

Reflux Esophagitis

Approach for persistent symptoms

Ghassan Hemadeh, MD

March 13, 2010

The learning objectives

Participants should be able to:

- Define refractory GERD
- Describe the appropriate first steps in management of patients with persistent reflux symptoms
- Identify the most probable diagnosis in these patients
- Identify the appropriate investigations following normal endoscopy.
- Know the limitations of different diagnostic investigations.
- Identify the most suitable treatment for patients with refractory GERD

Introduction I

- ❑ GERD prevalence has increased dramatically over the last decades mostly in the western world, affecting up to 20% of adult population ⁽¹⁾
- ❑ Classic symptoms of GERD are heart burn and acid regurgitations, but they are predictive only in 70% of GERD patients ⁽²⁾
- ❑ Most symptomatic patients do not develop ERD ⁽³⁾
- ❑ Study from Sweden shows 36.5% of symptoms free individuals undergoing endoscopies had reflux esophagitis ⁽⁴⁾

(1) Vakil N. Amj Gastroenterol 2006, 101: 1900-1920

(2) Klauser AG: Lancet 1990, 335:205-208

(3) Labenz J: Amj Gastroenterol 2006, 101:2457-2462

(4) Ronakainen J: Scand J Gastroenterol 2005, 40:275-285

Introduction II

- Medical therapy of GERD has improved since the introduction of PPI in the late 1980s
- Current practice is to give empirical treatment and reserve endoscopy for patients with alarming symptoms
- Problems with withholding early gastroscopy
 1. Missing a significant lesion
 2. Diagnosing patients as having NERD or FD while they have healed ERD on treatment

Introduction III

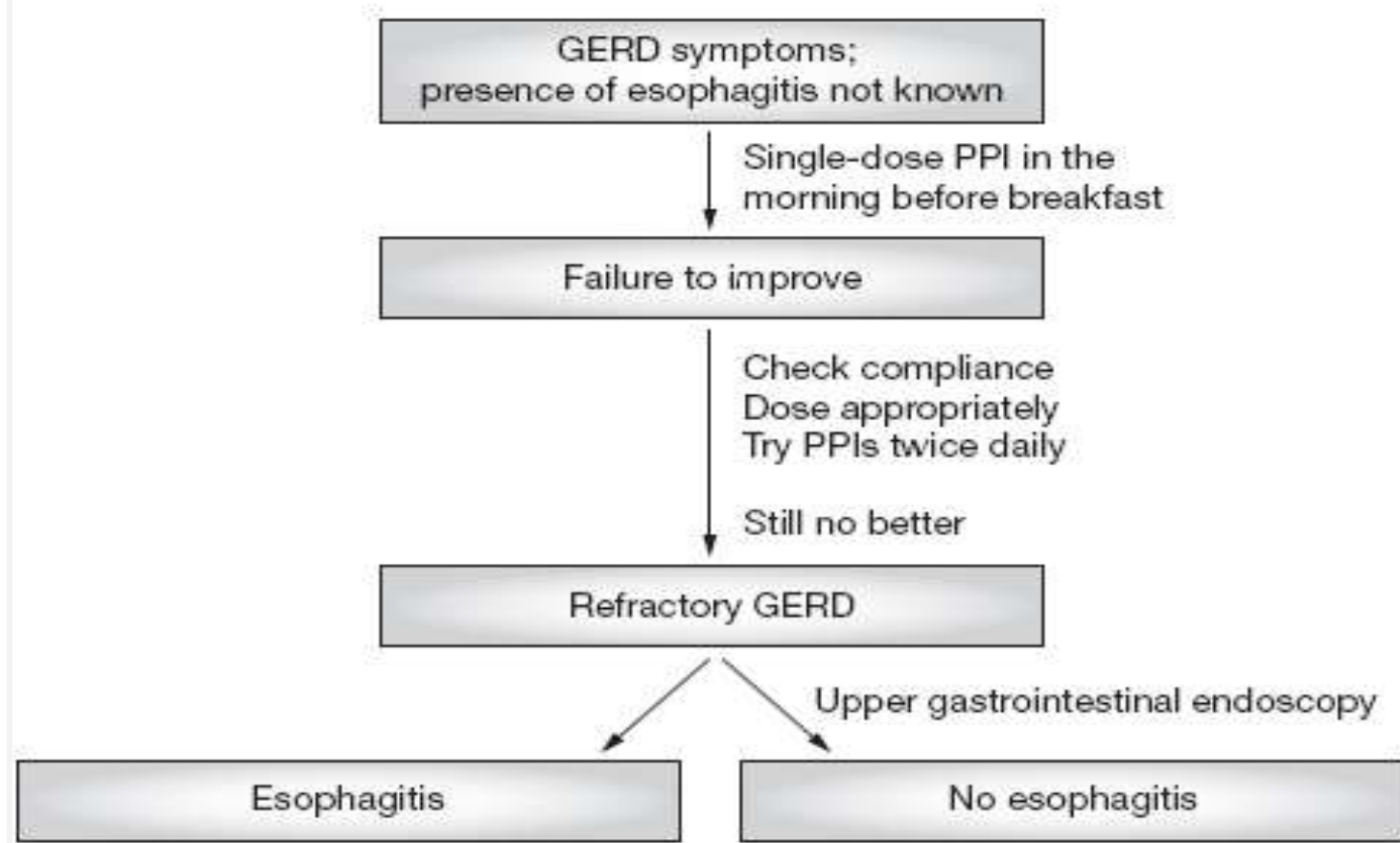
- 25%-42% of patients with GERD fails to respond to 4-8 weeks trial with PPI⁽¹⁾
- Patients who failed to improve maybe non compliant or taking their PPI inappropriately. ⁽²⁾
- Difficult to manage cases of GERD needs a practical approach for management.

1. Bardham ICD(1995). A liment pharmacol than 9:15-2.5
2. Barrison A Fetal.(2006) Clin Gastroenterol Hepatol 4:50-60

Refractory GERD

Patients who fails to respond to twice daily dosing of PPI before breakfast and dinner for 4-8 weeks fall into the category of **refractory GERD**.

Practical Approach to Manage Patients with Persistent GERD Symptoms?



Refractory GERD Upper Endoscopy

Esophagitis

No Esophagitis

Pill esophagitis

Possible diagnosis

Autoimmune skin disease

Nocturnal gastric acid break through

Z-E syndrome

Non acid GER

Genotype (PPI meta)

Missed

Eosinophilic esophagitis

Functional heart burn

Wrong diagnosis

*Achalasia

*Gastroparesis

Practical Approach to Manage Patients with Persistent GERD Symptoms?

Step I

- Increase the dose of PPI
- Twice daily high dose (25% response)⁽¹⁾
- Lansoprazole 30mg Bid compared to eso-omeprazole 40mg single dose.
- Accurate timing 1 hour before meals

(1) Martinez SD *et al.* (2003) *Non-erosive reflux disease (NERD), acid reflux and symptom patterns. Aliment Pharmacol Ther* 17: 537–545

Practical Approach to Manage Patients with Persistent GERD Symptoms?

Step II

Upper endoscopy if not done before to

1. R/O

- a. Refractory peptic ulcer disease
- b. Acid-resistant esophagitis

2. Categorize patients into ERD & NERD

Patients with normal endoscopy account approximately for 90% of patients with refractory GERD

JE Richter, 2007 Nature Clinical Practice Gastroenterology & Hepatology

Esophageal PH Testing

Step III

confirm excellent acid control in -ve endoscopy esophagitis and support non-acid etiology

- Cleveland Clinic Group → 7% on twice daily PPI with classical symptoms and 1% of atypical reflux symptoms patients still have abnormal acid reflux (1)

(1) Charbel S *et al.* (2005) *The role of esophageal pH monitoring in symptomatic patients on PPI therapy.* *Am J Gastroenterol* 100: 283–289

Refractory GERD with Esophagitis

- Pill esophagitis
- Autoimmune skin disease
with esophagitis
- Hypersecretory syndrome such as
Zollinger–Ellison syndrome
- Genotype that confers an altered
ability to metabolize PPIs
- Eosinophilic esophagitis

Pill Induced Esophagitis

- Classic presentation in young
- Elderly could be chronic (motility disorder or undiagnosed stricture)
- Most common site
Junction of proximal+middle 1/3
- Distal 1/3 can be involved with sparing of squamo columnar junction.
Drugs: doxycycline, alendronic acid, naproxen, KCl, ascorbic acid, quinidine and ferrous sulphate
- Aspirin+NSAID 1/3
- Prevention: take pills with at least 8 fl oz of water and avoid reclining or going to bed within 1 hour

1. Kikendall JW (2004) Pill-induced esophageal injury. In *The Esophagus*, edn 4, 572–584 (Eds Castell DO and Richter JE) Philadelphia: Lippincott Williams and Wilkins

2. Abid S et al. (2005) Pill-induced esophageal injury: endoscopic features and clinical outcomes. *Endoscopy* 37: 470–474

Autoimmune Skin Disease

- Epidermolysis bullosa acquisita
- pemphigus vulgaris
- Cicatricial pemphigoid
- Lichen planus → (dense histiocytic infiltrate)
- Middle age women often with dysphagia
- Endoscopy-diffuse erythema-blistering-whitish nodules-proximal stricture
- Bx of involved+uninvolved mucosa(Immuno fluorescence direct+indirect)

Acid Hypersecretion

30-45% of patients with Zollinger-Ellison syndrome have endoscopically visible esophagitis.

2/3 symptoms reduction on twice daily PPI .⁽¹⁾

In case of strictures need to decrease acid output to $< 1\text{m Eq 1h}$ to decrease the need for frequent dilatation.

Predictors for Esophagitis-Vomiting, low LES pressure, and obesity⁽²⁾

1. Miller LS et al. (1990) *Reflux esophagitis in patients with the Zollinger-Ellison syndrome. Gastroenterology* **98: 341–346**

2. Hirschowitz BI et al. (2004) *Risk factors for esophagitis in extreme acid hypersecretion with and without Zollinger-Ellison syndrome. Clin Gastroenterol Hepatol* **2: 220–229**

Genotype differences (PPI metabolism)

Cytochrome P450, family 2, subfamily C polypeptide 19(genotype)

Rapid metabolizer → reduce acid lowering effect

More common in Asians 12-20% than in white populations 3-6%

Eso omeprazole CYP3A4

Eosinophilic Esophagitis

Young men, intermittent solid food dysphagia, history of food impaction associated asthma or food allergy especially milk-egg, soy, peanuts or melons.

Eosinophilic Esophagitis Diagnosis

- Endoscopy-multiple rings, longitudinal furrows, pinpoint white exudates.
- Biopsy-proximal and distal > 15-20 eosinophils/HPF
- Peripheral eosinophilia is uncommon

Eosinophilic Esophagitis Treatment

Inhaled steroids twice daily for 3 months

- spacer should not be used
- Inspire deeply-depress the inhaler and swallow the aerosol
- Avoid food or drink for 2-3h
- Rinse mouth with water
- Fluticasone propionate 440mg twice daily ⁽¹⁾
- Leukotriene D4 antagonist(montelukast 10-40mg/daily)
- Oral steroid

prednisone 30mg/d for two weeks and taper over 6 week

- Oral PPI

1. Konikoff MR *et al.* (2006) A randomized, double-blind, placebo-controlled trial of fluticasone propionate for pediatric eosinophilic esophagitis. *Gastroenterology* **131**: 1381–1391

Refractory GERD without Esophagitis

- Nocturnal gastric acid breakthrough
- Nonacid GER
- Missed GER
- ‘Functional’ heartburn
- Wrong diagnosis
 - a. Achalasia
 - b. Gastroparesis

Causes

- It does not occur everyday
- Proximal placement of the PH probe
- Noxious effect of the nasal catheter limits eating and activity → false negative
- Bravo capsule (two days measures)
- One study measures acid exposure at 5 mm instead of 5cm proximal to LES

(11.7% instead of 1.8%) (1)

(1) Fletcher J *et al.* (2004) *Studies of acid exposure immediately above the gastro-oesophageal squamocolumnar junction: evidence of stat segment reflux.* *Gut* **53**: 168–173

Functional Heartburn

- Episodic retrosternal burning in the absence of pathological GER, motility disorder or structural abnormalities
- young-non obese-predmoniantly women (1)
- 30-50% ———> Normal endoscopy + heart burn + normal 24PH test results (2)
- Impedance studies (2006) 50-60% of sympomatic patients on twice daily PPI have no relation to missed or nonacid reflux (3)
- Visceral hyperalgesia ———> TCA, SSRI (4)

1. Zerbib F *et al.* (2006) *Esophageal pH-impedance monitoring and symptom analysis in GERD: a study in patients off and on therapy. Am J Gastroenterol* **101**: 1956–1963

2. Mainie I *et al.* (2006) *Acid and non-acid reflux in patients with persistent symptoms despite acid suppressive therapy: a multicenter study using ambulatory Galmiche JP et al. (2006) Functional esophageal disorder. Gastroenterology* **130**: 1459–1465

3. Smout AJPM (1997) Endoscopy-negative acid reflux disease. *Aliment Pharmacol Ther* **11 (Suppl 2)**: 81–85 38 Fass R and Tougas G (2002) Functional heartburn: the stimulus, the pain and the brain. *Gut* **51**: 885–892

4. Mayer EA and Gebhart GF (1994) Basic and clinical aspects of visceral hyperalgesia. *Gastroenterology*

107: 271–293

Non-Acid GER

Impedance testing measures the movement of liquids and gasses in the esophagus combined with PH testing

- Mostly weakly acidic (PH 4.0-6.5) occurring during daytime ⁽¹⁾
- Bile reflux 10-15%⁽²⁾
- One study-Baclofen⁽³⁾
- Role of surgery?

1. Sifrim D *et al.* (2001) *Acid, non-acid, and gas reflux in patients with gastro-esophageal reflux disease during ambulatory 24-hour pH-impedance recordings.* *Gastroenterology* **120**: 1588–1598

2. Vaezi MF *et al.* (1994) *Validation studies of Bilitec 2000: an ambulatory duodenogastric reflux monitoring system.* *Am J Physiol* **267**: G1050–G1075

3. Koek GH *et al.* (2003) *Effect of the GABAB agonist baclofen in patients with symptoms and DGE reflux refractory to proton pump inhibitors.* *Gut* **52**: 1397–1402

Nocturnal acid breakthrough (NAB)

- 60-80% of patients on twice daily PPT⁽¹⁾
- H2 blockers can control given at bedtime. Tolerance will develop within 1-4 weeks⁽²⁾
- Intermittent use?

1. Peghini PL *et al.* (1998) *Ranitidine controls nocturnal gastric acid breakthrough on omeprazole: a controlled study in normal subjects. Gastroenterology* **115**: 1335–1339

2. Wilder-Smith CH *et al.* (1990) *Tolerance to oral H₂-receptor antagonists. Dig Dis Sci* **35**: 976–983

Wrong Diagnosis

- Achalasia with minimal dilatation → manometry
- Delayed gastric emptying especially in patients with regurgitations rather than heartburn is the major complaint⁽¹⁾
- Low fiber diet + prokinetics

1. Dhir R and Richter JE (2004) Erythromycin in the short- and long-term control of dyspepsia symptoms in patients with gastroparesis. *J Clin Gastroenterol* **38**: 237–242

Conclusion

- Approximately 25% of patients who have reflux symptoms fail to respond to twice-daily PPI treatment for 4–8 weeks; these patients are said to have ‘refractory GERD’
- The first test to perform in patients with refractory GERD is upper endoscopy, primarily to assess the presence or absence of esophagitis and other gastric pathology
- Those patients who do not have esophagitis are more problematic to manage and have to undergo further tests, including prolonged pH monitoring, impedance testing for nonacid gastroesophageal reflux (GER), esophageal manometry or gastric function testing



Thank You