Testing for Fecal Calprotectin in Food Protein–Induced Enterocolitis Syndrome

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Dear Editor:

I read with interest the medical update by Vila Sexto [1] on food protein–induced enterocolitis syndrome (FPIES) and would like to add my thoughts on the importance of noninvasive tests such as fecal calprotectin (FC) in this condition. Several fecal biomarkers (eg, β-defensin, TNF-α, and eosinophil cationic protein) have been assessed in non–IgE-mediated gastrointestinal disorders, although FC appears to be the most reproducible and reliable [2]. It is important to emphasize that no single test can replace the information provided by the patient's symptoms and clinical assessment. Nevertheless, the availability of any biomarker would assist in diagnosis and counseling of patients and parents.

Calprotectin is a cytosolic Ca^{2}+/Zn–binding protein present in neutrophils and monocytes that has antimicrobial action (by depriving microorganisms of zinc), immunomodulatory action, and antiprofilerative action [3]. Increased FC levels suggest gut mucosal inflammation that is easily confirmed by endoscopy and histology in inflammatory bowel disease. At the cellular level, increased FC has been associated with increased neutrophil migration towards the intestinal lumen. Just as non–IgE-dependent mechanisms account for the inflammation seen in inflammatory bowel disease, a similar parallel is drawn for FPIES, wherein skin tests and levels of specific IgE against food proteins (eg, cow's milk protein [CMP], egg, wheat, and soy) are negative. Therefore, gut proteins such as β-defensin, eosinophil cationic protein, TNF-α, and calprotectin in fecal samples can act as surrogate markers of cellular response. The Table lists studies showing that estimation of FC may prove to be a useful biomarker in FPIES [2,4,5]. Beşer et al [4] showed a higher FC level in non–IgE-mediated disease before elimination of CMP that decreased after elimination of CMP, although levels were still higher than in IgE-mediated disease. Merras-Salmio et al [2] showed that the Mann-Whitney test *P* values were significantly different between geometric means of FC values in IgE-mediated vs non–IgE-mediated disease during elimination of CMP [2].

The exact cut-off limits of FC in FPIES remain to be determined, although these will undoubtedly be dependent on age, duration of the elimination diet, and intercurrent gastrointestinal infections. Further studies are required to determine whether FC is useful in non–IgE-mediated food allergies, since gastrointestinal involvement is more common here than in IgE-mediated disease.

References

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Table. Studies on Fecal Calprotectin in IgE- and Non–IgE Mediated Gastrointestinal Diseases

Study Location, y	Number of Children (Age Range)	Fecal Calprotectin Levels and Clinical Groups	Reference
Turkey, 2014	19 healthy children aged 1 to 31 mo 32 CMPA patients (24 IgE-mediated, 8 non–IgE-mediated)	Mean FC value was 296 (94) µg/g (healthy children) Pre-CMP elimination diet mean FC value Non-IgE group (n=8): 886 (278) µg/g Control group (n=19): 296 (94) µg/g *P*<.001	[4]
		Pre-CMP elimination, Mean FC value / Post-CMP elimination diet, Mean FC value IgE-mediated group (n=24): 392 (209) µg/g / 218 (90) µg/g Non–IgE-mediated group (n=8): 886 (278) µg/g / 359 (288) µg/g *P*=.001 / *P*=.025	
Finland, 2014	57 young children aged 0-4 y	Percentage change in geometric mean of FC, IgA and β-defensin 2 levels	[2]
		% change following introduction of CMP / FC / IgA / β-defensin 2 IgE-mediated group (n=18): 15% / –11% / 23% Non–IgE-mediated group (n=39): 18% / –2.2% / 39%	
		Fecal β-defensin 2 and IgA showed high levels of within-group variation but the differences between the groups were insignificant.	
Spain, 2016	82 infants aged 1-12 mo	Statistically significant relationship of high FC levels between infants with non-IgE-mediated CMPA and controls; FC<138 µg/g excludes FPIES	[5]

Abbreviations: CMP, cow's milk protein; CMPA, cow's milk protein allergy; FC, fecal calprotectin; FPIES, food protein-induced enterocolitis syndrome.

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