Risk Factors of Eosinophilic Esophagitis in Children with Esophageal Atresia

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ABSTRACT:
AIM: Eosinophilic Esophagitis (EoE) has been reported among esophageal atresia (EA) patients but the risk factors are unknown.

METHODS: 31 consecutive children (16M/15F, age <1-18 years) who had undergone upper gastrointestinal endoscopy with biopsies underwent review. Medical records were reviewed for risk factors including EGA, mode of delivery, anastomotic dilation, and family history of atopy, newborn feeds, inhaled steroid use, tracheomalacia and aspiration pneumonia.

RESULTS: Of 31 patients, 10 were diagnosed with EoE based on accepted histology (>15 eosinophils/HPF). In the EoE group 80% were male compared to 38% in the non-EoE group. There was no difference in family history of atopy, EGA, mode of delivery, use of breast milk, or presence of G-tube. Tracheomalacia affected 48% of non-EoE patients vs. 70% of EoE patients; 67% of non-EoE patients had aspiration pneumonia vs. 30% for those with EoE. Inhaled steroid exposure under 2 years of age was significantly higher in the non-EoE group (67% vs. 10%). Of 8 males in the non-EoE group 50% had early topical steroid exposure, where 13% did in the EoE group. Occurrence of esophageal strictures or multiple strictures dilations were not associated with risk of EoE. Age of initial dilation was later in EoE and 25% were >2y at first dilation. Steroid use at time of endoscopy was low (24% / 22%).

CONCLUSION: Male sex, like EoE in general, was a significant risk factor for EoE among EA patients, but there was no difference in family history of atopy. The use of steroids prior to the age of 2 was shown to potentially decrease the chance of developing EoE. Whether early topical steroid is somehow protective from EoE is not clear, as our numbers are small, but this observation needs further follow up.

BACKGROUND: Children with EA often have dysphagia. Historically the dysphagia was thought to be due to a combination of gastroesophageal reflux and dysmotility. Eosinophilic Esophagitis (EoE), a known cause of dysphagia, is a disorder characterized by the presence of an eosinophilic infiltrate in the esophagus that has been recruited by an inflammatory pathway. EoE most often occurs in non EA/TEF patients, those having EA/TEF have been reported as having EoE as a contributing factor for their dysphagia. We (Oliveira J, Pediatric Surg, 2008;43(5):810-4) and others have reported finding EoE in some of their EA/TEF patients. There are known risk factors for EoE in the general population, including a personal or family history of atopy. More recently early life events, such as delivery method and exposure to antibiotics may also lead to increase risk of EoE (Jensen et al., 2013). Risk factors relevant to EA/TEF patients are not known.

AIM: To review the medical histories of patients with Esophageal Atresia in order to determine possible risk factors and predictors of Eosinophilic Esophagitis in children with EA.

METHODS: The medical records of patients under the age of 18 with EA who had undergone upper endoscopy in a ten year span (n=31) were retrospectively reviewed. The patients were divided into two cohorts:
- Positive histology for EoE (n=10)
- Negative histology for EoE (n=21)

(accepted positive histology is >15 eosinophils / HPF)

a) Esophageal biopsy with EoE  b) Normal esophageal biopsy

Following variables were then obtained and analyzed:
- Gender
- Early use of inhaled steroids
- Diagnosis of atopic disease
- Diagnosis respiratory tract conditions
- Esophageal dilations
- Type of Fistula/EA
- Gestational age

Comparison between the two cohorts was then carried out.

RESULTS:

- 10/31 patients + histology EoE
- 21/31 had negative histology

Gender
- Non-EoE 38% / EoE group 80%

Airway Conditions
- Recurrent aspiration pneumonia:
  - Non-EoE 57% / 30% EoE
  - EA proximal & distal fistula (D)

Inhaled Steroid Use in first 2 years
- Non-EoE group (67%)  
  - EoE group (10%)  

The RR of developing EoE with early steroid exposure was 0.166.

Histology
- Non-EoE group, 29% had 1-5 eosinophils / HPF
- 50% of those with 1-5 eosinophils / HPF were on an inhaled topical steroid within two years of endoscopy
- 8 non-EoE patients were diagnosed with another type of Esophagitis

% of non-EoE patients with histological findings

Other
- Remaining factors, such as: gestational age, antibiotic use, delivery method, strictures and subsequent dilations, and heart disease did not found to be statistically significant

CONCLUSION: The EoE cohort had more than twice as many males than the non-EoE cohort. This is consistent with previous finding that the male gender is a risk factor for developing EoE.

Factors such as gestational age, type of EA/TEF, esophageal strictures and subsequent dilations were not found to be significant risk factors.

Patients who had regular exposure to inhaled steroids before the age of 3 were found to have a decreased risk of developing EoE with age, even with other risk factors (e.g. Atopic disease, eczema, seasonal rhinitis) associated with EoE. Inhaled steroid use at <2 y of age had less EoE.

FUTURE STUDIES:
The findings of this study suggest a need for further research into early inhaled topical steroid use in children with EA/TEF suspected of having EoE.

Other risk factors for EoE - like early antibiotic use - should be reviewed and looked at prospectively.

Microbiome studies in this group could be informative.

Whether the children in this study who were not to have <15 eosinophils in their respective biopsies (thus failing to meet the diagnostic criteria for EoE) while on an inhaled steroid actually had EoE remains unclear. Early endoscopy may help sort this out.

REFERENCES:

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