

Introduction to faecal calprotectin for GPs

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Introduction

Faecal calprotectin, a novel marker of intestinal inflammation and may play a role in clarifying the presence of pathology. Calprotectin is a stable protein that accounts for about 60% of neutrophil cytosolic protein. Calprotectin is released into the faeces when neutrophils gather at the site of any gastro-intestinal tract inflammation. Calprotectin can provide a non-invasive, inexpensive and objective method for assessing patients when considering the need for additional possible invasive procedures e.g. colonoscopy or imaging studies.

The faecal calprotectin test has a relatively high specificity and sensitivity (approximately 90%) for distinguishing between non-inflammatory bowel disorders (e.g. irritable bowel syndrome) and inflammatory bowel disease (e.g. ulcerative colitis and Crohn's disease).

Faecal calprotectin has displayed the most promise in the measurement of intestinal inflammation for which conventional diagnostic modalities are often invasive. It is also able to identify inflammation in the small bowel, an area which is not able to be examined fully with standard endoscopy equipment.

Faecal calprotectin can be measured in a single stool, rather than a 24-hour or four-day stool collection, thus improving convenience for patients and laboratory staff. Only 5 grams of faeces is required to be collected in a standard faeces collection pot. Additionally, calprotectin is very stable due to calcium binding, and specimens can be stored for up to 7 days at room temperature before being processed.

While faecal calprotectin is a very sensitive measure of intestinal inflammation, it is not specific for the cause of inflammation. Any cause of intestinal inflammation is able to produce an elevated concentration including inflammatory bowel disease (IBD), infective colitis, diverticulitis, certain drugs and colorectal cancer. Therefore the use of this investigation has potential application in clinical situations where the result will be clinically useful, namely distinguishing intestinal inflammation from functional disorders, and to monitoring the extent of inflammation during therapy for patients with IBD.

Triage of patients to Inflammatory Bowel Disease clinic

Unfortunately there is often a significant time delay between symptoms and a diagnosis of IBD. This leads to unnecessary suffering by the patients and sometimes a less favourable clinical outcome.

The faecal calprotectin assay will help fast track patients to the luminal and IBD clinics at St George's where there are facilities for rigid sigmoidoscopy and flexible sigmoidoscopy to aid rapid investigation and diagnosis.

Limitations of faecal calprotectin

While there is no doubt that faecal calprotectin can be used to separate those with irritable bowel syndrome and inflammatory bowel disease it cannot be relied on as the sole investigation. It helps to fast track those who need urgent endoscopic investigation but it is essential to remember that its use in diagnosing the following causes of diarrhoea has yet to be established:

- Coeliac disease
- Pancreatic exocrine insufficiency
- Microscopic colitis
- Colonic adenomas and colorectal cancers
- Bile salt malabsorption

Conclusions

Faecal calprotectin offers a non-invasive sensitive method of assessing the intestine for inflammation. The major application of the test is in distinguishing inflammation from non-inflammatory disorders; however there is a limitation in that the test does not determine the cause of inflammation. Clinical scenarios (where faecal calprotectin measurement has been shown to be useful) include diagnostic resource allocation for patients presenting with chronic diarrhoea and in determining whether or not gastrointestinal symptoms are inflammatory or functional in patients with known IBD.

Guidelines on the use of faecal calprotectin in General Practice in patients with lower gastrointestinal symptoms

New patients:

Age 16- 40, no alarm symptoms, full-fill Rome III criteria for Irritable Bowel syndrome

Rome III Criteria for I.B.S.

Rome III is a set of diagnostic criteria used to help diagnose IBS.

The basic criteria are as follows:

Recurrent abdominal pain or discomfort at least 3 days per month in the last 3 months associated with 2 or more of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

Red Flag symptoms which are not characteristic of I.B.S.

- Blood in stools
- Weight loss
- Pain during the night that interferes with sleep
- Diarrhoea during the night that interferes with sleep
- Fever/high temperature
- Severe watery diarrhoea

Check FBC, glucose, LFTs, U&Es, CRP, TFT, Ca, ferritin, folate, B12, Coeliac autoantibodies, faecal calprotectin and if diarrhoea stool MC&S.

1. If investigations abnormal refer to gastroenterology.
2. If all investigations normal / negative consider treating as I.B.S. and review in 4-6 weeks.
3. If better discharge.
4. If no better consider referral for further investigation.

Patient with known IBD

Symptoms suggestive of a flare. Check FBC, CRP, LFT, stool culture, *C difficile* toxin and faecal calprotectin.

1. Consider increasing dose of 5-ASA (treatment dose of Pentasa 2g b.d. and Asacol 2.4g b.d.). Consider course of prednisolone. Consider 5-ASA suppository or enema treatment.
2. Contact IBD nurse / patients usual medical / surgical team to arrange urgent OP review.

Further reading:

Poullis A et al. The emerging role of calprotectin in gastroenterology. *Journal of Gastroenterology and Hepatology* 2003;18(7):756-762.

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Tibble J et al. Surrogate markers of intestinal inflammation are predictive of relapse in patients with inflammatory bowel disease. *Gastroenterology*. 2000;119:15-22

Roseth AG et al. Assessment of disease activity in ulcerative colitis by fecal calprotectin, a novel granulocyte marker protein. *Digestion*. 1997;58:176-80.

Limburg PJ et al. Faecal Calprotectin levels predict colorectal inflammation among patients with chronic diarrhea referred for colonoscopy. *Am J Gastroenterol*. 2000;95:2831-7.

Carrocio A et al. Diagnostic accuracy of fecal calprotectin assay in distinguishing organic causes of chronic diarrhea from irritable bowel syndrome: a prospective study in adults and children. *Clinical Chemistry*. 2003;49:861-7.