Faecal calprotectin testing: the new NICE guidelines

The National Institute for Health and Care Excellence has issued new guidelines on the use of faecal calprotectin diagnostic tests for inflammatory diseases of the bowel. As Jason Cunningham explains, these guidelines may have a substantial impact and cause the number of test requests to rocket.

Gastrointestinal disease, including conditions such as inflammatory bowel disease (IBD; most commonly Crohn's disease and ulcerative colitis), irritable bowel syndrome (IBS), coeliac disease and food allergy, is a significant healthcare burden on the NHS.[1,2] Gastrointestinal symptoms are one of the most common complaints patients present with and frequently these symptoms are representative of several gastrointestinal diseases, making it difficult to diagnose on a clinical history alone.[3-6]

In terms of symptoms, IBS and IBD are the two gastrointestinal diseases that are most similar. Common symptoms across both conditions include abdominal pain, chronic diarrhoea, bloating, anaemia, fatigue and depression.[3-6] However, IBS and IBD are somewhat different in terms of pathology, treatment options, prevalence, prognosis and quality of life.

IRRITABLE BOWEL SYNDROME

Irritable bowel syndrome is a functional bowel disorder with no distinctive pathology; therapies are therefore targeted at symptoms and primarily focus on dietary and lifestyle advice, with pharmacological therapy covering antispasmodic agents, laxatives, antimotility agents and tricyclic antidepressants. Exacerbations may be triggered by diet or stress and can be characterised by frequent bouts of bowel disturbance, abdominal pain and bloating.

Although the true prevalence of IBS may be higher than estimated, current data suggest a prevalence of 10–20% in the general population, with data possibly varying due to differences in diagnostic criteria. Irritable bowel syndrome is not associated with the development of serious co-morbidities or a worse prognosis compared to the general population; however, it is associated with a significant reduction in the quality of life.[7]

INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease is a group of conditions that involve inflammation of the gastrointestinal tract, primarily Crohn's disease and ulcerative colitis. Crohn's disease and ulcerative colitis are relapsing and remitting inflammatory diseases.[8] Crohn's disease is a chronic inflammatory disease affecting the gastrointestinal tract; therapies aim to reduce symptoms, while minimising drug toxicity, and as such include inflammatory targeted therapies such as glucocorticosteroid and 5-aminosalicylate treatment, antibiotics, immunosuppressive agents and the use of tumour necrosis factor-α (TNFα) inhibitors.[9]

Crohn's disease can affect any part of the gastrointestinal tract (Fig 1) and commonly presents with symptoms such as abdominal pain, weight loss, diarrhoea, lethargy and anorexia. Some 0.5–1.0% of the population have Crohn's disease and the incidence has been increasing. Crohn's disease is associated with a relatively poor outlook; only 10% of patients will have prolonged remission, 20% need hospital admission each year, and 50% will need surgery within 10 years of diagnosis. Furthermore, Crohn's disease is associated with several serious intestinal complications

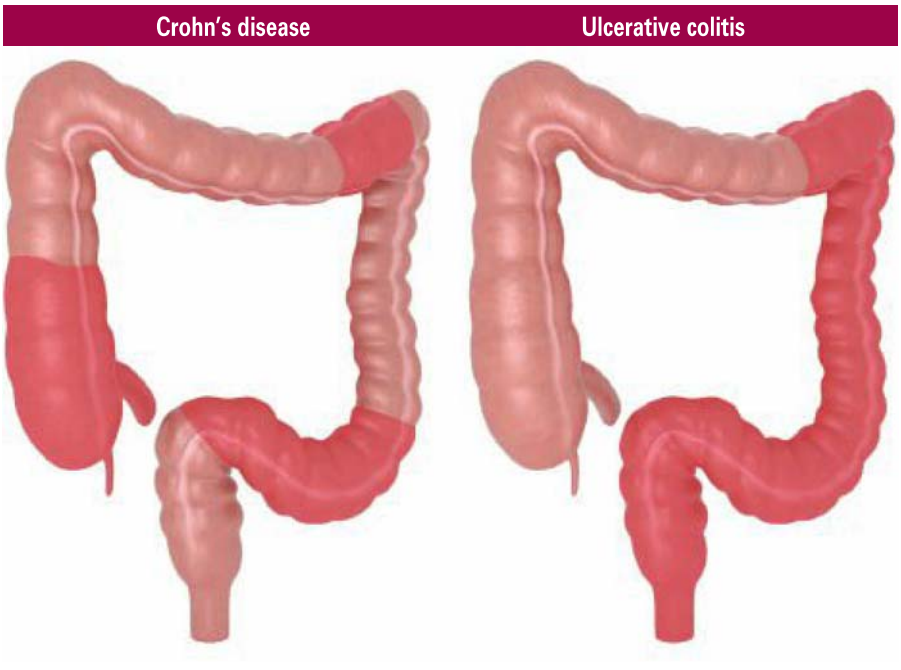

Fig 1. Illustration of inflammatory patterns in Crohn's disease and ulcerative colitis.

including narrowing of the bowel, which presents with acute abdominal pain and requires surgery, and bowel fistulas and colorectal cancer. Additionally, Crohn's disease has a reported 11% reduction in quality of life in patients with remissions and 39% in patients with active disease.[8]

Ulcerative colitis is the most common type of inflammatory disease of the bowel, and is characterised by inflammation of the rectum and a variable extent of the sigmoid colon and descending colon proximal to the rectum (Fig 1). Therapy, primarily using anti-inflammatory agents (eg aminosalicylates, beclometasone dipropionate and cyclosporine), aims to address symptoms, improve quality of life and maintain remission.[10] The inflammation associated with ulcerative colitis is sometimes intense with bloody diarrhoea but is more often milder; at presentation only 10% of patients have severe disease.[8]

Ulcerative colitis is more prevalent than Crohn's disease, occurring in 1–2% of the population. It has a slightly better prognosis than Crohn's disease, with approximately 50% of patients continuing to have mild disease or be in remission. However, in approximately 20% of patients it will be chronic, continuous and may spread along the entire length of the colon. Approximately 10% of patients will need a proctocolectomy to remove the rectum, sigmoid colon and descending colon, but the risk of mortality is comparable with the general population. Ulcerative colitis has a reported 9% reduction in quality of life in patients with remission and 29% in patients with active disease.[8]

In comparison to IBS, IBD (Crohn's disease and ulcerative colitis) is associated with an inflammatory pathology, has treatment options aimed at treating the pathology rather than symptoms, is less prevalent, is associated with a worse prognosis and is more detrimental to the quality of life;[7,8] therefore, it is vital to differentiate correctly between the two conditions and ensure correct patient management and treatment is expedited.

GUIDELINES

The National Institute for Health and Care Excellence (NICE) guidelines on the diagnosis and management of irritable bowel syndrome in primary care[7] state how a diagnosis of IBS can be made on the basis of a clinical history alone. However, they do suggest that patients presenting with abdominal pain or discomfort, bloating or a change in bowel habit for at least six months should be asked if they have, or been tested for, 'red flag' indicators of other conditions such as unexplained weight loss, anaemia, rectal masses, inflammatory biomarkers for IBD and, in patients aged over 60 years, a change in bowel habits. Patients with any of these indicators are then referred to specialist care.

The guidelines state that patients who meet the IBS diagnostic criteria should also have tests for full blood count (FBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tissue transglutaminase (tTG) and endomysial antibodies (EMA) to exclude other diagnoses. The guidelines also state that people who meet the IBS diagnostic criteria should not be referred for ultrasound, investigative endoscopy, thyroid function tests (TFTs), faecal occult blood, faecal parasite investigation or hydrogen breath test.[7] Considering that the two main tests for inflammation are ESR and CRP, and these tests can be influenced by non-intestinal disease and lack diagnostic accuracy, many patients are still referred for endoscopy.[8]

Recent data from NHS hospital episode statistics show that a disproportionate number of patients still undergo investigative endoscopy unnecessarily; approximately 1000 per 100,000 population are referred for this investigation for gastrointestinal symptoms each year, amounting to £610,000. Approximately 30% of these are not followed up, and are therefore unnecessary, amounting to £185,000.[11] There has clearly been a need for a diagnostic test that differentiates between IBD and IBS early in the patient pathway, providing clear diagnostic direction from first presentation of symptoms.

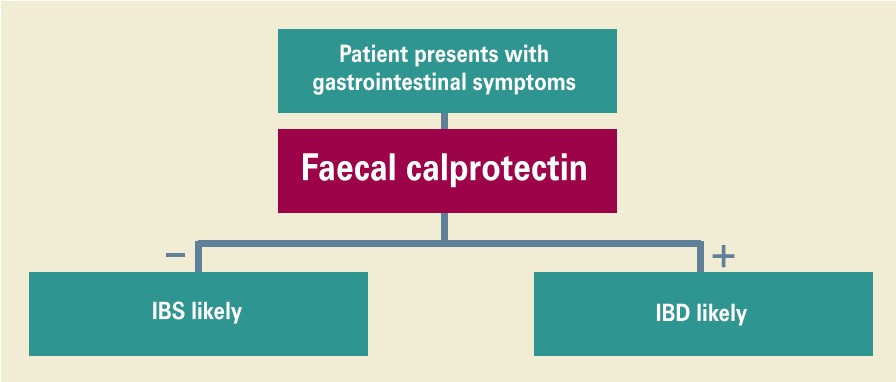

Fig 2. Illustration of the role of faecal calprotectin in patient diagnosis according to the new NICE guidelines on the use of faecal calprotectin diagnostic tests for inflammatory disease of the bowel.[8]

FAECAL CALPROTECTIN TESTING

Faecal calprotectin testing differentiates between IBS and IBD.[12] Calprotectin is a calcium- and zinc-binding protein found in high levels in neutrophils, acts primarily as an antimicrobial agent and is released when the gastrointestinal tract is inflamed.

> 'Although the true prevalence of IBS may be higher than estimated, current data suggest a prevalence of 10–20% in the general population'

It is resistant to enzyme activity and stays active in faeces for almost a week at room temperature.[13] Calprotectin is a highly sensitive and specific marker for the detection of intestinal inflammation, particularly mucosal inflammation, and therefore a positive test result is indicative of IBD.[14,15] In addition to diagnostic applications, there are data to suggest that calprotectin levels correlate with severity of Crohn's disease and ulcerative colitis,[12,16] and that it can be used to predict IBD relapses and optimise therapy in affected patients.[17–19]

WHAT DO THE GUIDELINES SAY?

The new NICE guidelines on faecal calprotectin diagnostic tests for inflammatory disease of the bowel were issued on 2 October 2013, and evaluate the use of faecal calprotectin in differentiating between IBS and IBD.[8] Faecal calprotectin testing is recommended as a clinical option for the differential diagnosis of IBS or IBD in the following cases:

- adults with recurrent-onset lower gastrointestinal symptoms for whom specialist assessment is being considered
- children with suspected IBD who have been referred for specialist assessment.

In addition, these guidelines have been implemented in the NICE pathways for the diagnosis of Crohn's disease, ulcerative colitis and IBS. In the Crohn's disease and ulcerative colitis pathways, faecal calprotectin testing is the first step following the presentation of a person with suspected disease, and is used in the diagnosis of IBS to exclude the possibility of IBD.[20–22]

WHAT DO THE GUIDELINES MEAN?

In essence, the new NICE guidelines advocate the use of faecal calprotectin as a first-line test in patients presenting with gastrointestinal symptoms indicative of IBS or IBD (Fig 2).This will lead to a change in practice, although, as is often the case with new guidelines, it can take time for clinicians to become aware of the new guidelines and implement them. However, when the potential cost savings are factored in to the

present clinical environment – the use of faecal calprotectin as a first-line test to determine the need for an investigative endoscopy could save approximately £180,000 per 100,000 population based on £25 per faecal calprotectin test[11] – the likelihood of implementation by clinical commissioning groups (CCGs) increases significantly.

Implementation of the guidelines at the CCG level will very quickly filter into practice and translate into test requests. An additional factor to consider is that faecal calprotectin testing has been identified as a topic that may benefit from support by the NICE Health Technology Adoption Programme, meaning that when this assessment comes into effect clinicians will be required to adopt faecal calprotectin testing. Bearing in mind the proportion of the population that may be presenting to their clinician with gastrointestinal symptoms, which will need a panel of diagnostic tests including faecal calprotectin, it is easy to anticipate an increase in the number of test requests. It is likely that clinicians will start to request a panel of tests, and, based on the guidelines above, a panel will most likely include common diagnostic tests (eg FBC), a coeliac disease screen and faecal calprotectin.

What the new guidelines will mean to pathology is something that each laboratory needs to reflect upon. This may largely replicate the impact that the coeliac guidelines[23] had on test requests; however, with a stronger cost benefit and a larger IBD/IBS patient population, it is reasonable to assume that the increase in faecal calprotectin test requests will be more rapid and dramatic – the number of test requests could rocket.

When considering the potential impact on laboratory working, individual laboratories will need to consider the potential impact on workload and whether or not their present kit is best suited for handling a significant increase in the number of requests. Several kits are available including fully-automated quantitative laboratory-based technologies, fully quantitative rapid tests and semi-quantitative point-of-care tests. The three most common tests supported for external quality assessment by UK NEQAS are EK-CAL, a quantitative enzyme-linked immunosorbent assay (ELISA; Bühlmann), Quantum Blue, a rapid immunoassay (Bühlmann), and EliA Calprotectin, a fully automated, quantitative fluorescence enzyme immunoassay test (Phadia); however, it rests with the individual laboratory to evaluate its preferences and needs in relation to the testing approach adopted. However, considering the potential impact the new faecal calprotectin guidelines could have on test requests, it may be wise to reflect sooner rather than later. ■

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