

# **Overview and comparison of the proton pump inhibitors for the treatment of acid-related disorders**

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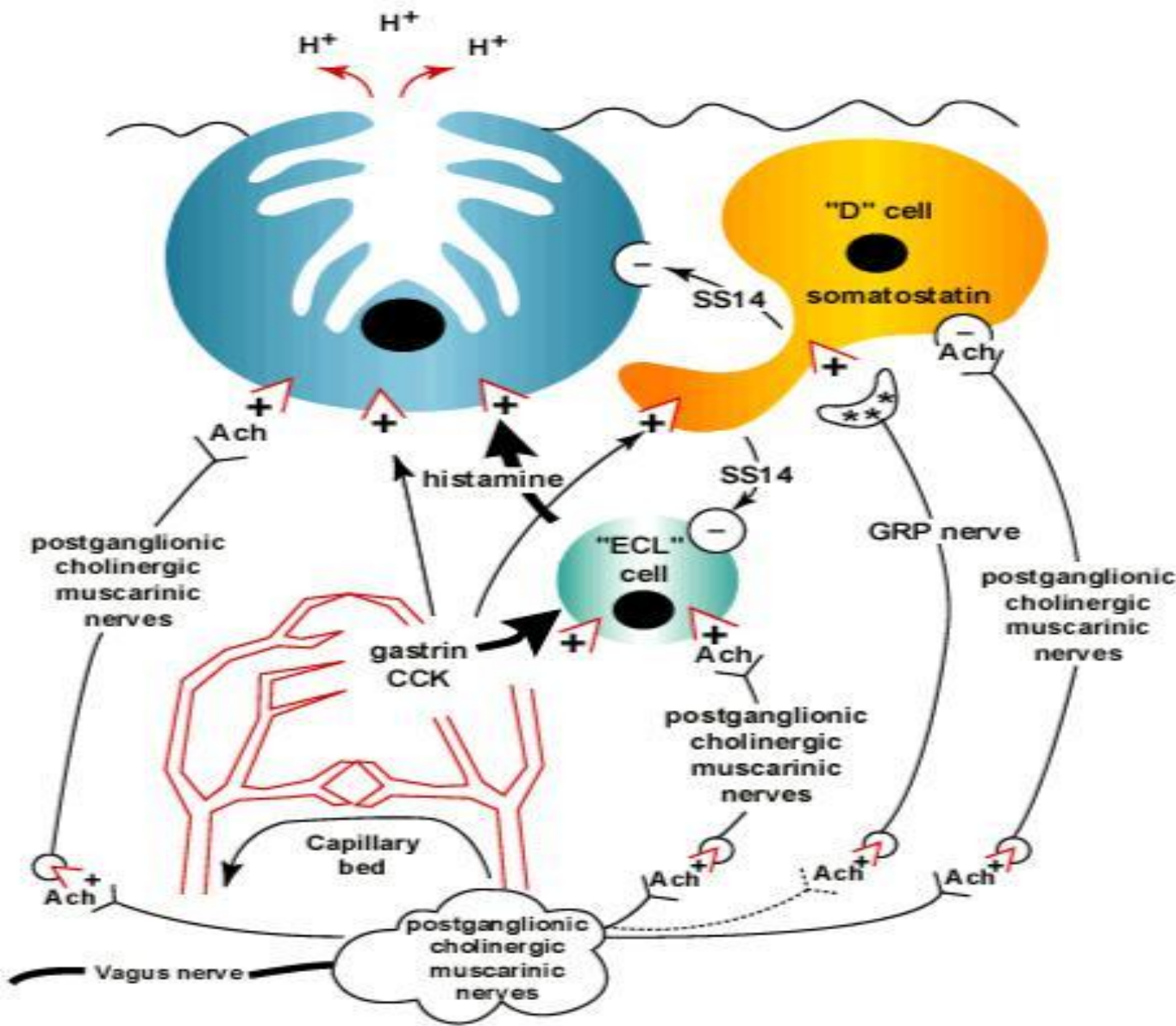
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# INTRODUCTION

- The introduction of proton pump inhibitors (PPIs) in the late 1980s optimized the medical treatment of acid-related disorders

# PHYSIOLOGY OF ACID SECRETION

- Acetylcholine is the chief neurocrine transmitter
- Histamine is the primary paracrine transmitter that binds to H<sub>2</sub>-specific receptors on the parietal cell basolateral membrane
- Gastrin stimulates the generation of hydrogen ions both directly and indirectly



# PHARMACOLOGY OF THE PROTON PUMP INHIBITORS

- PPIs, accumulate specifically and selectively in the secretory canaliculus, the highly acid space of the parietal cell. Within that space, PPIs undergo an acid catalyzed conversion to a reactive species, the thiophilic sulfenamide, which are permanent cations.

- conversion varies among the compounds and is inversely proportional to the pKa of the benzimidazole : rabeprazole > omeprazole/esomeprazole = lansoprazole/dexlansoprazole > pantoprazole

- The PPIs are the most potent inhibitors of gastric acid secretion available
- most effective when the parietal cell is stimulated to secrete acid postprandially
- PPIs should be administered before the first meal of the day
- Once-daily PPI dosing inhibits maximal acid output by about 66 percent after five days

# TREATMENT OF ACID-RELATED DISORDERS

PPIs are effective for treatment of all acid-related disorders

- ❖ Peptic ulcer disease —

PPIs heal gastroduodenal ulcers more rapidly than H<sub>2</sub>-receptor antagonists

- ❖ Eradication of *Helicobacter pylori*

— The role of PPIs in treatment of *H. pylori* is discussed separately



- ❖ Treatment and prevention of gastroduodenal ulcers associated with NSAIDs

— PPIs also appear to be as **effective** or more effective than misoprostol. PPIs are also effective for primary prevention of NSAID-associated ulcers.

- ❖ Zollinger-Ellison syndrome

- ❖ Treatment of gastroesophageal reflux disease — relieve symptoms and heal esophagitis in approximately 85 to 90 percent of patients

## ❖ Maintenance therapy

PPIs superior in maintaining remission and effective prophylactic doses are generally the same as those required for initial healing

## ❖ Complications of GERD

- Esophageal strictures
- Barrett's esophagus
- Extraesophageal symptoms

# Long-term safety

long-term safety of the PPIs include:

- prolonged hypergastrinemia
- gastric atrophy
- chronic hypochlorhydria
- associations with hip fractures
- community-acquired pneumonia

# Intravenous formulations

- Pantoprazole, lansoprazole, omeprazole, and esomeprazole are the only PPIs available as an intravenous formulation
- they are more frequently used in management of patients with bleeding peptic ulcers and for the prevention of stress-related mucosal damage.

# SUMMARY AND RECOMMENDATIONS

- The PPIs are the most potent inhibitors of gastric acid secretion available.
- PPIs are effective for treatment of all acid-related disorders including peptic ulcer disease, gastroesophageal reflux disease and Zollinger-Ellison Syndrome.
- While some differences have been reported, the magnitude of differences has been small and of uncertain clinical importance.