

Combining different therapeutic interventions in eosinophilic esophagitis may lead to unreplicable and misleading results

Dear Editor,

In an upcoming issue of *Diseases of the Esophagus*, Kruszewski *et al.* report the first prospective, although nonrandomized, comparative study between cow's milk elimination diet and topical steroids in pediatric eosinophilic esophagitis (EoE) patients.¹ The authors are to be congratulated because this is one of the EoE fields most in need for trials. In addition, they did not only evaluate just histological remission, but also the impact of therapeutic interventions on symptoms and quality of life.

Throughout the discussion, the authors elegantly address the limitations of the study. We find two major setbacks in the study. The first one is that proton pump inhibitor (PPI)-responsive esophageal eosinophilia was not ruled out in any of the included patients from November 2012, contrary to 2011² and further guidelines. The second downside is that both groups (cow's milk elimination diet vs. topical steroids) received PPI therapy concomitantly with the therapeutic intervention. At least one third of patients with suspected EoE can achieve clinical and histological remission on PPI therapy.² PPI therapy has been recently shown to improve symptoms in EoE patients, despite persistent esophageal inflammation.³ Furthermore, a recent abstract has suggested PPI may exert additive effects over topical corticosteroid therapy in an *in vitro* model of EoE.⁴ Consequently, we can infer that a significant proportion of patients in both groups (64% vs. 80%, *p* 0.4) achieved either clinical and/or histological improvement due to PPI therapy effects.

Combining different therapeutic interventions in EoE might guide us to misleading and unreplicable results. Skin testing-guided elimination diet is a prime example. The outstanding results (77%) published by Spergel *et al.* in 2005⁵ and 2007⁶ have not been replicated at any other centers yet. The main reason is likely that overall efficacy was due to a combination of three different strategies (skin testing-guided elimination, elemental diet in those in which skin testing-guided diet was too restrictive, and empiric elimination of cow's milk). When a single therapeutic intervention (e.g. six-food elimination diet) in EoE has been separately evaluated,^{7–9} results have been almost identical. A recent meta-analysis on seven observational studies¹⁰ provided an extremely homogenous remis-

sion rate of around 72%, regardless of the geographical area or age of the population being assessed (72.8% and 71.3% for children and adults, respectively).

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