GERD: An Update

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DDRI, TUMS, IAGH meeting
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Shariati Hospital, Tehran
GERD is a common disease

- Various studies have shown this
- Up to 40% in western reports
- Several Iranian studies:
  - Up to 18% (If minor symptoms included up to 27%)
- Many never refer
- Prevalence has increased significantly
- Why? No one clear answer, maybe:
  - Life style
  - Better hygiene \( \square \) less HP
  - Nitrates
GERD: Diagnosis

• No “Gold standard” for Dx
• Mostly relied on symptoms: HB/AR (also dysphagia, chest pain and some minors)
  • Sensitivity of HB/AR: 30-75%
  • Specificity of HB/AR: 62-96%
• The point is that w/o having a “gold standard” these figures are also shaky
• Endoscopy: Distal esophageal erosions seen in 30-50% of cases
• pH-metry, Multi-channel Intraluminal Impedance (MII): Left for difficult cases, refractory cases, and surgery candidates
The overall definition of GERD
Vakil N, et al. AJG 2006;101:1900–1920

GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications

Esophageal Syndromes
- Symptomatic Syndromes
  1. Typical Reflux Syndrome
  2. Reflux Chest Pain Syndrome
- Syndromes with Esophageal injury
  1. Reflux Esophagitis
  2. Reflux Stricture
  3. Barrett's Esophagus
  4. Esophageal Adenocarcinoma

Extraesophageal Syndromes
- Established Associations
  1. Reflux Cough Syndrome
  2. Reflux Laryngitis Syndrome
  3. Reflux Asthma Syndrome
  4. Reflux Dental Erosion Syndrome
- Proposed Associations
  1. Pharyngitis
  2. Sinusitis
  3. Idiopathic Pulmonary Fibrosis
  4. Recurrent Otitis Media
GERD: Some definitions
(Rome III criteria)

- Erosive GERD: Definite mucosal breaks in the distal esophagus
  - May have normal or abnormal acid exposure
- NERD: typical symptoms, Normal endoscopy, excessive acid exposure on MII/pH
- Hypersensitive esophagus: Typical symptoms, reflux on MII, normal acid exposure
- Functional heartburn: Typical symptoms, No reflux on MII, normal acid exposure
GERD: Pathophysiology

• Many reflux episodes are not associated with symptoms
• Many symptom episodes are not associated with GER
• Pathophysiology is largely unknown
Pathophysiology: Mechanisms of symptom perception
Bredenoord AJ, AJG Jan 2012
Symptom perception in GERD

- NERD pts
  - fewer acid reflux episodes and less esophageal acid exposure than patients with reflux esophagitis but,
  - perceive less intense stimuli because of greater esophageal sensitivity

- Factors contributing to greater esophageal sensitivity:
  - impaired mucosal barrier function,
  - peripherally mediated esophageal sensitivity (enhanced esophageal receptor signaling), and
  - centrally mediated esophageal sensitivity (physiological stressors, sensitization of spinal sensory neurons)
Other contributing factors to symptom perception

- Reflux characteristics other than acidity, e.g.
  - the presence of bile, pepsin, liquid, or gas in reflux, and
  - the proximal extent or volume of reflux
### The PARI database

Mean Age ± SD = 39.3 ± 14.6

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Pathophysiology: Mechanisms of symptom perception
Bredenoord AJ, AJG Jan 2012

- Esophagus
- Reflux extent (or volume?)
- Reflux acidity
- Reflux composition
  - Liquid
  - Gas
  - Bile
  - Pepsin?
- Lower esophageal sphincter
- Stomach

- Esophageal mucosa
  - Basal membrane
  - Pain receptor
  - Epithelial cell
  - Tight junction

- Central sensitization (brain)
  - Physiological stress?

- Central sensitization (spinal neurons)
  - Previous exposure to acid?

- Mechanical activation of pain receptors
  - Reflux-volume-induced esophageal distension

- Chemical activation of pain receptors
  - Acid
  - Bile
  - Pepsin?

- Activated pain receptor

- Impaired mucosal barrier function
  - Previous exposure to acid, pepsin (or bile?)

- Peripheral sensitization
  - Upregulation of pain receptors (acid-induced?)
  - Enhanced signalling (genetic factors?)
Other possible pathophysiologic mechanisms

- Animal studies:
  - Reflux induced in mice, significant esophagitis develops only when fed a diet containing nitrates
  - Dilated intercellular space (DIS), is induced by nitrates and acid, but not by acid alone

- Ecologic studies:
  - linked high nitrate content of drinking water to increased prevalence of acid regurgitation
    Nasseri-Moghaddam et al, AIM 2011

- Oral nitrate reductase activity is higher in pts w erosive GERD than normal controls
  Nasseri-Moghaddam et al, DDS 2011
GERD: Investigations

- History
  - Significant number of symptoms considered as atypical e.g. nausea, eructaion, chest pain, etc
  - Significant overlap w IBS
  - Significant overlap w PUD

- Endoscopy
- MII-pH
GERD: Treatment

- Life style modification
  - Diet
  - Stress
  - Habits
- Medications:
  - H2 blockers
  - PPIs
  - Newer drugs
Facts about PPIs as mainstay of Rx

• Are PPIs safe over long term?
  • Yes, no malignancy reported in humans up to 15 years of use (uncontrolled studies)
  • Recent SR of controlled trials: no malignancy up to 7 years
  • Osteoporosis: very low risk,
    • older people,
    • high dose
    • Long term
• Infections
  • Maybe in older people, not a big burden
• Renal problems:
  • Hypomagnesemia/renal injury
  • Interstitial nephritis
Facts about PPIs as mainstay of Rx

• Are PPIs safe during pregnancy?
  • Yes, all even in the first trimester
  • Omeprazole may be better in the pre-conception period
Facts about PPIs as mainstay of Rx

• Several PPIs available: Omeprazole, Pantoprazole, Lansoprazole, Rabeprazole, Esomeprazole and a couple of long-acting variants
• In most instances (80%) all have equal efficacy and clinical profile
  • Therefore the cheapest will do
• In some subgroups one may be better
  • Some refractory cases are CYP 2C19 related PPIs not metabolized by this pathway (e.g. Rabeprazole/Pariet) preferrable
  • Sometimes switching to another PPI may help (not CYP 2C19 related)
  • Acute cases need rapid onset of action (Rabeprazole/Pariet)
  • Pts on multiple drugs may be better off on Pantoprazole or Rabeprazole (almost no interaction with other drugs)
  • Drug resistant HP: Rabeprazole may add a small benefit
• Overall different PPIs have similar efficacy and safety profile
Facts about PPIs as mainstay of Rx

• Do PPIs decrease the anti-platelet effects of Clopidogrel?
  • In vitro studies: Yes
  • In vivo studies: No consistent effect, most probably no significant clinical interaction

• Do we need to select a special PPI to minimize this possible effect?
  • No consistent data, most probably NO
  • Some propose PPIs w less interaction (e.g. Pantoprazole, Rabeprazole/Pariet)
How should PPIs be administered?

- Step up vs step down therapy
- Single vs double dose administration
- Before meals
- Continue long term
- Taper before D/C
- Maintain at the lowest dose
Refractory GERD

• GERD pts unresponsive to PPIs after 4-8 weeks
• Differential diagnoses:
  • True refractory
  • Achalasia
  • Eosinophilic esophagitis
  • Malignancy
  • Lichen Planus and related disorders
  • Hypersensitive esophagus
  • Functional heartburn
Refractory GERD

- Review pt hx (attention to symptoms, concomitant IBS)
- UGIE + 4 quadrant upper and lower esophageal bx
- Ba swallow
- Manometry (high resolution)
- pH-metry/MII
Refractory GERD

• Abnormal acid-reflux causes symptoms
• Normal acid reflux causes symptoms (hypersensitive esophagus)
• Non-acid reflux causes symptoms

Esophageal pH/Impedance monitoring
• Non-GERD esophageal disorders cause symptoms

UGIE/esophageal Manometry/Ba swallo
• Extra-esophageal disorders cause symptoms

Test for heart/biliary/other disorders
• Symptoms are functional
Thank you for your attention