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MODERN APPROACHES TO THE TREATMENT OF GASTRIC AND DUODENAL PEPTIC ULCER DISEASE

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Abstract:

Peptic ulcer disease (PUD) of the stomach and duodenum remains a significant global health problem despite substantial advances in gastroenterology over recent decades, largely due to its high prevalence, recurrent nature, and potential for severe complications such as bleeding, perforation, and gastric outlet obstruction. The present scientific article aims to provide a comprehensive and evidence-based analysis of modern therapeutic approaches to gastric and duodenal peptic ulcer disease, with particular emphasis on pathogenetic treatment strategies, eradication of Helicobacter pylori, acid-suppressive therapy, and emerging pharmacological and endoscopic interventions. Contemporary concepts of ulcerogenesis are reviewed, highlighting the central role of acid-peptic aggression, mucosal defense mechanisms, infectious factors, and drug-induced mucosal injury, particularly non-steroidal anti-inflammatory drugs. Special attention is given to the evolution of treatment paradigms from symptom-oriented management to targeted etiological therapy guided by international consensus documents and clinical practice guidelines. The article synthesizes current data from randomized controlled trials, meta-analyses, and authoritative international recommendations, including the Maastricht VI/Florence Consensus Report, to evaluate the efficacy and safety of proton pump inhibitors, potassium-competitive acid blockers, antibiotic combinations, and adjunctive mucosal protective agents. In addition, modern diagnostic and therapeutic algorithms, challenges related to antibiotic resistance, and prospects for personalized treatment approaches are critically discussed. This work is intended to serve as a scientific and practical resource for clinicians, researchers, and healthcare professionals involved in the management of peptic ulcer disease in contemporary clinical practice.

Keywords:

Peptic ulcer disease; gastric ulcer; duodenal ulcer; Helicobacter pylori; proton pump inhibitors; potassium-competitive acid blockers; eradication therapy; evidence-based medicine; modern treatment.

Introduction

Peptic ulcer disease of the stomach and duodenum represents one of the most extensively studied yet persistently relevant conditions in clinical gastroenterology, owing to its multifactorial etiology, chronic recurrent course, and substantial burden on healthcare systems

worldwide, and despite a noticeable decline in incidence in some regions, it continues to affect millions of patients annually, particularly in developing and transitional healthcare settings where diagnostic and therapeutic resources may be limited. Traditionally regarded as a consequence of stress, dietary factors, and excessive gastric acid secretion, the understanding of peptic ulcer disease has undergone a profound paradigm shift following the discovery of *Helicobacter pylori*, which fundamentally altered concepts of pathogenesis and treatment by establishing an infectious basis for the majority of duodenal and a significant proportion of gastric ulcers, thereby transforming ulcer disease from a chronic relapsing condition into a potentially curable entity. Nevertheless, the clinical reality remains complex, as not all ulcers are associated with *H. pylori* infection, and the widespread use of non-steroidal anti-inflammatory drugs, antiplatelet agents, and anticoagulants has emerged as a dominant etiological factor, particularly in elderly and comorbid patient populations. Moreover, the increasing prevalence of antibiotic resistance, variability in patient adherence, and heterogeneity in host-pathogen interactions have introduced new challenges that necessitate continuous refinement of therapeutic strategies. Modern management of peptic ulcer disease therefore requires an integrated approach that combines accurate etiological diagnosis, rational selection of pharmacological agents, adherence to evidence-based guidelines, and individualized risk assessment to prevent complications and recurrence. In this context, the present article seeks to systematically examine contemporary methods for the treatment of gastric and duodenal peptic ulcer disease, focusing on advances in acid suppression, eradication regimens, adjunctive therapies, and emerging modalities, while critically appraising their clinical efficacy, safety profiles, and applicability in real-world practice. By consolidating current scientific evidence and clinical recommendations, this work aims to contribute to the ongoing optimization of peptic ulcer disease management and to provide a solid foundation for further research and clinical decision-making.

Materials and Methods

The present scientific work was conducted as a comprehensive narrative and analytical review of contemporary therapeutic strategies for gastric and duodenal peptic ulcer disease, structured in accordance with the IMRAD format and aligned with the methodological and ethical requirements of academic medical research accepted by national and international scientific councils. The methodological framework of the study was designed to ensure a systematic, transparent, and reproducible synthesis of current evidence concerning the modern management of peptic ulcer disease, with particular emphasis on pharmacological, endoscopic, and etiologically targeted treatment modalities. A structured literature search was performed using internationally recognized biomedical databases, including PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library, covering publications from January 2000 to December 2024, thereby capturing both foundational studies and the most recent advances in the field. Search terms and medical subject headings (MeSH) were selected to reflect key aspects of peptic ulcer disease and its treatment, including but not limited to “peptic ulcer disease,” “gastric ulcer,” “duodenal ulcer,” “Helicobacter pylori,” “eradication therapy,”

"proton pump inhibitors," "potassium-competitive acid blockers," "antibiotic resistance," and "evidence-based treatment," with Boolean operators applied to optimize sensitivity and specificity of retrieval. Inclusion criteria encompassed randomized controlled trials, systematic reviews, meta-analyses, clinical guidelines, and consensus statements published in English that addressed therapeutic interventions for adult patients with confirmed gastric or duodenal ulcers, while studies focusing exclusively on pediatric populations, animal models, or non-ulcer dyspepsia were excluded to maintain clinical relevance and methodological consistency.

In addition to database searching, manual screening of reference lists from key publications and international guidelines was undertaken to identify seminal works and consensus documents that may not have been captured through electronic searches alone, including successive Maastricht Consensus Reports, recommendations of the European Society of Gastrointestinal Endoscopy, and guidelines issued by leading gastroenterological associations. The methodological quality of selected studies was assessed qualitatively based on study design, sample size, clarity of diagnostic criteria, appropriateness of statistical analysis, and relevance of clinical endpoints, with particular attention paid to outcomes such as ulcer healing rates, eradication success, recurrence prevention, complication reduction, and adverse event profiles. Data extraction was performed in a structured manner, focusing on therapeutic regimens, duration of treatment, comparative efficacy, resistance patterns, and patient-related factors influencing treatment outcomes. Given the heterogeneity of study designs and therapeutic approaches, a formal quantitative meta-analysis was not pursued; instead, a critical narrative synthesis was employed to integrate findings and highlight convergent evidence, discrepancies, and areas of ongoing debate within the literature.

From a clinical-methodological perspective, the article adopts a pathogenetic approach to treatment evaluation, categorizing therapeutic interventions according to etiological factors, including *H. pylori*-associated ulcers, NSAID-induced ulcers, and idiopathic ulcers, and analyzing treatment strategies within each category. Acid-suppressive therapies were examined in detail, with comparative analysis of proton pump inhibitors and newer potassium-competitive acid blockers, considering pharmacodynamics, pharmacokinetics, dosing regimens, and clinical outcomes. Eradication therapies were evaluated in the context of evolving antibiotic resistance, with emphasis on first-line, second-line, and rescue regimens recommended by contemporary guidelines. Adjunctive therapies, such as mucosal protective agents, probiotics, and lifestyle modifications, were reviewed as supportive measures within integrated treatment algorithms. Ethical considerations were addressed by relying exclusively on previously published data, thereby obviating the need for institutional review board approval or informed consent, while ensuring adherence to principles of academic integrity and responsible scientific reporting. Through this methodological approach, the study aims to provide a rigorous and balanced overview of modern therapeutic options for gastric and duodenal peptic ulcer disease, grounded in current evidence and applicable to real-world clinical practice.

Results

The analysis of contemporary scientific literature demonstrates that modern therapeutic approaches to gastric and duodenal peptic ulcer disease have achieved substantially higher rates of ulcer healing, recurrence prevention, and complication reduction compared to historical treatment strategies, primarily as a result of effective acid suppression and targeted eradication of *Helicobacter pylori*. Across multiple randomized controlled trials and large-scale meta-analyses, proton pump inhibitor (PPI)-based therapy remains the cornerstone of ulcer treatment, with healing rates exceeding 85–95% for uncomplicated duodenal ulcers and 80–90% for gastric ulcers after 4–8 weeks of standard-dose therapy, depending on ulcer size, location, and patient adherence. Comparative studies indicate that newer potassium-competitive acid blockers (PCABs), particularly vonoprazan, provide more rapid and sustained suppression of gastric acid secretion than conventional PPIs, resulting in higher intragastric pH control and improved early ulcer healing, especially in patients with severe disease, nocturnal acid breakthrough, or CYP2C19 polymorphisms affecting PPI metabolism. In *H. pylori*-positive patients, eradication therapy was consistently associated with a significant reduction in ulcer recurrence, with eradication success rates ranging from 70% to over 90% depending on the regimen used, local antibiotic resistance patterns, and treatment duration. Standard triple therapy showed declining effectiveness in many regions due to increasing resistance to clarithromycin and metronidazole, whereas bismuth-containing quadruple therapy and non-bismuth concomitant regimens demonstrated superior eradication rates, frequently exceeding 85% in intention-to-treat analyses. Studies evaluating vonoprazan-based eradication regimens reported particularly high success rates, often surpassing those of PPI-based protocols, highlighting the potential of PCABs to overcome limitations associated with acid instability of antibiotics and suboptimal intragastric pH.

In patients with NSAID-induced peptic ulcers, withdrawal of the offending agent combined with acid-suppressive therapy resulted in ulcer healing rates comparable to those observed in *H. pylori*-associated disease, while continued NSAID use necessitated prolonged PPI therapy and was associated with higher rates of delayed healing and recurrence. Preventive strategies, including co-prescription of PPIs or use of selective COX-2 inhibitors, were shown to significantly reduce the incidence of NSAID-related ulcer complications, particularly upper gastrointestinal bleeding, in high-risk populations. The addition of mucosal protective agents, such as rebamipide or sucralfate, provided modest benefits in symptom relief and mucosal repair, although their impact on long-term outcomes was less pronounced when effective acid suppression was already in place. Endoscopic interventions, including hemostatic techniques for bleeding ulcers, demonstrated high immediate success rates exceeding 90%, with rebleeding rates substantially reduced when combined with high-dose intravenous or oral acid suppression. Collectively, these results underscore that modern, evidence-based treatment strategies—particularly those incorporating potent acid suppression, rational eradication therapy, and etiologically driven management—have transformed peptic ulcer disease into a largely controllable and, in many cases, curable condition, while also revealing persistent

challenges related to antibiotic resistance, patient heterogeneity, and the need for individualized therapeutic decision-making.

Discussion

The findings synthesized in this review confirm that the modern management of gastric and duodenal peptic ulcer disease represents one of the most successful examples of translational medicine, in which advances in pathophysiological understanding have been rapidly integrated into clinical practice, resulting in substantial improvements in patient outcomes. The transition from purely symptomatic treatment to etiologically oriented therapy, particularly following the recognition of *Helicobacter pylori* as a key causal factor, has fundamentally altered the natural history of peptic ulcer disease, transforming it from a chronic relapsing condition into a largely curable disorder in the majority of affected patients. The consistently high ulcer healing rates observed with contemporary acid-suppressive therapies underscore the central role of gastric acid in ulcerogenesis, while also highlighting the importance of sustained intragastric pH control for mucosal repair and stabilization of the ulcer base. Proton pump inhibitors, despite being in clinical use for several decades, continue to demonstrate robust efficacy and safety profiles, yet their limitations—such as delayed onset of action, variable metabolism, and incomplete nocturnal acid suppression—have become increasingly evident in specific patient populations.

In this context, the emergence of potassium-competitive acid blockers, particularly vonoprazan, represents a significant pharmacological advancement, offering more rapid, potent, and consistent acid suppression independent of meal timing and genetic polymorphisms affecting cytochrome P450 enzymes. The superior intragastric pH control achieved with PCABs provides a plausible mechanistic explanation for the improved early healing rates and enhanced effectiveness of *H. pylori* eradication regimens reported in recent studies. Nevertheless, the long-term safety profile of these agents, especially with prolonged use, remains an area requiring ongoing surveillance and post-marketing research. The discussion of eradication therapy outcomes further illustrates the dynamic nature of peptic ulcer disease management, as increasing antibiotic resistance has eroded the effectiveness of once-standard regimens and necessitated continual adaptation of treatment algorithms. The declining efficacy of clarithromycin-based triple therapy, documented across multiple geographic regions, reinforces the importance of local resistance data, antibiotic stewardship, and adherence to updated international guidelines when selecting eradication protocols.

The management of NSAID-induced and idiopathic ulcers presents additional clinical challenges, as these forms of peptic ulcer disease are not amenable to eradication therapy and often occur in patients with significant comorbidities requiring ongoing antithrombotic or anti-inflammatory treatment. The evidence reviewed indicates that preventive strategies, including risk stratification, co-prescription of acid suppressants, and judicious selection of analgesic and anti-inflammatory agents, are essential components of modern ulcer management, particularly in aging populations. Endoscopic and interventional advances have further improved outcomes in complicated ulcer disease, with high rates of hemostatic success and reduced mortality when

combined with optimized pharmacotherapy. Taken together, these considerations emphasize that while modern therapeutic tools are highly effective, optimal outcomes depend on an individualized, multifactorial approach that integrates etiological diagnosis, patient-specific risk factors, and evolving evidence. The persistence of challenges such as antibiotic resistance, treatment non-adherence, and healthcare disparities underscores the need for continued research, education, and refinement of clinical strategies in the management of peptic ulcer disease.

Conclusion

Modern approaches to the treatment of gastric and duodenal peptic ulcer disease have markedly improved the prognosis, quality of life, and long-term outcomes of affected patients, reflecting a successful convergence of pathophysiological insight, pharmacological innovation, and evidence-based clinical practice. Effective acid suppression, particularly through the use of proton pump inhibitors and emerging potassium-competitive acid blockers, remains the cornerstone of ulcer healing, while targeted eradication of *Helicobacter pylori* has become the definitive therapeutic strategy for preventing recurrence in infected individuals. Contemporary treatment algorithms emphasize etiological differentiation, rational selection of eradication regimens based on resistance patterns, and the integration of preventive measures for drug-induced ulcers, thereby enabling a more personalized and effective approach to care. Despite these advances, peptic ulcer disease continues to pose clinical challenges related to antibiotic resistance, comorbid conditions, and long-term medication use, highlighting the necessity for ongoing research and guideline updates. In conclusion, the continued refinement of therapeutic strategies, informed by high-quality clinical evidence and tailored to individual patient needs, is essential for sustaining and further improving the successful management of gastric and duodenal peptic ulcer disease in modern clinical practice.

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