

# Long term use of Proton Pump Inhibitors

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# Proton pump inhibitors

- (PPIs) have been on the market since the late 1980s and have replaced the histamine<sub>2</sub> receptor-antagonists (H<sub>2</sub>RAs)
- **In general, the safety of this class of drugs has been excellent**

# Proton pump inhibitors currently available

- 1-Omeprazole
- 2-Pantoprazol
- 3-Lansoprazole
- 4-Rabeprazole
- 5-Esomeprazol
- 6-Dexlansoprazole
- 7-Immediate-release omeprazole  
plus sodium bicarbonate

# Mode of action

- They block the terminal step in acid production .
- Irreversibly inhibit the function of the hydrogen potassium adenosine triphosphatase of parietal cell membranes.

# Indications

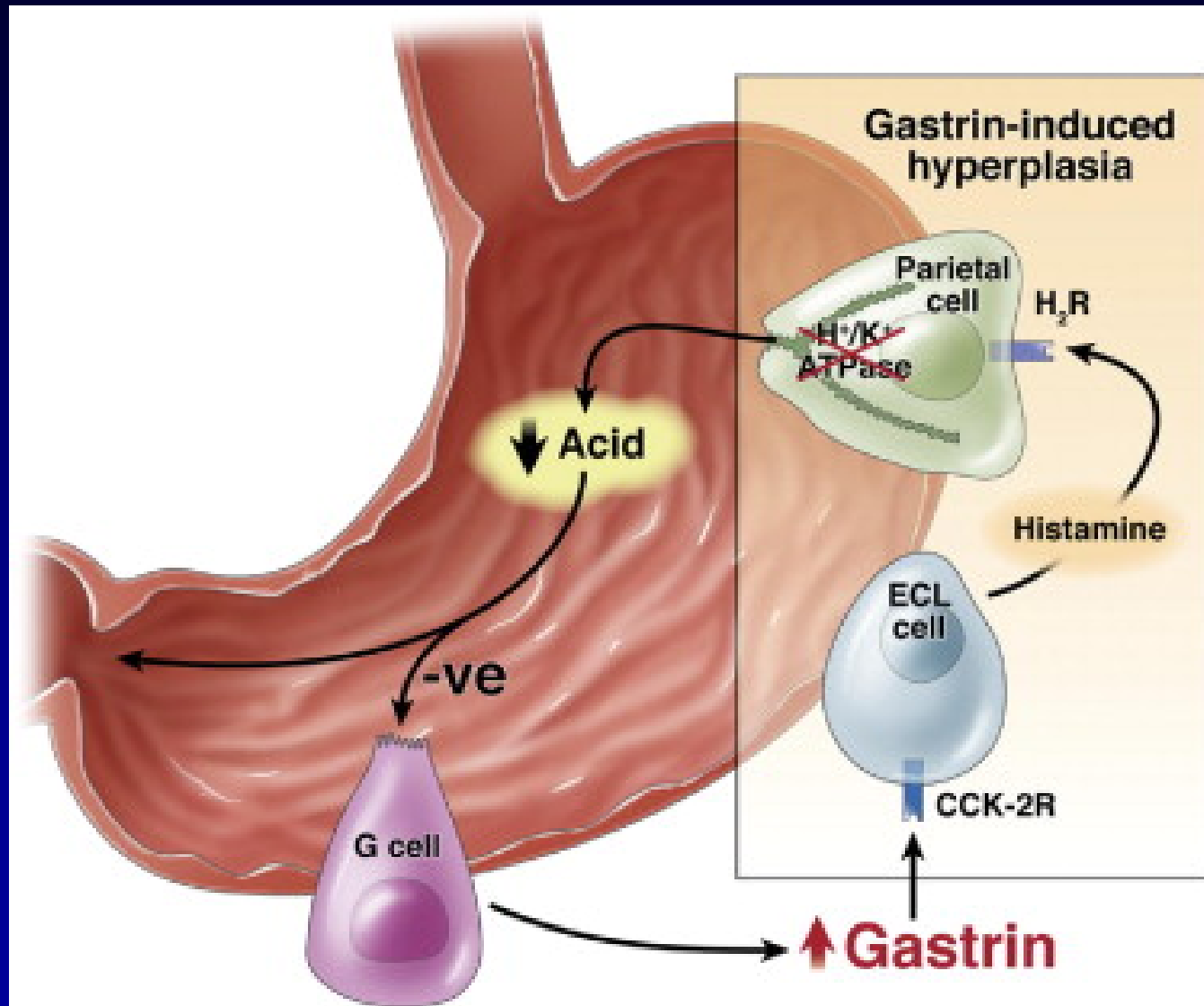
- Heartburn:
- GERD:
- Erosive esophagitis:
- Duodenal ulcer:
- Gastric ulcer:
- Helicobacter pylori Infection:
- NSAID-induced gastric ulcer:
- Zollinger-Ellison syndrome:

# Adverse Consequences of PPIs

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- Rebound hypersecretion of Acid
- Osteoporosis and fractures
- Enteric infections
  - Food-borne bacterial infections
  - *Cl. Difficile*
  - Spontaneous Bacterial Peritonitis ( SBP)
- Pneumonia.
- Interactions with clopidogrel.
- Interstitial nephritis.
- Iron deficiency anaemia.

# Gastrin Exerts a Powerful Trophic Effect on Enterochromaffin-like cells and Parietal cells





# Rebound Hypersecretion of Acid on PPI's

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- The greater the acid suppression, the greater the rebound.
- Once you start PPI's for GERD be prepared to use as long-term therapy.
- Discontinuation of PPI or switching to H2RA may be difficult

# PPI's and Osteoporosis

In the last several years, concern has been raised that PPIs could induce

Calcium malabsorption

Osteoporosis and

Hip fracture,

which can have devastating effects, including death

# PPIs AND ENTERIC INFECTIONS

- Profound acid suppression -----
  - Changes in the mix of dominant flora
  - Increase in total bacterial of all genera.
- Patients using PPIs who develop diarrhoea should be evaluated for ----
  - Cl. difficile* infection
  - Small bowel bacterial overgrowth

# PPI and SBP

Several reports suggest --

- ❖ There is a relationship between PPI use and the development of SBP.
- ❖ More in hospitalized cirrhotic patients with ascites .

# PPI and SBP

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- 2631 cirrhotics with ascites followed from 2002-2007
- PPI use strongly associated with SBP and hepatorenal syndrome
  - SBP on PPI 23.7%      No PPI 5.7%
  - HSR on PPI 15.3%      No PPI 1.9%
- Number needed to treat for harm from PPI use: 5.5 for 1 episode of SBP

# PPI and the Risk of Pneumonia

- Pneumonia is about 4.5 times higher in people exposed to acid-suppressive drugs (both PPIs and histamine-2-receptor antagonists)
- Patients who developed pneumonia also had higher significant comorbid conditions, including heart failure and chronic obstructive pulmonary disease.

# FDA alert: Avoid using PPI with clopidogrel

**November 17, 2009, the US (FDA) issued an alert.**

Use of omeprazole or , esomeprazole with clopidogrel should be avoided.

Causes -

Increased rates of

- Recurrent hospitalization for ACS
- Revascularization procedures and
- Death compared with patients taking clopidogrel without a PPI

# PPI and Iron deficiency anemia

- Both hydrochloric acid and ascorbic acid involved conversion of ferric to ferrous iron, which hampered by PPI.
- Iron absorption significantly suboptimal during PPI therapy.
- More in *H.Pylori* gastritis.
- More common in elderly and poorly nourished person



# PPI and Interstitial nephritis

Several case reports have implicated

- PPIs causes acute interstitial nephritis.
- Initial symptoms are nonspecific and included nausea, malaise, and fever,
- Despite the rarity of the syndrome, need a high level of clinical suspicion to detect acute interstitial nephritis for early in its course, especially soon after the PPI use.

# Proton-Pump Inhibitors and gastric Fundic-Gland Polyps

- Long-term use of proton-pump inhibitors (PPIs) increase risk for benign fundic-gland polyps.
- Fundic-gland polyps are round, slightly reddish polyps in the stomach.
- They do not become malignant.

# FUNDAL GASTRIC POLYPS



# Magnitude and Economic Impact of Inappropriate Use of long term PPI

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Several trials have demonstrated that

In general medicine wards about 71% of patients receiving some sort of acid- suppressive therapy (AST) without an appropriate indication.

**Should PPI's be First-Line  
Treatment for Newly-  
Diagnosed Dyspepsia or  
GERD?**

- **No!!**

# Which PPI is the best ?

There are no strong data .

FDA did not issue the same warning for all PPIs other than omeprazole and esomeprazole .

# Recommendation for PPI

- ❖ When treating acid-like dyspepsia or GERD, start with H2-receptor antagonist as initial therapy.
- ❖ If H2-RA's fail, use the lowest dose PPI once a day.
- ❖ If nocturnal symptoms predominate, try PPI before dinner, or add an evening H2RA before bid dosing of PPI.
- ❖ Never use Esomeprazol 40 as initial therapy.

# Recommendation

- ❖ Try different PPI's before going to high-dose PPI.
- ❖ Once symptoms have been controlled for several months, try to back down to lowest effective PPI dose periodically



# Conclusions

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- PPI are effective in management of acute acid peptic bleeding and stress ulcer prophylaxis but carry significant infectious risks.
- Up to 71% of acid suppression therapy may be inappropriate in hospital inpatients.
- Questions the indication for PPI's on a regular basis

THANK YOU

FOR YOUR ATTENTION