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THE ROLE OF FRACTIONATED EXHALED NITRIC OXIDE (FENO) IN EOSINOPHILIC ESOPHAGITIS AND THE RELATIONSHIP WITH DOWNSTREAM EOSINOPHILS

**Background:** Eosinophilic Esophagitis (EoE) is a chronic immune mediated disease of the esophagus characterized by symptoms of esophageal dysfunction and eosinophilic-predominant inflammation of the esophagus. It can lead to feeding difficulties, failure to thrive, and esophageal strictureing. Currently, the gold standard for diagnosis and assessing response to therapy is upper endoscopy and histopathological analysis of biopsies. A noninvasive, cost-effective, and low risk alternative that can aid in the management of EoE is not currently available. Previous studies assessing correlation of fractionated exhaled nitric oxide (FeNO) with degree of esophageal eosinophilic inflammation were low powered but noted a trend for association. To our knowledge, we have investigated the contribution of eosinophilic inflammation of stomach and duodenum to FeNO. We hypothesized that in an adequately powered sample, patients with esophageal eosinophilic inflammation will have elevated FeNO levels that would correlate with severity of esophageal eosinophilia on biopsies.

**Objectives/Goal:** To assess the utility of FeNO as a non-invasive biomarker of esophageal eosinophilic inflammation for monitoring disease activity
**Methods/Design:** Patients aged 6-21 years undergoing scheduled upper endoscopy with biopsy for suspected EoE were recruited in our prospective study. Patients on steroids and with persistent asthma requiring daily controller medication were excluded. FeNO measurements were obtained in duplicate using a NIOX MINO machine (Aerocrine, Inc.) prior to endoscopy. Based on the esophageal peak eosinophil count (PEC)/HPF on biopsy, patients were classified as EoE (PEC ≥15) or control (PEC ≤ 14). Mean FeNO levels were correlated with presence or absence of EoE, eosinophil counts on esophageal biopsy, and abnormal downstream eosinophilia in the stomach (PEC ≥ 10) and duodenum (PEC ≥ 20). Wilcoxon rank-sum test, Spearman correlation, and logistic regression were used for analysis. P value < 0.05 was considered significant.

**Results:** We recruited a total of 134 patients, of which 45 were diagnosed with EoE by histopathology. The median (IQR) FeNO level was 17 ppb (11-37, range: 7-81) in the EoE group and 12 ppb (8-19, range: 5-71) in the control group. After adjusting for atopic diseases, EoE patients had significantly higher FeNO levels as compared to patients without EoE (z = 3.33, p <0.001; Figure 1). A weak yet statistically significant positive association was found between the number of esophageal eosinophils and FeNO levels (r = 0.30, p <0.005). On subgroup analysis within the EoE cohort, higher FeNO levels were noted in patients with abnormal gastric (n = 23, 18 vs. 15) and duodenal eosinophilia (n = 28, 21 vs. 14); however, the difference was not statistically significant.

**Conclusions:** After ruling out atopy and downstream eosinophils as possible confounders, our study found significantly higher FeNO levels in the EoE cohort. Additionally, a weak yet statistically significant positive correlation was found between FeNO and number of esophageal eosinophils which differed from the existing literature correlating FeNO in EoE patients. Future, prospective studies following individual patients longitudinally, with each patient serving as their own control as they experience change in esophageal eosinophilia secondary to therapy, may yield more clinically useful results for assessing response to therapy.