The Effects of a Single Food Elimination Diet on the Concentration and Distribution of Immunoglobulins in Children with Eosinophilic Esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is an immune-mediated disease of the esophagus that is triggered by foods, especially milk. EoE is characterized histologically by eosinophil predominant inflammation of the esophageal mucosa. Immunoglobulin (Ig) G4 may be a marker of this inflammation. Children with active EoE for example have elevated serum levels of IgG4:IgE ratio to milk. However, little is known regarding whether serum levels of IgG4 and IgE or esophageal tissue expression of IgG4 can predict therapeutic response to milk elimination in pediatric EoE patients.

Hypothesis: Histologic response to milk elimination is associated with reductions in serum milk specific IgG4/IgE ratio and reductions in total IgG4 expression in esophageal tissue in pediatric EoE patients.

Methods: Milk specific IgG4 and IgE were measured by ImmunoCap in serum samples of EoE patients treated with a 12-week milk elimination diet. Total IgG4 expression and protein distribution in esophageal tissue were also assessed using RT-PCR and immunohistochemistry respectively. Patients were classified as diet responders or non-responders based on the number of eosinophils present in esophageal tissue or the percent reduction in eosinophils compared to before the diet.

Results: Responders (defined as >50% reduction in eosinophil count) to the elimination diet showed a 2-fold decrease in total milk-specific IgG4/IgE ($p=0.009$) and a 2-fold decrease in milk specific beta lactoglobulin IgG4/IgE ($p=0.027$) compared to non-responders. However, change in milk-specific IgG4/IgE from baseline was not a significant predicting factor for response ($p=0.10$). Serum milk-specific IgG4/IgE positively correlated with change (improvement) in esophageal histologic features ($r=0.86$) in responders. However, there was no significant difference in tissue level expression and distribution of IgG4 between responders and non-responders. Similar results were found when responders were defined by absolute eosinophil count (<15 eosinophils per high power field).

Conclusions: While the difference in reduction of milk-specific IgG4/IgE between histologic responders and non-responders to diet elimination therapy was significant, the ratio was not a significant determinant in predicting histologic response. The data does provide more evidence that the IgG4:IgE ratio may act as a general biomarker of inflammation in EoE.

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