Non-Acid Reflux: Detection, Clinical Relevance, Management

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GERD PATHOGENESIS

Heartburn

Nociceptor activation

Injury

LES

Acid

Esophageal Defense Mechanisms
MEDICAL TREATMENT: SUPPRESS GASTRIC ACID

PPI Efficacy: Randomized Controlled Trials

MEDICAL TREATMENT: SUPPRESS GASTRIC ACID

Incomplete Response to PPI:
30% for heartburn
worse for other symptoms

How do we deal with these patients?
How can we improve our diagnostic and therapeutic strategy?

KEY questions:
1. Do these patients have GERD?
2. If they have GERD, what explains the lack of response?

TESTING FOR GERD: TARGETS

Reflux Monitoring
TESTING FOR GERD: REFLUX MONITORING

pH-monitoring

5 cm above LES

Is there an abnormal amount (pathological) of reflux?
Is there an association between reflux episodes and symptoms?

Purpose: answer 2 questions
WIRELESS pH MONITORING

- Improved patient comfort and acceptance
- Less restriction of diet and daily activities
- Prolonged monitoring: 48 – 96 hours
- Increased yield

CONVENTIONAL MONITORING: pH

ACID REFLUX

- In patients with ongoing symptoms despite adequate acid suppression
- Reflux mechanism not changed

Nonacid reflux?
TESTING FOR WEAKLY ACIDIC or NONACID REFLUX

- pH testing
- Impedance-pH testing

ACID REFLUX

Z1, Z2, Z3, Z4, Z5, Z6

pH
The clinical value of impedance-pH monitoring is directly related to the relevance of weakly acidic or non-acid reflux.
PATHOGENESIS OF SYMPTOMS DUE TO NONACID REFLUX

Chemoreceptors
Mechanoreceptors

Acid, hyperosmolarity
Distension

SYSTEMATIC REVIEW: ROLE OF ACID, WEAKLY ACIDIC AND WEAKLY ALKALINE REFLUX IN GERD

• 21 studies involving 664 patients
  • 374 patients on PPI / 382 patients off PPI

Boeckxstaens and Smout  Aliment Pharmacol Ther 2010
SYSTEMATIC REVIEW: ROLE OF ACID, WEAKLY ACIDIC AND WEAKLY ALKALINE REFLUX IN GERD

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SYSTEMATIC REVIEW: ROLE OF ACID, WEAKLY ACIDIC AND WEAKLY ALKALINE REFLUX IN GERD

- Symptom-related reflux episodes

Boecksxtaens and Smout  Aliment Pharmacol Ther 2010
WEAKLY ACIDIC OR NON-ACID REFLUX: IS IT TREATABLE?

MANAGEMENT OF PERSISTENT REFLUX DESPITE PPI (ACID OR NON-ACID)

- Modulate anti-reflux barrier:
  - Pharmacologically: TLESR inhibitor: Baclofen, others
  - Surgically: Fundoplication
  - Endoscopically: Endoscopic anti-reflux procedure (Acid)
EFFECT OF BACLOFEN ON ACID AND NONACID REFLUX

- 18 subjects with heartburn
- Randomized crossover study: baclofen vs placebo

Vela, Aliment Pharmacol Ther 2003

Nissen Fundoplication in Refractory GERD

- 40 patients with heartburn / regurgitation despite PPI
- Impedance-pH monitoring:
  - on PPI before surgery
  - off PPI 3 months after fundoplication

Frazzoni et al. Dig Dis Sci 2011;56:1099
**Nissen Fundoplication in Refractory GERD**

- 3-year follow-up in 38 patients recently published
  - Good symptom control in 34 of 38
  - Reflux parameters improved

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Before surgery</th>
<th>After surgery</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>LES tone, mmHg</td>
<td>13 (8–20)</td>
<td>19 (14–25)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total refluxes</td>
<td>68 (45–94)</td>
<td>8 (4–17)</td>
<td>0.001</td>
</tr>
<tr>
<td>Abnormal %EAET</td>
<td>6 (16 %)</td>
<td>3 (8 %)</td>
<td>0.480</td>
</tr>
</tbody>
</table>

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**pH versus Impedance-pH prior to Fundoplication in Patients with Extraesophageal Reflux**

- 27 patients with objective evidence of GERD underwent fundoplication
- Prior to surgery: 48-h wireless pH OFF PPI
  - 24-h impedance-pH ON PPI
- 59% at least partial improvement of extraesophageal symptom on f-u

**Predictors of symptomatic improvement on multivariate model:**
- Concomitant heartburn
- % time pH <4 greater than 12%

**Factors that did NOT predict improvement:**
- no. reflux episodes by impedance
- SI/SAP during 48-h pH or 24-h impedance-pH study
- % time pH <4 greater than 5%

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Francis Laryngoscope 2011
ISSUES AND UNANSWERED QUESTIONS

- No controlled studies of surgery for nonacid or weakly acidic reflux
- How best to define an abnormal test?
- What parameters predict response to therapy?

PERSISTENT SYMPTOMS DESPITE ACID SUPPRESSION
SUMMARY

• 30-40% patients: incomplete control on PPI

• Ongoing symptoms: acid GER / nonacid GER / no GER
  • Impedance-pH superior for testing on medication
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  • Measureable by impedance-pH
  • Responsible for symptoms in some patients
  • Responds to treatment – RCT needed

• Stop PPIs if there is no evidence of GERD
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Thank you
Symptoms not due to reflux

- Nonacid reflux
- Acid reflux

Abnormal: GERD

Escalate Therapy