Calprotectin: Non-invasive Gold Standard for the Diagnosis of Bowel Inflammation

IBD or IBS?

Only a small proportion of patients with abdominal discomfort have an organic disease, but a correct diagnosis can rarely be made by simple clinical examination. The acute phase protein calprotectin (MRP 8/14) allows the discrimination between organic and functional intestinal diseases. Calprotectin is the major protein of the neutrophil cytosol. It is excreted in excess in stool during inflammatory bowel disease (IBD) but not during inflammatory bowel syndrome (IBS). The molecule plays an important role in inflammatory processes and has direct antibacterial effects. Calprotectin is a surrogate marker of neutrophil influx into the bowel lumen.

Diagnosis and therapy control of IBD-patients

Faecal calprotectin levels correlate significantly with histologic and endoscopic assessment of disease activity in ulcerative colitis as well as with faecal α1-antitrypsin levels and faecal excretion of ¹¹¹indium-labeled white blood cells in patients with Crohn’s disease. In laboratory analysis of IBD, calprotectin exhibits a higher specificity and sensitivity for bowel inflammations in comparison to lactoferrin and PMN-elastase. In addition, a rise in calprotectin level is earlier detectable than an increase of lactoferrin concentration providing a timely indicator of inflammatory processes in IBD patients. In clinical praxis, Calprotectin has therefore been established as the preferred faecal marker of IBD.

“Calprotectin is ideal for monitoring disease activity in IBD-patients”

Due to these special features, Calprotectin is ideal for monitoring disease activity in IBD-patients. Crohn’s disease and ulcerative colitis are related conditions characterized by periods of remission marked by episodes of clinical relapse. The clinical implications of predicting which IBD-patients are likely to relapse are considerable. Such knowledge allows targeted treatment at an earlier stage (with fewer side effects) to avert the relapse, as well as an assessment of new therapeutic strategies for maintaining symptomatic remission. Calprotectin is therefore the ideal parameter for monitoring disease activity (e.g. of M. Crohn or after polyp resection) and for the early detection of a relapse. Immunological semi-quantitative calprotectin rapid tests (e.g. PreventID® CalDetect, Preventis GmbH) even allow therapy monitoring at home which can be extremely useful in regions where access to medical facilities is difficult or for patients with limited mobility. The differentiation between negative values, slightly increased values and high calprotectin values is important for excluding functional intestinal diseases (e.g. IBS) and for the diagnosis and monitoring of organic intestinal diseases.

These features allow for serial monitoring of IBD disease activity and treatment success, especially in the evaluation of new and empirical drugs. Calprotectin analysis has been able to disclose treatment failure, allowing for these patients to avoid prolonged, useless courses of steroids.
Differential diagnostics of acute diarrhea

Calprotectin is also capable of discriminating between organic and functional diarrhea and provides a positive predictive marker for infectious diarrhea. Increased calprotectin concentrations (> 15 µg/g) indicate invasive pathogens as causative of diarrhea.

In contrast to an acute inflammatory diarrhea, leucocyte markers are not elevated in stool during an acute, non-inflammatory diarrhea. The determination of faecal calprotectin can discriminate between these two forms of diarrhea and thereby prevent a probationary antibiotic therapy. Patients suffering from a non-inflammatory diarrhea will receive dietary and symptomatic treatment. If the calprotectin level is elevated, further diagnostic clarification is necessary to indicate the appropriate drug therapy (see flowchart).

Algorithm depicting the role of faecal calprotectin in managing acute diarrhea:

Viruses (e.g., adenovirus, rotavirus, Norwalk virus) are the most common cause of diarrhea in the United States. Escherichia coli, Clostridium difficile, and Campylobacter, Salmonella, and Shigella organisms are common causes of bacterial diarrhea. Bacillus cereus, Clostridium perfringens, Staphylococcus aureus, Salmonella species, and others cause food poisoning. Entamoeba histolytica, Giardia, Cryptosporidium, and Cyclospora are parasitic/protozoal agents that cause diarrhea.
Easy & reliable lab diagnostics with monoclonal Calprotectin-ELISAs

Various ELISA-systems are available for laboratory determination of faecal calprotectin. Assays with monoclonal antibodies have been proven to be more sensitive and more specific than polyclonal antibodies and therefore deliver more reliable results in the discrimination of chronic and functional diarrhea as well as in the determination of inflammatory activity in ulcerative colitis patients. Overall, the monoclonal test system exhibits a better performance than the polyclonal test system. In general, lab diagnostics is facilitated by the fact that calprotectin resists metabolic degradation and is therefore highly stable in faeces (stable for one week at room temperature).

**Indications for calprotectin determination**

- Differentiation between organic intestinal diseases (e.g. IBD) and functional intestinal diseases (IBS)
- Monitoring disease activity (e.g. of M. Crohn or after polyp resection)
- Monitoring & early detection of a IBD-relapse
- Differentiation between organic diarrhoea and functional diarrhea

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