CELIAC DISEASE

Progress towards noninvasive diagnosis and follow-up

Noninvasive evaluation of intestinal damage for the diagnosis and follow-up of celiac disease may be one step closer to the clinic, according to the findings of a Dutch pilot study, performed at the Maastricht University Medical Center. "In the plasma/urinary markers intestinal fatty acid binding protein (I-FABP) and liver fatty acid binding protein (L-FABP) we have found a potentially helpful tool for early, noninvasive diagnosis and rapid evaluation after starting a gluten-free diet (GFD)," report Joep Derikx and Wim Buurman, two of the study investigators.

"Early diagnosis of intestinal pathology is a major focus for us," say the authors. "We became interested in [FABP] because we were looking for a small, gut-specific protein located on top of the villi … [that] would be rapidly released upon cell damage at the location of first injury (that is, mature enterocytes) in most intestinal diseases, including celiac disease." Previous work by Derikx *et al.* and others had already identified FABP as a plasma/urinary marker of damage to intestinal epithelial cells.

To assess the potential of FABP as a noninvasive marker for celiac disease, the investigators first assessed the distribution and microscopic localization of I-FABP and L-FABP in the gastrointestinal tract. Histologically normal samples of full-thickness intestinal tissue were taken from various parts of the gut—from the stomach to the sigmoid colon—during routine surgery on 39 patients. FABP expression was measured and quantified by western blot analysis and enzyme linked immunosorbent assay (ELISA). Immunohistochemical analysis was also performed with antibodies against human I-FABP and L-FABP. The

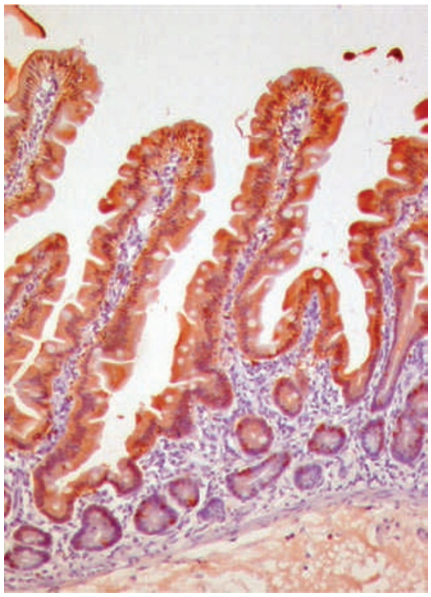

Image courtesy of J. Derikx

expression of I-FABP and L-FABP was found to be specific to mature enterocytes present on the tip of the villi of the small intestine, in particular the jejunum.

With the specificity of FABP expression confirmed, the authors then wanted to see whether serum concentrations of FABP would be able to discriminate between patients with celiac disease and controls. To establish a normal serum FABP value they measured the serum FABP concentrations of 62 healthy volunteers by ELISA. 13 patients with celiac disease then had their serum FABP concentrations measured at the point of diagnosis, which was made by biopsy of the small intestine. Compared with the mean normal serum I-FABP value (172.7 ± 20.2 pg/ml), the mean serum I-FABP concentration in patients with celiac disease was significantly elevated (784.7 ± 145.5 pg/ml, $P<0.001$). The mean serum L-FABP concentration was also significantly increased in patients with celiac disease compared with those in healthy controls (48.4 ± 11.6 ng/ml versus 10.4 ± 0.7 ng/ml, $P<0.001$).

The final study objective was to assess whether serum FABP concentrations normalize after the introduction of a GFD. Serum I-FABP and L-FABP concentrations were therefore measured in 10 patients within 1 year of starting a GFD. The mean serum concentration of I-FABP decreased significantly (from 725.5 ± 134.4 pg/ml to 266.8 pg/ml [range 41.0–642.6 pg/ml; $P=0.002$]), as did the mean serum L-FABP concentration (from 40.9 ± 10.0 ng/ml to 15.3 ng/ml [range 7.3–34.3 ng/ml; $P=0.025$]). In light of these findings, the authors suggest that "…assessment of circulating FABP concentrations may be very valuable to monitor the effect of a GFD on recovery of the intestinal mucosa in celiac disease."

A multicenter study is now underway to further assess how valuable FABP might be in the clinical management of celiac disease. The usefulness of urinary FABP concentrations for diagnosis is being compared with biopsy in children with suspected celiac disease. The potential of urinary FABP measurement to replace endoscopy and biopsy is also being assessed by studying the correlation between urinary FABP levels and intestinal damage. "In addition," say Derikx and Buurman, "we are following these children during the start of a GFD (and eventual gluten challenge) and measuring FABP values prospectively in order to find out whether FABP is an accurate marker to evaluate diet effect and therapy compliance noninvasively."

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