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REVIEW

Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on the utility of the determination of faecal calprotectin in inflammatory bowel disease☆

Jordi Guardiola[a,*], Triana Lobatón[b,g], Elena Cerrillo[c,g], Rocío Ferreiro-Iglesias[d], Javier P. Gisbert[e,g], Eugeni Domènech[b,g], María Chaparro[e,g], Maria Esteve[f,g], Francisco Rodríguez-Moranta[a], on behalf of GETECCU

[a] *Servei d'Aparell Digestiu, Hospital Universitari de Bellvitge, Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), Universitat de Barcelona, Hospitalet de Llobregat, Barcelona, Spain*
[b] *Servei d'Aparell Digestiu, Hospital Universitari Germans Trias i Pujol, Badalona, Barcelona, Spain*
[c] *Servei d'Aparell Digestiu, Hospital Universitari i Politècnic La Fe, Valencia, Spain*
[d] *Servicio de Aparato Digestivo, Hospital Clínico Universitario de Santiago de Compostela, Santiago de Compostela, La Coruña, Spain*
[e] *Servicio de Aparato Digestivo, Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IIS-IP), Universidad Autónoma de Madrid, Madrid, Spain*
[f] *Servei d'Aparell Digestiu, Hospital Universitari Mútua Terrassa, Terrassa, Barcelona, Spain*
[g] *Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Spain*

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Abstract The management of inflammatory bowel disease (IBD) is currently based on the objective evaluation of intestinal lesions. It would therefore be interesting to have access to simple and non-invasive tools to monitor IBD activity and to identify the presence of lesions. Faecal calprotectin (FC) is the main cytosolic protein of neutrophils, it is resistant to bacterial degradation and it is stable at room temperature for several days, characteristics that make it suitable for use in clinical practice. It can be used to differentiate between inflammatory and functional processes, it correlates with endoscopic activity, it is associated with clinical and endoscopic response to treatment and it has short-term prognostic value. This paper offers an up-to-date perspective on the information that FC can provide clinicians to aid diagnosis, monitoring and management of IBD.

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* Corresponding author.
E-mail address: jguardiola@bellvitgehospital.cat (J. Guardiola).

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Recomendaciones del Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa (GETECCU) sobre la utilidad de la determinación de calprotectina fecal en la enfermedad inflamatoria intestinal

Resumen Actualmente, el manejo de la enfermedad inflamatoria intestinal (EII) se basa en la evaluación objetiva de las lesiones intestinales. Por ello, es de interés disponer de herramientas sencillas y no invasivas con las que monitorizar la actividad de la EII e identificar la presencia de lesiones. La calprotectina fecal (CF) constituye la principal proteína citosólica de los neutrófilos, es resistente a la degradación bacteriana y estable a temperatura ambiente durante días, características que la hacen adecuada para su uso en la práctica clínica. Es útil para diferenciar entre procesos inflamatorios y funcionales, se correlaciona con la actividad endoscópica, se asocia con la respuesta clínica y endoscópica al tratamiento y tiene valor pronóstico a corto plazo. El presente documento pretende ofrecer una visión actualizada sobre la información que la CF puede proporcionar al clínico en el diagnóstico, la monitorización y el manejo de la EII.

Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are chronic, progressive inflammatory diseases characterised by alternating periods of activity and remission of unpredictable duration. Management of inflammatory bowel disease (IBD) is currently based on the objective assessment of intestinal lesions and, in general, decision-making guided purely by clinical symptoms is not considered appropriate. There are two reasons for this. First of all, gastrointestinal symptoms do not accurately reflect the presence or severity of gastrointestinal lesions. More than a third of patients in clinical remission have endoscopic lesions and, in more than 10% of symptomatic patients, the endoscopy is normal.[1,2] It is therefore easy to see how making therapeutic decisions based purely on the symptoms can lead to serious errors. Secondly, improvement or disappearance of intestinal lesions is known to be associated with a less severe disease course, with less likelihood of complications or the need for hospitalisation or surgery.[3,4] All this has renewed interest in endoscopy and imaging techniques in the assessment of patients with IBD. These methods provide valuable information about the severity and extent of lesions and the development of complications. However, in view of their high cost, limited availability and invasive nature, they are not suitable for periodic monitoring of the disease.

It would therefore be of great benefit to clinicians to have simple and non-invasive tools with which to monitor IBD activity and identify the presence of lesions. A number of serum biomarkers have been proposed, with the most widely used being C-reactive protein (CRP). However, CRP is nonspecific and can be elevated in extraintestinal inflammatory processes.[5] An ideal biomarker should accurately distinguish between the existence and absence of lesions, and be related to their severity and the response to treatment. It should also be widely accessible, easy to use and affordable. To a greater or lesser extent, faecal calprotectin (FC) meets these requirements and it is presently the best characterised commercially available biomarker in IBD.

FC is a calcium-binding protein with antimicrobial, antiproliferative and pro-inflammatory properties. It is derived predominantly from neutrophils, of which it is the main cytosolic protein and, to a lesser extent, from monocytes and activated macrophages. FC is released in very early stages of the inflammatory process and its concentration in the stool is directly proportional to the presence of neutrophils in the intestinal lumen.[6] FC levels show good correlation with the excretion of indium-111-labelled leucocytes[7] and with the permeability of the intestinal mucosa.[8] It is resistant to bacterial degradation and stable at room temperature for days, with these characteristics making it suitable for use in clinical practice.

The aim of this document is to provide an update on the utility of FC in patients with IBD in clinical practice.

Available methods for measuring faecal calprotectin

What methods are available for determining faecal calprotectin?

The most commonly used methods are enzyme-linked immunosorbent assay (ELISA) and lateral-flow immunochromatography, which is used in so-called ''rapid tests''. The antibodies used in both techniques can be polyclonal or monoclonal. The kits that use monoclonal antibodies are preferable as they have shown greater precision.[9,10]

The ELISA tests are the most validated, are cheaper and provide a quantitative result that usually covers a wider range of values. However, they require a specialised laboratory and several dozen samples have to be accumulated in order to make the cost of each determination affordable, with the consequent delay in obtaining the results. In contrast, immunochromatographic tests (rapid tests) have the advantages of not requiring a laboratory and each sample being analysed individually, with the result available in a few minutes. Using a reader with the appropriate software, some of immunochromatographic tests can provide a quantitative