ulcer. Gastric ulcers and reflux esophagitis are also treated with lansoprazole at a dose of 30 mg/day, for 4 to 8 weeks, with cure rates of approximately 85 to 95% for both indications.

Lansoprazole was well tolerated in short-term clinical trials, with an incidence of adverse reactions comparable to other PPIs [60].

Antacids are medications commonly used in self-medication. They initially constituted the first line of defense against the UGD [61]. But the discovery of PPIs revolutionized the treatment of peptic ulcer disease.

Currently, the use of antacids is limited to the relief of mild GERD, accompanied by heartburn.

They are a combination of several compounds with calcium, magnesium or aluminum salts as active ingredients.

Their effect on the stomach is due to partial neutralization of gastric HCl and inhibition of pepsin [62]. Antacids are indicated in the following cases: esophagitis, active UGD (first prescribed while awaiting basic treatment), GERD, pancreatic biliary and hepatic insufficiency, diarrhea caused by bile acids, and non-ulcerative dyspepsia [62].

Most side effects of antacids are minor when used rationally and in small quantities.

However, when used in large doses and for long periods [63], adverse effects can be severe, such as sudden death from cardiac poisoning with Mg^{2+} [64, 65].

Like any medication, antacids have well-known drug interactions, but they can be avoided by interspersing the times of taking other medications (±2 hours). Therefore, they must be administered 90 minutes after a meal and if necessary, at bedtime [63].

Sucralfate has 3 types of properties:

- Mechanical protection of the digestive tract: It transforms into a viscous, adhesive, strongly polarized substance, capable of attaching to lesions of the esophageal, gastric, duodenal and colonic mucous membranes. This affinity for damaged mucous membranes is explained by an electrostatic interaction between the negatively charged sucralfate and the positively charged inflammatory proteins. The complex formed protects the lesions [66].
- An anti-bile salt and anti-pepsin action: sucralfate has an adsorbing power for pepsin and bile salts, which allows it to oppose their attack on damaged tissues
- Stimulation of physiological protective factors of the gastroduodenal mucosa: endogenous prostaglandins, mucus and bicarbonates. In addition, it inhibits damage to the gastroduodenal mucosa induced by NSAIDs [67].

The sucralfate substance also helps treat chemotherapy-induced mucositis, radiation proctitis, Bechet's disease ulcers and burns. It is approved by the FDA for the short-term treatment of duodenal ulcers, the dose being 1 g four times daily for eight weeks, then with 1 g twice daily as maintenance therapy. Its effectiveness is comparable to that of cimetidine or intensive antacid treatment [68].

The most common side effects of this substance are constipation, hypophosphatemia, aluminum intoxication rarely observed in patients in the terminal phase of treatment [69].

Misoprostol is a synthetic analogue of prostaglandin E_1. It is effective in healing and preventing NSAID-induced gastric injury. It has a «cytoprotective» activity, manifested by inhibiting the secretion of gastric acid and limiting the extension of gastrointestinal lesions.

The recommended dosage of misoprostol in adults is 200µg 4 times a day for 4 to 8 weeks [70].

However, this medication is not without adverse effects due to its systemic action like any prostaglandin:

- Diarrhea is often noted following stimulation of intestinal motility.
- Stimulation of uterine contractility, with bleeding in pregnant women,

hence its contraindication in this case [71].

Bismuth is an intestinal antiseptic, gastroprotective, which disrupts the integrity of bacterial cell walls [72]. It lyses *H. pylori* near the gastric surface, as it can prevent its adhesion to the gastric epithelium or inhibit its urease, phospholipase and proteolytic activity. Bismuth compounds are often used in combination with antibiotics to eradicate *H. pylori* due to their complementary effects. Bismuth concentrations are reached in the antral mucus for two hours after each dose.

Its mechanism of action is summarized in these following steps [73].

1). Inhibition of several enzymes produced by *H. pylori*, including catalase, urease, and lipase/phospholipase.

2). Inhibition of *H. pylori* adhesion to superficial epithelial cells.

3). Inhibition of ATP synthesis. Inhibition of proteins, membrane function and cell wall synthesis. It is present in the form of colloidal bismuth subcitrate (CBS) and ranitidine bismuth citrate (RBC).

These compounds present synergy with one or two antibiotics used to eradicate *H. pylori*. Side effects of high doses of bismuth primarily include central nervous system toxicity [74].

So far, no resistance from *H. pylori* to different bismuth compounds has been reported, despite treatment failures often due to the acquisition of bacterial resistance

The eradication of *H. pylori* is recommended for all subjects with PUD. First-line treatment achieves an eradication rate greater than 80%.

The prescriber rarely knows the patient's sensitivity before initiating treatment. Therefore, its choice must be made empirically, based on regional patterns of bacterial resistance, local recommendations and drug availability. Standard triple therapy is a reasonable initial treatment when resistance to clarithromycin is low [75].

Eradication cures most PUs and significantly reduces the risk of bleeding. A scientific study found that treatment of *H. pylori* is more effective than

non-eradicative antisecretory therapy (with or without long-term maintenance antisecretory therapy), in preventing bleeding due to PUD [76]. Current data suggest that increasing the treatment duration up to 14 days significantly increases the eradication rate (Fig. 1.3.) [77].

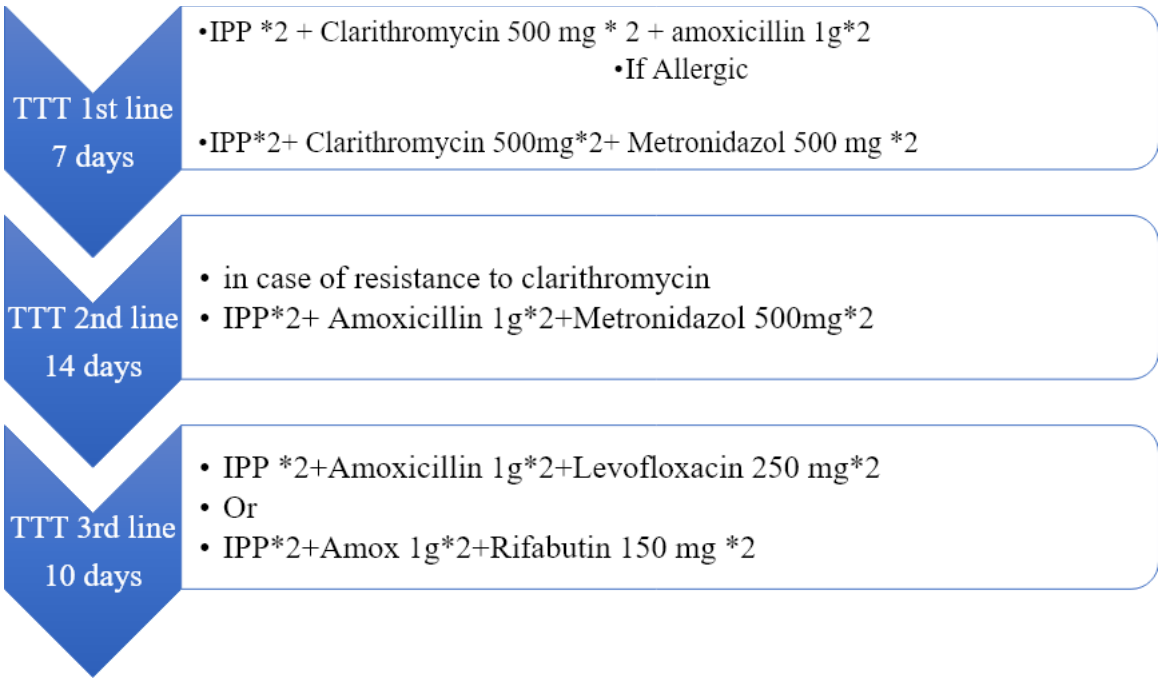


Fig. 1.3. Eradication of *H. pylori* [78].

A triple therapy of 7 to 10 days comprising a PPI, 1 g of amoxicillin and 500 mg of clarithromycin, twice a day, is the first-line treatment to eradicate *H. pylori*. But, due to its excessive use, it has developed increasing resistance to clarithromycin, observed by a decline in eradication rates (below 80%) [78].

Therefore, this diet is not recommended when the prevalence of *H. pylori* resistant to clarithromycin exceeds 15 to 20%. Another form of triple therapy replaces amoxicillin with metronidazole 500 mg twice a day. It has been shown that the addition of probiotics to triple therapy, in particular *Saccharomyces boulardii* and *Lactobacillus*, increases eradication rates by 9% and 5% respectively, and reduces the adverse effects of treatment, mainly diarrhea (absolute reduction in 14% and 7%, respectively [79].

Quadritherapy :

A. Sequential therapy:

It is a 5-day treatment, with a PPI, 1g of amoxicillin twice a day, followed by a 5-day treatment with a PPI, 500 mg of clarithromycin and 500 mg of metronidazole or 500 mg of tinidazole, twice a day. The eradication rate is 84%, with an eradication rate of 73% for strains resistant to clarithromycin.

The tolerance and compliance rates of sequential therapy are similar to those of triple therapy, but the cost is lower, especially if we take into account the cost of failure of first-line treatment (triple therapy) [78].

B. Non-bismuth-based quadruple therapy (concurrent therapy):

This therapy consists of adding 500 mg of metronidazole or 500 mg of tinidazole twice a day to standard triple therapy. It is simpler than sequential therapy with similar eradication rates [80].

Additionally, it may be more effective than sequential therapy in patients with antibiotic resistance to clarithromycin and metronidazole.

Its eradication rate is the highest, around 90%, even in areas with high resistance to clarithromycin and metronidazole [81], but it is more expensive than sequential therapy because clarithromycin is taken for 10 days.

C. Bismuth-based quadruple therapy:

This is the traditional quadruple therapy, which includes a bismuth salt (420 mg potassium subcitrate or 525 mg subsalicylate), 375 to 500 mg of the tetracycline and 250 mg of the metronidazole, all taken twice a day, plus a PPI twice a day. Bismuth-based quadruple therapy is often used as a rescue treatment in the event of failure of first-line treatment. It can also be administered as a first-line treatment, in areas of high resistance or when cost is an important factor [82].

A combined capsule (Pylera®) (Fig. 1.4,), containing 3 active ingredients: bismuth potassium citrate, metronidazole and tetracycline, has been marketed to reduce the number of tablets, in order to facilitate administration and avoid forgetting.

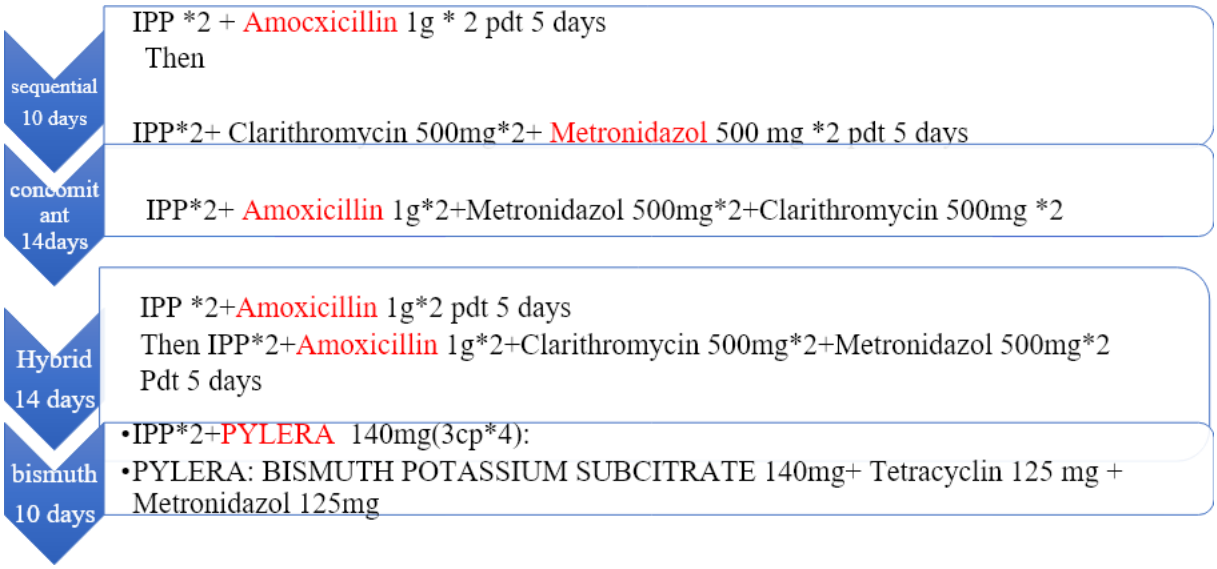


Fig. 1.4. Eradication of *H. Pylori* with Pylera® [80].

Several factors can explain the failure to eradicate *Helicobacter pylori*. The main factors are poor compliance with treatment, ignorance of the methods of administration of treatment by most patients, which can vary the eradication rate from 10% to 15%.

Conclusions for chapter 1

1. Peptic ulcers represent a significant gastrointestinal health challenge, affecting individuals worldwide and contributing to substantial healthcare costs. While the prevalence of peptic ulcers has declined in recent years, they continue to be a source of morbidity and require ongoing attention from healthcare providers.

2. Understanding the pathophysiology of peptic ulcers is crucial for effective management. These ulcers typically arise due to an imbalance between aggressive factors, such as gastric acid secretion and *Helicobacter pylori* infection, and protective factors, including mucosal integrity and blood flow. Chronic irritation from factors such as NSAID use further exacerbates mucosal damage, leading to ulcer formation.

3. The etiology of peptic ulcers encompasses a range of factors, including *H. pylori* infection, NSAID use, lifestyle factors (such as smoking and alcohol consumption), genetic predisposition, and socioeconomic influences. Identifying and addressing these underlying causes are essential components of successful ulcer management.

4. Treatment strategies for peptic ulcers aim to alleviate symptoms, promote healing, and prevent complications. Pharmacological interventions, such as proton pump inhibitors (PPIs), H_2-receptor antagonists, and antibiotics for *H. pylori* eradication, are central to ulcer therapy. Additionally, lifestyle modifications, including dietary changes and stress reduction techniques, play a crucial role in symptom management and ulcer prevention. In severe cases or when complications arise, such as gastrointestinal bleeding or perforation, endoscopic therapy or surgical intervention may be necessary to address the underlying pathology and prevent further harm.

5. Peptic ulcers require a multifaceted approach to diagnosis and management that considers the complex interplay of epidemiological, pathophysiological, and etiological factors. By addressing these aspects comprehensively, healthcare providers can deliver optimal care and improve outcomes for individuals affected by peptic ulcers.

CHAPTER 2
MATERIALS AND METHODS

The practical part of the study was conducted in cooperation with Rmail Pharmacy, Sidi Kacem, Morocco. We have developed two versions of the questionnaires, which are presented in Fig. 2.1 and Fig. 2.2:

1) Questionnaire for pharmacists on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers.

2) Questionnaire for pharmacy visitors on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers.

We analyzed 42 questionnaires of pharmacists and 40 questionnaires of pharmacy visitors on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers.

The survey was conducted using two versions of the questionnaire. There were Google questionnaires and paper questionnaires. Pharmacists and pharmacy visitors choose the convenient version of the questionnaire themselves.

The objective of this questionnaire is to understand both the opinions of pharmacists and visitors on the use of drugs treating ulcers such as peptic and gastric ulcers with the aim of collecting as much information as possible which can help us in prevention, and also in subsequently understanding the role of the pharmacist in the prevention and treatment of peptic and gastric ulcer disease.

The questions concerning the criteria of efficiency of treatment and about the factors, that from the point of patient are the most important for the effectiveness of the treatment were in both questionnaires same. In the questionnaire for patients, the questions and answers were adopted for better understanding, how the pharmacists can provide an appropriate prevention, and also test the level of pharmacists in their know-how regarding prevention and the method pursued to avoid any complications caused either by the wrong choice of medications or late follow-up of patients.

QUESTIONNAIRE FOR PHARMACIST

ON MEDICATIONS ARE MOST FREQUENTLY REQUESTED BY PATIENTS FOR THE TREATMENT OF PEPTIC AND GASTRIC ULCERS

To fill in the questionnaire, circle the correct answers or write the necessary information by hand. Thank you for your cooperation!

Which of the following medications do patients most commonly request for the treatment of peptic and gastric ulcers?

- ☐ Proton pump inhibitors (PPIs)
- ☐ H2-receptor antagonists (H2 blockers)
- ☐ Sucralfate
- ☐ Antacids
- ☐ Misoprostol
- ☐ others (specify please)

Are there any notable differences in patient requests between medications for peptic ulcers and those for gastric ulcers?

☐ Yes. ☐ No.

How often do patients inquire about specific brands or formulations for treating peptic and gastric ulcers?

☐ Frequently ☐ Occasionally ☐ Rarely
☐ Never

Have you observed any shifts in patient preferences for ulcer medications over time?

☐ Yes. ☐ No.

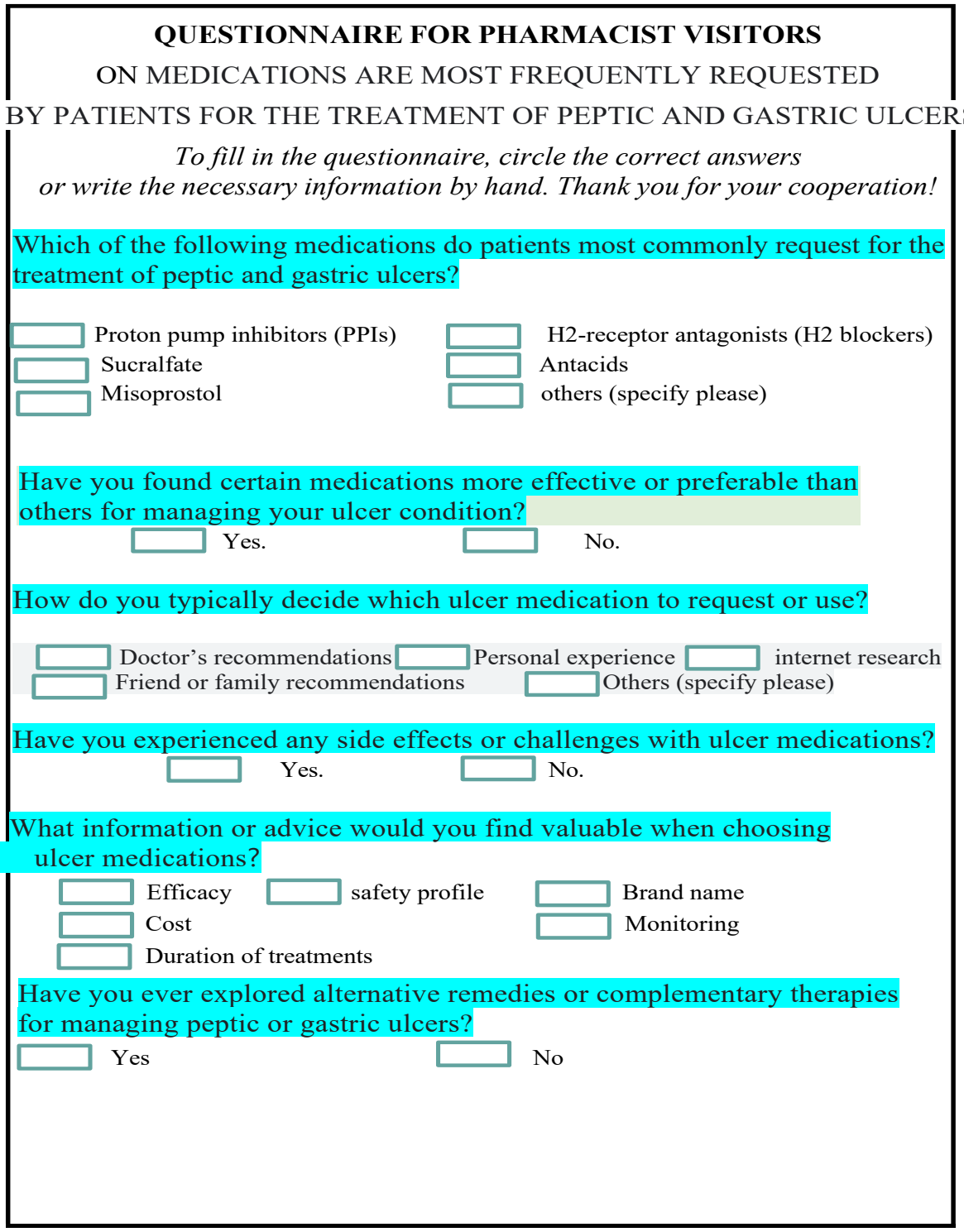
what factors do you believe influence patients choice when requesting medications for peptic and gastric ulcers?

☐ Price ☐ Brand loyalty ☐ Doctor's recommendation
☐ Side effect profile ☐ Effectiveness
☐ Others (please specify)

How do you address patient concerns or inquiries about potential interactions between ulcer medications and other drugs they may be taking?

☐ Educate the patient about potential interactions ☐ Consult a doctor
☐ Encourage open communication ☐ Provide resources ☐ Offer reassurance

Fig. 2.1. Version of the questionnaire for pharmacists on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers



QUESTIONNAIRE FOR PHARMACIST VISITORS

ON MEDICATIONS ARE MOST FREQUENTLY REQUESTED

BY PATIENTS FOR THE TREATMENT OF PEPTIC AND GASTRIC ULCERS

To fill in the questionnaire, circle the correct answers or write the necessary information by hand. Thank you for your cooperation!

Which of the following medications do patients most commonly request for the treatment of peptic and gastric ulcers?

☐ Proton pump inhibitors (PPIs) ☐ H2-receptor antagonists (H2 blockers)
☐ Sucralfate ☐ Antacids
☐ Misoprostol ☐ others (specify please)

Have you found certain medications more effective or preferable than others for managing your ulcer condition?

☐ Yes. ☐ No.

How do you typically decide which ulcer medication to request or use?

☐ Doctor's recommendations ☐ Personal experience ☐ internet research
☐ Friend or family recommendations ☐ Others (specify please)

Have you experienced any side effects or challenges with ulcer medications?

☐ Yes. ☐ No.

What information or advice would you find valuable when choosing ulcer medications?

☐ Efficacy ☐ safety profile ☐ Brand name
☐ Cost ☐ Monitoring
☐ Duration of treatments

Have you ever explored alternative remedies or complementary therapies for managing peptic or gastric ulcers?

☐ Yes ☐ No

Fig. 2.2. Version of the questionnaire for pharmacist's visitors on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers

Conclusions for chapter 2

1. The practical part of the study was conducted in cooperation with Rmail Pharmacy, Sidi Kacem, Morocco.

2. Two versions of the questionnaires were developed: Questionnaire for pharmacists on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers; Questionnaire for pharmacy visitors on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers.

3. We analyzed 42 questionnaires of pharmacists and 40 questionnaires of pharmacy visitors on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers.

CHAPTER 3
THE ROLE OF THE PHARMACIST IN THE PREVENTION AND TREATMENT OF PEPTIC ULCER DISEASE (EXPERIMENTAL PART)

3.1. Survey of pharmacists concerning efficiency and safety of peptic ulcer disease treatment

We analyzed questionnaire from 42 pharmacists about the medications are most frequently requested by patients for the treatment of peptic and gastric ulcers.

The results of pharmacist's survey on medications which are most frequently requested by patients for the treatment of peptic and gastric ulcers (Fig. 3.1.).

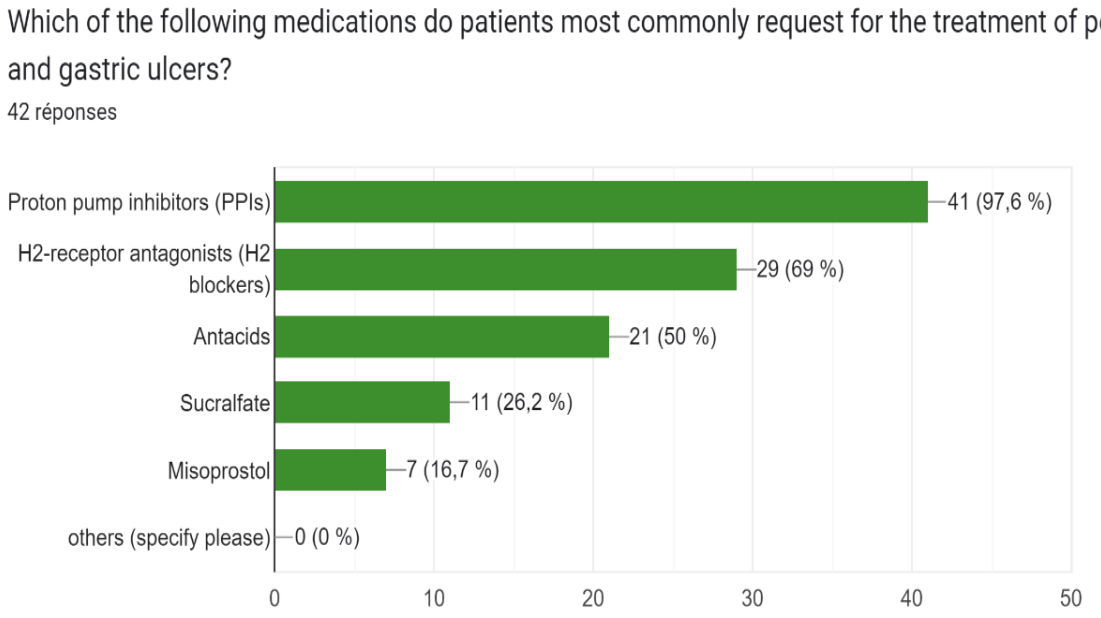


Fig. 3.1. The results of pharmacist's survey on medications which are most frequently requested by patients for the treatment of peptic and gastric ulcers

In response to the question which of the following medications do patients most commonly request for the treatment of peptic and gastric ulcers? 97.6% of respondents answered proton pump inhibitors (PPIs), 69% answered H_2-receptor antagonists; 50% answered antacids; 26.2% answered sucralfate, 16.7% answered misoprostol (Fig 3.1).

Figure 3.2. demonstrates the results about notable differences in patient requests between medications for peptic ulcers and those for gastric ulcers: 45.2% answered Yes; 54.8% answered No.

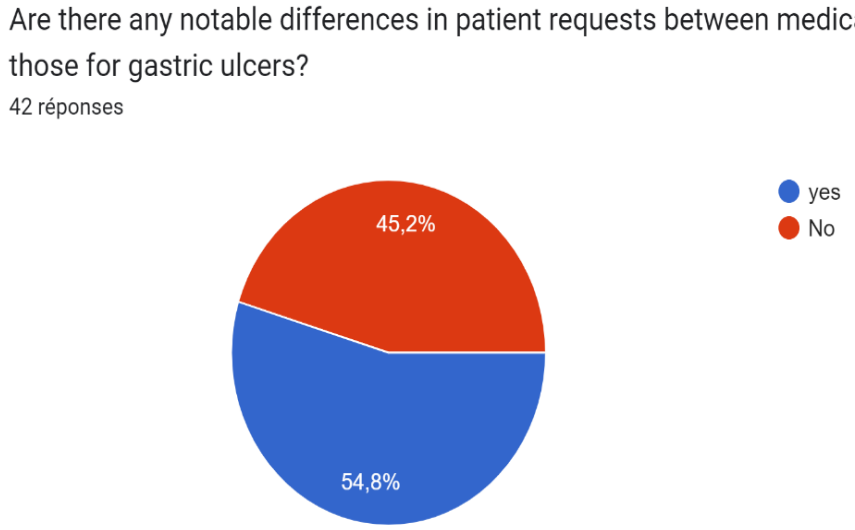


Fig. 3.2. Notable differences in patient requests between medications for peptic ulcers and those for gastric ulcers?

3.2. Survey of pharmacy visitors concerning efficiency and safety of peptic ulcer disease treatment

We analyzed questionnaire from 40 visitors' pharmacy about the medications which are most frequently requested by patients for the treatment of peptic and gastric ulcers.

The results of pharmacist's survey on medications are most frequently requested by patients for the treatment of peptic and gastric ulcers in response to the question Which of the following medications have you been prescribed or used for treating peptic or gastric ulcers? 90% of respondents answered proton pump inhibitors (PPIs); 67.5% answered H_2-receptor antagonists; 52.5% answered antacids; 10% answered sucralfate, 12.5% answered misoprostol (Fig. 3.3.).

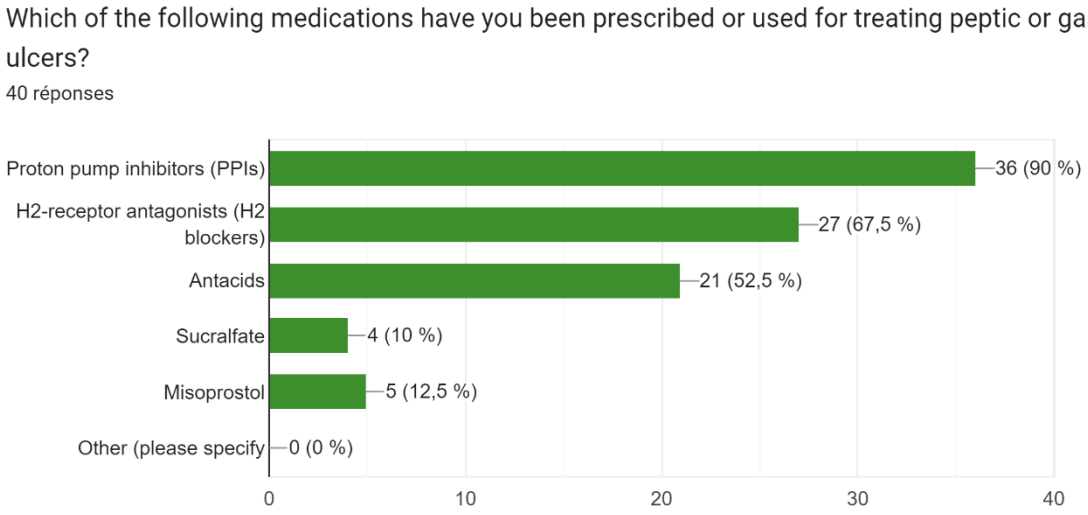


Fig. 3.3. The results of pharmacy visitors survey on medications which are most frequently requested by patients for the treatment of peptic and gastric ulcers

In this research we also studied what information or advice would you find valuable when choosing ulcer medications?

- Efficacy: 82.5%;
- Safety profile: 70%;
- Brand name: 55%;
- Cost: 65%;
- Monitoring: 10%;
- Duration of treatment: 17.5%.

3.3. Discussion of the practical cases

3.3.1. Case of the patient coming to the pharmacy with pain gastric

Since the community pharmacist is the health actor closest to the patient. This patient comes spontaneously to the pharmacy, without a prescription, to look for medication to treat stomach pain. The pharmacist must always be vigilant regarding the differentiation between gastric pain, which could be linked to gastritis or GERD, of those could be linked to a gastric or duodenal ulcer (Fig. 3.4).

Gastritis is an inflammation of the gastric mucosa (acute or chronic), which causes cramp-like pain, occurs at the end of meal. However, it is not characterized by damage to the mucosa. gastric, unlike UGD (pain occurs 1h 30 to 2 hours after meals).

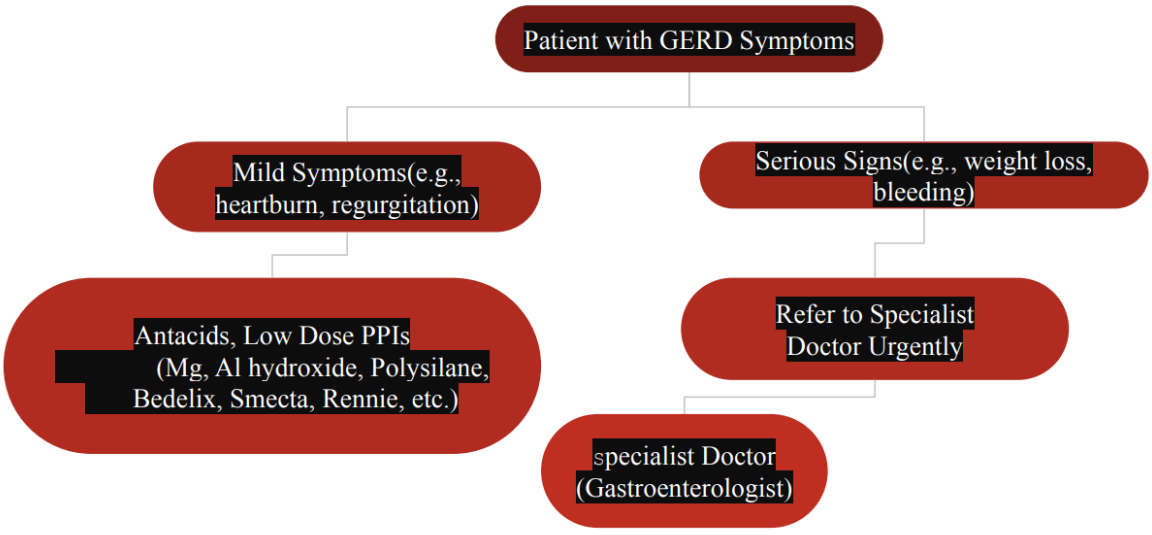


Fig. 3.4. The algorithm of conversation with patient with GERD symptoms

The patient with GERD symptoms is originally split into two branches in this diagram: those with mild symptoms and those with significant indicators. The

pharmacist can suggest antacids, low-dose PPIs, and gastrointestinal products as treatments for minor symptoms. It is imperative that the pharmacist promptly refers a patient who exhibits severe symptoms of possible consequences to a specialist doctor, usually a gastroenterologist, for additional assessment and care.

3.3.2. Case of the patient already having a peptic ulcer

The pharmacist participates in improving treatment compliance, by explaining to the patient all the instructions for using their new treatment.

The announcement of peptic ulcer, with or without *Helicobacter pylori* infection, can sometimes disturb the patient and prevent him from listening to the instructions given by his doctor. Since the community pharmacist is going to dispense his treatment, he re-explains in detail, specifying its instructions for use, its undesirable effects, etc. By dint of the theoretical and practical training of the pharmacist, he can adapt his vocabulary according to the intellectual level of the patient so that he assimilates his treatment.

Explanation of the treatment and its instructions for use:

In the event of PUD caused by *Helicobacter pylori* infection, the pharmacist explains to the patient that his treatment is composed of a combination of several ATB to eliminate the bacteria, an IPP to reduce the secretion of gastric acid, in order to boost the activity of antibiotics. Thus, it is necessary to insist on the obligation to correctly take one’s treatment and complete it to the end, without stopping immediately. If not, the patient is exposed not only to recurrence of peptic ulcer, but also to complicated bacterial resistance.

Instructions for use

If the IPP is prescribed once a day, it is administered for 30 to 60 minutes before breakfast, and if it is prescribed twice a day, we administer it 30 minutes before breakfast and 30 minutes before dinner, to control nocturnal hyperacidity (table 3.1).

Table 3.1

Instructions for antiulcer drugs use

Important Instructions	
Medications	**Instructions**
Capsules	Must be swallowed whole, with a good glass of water without crushing or chewing them.
Antacids	a) Administer 90 minutes after,meals, and if necessary at bedtime. b) Intersperse times of taking. c) Other medications (±2H). d) Avoid drug interactions with antacids.
Antibiotic therapy (*H.pylori*-positive)	a) Amoxicillin: take at the start of the meal. b) Clarithromycin, Metronidazole: take in the middle of the meal to limit digestive problems. c) Administer antibiotics at the same time in the middle of the meal to encourage compliance. d) Propose a dosing plan to facilitate patient uderstanding, especially for elderly subjects.

A concise summary of the crucial directions for medicine administration is given in this table, which also includes information on capsules, antacids, and antibiotic therapy for patients who test positive for *H. pylori*. The administration directions for each drug are included in the list of instructions.

If you forget to take a dose: the forgotten medication(s) will be administered as soon as possible, without doubling the dose. The treatment will be continued until you have taken all of the medications initially planned.

Explanation of side effects

The patient should be aware of the frequent side effects of treatment, to reduce anxiety if one of these effects occurs. In this case, the patient must immediately inform his pharmacist or doctor, to decide on the continuation of treatment (table 3.2).

Table 3.2

The main side effects of antiulcer drugs

Medication	Adverse Effects	Management/Considerations
Amoxicillin	- Digestive disorders (diarrhea, dyspepsia)	- Ensure no penicillin allergy
	- Headaches	
	- Allergic reactions (urticaria, angioedema)	
Clarithromycin	- Severe digestive problems	- Simultaneous administration of probiotics (Saccharomyces boulardii) and hydration
	- Oral candidiasis, stomatitis	
	- Tongue discoloration	
Metronidazole	- Dry mouth	- Avoid alcohol + metronidazole combination to prevent disulfiram-like reaction
	- Metallic taste	
	- Discoloration of tongue and urine	
H_2 antihistamines	- Minor digestive disorders (diarrhea, constipation)	- Monitor for rare side effects such as rash, dizziness, hematological disorders, sinus bradycardia
	- Headache	
Cimetidine	- Confusional syndromes	- Consider replacing with another H_2 blocker
	- Anti-androgenic effects (especially in elderly)	- Balanced sodium intake for effervescent forms
PPIs	- Minor and transient: nausea, vomiting, headache	- Generally well-tolerated
Sucralfate	- Constipation	- Maintain good hydration
	- Hypophosphatemia	- Rarely observed aluminum poisoning in terminal phase of treatment
	- Aluminum toxicity in chronic renal failure	- Avoid prolonged high-dose administration in chronic renal failure patients (risk of encephalopathy)
Misoprostol	- Diarrhea	- Contraindicated in pregnant women
	- Bleeding in pregnant women	- Use with caution in elderly with hypotension

The side effects of several drugs that are frequently prescribed for gastrointestinal diseases are listed in this table, along with treatment techniques and other important information for each drug.

All this information must be clarified to the patient by his pharmacist, in order to avoid relapses and improve compliance with treatment.

Explanation of the hygienic and dietary rules

The pharmacist accompanies the delivery of medications, through a set of hygienic-dietary rules and advice, in order to improve the progression of his illness and to promote complete recovery (table 3.3).

Table 3.3

Hygienic and dietary rules

Advice	Description	Considerations/Management
Dietary Advice	- Split diet into 4 to 6 small meals to increase pH and reduce gastric pain.	- Avoid prolonged fasting to prevent ulcers. - Chew food well. - Avoid aggressive foods: acidic, too sweet or salty, pungent, high-fat, carbonated, alcoholic, caffeinated. - Favor "soft" foods during acute phases. - Milk intake (2 to 2.5L/day) for analgesic effect on gastric juice secretion.
Stopping Smoking	- Explain tobacco's role in gastrointestinal disorders and cancer. Offer nicotine-based alternatives.	- Smoking cessation enhances drug treatment effectiveness, reduces recurrence risk by 50%. - Offer nicotine spray, chewing gum, patches, lozenges, or replace nicotine in cigarettes.
Avoid Self-Medication	- Discourage self-medication. Seek pharmacist/doctor advice before adding medications.	- Prohibit NSAIDs; prefer paracetamol for pain relief.
Avoid Stress	- Explain stress impact on health, especially gastric mucosa. Advise antacids/PPIs during painful stress attacks.	- Stress ulcer risk; stressed patients may already be under preventive treatment.

A detailed summary of the many suggestions and pieces of guidance for treating gastrointestinal diseases is given in this table. For improved patient care, each piece of advice is supported with management techniques and considerations.

3.3.3. Analysis of some cases (prescriptions) during internship period in the pharmacy

Table 3.4

Prescriptions cases during internship period in the pharmacy

Case	Patient information	Prescriptions	Recommendations
1	Male, aged 50, presenting with epigastric pain and a history of chronic NSAID use for arthritis.	omeprazole (PPI) 20 mg once daily for 4 weeks, along with sucralfate to provide mucosal protection.	Avoid spicy and acidic food.
2	Female, aged 60, with a duodenal ulcer positive for Helicobacter pylori infection.	Prescribed a triple therapy regimen consisting of a proton pump inhibitor (e.g., omeprazole), clarithromycin, and amoxicillin for 14 days, followed by omeprazole monotherapy for an additional 4 weeks.	Avoid clear of fatty, acidic, and spicy foods since they can make symptoms worse. Maintain a bland diet.
3	Male, aged 45, smoker, diagnosed with a gastric ulcer and signs of recent bleeding.	Prescribed high-dose PPI therapy (e.g., pantoprazole 40 mg twice daily).	cessation of smoking and avoidance of NSAIDs.
4	Female, aged 55, with recurrent gastric ulcers despite PPI therapy and confirmed NSAID intolerance.	Prescribed misoprostol, a prostaglandin analog, to replace NSAIDs for arthritis pain management, along with continued PPI therapy.	Schedule regular follow-up appointments with the doctor.

5	Male, aged 35, presenting with a duodenal ulcer and concomitant chronic kidney disease on hemodialysis.	Prescribed PPI therapy (e.g., esomeprazole) at a reduced dosage to account for renal impairment, along with regular monitoring of electrolytes and avoidance of nephrotoxic medications.	Maintain regular follow-up appointments with doctor for monitoring of renal function and electrolyte levels.
6	Male, age 45 male with peptic ulcer.	Omeprazole 20mg, twice daily (morning and evening) for 14 days; Clarithromycin 500mg, twice daily (morning and evening) for 14 days; Amoxicillin 1g, twice daily (morning and evening) for 14 days.	Avoid NSAIDs (Nonsteroidal anti-inflammatory drugs) like ibuprofen, unless advised otherwise by doctor and avoid spicy, acidic, and fatty foods that may exacerbate symptoms. Stick to a bland diet.
7	Female age 35 diagnosis peptic ulcer.	Prescribed Lansoprazole 30mg, once daily; Misoprostol 200mcg, four times daily; Tetracycline 500mg, four times daily.	Take medications as prescribed and finish the entire course.
8	Female 40 with pain peptic ulcer.	Pantoprazole 40mg, once daily; Bismuth subsalicylate 262mg, four times daily; Metronidazole 500mg, three times daily.	Follow a bland diet until symptoms improve; Elevate the head of the bed while sleeping to reduce reflux; Keep a food diary to identify triggers and avoid them.

These case studies point out the significance of individualized therapies in the management of peptic ulcers by demonstrating a variety of prescription approaches specialized to specific patient characteristics, ulcer severity, and underlying medical conditions.

3.4. Discussion of the results

Several important topics would be covered in a broad discussion of the findings from the case studies that were presented and the recommendations for treating peptic ulcers:

- Pharmacological Interventions' Efficacy: The case studies show how well pharmacological treatments for peptic ulcers work, including prostaglandin analogs, proton pump inhibitors (PPIs), *H. pylori* eradication therapy, and cytoprotective medicines. These drugs are essential for lowering stomach acid production, encouraging ulcer repair, and averting consequences.
- Customized Therapy Strategies: Every case study emphasizes the significance of customizing treatment strategies based on patient-specific variables such as underlying comorbidities (e.g., diabetes, chronic kidney disease), medication use (e.g., NSAIDs, corticosteroids), lifestyle factors (e.g., alcohol consumption, smoking), and ulcer characteristics (e.g., location, severity). Customized treatment plans are necessary to maximize benefits and reduce side effects.
- The role of lifestyle modifications is crucial in managing peptic ulcers. These modifications involve reducing back on alcohol, changing one's diet, managing stress, and quitting smoking. These therapies address modifiable risk factors and facilitate ulcer healing in addition to medication.
- Difficulties in Complex Cases: Managing cases that provide major obstacles, such those with acute bleeding ulcers or ulcers that are resistant to normal care, can be difficult. In such circumstances, aggressive measures to control bleeding and avoid consequences, including as endoscopic hemostasis, blood transfusion, and surgical repair, may be required.
- The significance of follow-up and monitoring cannot be overstated. Evaluating the effectiveness of treatment and making necessary adjustments to therapy depend on regular follow-up on the patient's reaction to treatment,

which includes symptom improvement and endoscopic assessment of ulcer healing. To keep an eye out for ulcer recurrence and make sure that underlying risk factors are continuously managed, long-term follow-up is essential.

- The cost of medications, possible side effects, drug interactions, and patient preferences are all important considerations for clinicians when choosing treatment plans. Optimizing treatment outcomes and encouraging patient adherence require finding a balance between cost, safety, and efficacy.

In conclusion, the findings and recommendations made in the case studies. illustrate the complex nature of managing peptic ulcers and highlight the necessity of tailored, all-encompassing strategies that incorporate medication, lifestyle changes, and continuous monitoring in order to provide patients with the best possible outcomes.

3.5. Prevention of peptic ulcer disease and its complications: practical recommendations

The pharmacist plays an important role in the prevention of PUD, and this, directing the patient to take the necessary measures to prevent complications. The most effective actions mainly concern prevention peptic ulcers and their complications induced by NSAIDs and also the prevention of recurrences.

Subject who has never had an ulcer

The pharmacist must explain to the patient in the event of chronic taking of NSAIDs, their undesirable effects on the digestive tract, in order to minimize their taken. He may also suggest other alternatives. The risk of ulcer also increases when taking NSAIDs, associated with *Helicobacter pylori* infection. The eradication of this pathogen is therefore recommended in these patients taking NSAIDs. Prevention of recidivism, among These patients require maintenance treatment

with PPI.

There are obviously ulcers linked to taking NSAIDs in the absence contamination by *H.pylori.* There is an increased risk of ulcers more marked hemorrhagic when both factors are present. The effects eradication differs, from one chronic user to another user NSAID beginner. For the first case, eradication does not bring any benefit on maintaining remission after healing by PPI, it is less effective than maintenance treatment on the prevention of rebleeding.

On the other hand, patients developing a hemorrhagic ulcer, under treatment with low-dose aspirin, eradication of the bacteria reduces the rate of rebleeding.

Subject with ulcer or already having a history of ulcer

In patients with PUD or already have a history of ulcer, the change of the NSAID molecule and dosage adaptation, are the first measures to be implemented. Tests have shown that tolerance digestive system differs from one NSAID to another in the same subject. NSAIDs coxebs are better tolerated than conventional NSAIDs.

Curative treatment of patients with peptic ulcers under NSAIDs are mandatory, in order to avoid digestive complications (hemorrhages, perforations).

It is based primarily on the administration of IPPs; If dyspeptic disorders persist, screening and eradication are necessary systematic occurrence of *Helicobacter pylori* in these patients.

The implementation of gastro-protection by IPP in association with a coxeb is necessarily offered, in patients who have a history of complicated UGD. In addition, it is necessary to clearly explain to the patient ways to optimize compliance, that means taking the entire treatment prescribed, to properly protect the gastric mucosa against attacks due to NSAIDs and avoid recurrences.

To sum up, a comprehensive strategy for treating NSAID-induced ulcers includes discontinuing NSAID use if at all possible, starting PPI therapy to heal ulcers, checking for and treating *H. pylori* infections (Triple and quadruple therapy) [78] [80]. starting maintenance therapy to stop recurrence, routine

monitoring, and patient education. Referrals to consultants might be required in circumstances that are difficult.

Prevention of serious accidents induced by NSAIDs

Prevention aims to prevent digestive disorders induced by NSAIDs, ulcerations of the gastric mucosa and their complications (table 3.5). They must be recommended for patients with risk factors (elderly people, infection with *H. pylori*, alcohol consumption, tobacco, etc.). Ethically, any patient treated with NSAIDs must be informed by their doctor or pharmacist about the side effects of this treatment and the possibilities of prevention of digestive complications. Preventive treatment is essentially based on H_2-blockers and PPIs.

Table 3.5

Prevention of serious accidents induced by NSAIDs

Drugs	Description
Famotidine	High-dose famotidine (40 mg, twice daily) reduces incidence of PUD in long-term NSAID users.
	Provides protection against gastric ulcerations in low-dose aspirin users.
Misoprostol	Prevents ulcerative complications (hemorrhages and perforations).
	Association with non-selective NSAIDs reduces risk of ulcer complications by approximately 40%.
	Disadvantages: poor digestive tolerance, four doses per day.
	Artotec® withdrawn as a result of abuse (Artotec®50mg/0.2mg or Artotec®75mg/0.2mg). the Ministry of Health has withdrawn its AMM on 07/18/2018, because it was used for other illegal purposes (abortion).
Selective NSAIDs	COX-2 inhibition reduces peptic ulcer complications.
	Reduces risk by 50-60% compared to conventional NSAIDs.
	Similar security level to NSAID-PPI combination.
	Better tolerance on gastric and duodenal mucosa compared to PPIs.

To summarize, the prevention of digestive risk linked to NSAIDs is based either on the addition of a protective treatment, or on the development of new less toxic molecules for the digestive mucosa.

Anti H. pylori vaccination

Helicobacter pylori infection leads to chronic gastritis, PUD or even gastric adenocarcinoma, which is the 3rd cause of death by malignant tumor. Therapeutic eradication of this pathogen is ensured through different antibiotic therapy regimens. But it is also necessary to ensure prophylactic vaccination strategy like any threatening disease of the global society [83].

In addition, the development of an anti *H. pylori* vaccine is not a priority current strategy of the large pharmaceutical industries, despite the dangerousness of the disease and its importance in the world. Since the involvement of these companies is likely to be crucial for the advanced development, it is therefore necessary to establish collaboration between industries [84].

A prophylactic vaccine against *Helicobacter pylori* would therefore be a tool powerful in preventing gastric cancer. However, production trials of an advanced vaccine model, exploiting the antigenic properties of certain proteins, failed to prevent infection in humans. They are arrested at the first phase of clinical trial.

The vaccine development strategy was carried out over several animal models: mice, monkeys [84]. These studies showed that immunization is still possible using urease as antigen in the animal. According to this result, current clinical trials have also used urease as antigen, which is administered orally, with naive LT (heat-labile enterotoxin from E. coli). But they observed only a modest reduction of gastric colonization by *H. pylori* [84].

Another clinical study aims to test safety in healthy adults health, by administering orally a whole cell vaccine of *H.pylori*, inactivated by formalin, administered with or without naive LT (heat-labile enterotoxin of *E. coli*) as a mucosal adjuvant [85].Until present, no observation of effectiveness in humans.

Therefore, the marketing of a vaccine against *H. pylori* that is effective in the man still appears distant.

PRACTICAL RECOMMENDATIONS

The pharmacist is one of the most reliable health professionals, accessible, and is the first point of contact for many patients. He plays an essential role in the care of patients suffering from peptic ulcers. So, it is necessary for him to know the common and rare symptoms of Peptic ulcer, and that it is capable of ensuring good monitoring of the therapeutic regimen, to guarantee patients effective and personalized treatment. In addition, the pharmacist must ensure patient education regarding the possible risk factors, drug interactions, effects unwanted, the rate of intake, the dosage.

The pharmacist's intervention must be directed towards: The provision of personalized treatment + advice on hygienic and dietary rules, to ensure better compliance of treatment.

- The insistence on the importance, the deadline, the aim and the modalities of carrying out diagnostic examinations (urea breath test marked, fibroscopy, etc.), before and after treatment.
- The patient's obligation to follow all necessary precautions, in order to to avoid relapses and complications of peptic ulcer.

If ignored, peptic ulcers, which are characterized by open sores in the lining of the stomach, small intestine, or esophagus, can cause severe discomfort and consequences. *Helicobacter pylori* infection, chronic nonsteroidal anti-inflammatory medication (NSAID) use, excessive alcohol intake, smoking, and stress are common causes. Pharmacists are essential in teaching patients how to lower their risk of developing peptic ulcers and successfully treat their symptoms. Pharmacists may empower people to adopt healthy lifestyle habits and make educated decisions regarding medication usage by offering tailored recommendations and guidance. Here are some helpful suggestions that pharmacists can make to support digestive health and help avoid peptic ulcers:

➢ Avoid prolonged use of nonsteroidal anti-inflammatory medicines (NSAIDs) for extended periods of time without a prescription.

- Take NSAIDs for as little time as possible at the lowest dose that works.
- For mild to severe pain, take into account other pain management choices including acetaminophen.
- Take antacids or NSAIDs with food to help shield the lining of your stomach.
- If NSAIDs are required, use gastroprotective medications such as H_2-receptor antagonists or proton pump inhibitors (PPIs).
- To reduce systemic exposure, take into consideration topical NSAID formulations for regional pain treatment.
- Adopt good medication management practices, such as routinely discussing your current medication regimen with your doctor.
- Discuss with your doctor about the advantages and disadvantages of NSAID medication, particularly for those who have a history of ulcers.
- Avoid excessive alcohol intake since it may irritate the lining of the stomach.
- Give up smoking since it can impede healing and raise the risk of peptic ulcers.
- Use stress-reduction methods including yoga, meditation, and deep breathing.
- To promote general digestive health, eat a diet high in fruits, vegetables, whole grains, and lean meats.
- Eat less hot, acidic, or fatty foods as these can aggravate the symptoms of an ulcer.
- Drink lots of water throughout the day to stay hydrated.
- Maintain proper cleanliness to ward against infections that could hasten the formation of ulcers.
- Engage in regular exercise to stay at a healthy weight and lower your chance of developing ulcers linked to obesity.
- To stop acid reflux, avoid reclining or lying down right after eating.
- In case you are having symptoms of reflux at night, raise the head of your

bed.

- A healthy balance of intestinal flora may be maintained by taking probiotics on a regular basis.
- See the doctor on a frequent basis to ensure that your treatment is being monitored and adjusted as necessary.

Conclusions for chapter 3

1. Therapeutic and biological monitoring of the patient must be ensured by the various public health actors, in particular the community pharmacist, who through its personalized therapeutic education of the ulcer patient, allows to avoid recurrences and complications of peptic ulcer. Most people today have become stressed, and therefore predisposed upon the revelation or worsening of the disease. without discounting the influence of diet, alcohol, smoke, and medications that cause ulcers on ulcer training.

2. The analysis of 42 questionnaires of pharmacists and 40 questionnaires of pharmacy visitors shows that the most frequently medications requested for the treatment of peptic and gastric ulcers are proton pump inhibitors, H_2-receptor antagonists, antacids, sucralfate and misoprostol. It was determined the most valuable information when choosing ulcer medications: efficacy (82.5%); safety profile (70%); brand name (55%); cost (65%); monitoring (10%); duration of treatment (17.5%). In this work, we have systematized the data on rational use of antiulcer drugs and presented them in the form of leaflets for pharmacists and pharmacy visitors.

3. Analysis of practical cases emphasizes the significance of customizing treatment strategies based on patient-specific variables such as underlying comorbidities (e.g., diabetes, chronic kidney disease), medication use (e.g., NSAIDs, corticosteroids), lifestyle factors (e.g., alcohol consumption, smoking), and ulcer characteristics (e.g., location, severity). Customized treatment plans are necessary to maximize benefits and reduce side effects.

4. The pharmacist plays an important role in the prevention of PUD, and this, directing the patient to take the necessary measures to prevent complications. The most effective actions mainly concern prevention peptic ulcers and their complications induced by NSAIDs and also the prevention of recurrences. Preventive treatment is essentially based on H_2-blockers and PPIs.

CONCLUSIONS

1. Peptic ulcers represent a significant gastrointestinal health challenge, affecting individuals worldwide and contributing to substantial healthcare costs. While the prevalence of peptic ulcers has declined in recent years, they continue to be a source of morbidity and require ongoing attention from healthcare providers.

2. The analysis of 42 questionnaires of pharmacists and 40 questionnaires of pharmacy visitors shows that the most frequently medications requested for the treatment of peptic and gastric ulcers are proton pump inhibitors, H_2-receptor antagonists, antacids, sucralfate and misoprostol.

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7. Therapeutic and biological monitoring of the patient must be ensured by the various public health actors, in particular the community pharmacist, who through its personalized therapeutic education of the ulcer patient, allows to avoid recurrences and complications of peptic ulcer.

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