Fecal Calprotectin to Screen for IBD?

Source: *Van de Vijver E, Schreuder AB, Cnossen WR, et al. Safely ruling out inflammatory bowel disease in children and teenagers without referral for endoscopy. Arch Dis Child. 2012; 97(12):1014-1018; doi:10.1136/archdischild-2011-301206*

PICO

Question: Among children with suspected inflammatory bowel disease (IBD), can fecal calprotectin be used as a reliable screening test to identify patients likely to have a positive endoscopy for IBD?

Question type: Diagnostic

Study design: Prospective

Researchers in Belgium and the Netherlands conducted a diagnostic accuracy study to determine if the use of fecal calprotectin as a screening test for inflammatory bowel disease (IBD) could reduce the number of children undergoing endoscopy. Participants included children and teens 6 to 18 years of age with abdominal complaints suggesting IBD who were evaluated in pediatric clinics of 6 general hospitals and 1 tertiary care hospital in northern Holland. Inclusion criteria included persistent diarrhea for >4 weeks or recurrent (>2 episodes in 6 months) abdominal pain and diarrhea, and at least 1 of the following: rectal bleeding, unintended weight loss, linear growth retardation, perianal symptoms (skin tag, fistula, fissure, or abscess), anemia, other extraintestinal manifestations (erythema nodosum, arthritis, uveitis), or increased inflammatory markers (ESR or CRP). At entry, a stool sample was analyzed for fecal calprotectin levels and cultured for pathogens. Pediatric gastroenterologists were blinded to calprotectin results and independently determined whether endoscopy was needed. Confirmation of IBD was based on histologic examination. Patients were classified as not having IBD based on a negative ileocolonoscopy, or if ileocolonoscopy was not performed, a definitive diagnosis other than IBD and/or complete resolution of symptoms within 6 months.

IBD was confirmed in 42 of 117 (36%) patients, 41 by pathology and 1 by positive magnetic resonance enterography after a negative gastroscopy and ileocolonoscopy. Fecal calprotectin was elevated (>50 µg/g) in all 42 patients (sensitivity 100%) and in 20 of the 75 patients without IBD (specificity 73%). In the absence of gastrointestinal infection, specificity rose to 81%. Extraintestinal manifestations of IBD and elevated markers of inflammation were significantly more common in patients with confirmed IBD ($P < .05$). Negative pathology results were found in 38% of the patients referred for ileocolonoscopy. If the decision to perform endoscopy was based on an abnormal fecal calprotectin, the number with negative results dropped to 32%. With an abnormal fecal calprotectin in the absence of infection, only 22% would have a negative ileocolonoscopy, and no cases of IBD would have been missed.

The authors conclude that the combination of a simple case definition for suspected IBD with a positive fecal calprotectin increases specificity and reduces unnecessary referrals for endoscopy.

Commentary by

Emily C. Webber, MD, Pediatric Hospital Medicine, Riley Hospital for Children at Indiana University Health, Indianapolis, IN

Dr Webber has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Calprotectin is a calcium-binding protein present in neutrophil granulocytes, but unlike other candidates for stool markers of intestinal inflammation (neutrophil elastase, lactoferrin, TNF-alpha, leukocyte esterase), calprotectin is proteolysis-resistant. Bunn et al (see *AAP Grand Rounds,* November 2001;6(5):52-53[1]) attempted to define normal levels of stool calprotectin and evaluate its validity for the diagnosis of IBD in the context of histopathology and technetium-99 scanning. Despite multiple positive studies, calprotectin has not found a niche as a screening test in the general population.

The authors of the current study published a meta-analysis showing that elevated fecal calprotectin identifies children most likely to have IBD, but found the test to be accurate when screening adults but not children.[2] The pretest probability of IBD in children already determined to need endoscopy is higher than in the general population.[2,3] Diamonte et al demonstrated pretest probability to be 60% in a tertiary care center population.[3] But the question remained: could calprotectin be used as a screening test in general pediatric practice to reduce the number of children referred for endoscopy?

The inclusion criteria for the current study were straightforward, effective, and a reflection of what a referring general pediatrician would use, and identified a population with a pretest probability of 36%. The challenge resides in the high risk of false positive fecal calprotectin, which can occur with intestinal infections or with the use of NSAIDs or proton pump inhibitors, both of which are commonly used in children who are eventually diagnosed with functional abdominal pain. However, these values are usually only mildly elevated, while the majority of confirmed IBD patients have fecal calprotectin >500 µg/g.[4]

Importantly, a normal calprotectin level reduced the probability of IBD to zero and can therefore be used to *rule out* IBD. With a thorough history and physical and a normal fecal calprotectin, pediatricians can adopt watchful waiting. This is an advantage over CRP, which was recently shown to be normal in children with new IBD diagnoses.[5]

Despite these encouraging results, the authors appropriately caution against translating fecal calprotectin into practice for general pediatricians or family practitioners, given the lower IBD prevalence in the general population coupled with the high incidence of false positives. They instead endorse using a clinical case definition for suspected IBD as well as positive fecal calprotectin to shape referral practices. With widespread efforts to reduce unnecessary tests and costs for our patients, finding an objective, reliable adjunct to rule out diseases like IBD should be a desirable goal.

References

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