Eosinophilic Oesophagitis

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Eosinophilic oesophagitis - Outline

- Definition
- Incidence and prevalence
- Pathology
- Presentation
- Endoscopic evaluation
- Other testing
- Management – dietetic
- Management – topical steroids
- Management – alternative strategies
- Summary
- References
Eosinophilic Oesophagitis - Definition

- EOE is a chronic immune/antigen oesophageal inflammatory disease associated with dysfunction mediated through eosinophil predominant inflammation.
- It needs to be disaggregated from other causes of eosinophil associated oesophagitis
- It may occur in combination with acid related oesophagitis
- Long term consequences are largely unquantified but progression to dysplasia and carcinoma are believed to be rare
# TABLE 3.

## Gastrointestinal Food Allergic Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Key Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IgE-mediated</strong></td>
<td></td>
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<tr>
<td>Oral allergy</td>
<td>Oral pruritus, mild angioedema of oral cavity</td>
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<tr>
<td>Gastrointestinal immediate hypersensitivity</td>
<td>Acute nausea, vomiting, pain, diarrhea</td>
</tr>
<tr>
<td><strong>Mixed IgE and non–IgE-mediated</strong></td>
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<tr>
<td>Eosinophilic esophagitis</td>
<td>Dysphagia, post-prandial nausea and vomiting, epigastric pain</td>
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<tr>
<td>Eosinophilic gastroenteritis</td>
<td>Vomiting, abdominal pain, diarrhea, malabsorption, and failure to thrive</td>
</tr>
<tr>
<td><strong>Non–IgE-mediated</strong></td>
<td></td>
</tr>
<tr>
<td>Food protein-induced enterocolitis</td>
<td>Vomiting, diarrhea, poor growth, lethargy, dehydration</td>
</tr>
<tr>
<td>Food protein-induced enteropathy</td>
<td>Malabsorption, emesis, poor growth, diarrhea</td>
</tr>
<tr>
<td>Food protein-induced proctocolitis</td>
<td>Bloody diarrhea, mucous in stools, normal growth</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>Malabsorption, failure to thrive, diarrhea</td>
</tr>
</tbody>
</table>

*IgE = immunoglobulin E.*
Adverse reactions to foods

Immune mediated

Food allergy

Non-immune mediated

Toxic reactions

Toxins
- Bacterial toxins
- Aflatoxins
- Scombroid poisoning

Food intolerance

Pathophysiology explained

Pathophysiology unexplained

IgE-mediated
- Urticaria
- Angioedema
- Bronchospasm
- Rhinitis
- Laryngospasm
- Diarrhoea/vomiting
- Anaphylaxis
- Oral Allergy

Non-IgE-mediated
- Food protein-induced enterocolitis syndrome
- Food protein-induced proctocolitis
- Food protein-induced enteropathies

Mixed IgE- and non-IgE-mediated
- Cow’s Milk Protein Allergy
- Eosinophilic Oesophagitis
- Eosinophilic Gastroenteritis

Coeliac Disease

Pharmacological
- Caffeine
tyramine

Enzyme deficiencies
- Lactose/fructose
- Malabsorption

Non specific gut and non-gut reactions to food
- Includes Irritable Bowel Syndrome & other functional GI disorders:
  - Luminal distension
  - Heightened gastrocolic reflex
  - Altered perception
  - Behavioural factors:
    - Expectation/conditioning
  - Psychological factors

Source: Aliment Pharmacol Ther © 2014 Blackwell Publishing
EOE – Historical perspective

- Paediatric endoscopy started to be described in the 1980’s
- First major papers described eosinophilic infiltration as part of acid related reflux
- Kelly 1995 described a group of children with intense eosinophilic oesophagitis resistant to maximal treatment
- Suggested that response to elemental feed and postulated an allergic cause
- Kelly et al Gastroenterology 1995 109 1503-12
EOE - Demographics

- 3 separate groups presenting in childhood, under 3, 5-10 and teenage
- Additional peak in presentation in young adults 25-35
- Male predominant disease 66 – 75% in most large studies
- 10-15% of children presenting with oesophagitis have EOE
- 68% have a history of atopic disease versus 43% age matched controls with GORD
- Rising prevalence 2/100,000 to 27/100,000 in Swiss study over 16 years
2013 Distribution of EoE

- Canada
- United States
- Mexico
- Brazil
- Switzerland
- Spain
- Belgium
- England
- Netherlands
- Italy
- Germany
- France
- Israel
- Middle East
- Africa
- Japan
- Asia
- Australia
EOE - demographics

- Childhood incidence 10/100,000
- Very rare in children of African/American origin
- Seen within Respiratory Allergy Dermatology ENT and General Paediatrics
- 15-20 new cases per year in my catchment area
EOE- presentations

- Age 0-4: Late onset vomiting
  Progressive food refusal
  Failure to thrive  Usually severely atopic

- Age 5-10: Vomiting, Retrosternal pain, non specific upper abdominal pain

- Ages 11-18: Pain on swallowing, difficulty swallowing, high fluid requirement with meals
  Food bolus obstruction
Figure 1

- Environmental exposure
- Food or aeroallergens
- Drugs
- Sensitization-Th2 Activation
- Allergic Genetic Background
- Eosinophilic Esophagitis Genetic Predisposition
- SNP in the 3'UTR of eotaxin-3 gene
EOE pathophysicsology

- Sensitization with allergen(s)
- Recognition by TH2 cells and initiation of inflammatory cascade
- Production of Il 4,5 and 13
- Switching on and elaboration of Eotaxin 3
- Recruitment of further eosinophils into surface epithelia
- Degranulation of eosinophils and attraction of mast cells
- Switching on of fibroblast via TGF beta leading ultimately to remodeling/fibrosis
EOE - Endoscopic changes

- Early changes – thickening of mucosa, white papules
- Medium changes – linear furrows, checkerboard appearance
- Late changes – signs of trachealisation, circular rings of fibrous tissue, stricture formation
EOE-Histology

- 4-5 biopsies at least 2 sites 5cm apart
- 2 biopsies showing >15 eosinophils per HPF +/- microabscess
- Basal cell hyperplasia > 50%
- Superficial layering of eosinophils in surface layer
Esophageal Histology: useful

- Normal esophagus
- GER
- Eosinophilic esophagitis

Small number of intraepithelial eosinophils
Basal cell thickening
Lengthening of stromal papillae
# EOE v GORD histology changes

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<thead>
<tr>
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<th>EOE</th>
<th>GORD</th>
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<tr>
<td>Eosinophils</td>
<td>75 +/-56</td>
<td>3 +/- 4</td>
</tr>
<tr>
<td>Basal zone</td>
<td>83%</td>
<td>59% (Normal &lt;33%)</td>
</tr>
</tbody>
</table>

- Mulder et al JPGN 2013 56 263-70
EOE - Treatment

- Dietary
  - Elimination diet
  - Targeted food elimination through allergy testing
  - Empiric food elimination

- Swallowed steroids

- Systemic steroids

- Immunomodulators
EOE – Dietary treatment

- Spergel reviewed investigation and intervention in 941 patients 2000-11
- Investigation based on Skin prick and Patch testing all relating to foods
- 74% reacted to cows milk and 30% cured by milk avoidance alone
- 50% needed 2 foods to be eliminated- commonest egg, wheat, soy, peanut
- +25% needed 4 or more foods to be eliminated
- Additional 15-17% required a full elimination diet with amino acid feed

- Spergel et al Determination of foods to eliminate in EOE
  J Allergy Clin Immunology 2012 131 461-7
EOE Dietary Treatment

- 2 approaches adopted
- Do extensive testing and treat by excluding all allergens + milk
- No testing but exclude milk, egg, wheat, soy and meats
- No difference in results 75% remission v 77% remission
- Small proportion of children have immediate hypersensitivity reactions 10-15%
The pie chart shows the percentage of different allergens:
- Milk: 74%
- Wheat: 26%
- Egg: 17%
- Soy: 10%
- Peanut/Treenut: 6%
- Seafood: 0%
# EOE – Dietary Treatment Biopsy Proven

- Allergy testing alone 52%
- Milk exclusion alone 30%
- Milk, egg, wheat 48%
- Six food exclusion (MEWSPS) 53%
- MEWS and all meats 77%
- Allergy testing and milk 75%
- Vegan diet 48%
Non Dietary Treatment

- Sodium Cromoglycate
- Leukotriene receptor antagonists
- Immunosuppressives
- Biologics (mainly anti IL 5)

- NO EVIDENCE THAT THERE IS ANY PART TO PLAY IN ACUTE OR CHRONIC TREATMENT
Non Dietary Treatment – Swallowed steroids

- 2 main forms both used off licence
- Swallowed Fluticasone (FP) usually bd
- Inhaled directly but into throat only and swallowed
- Oral Viscous Budesonide (OVB) usually bd
- Made up with either sugar, sucralose or Splenda and swallowed (ensure teeth cleaning but no swallowing of liquid after)
- Main complication oral/ oesophageal candidiasis
- High relapse rate when discontinued if not + dietary treatment
Swallowed Fluticasone (FP)

Dose range 88mg – 440mg/day usually in 2 divided doses

- Works best in those without allergy
- Symptomatic improvement 67%
- Histological improvement 50%
- Almost total relapse rate after stopping
Oral Viscous Budesonide (OVB)

- First described in patients who had failed to improve with FP
- 80% clinical and histological remission
- DBPC trial in 36 children
- Symptom relief 74% v 22%, histological Rx 68-5, placebo 62-56
- Dosing study in 81 Children
- Low dose 350 or 500ug did not work
- Medium or high (1400ug to 4000ug) similar 80% symptom + histology improve
EOE current management

- Individualized to patient
- Not currently doing SPT unless anaphylaxis suggested by history
- Dietary restriction, always Milk, Egg and Wheat
- Prefer Milk, Egg, Wheat, Soy and all Meat – difficult to achieve
- OVBudesonide 500ug bd under 10, 1000ug bd over 10
- Repeat biopsy in 6 months or earlier if non settling clinically
EOE-Conclusions

- Increasing Incidence of long term condition with substantial morbidity
- Seen in many General Paediatric Clinics
- Upper GI Endoscopy mandatory for accurate diagnosis and management
- Combination therapy of dietary restriction and OVB probably ideal to achieve symptomatic and histological control which is required to prevent long term obstructive complications
- ASTHMA OF THE OESOPHAGUS AN APPROPRIATE TERM AS THE LONG TERM REMODELLING IS PROBABLY COMMON TO BOTH DISEASES
EOE – MAIN REFERENCES


EOE Key References


