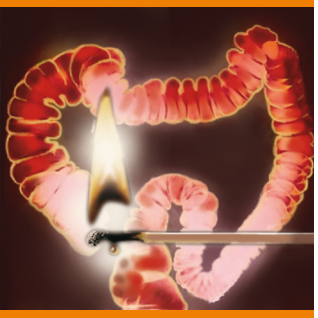


CED oder Reizdarmsyndrom?

PreventID® *CalDetect®*

Schnelltest zum Nachweis des Entzündungsparameters Calprotectin im Stuhl

PreventID® *CalDetect®* ist ein semiquantitativer immunologischer Schnelltest zum Nachweis von Calprotectin im Stuhl. Der Nachweis von fäkalem Calprotectin dient der Diskriminierung zwischen einer chronisch entzündlichen Darmerkrankung und einem Reizdarmsyndrom und eignet sich zur Therapie- und Verlaufskontrolle bei chronisch entzündlichen Darmerkrankungen. Die Verwendung von drei Testlinien ermöglicht die Einstufung in verschiedene Grade einer Calprotectin-Positivität und damit eine Beurteilung des individuellen Krankheitsverlaufs.

Calprotectin liegt hauptsächlich im Zytoplasma neutrophiler Granulozyten vor, dort macht es ca. 60% der löslichen Proteine aus. Das Molekül wird nach Aktivierung von Neutrophilen freigesetzt und spielt eine zentrale Rolle bei der Immunabwehr. Freigesetztes Calprotectin findet sich in Serum, Körperflüssigkeiten oder Stuhl und dient als wertvoller Entzündungsmarker.
Fäkales Calprotectin wird als Surrogatmarker des Neutrophileneintritts in das Darmlumen angesehen. Das Akute-Phase-Protein zeigt eine hohe Stabilität im Stuhl (bis zu 1 Woche bei Raumtemperatur!) und die Bestimmung des fäkalen Calprotectins ist als Marker für entzündliche Darmerkrankungen anerkannt.

Die Bestimmung von Calprotectin ermöglicht eine zuverlässige Differenzierung zwischen organisch bedingten intestinalen Erkrankungen und funktionellen intestinalen Erkrankungen (z.B. Reizdarmsyndrom). Die Bestimmung von Calprotectin eignet sich außerdem zur Verlaufskontrolle der Krankheitsaktivität - z.B. bei Morbus Crohn oder nach Polypektomie - sowie zur Vorhersage von Schüben bei chronisch entzündlichen Darmerkrankungen. Calprotectin kann zusätzlich als positiver prädiktiver Marker für invasive Erreger und damit als Screeningparameter für infektiöse Diarrhöen (Diskriminierung zwischen einer organischen und einer funktionellen Diarrhö) genutzt werden.

Patienten, für die eine Calprotectin-Messung in Frage kommt:

Zum Ausschluss einer CED:

- Erwachsene Patienten mit Symptomen, die mit einer CED übereinstimmen, bei denen das CRP jedoch normal ist und eine Röntgenuntersuchung oder Koloskopie in Erwägung gezogen wird
- Patienten mit einer geringen Abnormalität unklarer Herkunft im Röntgenbild
- Kinder, die aufgrund des dringenden Verdachts einer CED endoskopiert werden sollen
- Schwangere mit CED-Symptomen, bei denen das CRP normal ist

Zur Abschätzung der Krankheitsaktivität:

- Patienten mit bekannter CED und fehlendem CRP-Anstieg
- Patienten mit bekannter CED und erhöhtem CRP aufgrund extraintestinaler Erkrankungen

Differenzierung zwischen organischer und funktioneller Darmerkrankung

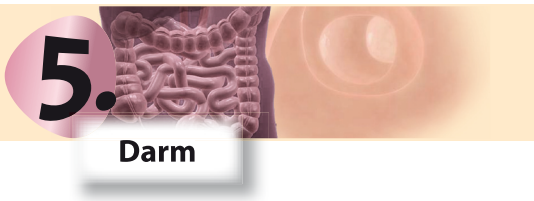
Die Unterscheidung zwischen einem Reizdarm und einer chronisch-entzündlichen Darmerkrankung (CED) gestaltet sich häufig schwierig und führt zu vielen nicht notwendigen Koloskopien. Eine schnelle Abklärung eines entzündlichen Geschehens (verursacht z.B. durch chronisch entzündliche Darmerkrankungen, Infektionskrankheiten, Polypen, Kolonkarzinome) ist mit dem PreventID® *CalDetect®* möglich. Bei gastrointestinalen Erkrankungen entzündlicher und neoplastischer Genese ist fäkales Calprotectin erhöht. Daher eignet sich dieser Parameter zur Differenzierung zwischen organischen Erkrankungen des Intestinaltrakts (z.B. chronisch entzündlichen Darmerkrankungen, Polypen) und funktionellen Erkrankungen (z.B. Reizdarmsyndrom) (Tibble et al. 2000, Tibble et al. 2002).

⇢

preventis
Ihr Partner für patientennahe Diagnostik

PreventID® *CalDetect®*

Arztinfo



Weitere Infos zu diesem und anderen Tests senden wir Ihnen auf Anfrage gerne zu.

Verlaufskontrolle bei der Therapie von CED

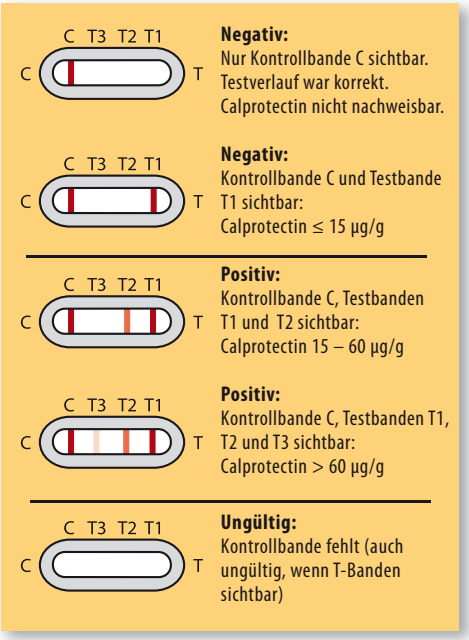
Die Einschätzung der entzündlichen Aktivität bei M. Crohn über klinische oder laborchemische Daten korreliert nur schwach mit Ergebnissen einer Endoskopie. Der bisherige „Gold-Standard" für die Aktivitätsbeurteilung bei CED ist die Messung der fäkalen Exkretion Indium-markierter neutrophiler Granulozyten. Der Indium-Granulozytentest ist jedoch sehr aufwändig (Krankenhausaufenthalt, Isotopenbestimmung) und belastet die Patienten insbesondere mit Radioaktivität. Eine wiederholte Anwendung bei Kindern sollte vermieden werden. Bei Schwangeren sollte dieser Test nicht durchgeführt werden. Mit der Bestimmung von Calprotectin steht ein neuer Marker zur Verfügung, der die entzündliche Aktivität bei M. Crohn widerspiegelt (Tibble 2000; Gaya et al. 2005). Der Nachweis aus Stuhl korreliert sehr gut mit den histologischen und endoskopischen Befunden der Krankheitsaktivität bei Morbus Crohn und Colitis ulcerosa sowie mit dem Indium-Granulozytentest. Ansteigende Calprotectinwerte deuten frühzeitig und mit großer Sicherheit auf ein Rezidiv hin.

Differenzialdiagnose der chronischen Diarrhö

Calprotectin eignet sich sowohl zur Diskriminierung zwischen einer organischen und einer funktionellen Diarrhö als auch als positiv prädiktiver Marker für eine infektiöse Diarrhö (Schirrmacher et al. 2004, Bergis et al. 2005). Ein erhöhter Calprotectin-Wert (> 15 µg/g) deutet auf eine durch invasive Erreger bedingte Diarrhö hin (Schirrmacher et al. 2004).

Einfache Testdurchführung des PreventID® *CalDetect®*

Vor der Testdurchführung eine Stuhlprobe im Probenröhrchen sammeln. Die gelöste Stuhlprobe in das Probenauftragsfenster eintropfen. Nach wenigen Minuten kann das Ergebnis im Ergebnisfenster abgelesen werden.



Interpretation des Testergebnisses

Nach der Testdurchführung lässt sich - je nach sichtbar gewordenen Farbbanden - semiquantitativ eine Aussage über die Calprotectin-Konzentration treffen (s. nebenstehende Abbildung).

Positive Ergebnisse:

Calprotectin-Konzentration 15 - 60 µg/g: Es liegt eine Entzündung im Darmtrakt vor.

Calprotectin-Konzentration > 60 µg/g: Es liegt eine ausgeprägte Entzündung im Darmtrakt vor (Werte in dieser Höhe können z.B. bei M. Crohn- oder Colitis ulcerosa Patienten vorliegen).

Beste klinische Zuverlässigkeit

Der PreventID® *CalDetect®* hat sich in der klinischen Praxis der Differentialdiagnostik von chronisch entzündlichen Darmerkrankungen und Reizdarmsyndrom bewährt und verfügt hier über eine besonders hohe Spezifität (94,5%) und beste Sensitivtät (100%) bei einem cut-off von 15 mg/kg (Otten et al., 2008).

Literatur

Aschauer GJM et al. (2010), Labmed 2010, P054
Tursi A et al. (2009), Int J Colorectal Dis 24:49–55
Otten MT et al. (2008), Clin Chem Lab Med 46(9)
Vestergard TA et al. (2007), Scand J Clin Lab Invest 1 - 5
Schröder O et al. (2007), Aliment Pharmacol Ther Oct 1;26(7):1035-42
Shastri Y et al. (2006), Gastroenterology 130 (4): AGA Abstracts: A-200
Bergis D et al. (2005), Z Gastroenterol 43: 948 (P512)
Gaya DR et al. (2005), QJM 98: 435-441
Schirrmacher S et al. (2004), Z Gastroenterol 42: 785-944 (P013)
Tibble JA et al. (2002), Gastroenterology 123: 450-460
Tibble JA et al. (2000), Gut 47: 506-513

preventis

preventis GmbH
Wiesenstr. 4
D - 64625 Bensheim
Tel.: +49(0)6251/70711-0
Fax: +49(0)6251/70711-25
www.preventis-online.de
info@preventis-online.de

CE

März 2011

Int J Colorectal Dis (2009) 24:49–55
DOI 10.1007/s00384-008-0595-9

ORIGINAL ARTICLE

Faecal calprotectin in colonic diverticular disease: a case–control study

Antonio Tursi · Giovanni Brandimarte · Walter Elisei · Gian Marco Giorgetti · Cosimo Damiano Inchingolo · Fabio Aiello

Accepted: 1 October 2008 / Published online: 22 October 2008

Abstract
Background and aims Information about faecal calprotectin (FC) in colonic diverticular disease (DD) are lacking. We assessed FC in colonic DD, comparing it with irritable bowel syndrome (IBS) patients and healthy controls. Moreover, we compared FC levels in different degrees of DD and assessed FC in symptomatic DD before and after treatment.
Materials and methods Forty-eight consecutive patients with a new endoscopic diagnosis of DD (16 with asymptomatic diverticulosis, 16 with symptomatic uncomplicated DD, 16 with acute uncomplicated diverticulitis), 16 healthy controls, and 16 IBS patients were studied. FC was assessed by semi-quantitative method and compared with histological inflammation. Moreover, FC was reassessed in symptomatic DD after 8 weeks of treatment.
Results/findings FC was not increased in healthy controls and IBS patients. No difference was found between asymptomatic diverticulosis, healthy controls, and IBS patients (p=n.s.). We found higher FC values in acute uncomplicated diverticulitis ($p<0.0005$) and in symptomatic uncomplicated DD ($p<0.005$) than in healthy controls and in IBS patients. FC values correlated with inflammatory infiltrate ($p<0.0005$). FC decreased after treatment to normal values both in acute uncomplicated diverticulitis ($p<0.0005$) and in symptomatic uncomplicated DD ($p<0.005$) after treatment.
Interpretations/conclusions FC may be useful to detect colonic inflammation in DD and in distinguishing symptomatic DD from IBS, as well as in assessing response to therapy in DD.

Keywords Diverticular disease · Faecal calprotectin · Irritable bowel syndrome · Microscopic inflammation

A. Tursi (✉)
Digestive Endoscopy Unit, "Lorenzo Bonomo" Hospital,
Via Torino, 49,
70031 Andria, BA, Italy
e-mail: antotursi@tiscali.it

G. Brandimarte · W. Elisei
Department of Internal Medicine, Division of Gastroenterology,
"Cristo Re" Hospital,
Rome, Italy

G. M. Giorgetti
Clinical Nutrition Unit, "S. Eugenio" Hospital,
Rome, Italy

C. D. Inchingolo
Department of Pathology, "Lorenzo Bonomo" Hospital,
Andria, Bari, Italy

F. Aiello
Department of Statistical and Mathematical Sciences,
University of Palermo,
Palermo, Italy

Introduction

Diverticulosis was once regarded as an uncommon anatomic variant but has become a routine finding in older patients in western countries. In particular, its prevalence has risen from 5% to more than 50% in the last century [1].

Recent observations suggest that diverticular disease (DD) could be considered as a chronic inflammatory bowel disease (IBD). In fact, mesalazine, a 5-ASA anti-

inflammatory drug widely used in the treatment of IBD, has been recently found very effective in treating both symptomatic uncomplicated and symptomatic recurrent DD [2]. The inflammatory background has been recently confirmed by a histological study that found an inflammatory infiltrate in DD higher than healthy controls and related to different degrees of DD [3].

Faecal calprotectin (FC) is a cytoplasmic antimicrobial compound prominent in granulocytes, monocytes, and macrophages. It accounts for approximately 60% of the total cytosolic protein. It is released from cells during cell activation or death, and it is stable in faeces for several days after excretion [4]. This has been shown to be a sensitive marker of activity in Crohn's disease (CD) and to be correlated well with endoscopic and histological activity in ulcerative colitis (UC) [5–8]. Finally, this inflammatory marker is considered a stronger predictor of relapse in UC than in CD [9].

Increased levels of faecal calprotectin may also be found in patients harbouring colonic polyps [10] but not in celiac disease [11]. A recent study found slightly increasing faecal calprotectin levels in diverticulosis than in healthy controls, but information about a specific correlation between levels of faecal calprotectin and clinical degree of colonic DD are lacking [11].

Aims of this study were, therefore:

1. to assess the faecal calprotectin in colonic DD and to compare it with those assessed in a group of subjects affected by irritable bowel syndrome (IBS), matched for sex and age. We enrolled another group constituted by healthy subjects matched for sex and age as well;
2. to assess the faecal calprotectin values in different degrees of colonic DD and to compare them with mucosal inflammation;
3. to assess the effect of medical treatment of symptomatic DD on FC levels.

Materials and methods

Patients

We enrolled in this study 48 consecutive patients who had undergone a total colonoscopy, affected by different degrees of colonic DD, and in which DD was diagnosed for the first time.

The patients were divided as follows:

- 16 patients affected by asymptomatic diverticulosis who had undergone a total colonoscopy for colon cancer screening but without any symptom nor signs of diverticular inflammation;
- 16 patients affected by symptomatic uncomplicated DD (symptomatic DD without signs of diverticular inflammation) who had undergone a total colonoscopy for long-lasting or recurrent abdominal pain [12];
- 16 patients affected by acute uncomplicated diverticulitis (symptomatic DD with signs of diverticular inflammation but without complications) who had undergone a total colonoscopy for abdominal pain with signs of inflammation (increased erythrosedimentation rate, serum C-reactive protein and/or white cell count) and after exclusion of complications by abdominal computed tomography scan [12–14].

Patients affected by colonic polyps (including hyperplastic polyps) or colon cancer were excluded. Other exclusion criteria were: personal or family history of colonic neoplasia, IBD (including segmental colitis associated to diverticula [15]), large bowel resection. Moreover, patients taking non-steroidal anti-inflammatory drugs or COXibs for less than 4 weeks were also excluded.

The control groups consisted of two groups:

- 16 subjects matched for sex and age, affected by IBS. All that patients suffered from abdominal pain and had undergone a total colonoscopy but without evidence of any disease (both DD, IBDs and polyps or cancer). In addiction, those patients underwent first-step haematology and chemistry tests (including erythrocyte sedimentation rate, serum C-reactive protein, blood cell counts, electrolytes and thyroid, liver and renal function), serologic assays for suspected celiac disease (anti-gliadin IgA and IgG and anti-transglutaminase IgA and IgG), stool examination for occult blood, ova and parasites and a lactose H_2 breath test. Those patients were considered to be suffering from IBS according to the Rome II criteria [16];
- 16 healthy subjects matched for sex and age, designed as healthy controls, who underwent total colonoscopy for colon cancer screening but without evidence of any disease (both DD, inflammatory diseases and polyps or cancer).

Also in those groups, patients taking non-steroidal anti-inflammatory drugs or COXibs were excluded.

Endoscopic procedures

All patients underwent the same standard bowel preparation prescribed in our centres consisting of an oral polyethylene glycol solution (Selg-Esse, Promefarm, Milano, Italy) to be taken in the evening. The day after, a pancolonoscopy (clean colon colonoscopy) was performed and six bioptic samples of colonic mucosa were collected in the sigmoid tract for histological examination.

In DD, biopsies were taken from the mucosa between diverticula. The presence of inflammatory infiltrate was assessed by a semi-quantitative lymphocytic and neutrophils count on ten colonic fields with high power field (HPF) technique at ×40 magnification, assessed not only in the epithelium but also in the whole lamina propria. Haematoxilin and eosin staining was performed to assess the histology of the sigmoid tract.

Histological assessment

Count lymphocyte assay (CLA) for T cells was performed by immunohistochemical detection of lymphocytes by an anti-CD3 monoclonal antibodies. Lymphocyte infiltration was graded as follows: three to five cells, normal lymphocytic infiltrate (score=0); six to eight cells, mild (score=1); nine to ten cells, moderate (score=2); >10 cells, severe (score=3). Neutrophilic infiltrate was also evaluated in order to assess active or non-active inflammation by using an arbitrary and semi-quantitative grading: non-active (absence of neutrophilic infiltrate, score=0); mild active (focal presence of neutrophils, score=1); moderate (presence of neutrophils intermediate between mild and severe, score=2); severe (diffuse neutrophilic infiltrate, score=3). Neutrophils were localised by myeloperoxidase staining as well as immunohistochemical reactivity using an anti-CD15 monoclonal antibodies.

Faecal calprotectin assessment

In all patients, we assessed faecal calprotectin after performing colonoscopy and before starting therapy. Each subject was instructed to collect and return a single stool sample within 24 h of defecation. Upon receipt, the stools were stored at 2–8°C according to the manufacturer's instructions.

Stool samples were prepared and analysed using a new quick and cheap test (CAL Detect®, Sofar SpA, Trezzano Rosa, Milan, Italy). This semi-quantitative test was developed from the quantitative enzyme-linked immunosorbent assay method regarded as the gold standard. The result of this test was given in one to four bands of colour, the numbers indicating increasing calprotectin concentration.

After unscrewing the cap of the sample collection device, the stick of the attached collection was stuck into the faeces for approximately 2 cm. The sample collection stick was retracted with the adhering faecal sample and inserted into the collection device containing an extraction buffer solution. The caps were screwed on firmly and shaken well. After repeating these two steps one more time, the tip of the sample collection device was broken off carefully and two drops of the extracted solution were squeezed into the round sample opening. The manufacturer suggests the following interpretation of the results:

1. a solitary control line (C) in the results windows indicates that the test has run correctly and calprotectin is undetectable;
2. the presence of two colour bands (C and T1) within the results windows indicates a calprotectin concentration ≤15 μg/g: absence of bowel inflammation;
3. the presence of three colour bands (C, T1 and T2) within the results windows indicates a calprotectin concentration between 15 and 60 μg/g: an inflammatory process is going on in the mucosa;
4. the presence of four colour bands (C, T1, T2 and T3) within the results windows indicates a calprotectin concentration higher than 60 μg/g: a high-grade inflammatory process is going on in the mucosa.

These results could be interpreted after 3 min.

Follow-up

After the assessment of DD degree and after the assessment of faecal calprotectin, the patients affected by symptomatic DD were medically treated. Patients with asymptomatic diverticulosis did not undergo any treatments. Patients suffering from acute uncomplicated diverticulitis were treated with mesalazine 2.4 g/day plus rifaximin 800 mg/day for 10 days, followed by mesalazine 1.6 g/day for 8 weeks [17]. Patients suffering from symptomatic uncomplicated DD were treated with mesalazine 1.6 g/day for 8 weeks [17]. At the end of the eighth week of treatment, FC was reassessed in all those patients.

Statistics

The means of faecal calprotectin of the different groups underwent statistical evaluation. Moreover, the means of faecal calprotectin before and after treatment also underwent statistical evaluation. Statistical evaluation was carried out by using Wilcoxon test with Yate's correction for small numbers and Mann–Whitney two samples *U* test, as appropriate.

The means of FC was compared also to inflammatory infiltrate. The correlation between FC values and inflammatory infiltrate was assessed as co-graduation. Since we should compare different ties, it was carried out by using the Goodman and Kruskal gamma coefficient. Statistically significant difference was considered positive when $p<0.05$.

Ethics approval

This study was approved by the Institutional Review Board and each subject gave written informed consent to participate to the study.

Results

The diverticular patients, the healthy controls, and the IBS patients did not differ for age distribution (see Table 1). We also failed to find increasing FC in asymptomatic diverticulosis. It was detected in 13/16 (81.25%) of patients: in all cases, but one, it was <15 μg/g, and 1/16 patient (6.25%) showed concentration between 15 and 60 μg/g (see Fig. 1). Although any statistical differences with healthy controls (p=0.312, n.s.) and IBS patients (p=0.117, n.s.) were found, the FC more easily detectable in those patients may be probably related to the increased inflammatory infiltrate in asymptomatic diverticulosis [3].

FC increased only in symptomatic DD. We found higher FC values in acute uncomplicated diverticulitis, and in symptomatic DD than healthy controls, showing a statistically significant difference (p<0.0005 in acute uncomplicated diverticulitis and p<0.005 in symptomatic DD; see Fig. 1). The same results were obtained comparing FC values in acute uncomplicated diverticulitis, symptomatic DD, and IBS patients (p<0.0005 in acute uncomplicated diverticulitis and p<0.005 in symptomatic DD; see Fig. 1).

FC did not increase in IBS patients. It was detected in 7/16 (43.75%) patients, and also in this population, FC was always <15 μg/g (absence of inflammation) without any statistical differences with healthy controls (p=0.312, n.s.; see Fig. 1). Also, in healthy controls, we did not find an increase in FC values. It was detectable in 5/16 (31.25%) patients, but in all cases, it was <15 μg/g (absence of inflammation; see Fig. 1).

FC values seem to correlate with inflammatory infiltrate. Looking at Fig. 2, we can see that FC values increase according to the increase of inflammatory infiltrate, showing a statistically significant correlation (p<0.0005). We can note that lower FC values are detectable both in healthy people and in asymptomatic diverticulosis; on the contrary, those values rapidly increase in symptomatic DD and acute diverticulitis, whilst the lymphocytic infiltrate does not increase so rapidly. This is probably related to the presence of a neutrophilic infiltrate in these last degrees of DD.

Focal presence of lymphocytes was detected in healthy controls, but only two of them showed a lymphocytic infiltration >5 (mean/median lymphocytic score=3.68/4.0). Lymphocytic infiltration was also detected in six IBS patients (mean/median lymphocytic score=3.69/5.0). Conversely, significant inflammatory infiltrate was found only in DD. Lymphocytic infiltrate seems to be increased according to the disease severity, ranging from a mean/median value of 5.62/6.0 in asymptomatic diverticulosis to a mean/median value of 7.31/7.0 in symptomatic DD and 12.44/12.5 in acute uncomplicated diverticulitis.

Scattered neutrophils were sometimes found in symptomatic DD (mean neutrophilic score=0.5), but a neutrophilic infiltrate was found only in acute uncomplicated diverticulitis. In none of these patients we found a severe neutrophilic infiltrate and it was absent in one patient; on the other hand, it was found as mild infiltrate in 11 patients and as moderate in six patients. The mean neutrophilic score was 1.65.

Finally, FC decreased after treatment in both degrees of symptomatic DD. After treatment with mesalazine/rifaximin for 10 days, followed by mesalazine alone for further 8 weeks, FC values decreased to normal values in acute uncomplicated diverticulitis, showing a statistically significant difference (p<0.0005; Fig. 3). Also, in symptomatic uncomplicated DD, we obtained the same results. After 8 weeks of treatment with mesalazine, FC values decreased to normal values: also, in this case, we found a statistically significant difference (p<0.005; Fig. 4).

Discussion

The clinical approach to DD in clinical practice has changed. For many years, DD has been considered as a "bacterial-related disease": the bacterial overgrowth related to the diverticulum obstruction by inspissated stool in its neck, led to diverticular inflammation ultimately leading to perforation [2]. However, recent studies have found mesalazine and probiotics effective in the treatment of DD [18, 19]. These results seem to be related to surprising similarities between DD and IBD: in fact, an inflammatory infiltrate may be detectable in the colonic mucosa of patients affected by DD rather than in healthy controls and inflammatory grading seems to be related to the clinical

Table 1 Demographic characteristics of the studied population

	Healthy controls	Irritable bowel syndrome	Asymptomatic diverticulosis	Symptomatic uncomplicated DD	Acute uncomplicated diverticulitis
Males/females	7/13	6/12	8/10	7/11	6/12
Median age in years (SD)	60.6 (±12)	58.2 (±13)	63.6 (±13)	64.6 (±11)	61.4 (±11)
p value	//	n.s.	n.s.	n.s.	n.s.

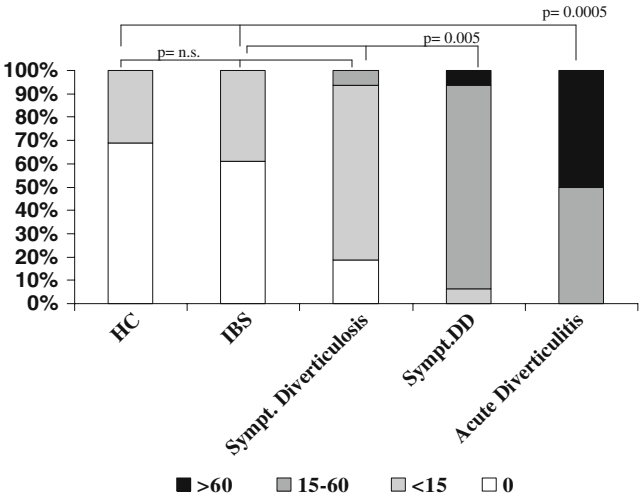


Fig. 1 Faecal calprotectin in healthy controls, IBS and different degrees of diverticular disease. *HC* healthy controls, *IBS* irritable bowel syndrome, *DD* diverticular disease

severity of the disease [3]. However, this method is quite cumbersome in clinical practice in distinguishing different degrees of DD. Since FC seems to be a useful non-invasive marker in detecting colonic inflammation [20], we performed this study attempting to find the role of FC in detecting colonic inflammation in DD.

The most interesting finding of this study is that FC may be an interesting tool in differentiating symptomatic uncomplicated DD from IBS. A relevant clinical problem is to distinguish symptomatic uncomplicated DD from IBS. Since symptomatic uncomplicated DD and IBS share most symptoms (abdominal pain/discomfort, flatulence, alteration of bowel movements), we cannot exclude that DD and IBS may coexist in the same patient.

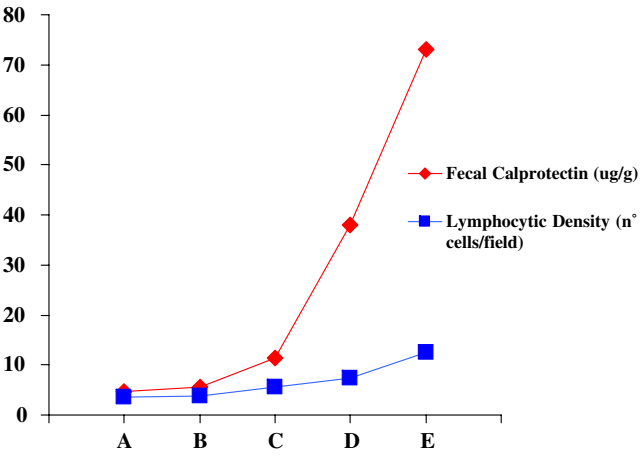


Fig. 2 Correlation between lymphocytic density and faecal calprotectin. *A* healthy controls, *B* IBS patients, *C* asymptomatic diverticulosis, *D* symptomatic diverticular disease, *E* acute uncomplicated diverticulitis

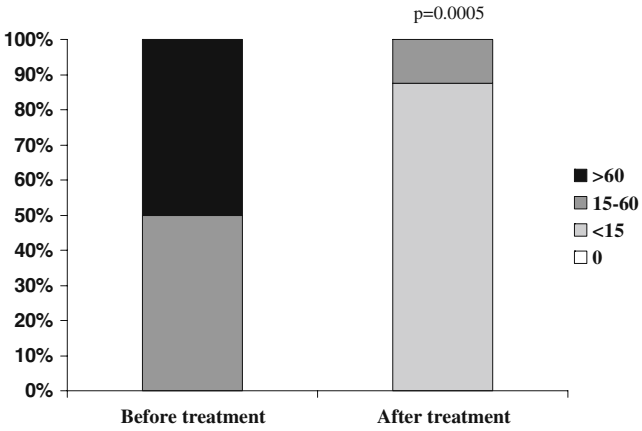


Fig. 3 Faecal calprotectin before and after treatment in acute uncomplicated diverticulitis

Two studies in the earlier 2000s found FC effective in distinguishing IBDs from IBS, showing high sensitivity and specificity [21, 22]. We found, for the first time, that FC may be effective in distinguishing symptomatic uncomplicated DD from functional diseases. The use of a non-invasive tool able to detect inflammation may be useful in distinguishing symptoms coming from colonic inflammation from functional symptoms. This approach may be useful, therefore, in starting a specific therapy avoiding the risk of over-treatment.

Another interesting finding of this study is that we found, for the first time, that FC increased in all degrees of symptomatic DD except asymptomatic diverticulosis with values significantly higher than in healthy controls. These results are in line to those recently described by Montalto et al. who found that FC did not differ in untreated celiac disease patients from those in healthy controls [11]. In fact, celiac disease shows a slight increase in the number of plasma cells and lymphocytes in the lamina propria [23], similar to that found in asymptomatic diverticulosis [24].

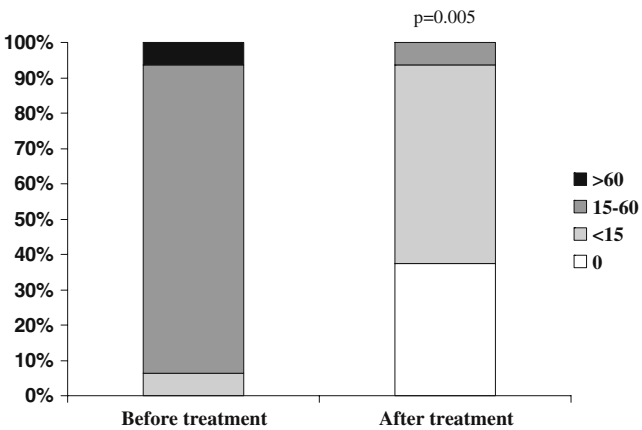


Fig. 4 Faecal calprotectin before and after treatment in symptomatic uncomplicated diverticular disease

We found that FC values are related to the degree of the DD. This is another interesting point, since different FC sensitivities in different degrees of DD have not been reported previously. FC values may be useful in distinguishing milder to severe colonic inflammation. The increasing FC values in patients affected by acute uncomplicated diverticulitis are consistent with the different colonic inflammatory infiltrates detected in different degrees of DD. In fact, inflammatory infiltrate in symptomatic uncomplicated DD is characterised by a prevalently lymphocyte infiltration of the mucosa, whilst acute uncomplicated diverticulitis is characterised by a diffuse lymphocyte infiltration with numerous neutrophils [3] (see Fig. 1).

The last interesting finding of this study is that FC values decreased after treatment in both symptomatic uncomplicated DD and acute uncomplicated diverticulitis, showing values similar to those of healthy controls and IBS patients (Figs. 3 and 4). This is an important point in clinical practice. Some symptomatic score have been developed in assessing clinical response to therapy [18, 19]. Moreover, we found, on biopsy samples, that inflammatory infiltrate may decrease with treatment [20], but this method to assess inflammatory decrease is quite cumbersome. Objective methods assessing the real reduction of inflammation in DD are, therefore, lacking. We found, for the first time, that FC values decreased after treatment in DD. FC seems to be, therefore, also effective in monitoring therapeutic response in DD, may be a useful tool in monitoring the clinical outcome in DD and may assess the real recurrence of the disease from symptoms coming from overlapping IBS. In this way, FC may play the same role in monitoring the disease activity in IBDs. In fact, FC has been proven effective in monitoring the disease's activity, and it has been proposed that FC is a stronger predictor of relapse in UC than CD [25]. On the other hand, it is less probable that FC may be useful in differentiating symptomatic DD from IBD. Most patients affected by symptomatic DD or IBD may show the same symptoms (diarrhoea, abdominal pain, rectal bleeding, etc). It is probable that these patients may show positivity for one or more biological markers of inflammation (FC, C-reactive protein, faecal blood test, etc.) and, therefore, none of them may be useful to differentiate symptomatic DD from active IBD. Further prospective studies are needed to investigate this point.

Despite these results, we cannot forget the limitation in using FC in detecting inflammation. Sensitivity, specificity, positive and negative predictive value may vary by using different methods in detecting FC. In fact, the quantitative method showed higher sensitivity and specificity in detecting inflammation than the qualitative method [26]. Another limitation may be related to sample collection. We used a semi-quantitative method, which showed a good sensitivity and specificity but requires careful evaluation in patients with small or aqueous faeces [27].

In conclusion, our results suggest that FC may be a useful tool in detecting inflammation in the colon harbouring diverticula. FC may be useful in distinguishing symptoms coming from diverticular inflammation from those coming from IBS. Moreover, FC values seem to be related to the degree of the DD, are higher than in healthy people and IBS people and decrease after treatment.

References

1. Floch MH, Bina I (2004) The natural history of diverticulitis: fact and theory. J Clin Gastroenterol 38(suppl. 5):2–7
2. Tursi A (2004) Acute diverticulitis of the colon—current medical therapeutic management. Expert Opin Pharmacother 5:145–149
3. Tursi A, Brandimarte G, Giorgetti GM, Elisei W, Inchingolo CD, Danese S, Aiello F (2008) Assessment and grading of mucosal inflammation in colonic diverticular disease. J Clin Gastroenterol 42:699–703
4. Costa F, Mumolo MG, Bellini M, Romano MR, Ceccarelli L, Arpe P, Sterpi C, Marchi S, Maltinti G (2003) Role of faecal calprotectin as non-invasive marker of intestinal inflammation. Dig Liver Dis 35:642–647
5. Tibble JA, Teahon K, Thjodleifssan B et al (2000) A simple method for assessing intestinal inflammation in Crohn's disease. Gut 47:506–513
6. Roseth AG, Aadland E, Jahnsen J, Raknerud N (1997) Assessment of disease activity in ulcerative colitis by faecal calprotectin, a novel granulocyte marker protein. Digestion 58:176–180
7. Roseth AG, Fagerhol M, Aadland E, Schjonsby H (1992) Assessment of neutrophil dominating protein calprotectin in feces. A methodological study. Scand J Gastroenterol 27:793–798
8. Teahon K, Roseth AG, Foster R, Bjarnason I (1997) fecal calprotectin: a simple sensitive quantitative measure of intestinal inflammation in man. Gastroenterology 112(suppl.):A1103
9. Costa F, Mumolo MG, Ceccarelli L, Bellini M, Romano MR, Sterpi C, Ricciuti A, Marchi S, Bottai M (2005) Calprotectin is stronger predictive marker of relapse in ulcerative colitis than in Crohn's disease. Gut 54:364–368
10. Pezzilli R, Barrassi A, Morselli Labate AM, Tinozzi S, Fantini I, Gizzi G, Latzniker M, Villani V, Melzi D'Eril G, Corinaldesi R (2008) Fecal calprotectin levels in patients with colonic polyposis. Dig Dis Sci 53:47–51
11. Montalto M, Santoro L, Curigliano V, D'Onofrio F, Cammarota G, Panunzi S, Ricci R, Gallo A, Greco A, Gasbarrini A, Gasbarrini G (2007) Faecal calprotectin in untreated coeliac patients. Scand J Gastroenterol 42:957–961
12. Köhler L, Sauerland S, Neugebauer E, for the Scientific Committee of the European Association for Endoscopic Surgery (E.A.E.S.) (1999) Diagnosis and treatment of diverticular disease. Results of a Consensus Development Conference. Surg Endosc 13:430–436
13. Pereira JM, Sirlin CB, Pinto PS, Jeffrey RB, Stella DL, Casola G (2004) Disproportionate fat stranding: a helpful CT sign in patients with acute abdominal pain. RadioGraphics 24:703–715
14. Tursi A, Brandimarte G, Giorgetti GM, Elisei W, Maiorano M, Aiello F (2008) The clinical picture of uncomplicated versus complicated diverticulitis of the colon. Dig Dis Sci 53:2474–2479
15. Lamps LW, Knapple WL (2007) Diverticular disease-associated segmental colitis. Clin Gastroenterol Hepatol 5:27–31

16. Thompson WG, Longstreth GF, Drossmann DA, Heaton KW, Irvine EJ, Müller-Lissner SA (1999) Functional bowel disorders and functional abdominal pain. Gut 45(suppl. II):II43–II47
17. Tursi A (2007) New physiopathological and therapeutic approaches to diverticular disease of the colon. Expert Opin Pharmacother 8:299–307
18. Di Mario F, Aragona G, Leandro G, Comparato G, Fanigliulo L, Cavallaro LG, Cavestro GM, Iori V, Maino M, Moussa AM, Gnocchi A, Mazzocchi G, Franzè A (2005) Efficacy of mesalazine in the treatment of symptomatic diverticular disease. Dig Dis Sci 50:581–586
19. Tursi A, Brandimarte G, Giorgetti GM, Elisei W (2006) Mesalazine and/or *Lactobacillus casei* in preventing recurrence of symptomatic uncomplicated diverticular disease of the colon: a prospective, randomized, open-label study. J Clin Gastroenterol 40:312–316
20. Shitrit AB, Braverman D, Stankiewics H, Shitrit D, Peled N, Paz K (2007) Fecal calprotectin as a predictor of abnormal colonic histology. Dis Colon Rectum 50:2188–2193
21. Tibble JA, Sigthorsson G, Foster R, Forgacs I, Bjarnason I (2002) Use of surrogate markers of inflammation and Rome criteria to distinguish organic from non-organic intestinal disease. Gastroenterology 123:450–460
22. Carroccio A, Iacono G, Cottone M, Di Prima L, Cartabellotta F, Cavataio F, Scalici P, Montalto G, Di Fede G, Ricci G, Notarbartolo A, Averna MR (2003) Diagnostic accuracy of fecal calprotectin assay in distinguish organic causes of chronic diarrhea from irritable bowel syndrome: a prospective study on adults and children. Clin Chem 49:861–867
23. Marsh MN, Crowe PT (1995) Morphology of the mucosal lesion in gluten sensitivity. Baillieres Clin Gastroenterol 9:273–293
24. Tursi A, Brandimarte G, Elisei W, Giorgetti GM, Inchingolo CD, Aiello F (2008) Effect of mesalazine on epithelial cell proliferation in colonic diverticular disease. Dig Liver Dis 40:737–742
25. Desai D, Faubion WA, Sandborn WJ (2007) Review article: biological activity markers in inflammatory bowel disease. Aliment Pharmacol Ther 25:247–255
26. Langhorst J, Elsencruch S, Koelzer J, Rueffer A, Michalsen A, Dobos GJ (2008) Noninvasive markers in the assessment of intestinal inflammation in inflammatory bowel diseases: performance of fecal lactoferrin, calprotectin, and PMN-elastase, CRP, and clinical indices. Am J Gastroenterol 103:162–169
27. Vestergaard TA, Nielsen SL, Dahlerup JF, Hornung N (2007) Fecal calprotectin: assessment of a rapid test. Scand J Clin Lab Invest i:1–5

irradiation magnetic field to tumor cells were established: 120 mT and 320 mT. The entrapment of magnetized immunocytes into tumor cells was verified with anti-CD8, -CD14, and -CD56 fluorescent antibodies. The production ability of IL4 and IFN was measured to evaluate the activation of magnetized immunocytes, and dead cell rate was determined by viability fluorescent multistaining to assess antitumor effect. Results: The APC and CTL combination group and the NK cell-alone group provided completely contrasting results with respect to their antitumor effect for HT29 and DLD1 cells. The death of not less than 40% of HT29 cells was successfully verified in the APC and CTL combination group. However, the death of HT29 cells could not be verified at all in the NK cell-alone group. Dead cells, when found, were NK cells. In contrast, the death of DLD1 cells could not be verified in the APC and CTL combination group. However, nearly 50% of NK cells died. In HT29 cells, furthermore, the antitumor effect-enhancing effect of the magnetized cytokine combination was effective in the APC and CTL group. In DLD1 cells, NK cells tended to be continuously effective; the activation of respective immunocytes and the enhancement of their antitumor effect were verified. Conclusions: Prolonged stay of magnetized immunocytes at the site of tumor was verified to enhance antitumor effect. Furthermore, our data suggested the magnetized cytokines' potential of controlling the negative feedback at the site of tumor.

W1299

Prevention of GI Absorption of Bacterial Toxins: An *In Vitro* Evaluation of the Potential for Prophylactic Use of a Novel Oral Adsorbent (AST-120)

Keith Anderson, Laurent Fischer

Background:AST-120 is currently in clinical trials for fistulizing Crohn's disease, Pouchitis, IBS, PPI-resistant GERD and Hepatic Encephalopathy. AST-120 is a carbonaceous microsphere with very high specific surface area (>1600 m^2/g). After oral administration, AST-120 is not systemically absorbed. It selectively and irreversibly adsorbs a broad range of organic compounds putatively involved in inflammation of the digestive tract. Bacterial toxins have been implicated in exacerbating and perpetuating inflammation in the gut. This work details an *In Vitro* examination of the potential for AST-120 to bind known exotoxins in support of a mechanistic-based approach for prevention and/or reduction in symptomatology of disease related to presence of bacterial toxins. Methods: E. coli, S.dysenteriae, V.cholerae and C.difficile were obtained from ATCC(Manassas,VA). Bacterial cultures were incubated in Tryptic Soy Broth (TSB) overnight at 37°C. When cultures reached target density, the cells were lysed via centrifugation at 900g for 20-30 min at 4°C and supernatants were resuspended in phosphate buffered saline (pH 7.4). 0.25g of AST-120 was added to 25 mL of PBS/toxin combinations representing low, medium and high toxin concentrations. Flasks were incubated over a 6h period at 37°C while shaking at 78 rpm. Residual toxin concentrations were quantitated by standardized test kits applying immunoassay technology for the E. coli STa toxin or reverse passive latex agglutination technology for Shiga toxin (STx), Cholera toxin CT) and C.difficile Toxin (Toxin A). Results: The specific binding affinity of AST-120 for bacterial toxins is detailed in the table below. Discussion: AST-120 has demonstrated binding affinity for known potent bacterial exotoxins. Although the features of AST-120 are not optimized for adsorption of proteins, it has been confirmed that binding capacity for these exotoxins are retained. It is postulated that the ability of AST-120 to improve symptomatology in inflammatory disease processes is, in part, conferred by the ability to irreversibly adsorb bacterial exotoxins thus preventing end organ damage. AST-120 is a broad range scavenger of inflammatory mediators and/or stimulants present in the GI tract and has been designed for chronic treatment of inflammatory GI diseases. Further investigation for use of AST-120 in prevention of clinical complications linked to bacterial toxins is warranted.

Toxin	Specific Binding Capacity (relative to AST-120)
E. coli heat stable enterotoxin (STa)	925 ng / g
S. dysenteriae Type 1 Shiga Toxin (STx)	413 ng / g
V. cholerae Cholera toxin (CT)	425 ng / g
C. difficile Toxin A	150 ng / g

W1300

AST-120: A Novel, Engineered Carbon Microsphere Product for Use in Chronic Inflammatory Bowel Disease and Liver Dysfunction

Keith Anderson, Shigemi Tomiyama, Toyohiko Nitta

Background:AST-120 is currently in clinical trials for fistulizing Crohn's disease, Pouchitis, IBS, PPI-Resistant GERD, and Hepatic Encephalopathy. AST-120 consists of microspheres 200-400 µm in diameter with an extremely high specific surface area of > 1600 m^2/g. The microspheres consist of a carbon scaffold (> 94% carbon) with a defined acidic/alkaline functionality at the surface,which has been optimized to adsorb select low MW pro-inflammatory mediators. The bulk of the adsorptive surface resides in the interior of the product,providing a highly porous network of channels inside the microspheres. The engineered design of AST-120 has created a broad-spectrum oral adsorbent (compounds < 10kD MW) which can be administered on a chronic basis. This study details differential features of AST-120 that support clinical applications for chronic use. Methods: 10mg/dL solutions of test compounds were prepared in pH 7.4 phosphate buffer. AST-120 or activated charcoal (AC, USP) were suspended in above buffer systems at 50 mg/mL for low MW organics and at 2.5 mg/mL for higher MW proteins. Suspensions were incubated for 3hr under constant agitation at 37°C (lipase,chymotrypsin and trypsin experiments conducted at 21°C). Residual analyte was detected by total organic carbon or UV_{282} spectrometry and quantitated against appropriate controls. Results: Normalized % removal from solution in a head-to-head comparison of known inflammatory mediators and digestive enzymes (bold) are presented in the table below. Discussion: The binding kinetics of AST-120 are delayed, thus allowing use of concomitantly administered medications without altering PK or absorption profiles. AST-120 represents a product that binds putative pro-inflammatory mediators to an equivalent or greater extent than Activated Charcoal, with significantly reduced binding affinity to higher MW proteins, especially digestive enzymes, allowing patients to maintain nutritional status during chronic courses of therapy.

Compound	AST-120	Activated Charcoal, USP
DL-β-aminoisobutyric acid	88.0	41.9
Aspartylglycine	93.3	82.7
Dimethylamine	49.8	22.0
Putrescine	83.9	72.4
Guanidinosuccinic acid	64.1	66.6
Creatinine	96.0	95.9
Indoleacetic acid	97.3	97.5
p-hydroxyphenylacetic acid	96.6	98.4
α- amylase	2.7	99.9
Pepsin	7.1	99.7
Lipase	30.6	99.4
Chymotrypsin	10.2	99.6
Trypsin	4.3	99.5

W1301

Sensitivity and Specificity of a Rapid Fecal Calprotectin Test in Patients with Chronic Non Bloody Diarrhea

Gerassimos J. Mantzaris, Anastassios Roussos, Angeliki Christidou, Stavroula Koilakou, Konstantinos Papamichail

Background: Calprotectin (C) is a neutrophil derived protein; high amounts are detected in the feces as a result of intestinal inflammation, ischaemia, or cancer. Fecal C (FC) is highly sensitivity in discriminating organic from functional diarrhea and is a reliable test in monitoring Crohn's disease (CD). Recently, a rapid FC hemi-quantitative immuno-chromatographic test has been developed which uses monoclonal antibodies (PreventID® CalDetect, Preventis, Bensheim, Germany). The cut off value for a negative test is <15 µg/g; FC values in the range of 15-60 µg/g are positive, and >60 µg/g strongly positive. Aim: To assess the reliability of PreventID in the differential diagnosis of organic from functional chronic non bloody diarrhea. Methods: In a prospective, single centre study patients with chronic non bloody diarrhea (>4 liquid bowel motions/day for >1 month) were instructed to collect 3 fresh fecal samples in a sample collection device which contained a buffer solution. The device was stored at 2-8oC and was turned over to our Unit within 5 days. The test was run by a physician unaware of patient's symptoms. Patients then underwent a thorough investigation including hematology, biochemistry, serology, gastroscopy and colonoscopy with segmental biopsies, and enteroclysis, if indicated. For CD patients, the clinical and endoscopic activity of CD was calculated using the Crohn's Disease Activity Index (CDAI) and the Crohn's Disease Endoscopic Index of Severity (CDEIS), respectively; histology was assessed according to D'Haens et al (Gastroenterology 1998;114:262). Results: 85 consecutive patients were included in a one-year study [35 males, age 35 (17-55)(median, range). The final diagnosis was irritable bowel syndrome (IBS) in 45 patients, CD in 30, microscopic colitis in 3, pseudomembranous colitis in 3, and NSAIDS enteropathy in 4. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of FC in the differential diagnosis of chronic non bloody diarrhea is depicted in the table as percentage with 95% CI. There was a stronger correlation between FC and CDEIS than between CRP and CDEIS in CD. However, FC was positive even in clinically and endoscopically mild organic colitides where serum CRP was normal. Conclusion: PreventID® CalDetect office test allows rapid and reliable differentiation between organic and functional diarrhea and may be used for selecting patients for further extensive laboratory and endoscopic evaluation.

Disease/FC	Sensitivity	Specificity	PPV	NPV
organic vs IBS	95.0 (90-98)	93.3 (88-98)	92.7 (87-98)	95.4 (91-98)
CD vs IBS	97.0 (95-99)	93.0 (89-97)	92.0 (88-96)	97.6 (95-99)

W1302

Hydrogen Breath Test for Bacterial Overgrowth and IBS

Linda Gillberg, Christina Prior, Ulrika Mjörnell, Lars Blomquist, Per M. Hellström

H2 breath test (HBT) is used for diagnosing small intestinal bacterial overgrowth by identifying abnormal breath H2 profiles. Controversies exist of how to interpret the HBT and if patients with irritable bowel syndrome (IBS) are improved by antibiotic treatment. A follow-up study was done to evaluate the use of H2 peak value and area under the curve (AUC) as means to define abnormal HBT and evaluating IBS patients responding to antibiotics. Methods and Results: Totally 668 patients performed HBT from 2000 until 2007. IBS was defined by Rome II criteria. Patients included in the evaluation had antibiotic treatment in succession with their HBT. A control group with no prior gastrointestinal symptoms or disease was studied. Subjects were excluded if antibiotics prior to the test improved symptoms. The HBT was done with 10g of lactulose. Of the 668 patients in the database, 220 were included for evaluation and categorised into 5 groups: controls (n=47), responders (n=87), responders with follow-up test (n=31), non-responders (n=39) and non-responders with follow-up test (n=16). In these groups, 49%; 81%; 54% and 63% had IBS, respectively. In controls, the upper 95% CI for orocecal transit time was estimated to 80 min. The time frame 0-80 min was used for calculation of H2 peak values (parts per million, ppm) and AUC (ppm*min). The peak values (±SD) were: controls 19±16, responders 30±24, responders follow-up 16±24, non-responders 24±21 and non-responders follow-up 33±31. Comparing H2 pre-

Clin Chem Lab Med 2008;46(9):xxx-xxx © 2008 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2008.246

Diagnostic performance of rapid tests for detection of fecal calprotectin and lactoferrin and their ability to discriminate inflammatory from irritable bowel syndrome

Charlotte M.T. Otten[1], Liselotte Kok[2], Ben J.M. Witteman[3], Ruben Baumgarten[4], Ellen Kampman[1], Karel G.M. Moons[2] and Niek J. de Wit[2,*]

[1] Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands
[2] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands
[3] The Department of Gastroenterology and Hepatology, Gelderse Vallei Hospital, Ede, The Netherlands
[4] Department of Clinical Biochemistry and Hematology, Gelderse Vallei Hospital, Ede, The Netherlands

Abstract

Background: Ruling out somatic bowel disease, such as inflammatory bowel disease (IBD), is an important goal in the management of abdominal complaints. Endoscopy is commonly used but is invasive and expensive. Mucosal inflammation in IBD can be detected through fecal biomarkers, though the present enzyme-linked immunoabsorbent assay (ELISA) tests require laboratory facilities. We validated the diagnostic performance of two new fecal rapid tests (FRTs) for the detection of calprotectin and lactoferrin and assessed their potential to differentiate IBD from irritable bowel syndrome (IBS).
Methods: The calprotectin and lactoferrin FRTs and ELISA tests were performed on the fecal samples of 114 patients referred for endoscopy, 80% of whom had IBS and 20% IBD, and validated against the endoscopic diagnosis.
Results: The sensitivity and negative predictive value of the calprotectin FRT were both 100%, whereas they were 78% and 95%, respectively, for the lactoferrin FRT. The specificity and positive predictive value were slightly higher for the lactoferrin FRT. Both FRTs had similar diagnostic accuracy as the corresponding ELISA tests.
Conclusions: The calprotectin and lactoferrin rapid tests are as good as the ELISA tests in detecting colonic inflammation. Given their simple use, FRTs can support the non-invasive exclusion of IBD, notably in primary care.
Clin Chem Lab Med 2008;46

*Corresponding author: Dr. N.J. de Wit, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands
Phone: +31-88-5768247,
E-mail: N.J.deWit@umcutrecht.nl
Received February 14, 2008; accepted April 28, 2008

Keywords: biomarkers; enzyme-linked immunosorbent assay (ELISA); fecal calprotectin; fecal lactoferrin; inflammatory bowel disease; irritable bowel syndrome.

Introduction

Chronic abdominal complaints are highly prevalent in primary care practice. In the majority of patients, they have a functional background. Irritable bowel syndrome (IBS) is the most prevalent functional intestinal condition. Most patients with IBS can be managed adequately in primary care. Despite expert based diagnostic criteria, such as the Rome criteria, it remains difficult to differentiate IBS from organic and more severe colonic abnormalities, such as inflammatory bowel disease (IBD) and even colon carcinoma, using symptoms and signs only. Existing diagnostic items are insufficient to rule out organic disorders due to a substantial overlap in symptomatology and other test results with non-organic or functional diseases (1). Hence, at least 20% of patients with chronic abdominal complaints are still referred to hospital for invasive tests, such as endoscopy, to rule out organic disorders (2). In approximately 70% of these referred patients, no severe abnormalities are found at endoscopy (3). Thus, endoscopy is not indicated in all primary care patients with chronic abdominal complaints. Less invasive and cheaper diagnostic tests that could more effectively rule out IBD in primary care patients with chronic abdominal complaints are needed to reduce the number of unnecessary referrals for endoscopy.

Calprotectin and lactoferrin are degradation products of neutrophil granulocytes in the mucosal layer of the colon. Neutrophil granulocytes play an important role in the inflammation process in IBD. Patients suffering from IBD have a larger intestinal permeability than healthy individuals, resulting in an increased transport of neutrophil granulocytes into the gut (4, 5). Granulocytes reaching the lumen lead to apoptosis, releasing lactoferrin and calprotectin into the gut (6). This explains the increased concentration of calprotectin and lactoferrin in the feces in the case of inflammation. Both calprotectin and lactoferrin resist enzymatic degradation, in vivo and in vitro, and show a high stability in feces (more than 1 week at room

temperature) (7–10). Bowel inflammation can thus be diagnosed by measuring calprotectin and lactoferrin in fecal samples, using enzyme-linked immunoabsorbent assay (ELISA) methods in the laboratory. Several studies have demonstrated significantly different concentrations of both biomarkers in the feces of patients with IBD and IBS (11–13). Increased fecal concentrations of calprotectin and lactoferrin after exacerbation of Crohn's disease and colitis ulcerosa can also be measured by ELISA methods, as well as mucosal healing after the start of treatment for IBD (4, 14–18).

Unfortunately, ELISA methods detecting fecal biomarkers are relatively time consuming and expensive. They require laboratory facilities and cannot be performed in the general practitioner's office. Recently, two new point-of-care or fecal rapid tests (FRTs) for calprotectin and lactoferrin have been developed that can support non-invasive differentiation of colonic inflammation from other (functional) diagnoses in primary care patients with chronic abdominal complaints.

Our aim was to evaluate the diagnostic accuracy of these two new rapid calprotectin and lactoferrin fecal tests in assessing colonic inflammation in patients with chronic abdominal complaints. In addition, the association of the results of the two rapid tests is compared with the results of the calprotectin and lactoferrin ELISA tests.

Patients and methods

Design and patients

This diagnostic study involved a cross-sectional design. Consecutive patients with lower gastro-intestinal abdominal complaints, including bloating, change in defecation frequency or consistency, or blood and mucus in the feces, referred for endoscopy or sigmoidoscopy to the endoscopy unit of the Gelderse Vallei Hospital, a major regional hospital in The Netherlands, were included in the study. Patients younger than 18 years, patients with a history of colonic surgery and those with iron deficiency were excluded from the study. All patients referred between May and June 2007 who met the inclusion criteria were invited by phone to participate in the study. After consenting, participants were sent a fecal sample tube and an information leaflet on how to collect and store the sample. On the day of endoscopy, patients returned their fecal sample and informed consent form. FRTs were performed at the endoscopy unit before the procedure. Fecal samples were frozen for ELISA determination at a later stage. Both calprotectin and lactoferrin are reported to be stable at a temperature of –20°C for 3–6 months (19). The study protocol was approved by the local Ethical Committee.

Index tests

The calprotectin rapid test (Prevent ID® CalDetect Preventis, Bensheim, Germany) is a semi-quantitative immunochromatographic test to detect the presence of calprotectin in feces. The test was performed according to the manufacturer's instruction (www.preventis-online.de). Briefly, the collection stick of the sample collection device was dipped in the fecal sample and then into the extraction buffer of the sample collection device and shaken thoroughly. This was repeated once. Two drops of the diluted fecal sample were added to the calprotectin rapid test device. The diluted feces were allowed to migrate laterally, thus providing a control line indicating the test worked properly. In the presence of calprotectin, one, two or three test lines appeared, corresponding with calprotectin concentrations of <15 mg/kg, between 15 and 60, or >60 mg/kg. In line with the instructions of the manufacturer, the test was evaluated positive when at least the second test line appeared, i.e., concentration ≥ 15 mg/kg. The test results were interpreted after 10 min.

The lactoferrin rapid test (IBD EZ VUE™, TECHLAB, Blacksburg, VA, USA) is an immunochromatographic test for the qualitative detection of lactoferrin. According to the manufacturer's instruction (www.techlab.com/product_details), a portion of 0.05 g feces was weighted on an analytic balance and mixed with 2.5 mL diluent (10× concentration of a buffered protein solution containing 0.2% thimerosal). Four drops of this diluted feces were added to the test device and allowed to migrate on the absorbent strip. If the test worked properly, a control line appeared. The test result could be read from the test line, which was positive at concentrations of lactoferrin ≥ 128 ng/mL. The results were read after 3 min.

Both FRTs were performed and interpreted by two of the authors (C.O. and L.K.) at the endoscopy department, before endoscopy.

ELISA test

Fecal calprotectin (Phical test®, CALPRO AS, Oslo, Norway) and lactoferrin (IBD-SCAN®, TECHLAB, Blacksburg, VA, USA) concentrations were also measured by ELISA methods (19, 20). Both ELISA tests were carried out by the laboratory staff of the hospital. Until analysis, the fecal samples were stored at –20°C for a maximum of 1 month. According to the manufacturer's cut-off value, the ELISA calprotectin test was considered positive if the concentration was higher than 50 mg/kg, and for the ELISA lactoferrin test if the concentration was higher than 7.25 mg/mL.

The two rapid tests and the two ELISA tests were all performed and interpreted without knowledge of the other test results, and blinded for patient history, physical examination and endoscopy results.

Diagnostic outcome (reference standard)

The outcome of the present study was defined as the presence or absence of IBD. To this aim, all patients underwent colonoscopy or sigmoidoscopy according to routine procedure, performed by experienced gastroenterologists (more than 700 colonoscopies annually, cecal intubation rate 97%) at the endoscopy department. According to routine clinical practice, the diagnosis was based on the endoscopic picture, biopsies were taken if necessary to confirm the diagnosis. The endoscopists were blinded for the results of the rapid tests and ELISAs.

Statistical analysis

We calculated for both rapid tests the sensitivity, specificity, positive and negative predictive values (PPVs and NPVs), and positive and negative likelihood ratios (LR+, LR–) with 95% confidence intervals for the detection of IBD, in comparison with the result of the colonoscopy or sigmoidoscopy. For the calprotectin rapid test, these characteristics were calculated for the two possible cut-off points, i.e., ≥ 15 mg/kg and ≥ 60 mg/kg. This was not possible for the lactoferrin rapid test, as this is a qualitative test.

We also calculated these diagnostic accuracy parameters for the two ELISA tests using the standard applied cut-off

points of the manufacturer, i.e., >50 mg/kg for the calprotectin ELISA test and >7.25 μg/mL for the lactoferrin ELISA test.

The correlation between the results of the ELISA tests and the two rapid tests were also assessed, using the kappa statistic.

Results

In total, 180 consecutive patients referred for colonoscopy or sigmoidoscopy by either the general practitioner (GP) (80%) or the gastroenterologist (20%) were invited to participate in the study. Of these, 36 refused participation; 144 patients (80%) were included in the study. The endoscopy procedure had to be aborted in two patients because of discomfort during the procedure. In addition, three other patients were excluded because they did not have active bowel complaints at the time of feces collection and endoscopy. From the remaining 139 patients (77%), a diagnosis at endoscopy was available. In 25 of these patients, somatic bowel disorders other than IBD were diagnosed: polyps (n=16), cancer (n=4, aged 64–58–61–75 years) or other (n=5). As our aim was to study whether the rapid tests could differentiate IBD from IBS, we analyzed the 114 patients (Table 1), of whom 109 (96%) underwent colonoscopy, and five (4%) sigmoidoscopy. Of these 114 patients, 23 were diagnosed with IBD (20%) and 91 with IBS (80%). In half of the patients with IBD, biopsies were taken; six patients had Crohn's disease, five had ulcerative colitis, and 12 had unspecified colitis.

Table 1 Patients referred for lower gastrointestinal endoscopy (n=114).

n=114	IBS	IBD
Number of patients	91	23
Age (mean), years	52.3	44.5
Women, n (%)	49 (53.8)	12 (52.2)
Symptomatology (n=113)		
Rectal blood loss	24 (26.4)	13 (55.8)
Constipation	51 (56.0)	8 (34.8)
Diarrhea	61 (67.0)	20 (87.0)
Pain	68 (74.7)	17 (73.9)
Bloating	49 (53.8)	16 (69.6)

Patients' characteristics and presenting symptoms are in absolute numbers and %.

Patients with IBS were older (mean age 52.3 years) than those with IBD (44.5 years). Of the patients with IBD, 56% presented with rectal blood loss and 87% with diarrhea, compared to 26% and 67% of patients with IBS, respectively.

The sensitivity of the calprotectin FRT was 100% at the cut-off point ≥15 mg/kg and 60.6% at the cut-off point ≥60 mg/kg (Table 2). The corresponding specificities were 94.5% and 97.8%, respectively. The PPVs for detecting IBD were 82.1% and 87.5% for the cut-off points ≥15 and ≥60 mg/kg, respectively, and NPVs were 100% and 90.8%, respectively. For the lactoferrin rapid test, sensitivity was 78%, specificity 99%, and the PPV and NPV were both 94.7%.

The sensitivity value of the calprotectin and lactoferrin ELISA tests were 95.7% and 78.3%, with specificity values of 86.8% and 90.1%, respectively. The PPVs for diagnosing IBD were 64.7% for the calprotectin ELISA and 66.7% for the lactoferrin ELISA, with NPVs of 98.8% and 94.3%, respectively.

The correlation between the calprotectin and lactoferrin rapid tests showed a kappa statistic of 0.76 (Table 3), whereas this was 0.67 between the two ELISA tests. The correlation between the lactoferrin FRT and lactoferrin ELISA test was 0.68, and between the calprotectin FRT and ELISA test 0.69.

Finally, the diagnostic performance of the combination of the two FRTs at endoscopy was determined (Table 4). If both test results were positive (with calprotectin FRT at the cut-off point ≥15 mg/kg), the probability of the presence of IBD was 95% (18/19). If the calprotectin test was positive, but the lactoferrin test negative, the probability of IBD was 44% (4/9). There were no patients with a positive lactoferrin test and negative calprotectin test, and if both tests were negative, the probability of IBD was also 0%. If either

Table 2 Diagnostic accuracy parameters (with 95% confidence intervals) of the calprotectin FRT and lactoferrin FRT and the two ELISA tests for distinguishing IBS from IBD as determined by colonoscopy or sigmoidoscopy (n=114 patients).

	Calprotectin FRT (cut-off point ≥15 mg/kg)	Calprotectin FRT (cut-off ≥60 mg/kg)	Lactoferrin FRT	ELISA calprotectin (cut-off >50 mg/kg)	ELISA lactoferrin (cut-off >7.25 mg/mL)
Specificity, %	94.5 (78.1–98.0)	97.8 (91.5–99.6)	99.0 (93.0–99.9)	86.8 (77.7–92.7)	90.1 (81.6–95.1)
Sensitivity, %	100 (78.1–98.0)	60.6 (38.8–79.5)	78.0 (65.0–92.0)	95.7 (76.0–99.8)	78.3 (55.8–91.7)
PPV, %	82.1 (62.4–93.2)	87.5 (60.4–97.8)	94.7 (71.9–99.7)	64.7 (46.5–89.0)	66.7 (46.0–82.8)
NPV, %	100 (94.7–100)	90.8 (82.8–95.5)	94.7 (87.6–98.0)	98.8 (92.3–99.9)	94.3 (86.5–82.8)
LR+	18.2 (7.7–42.7)	27.7 (6.7–113.3)	75.1 (0.5–534.2)	7.3 (4.3–12.4)	7.9 (4.1–15.3)
LR–	0	0.4 (0.2–0.7)	0.2 (0.1–0.5)	0.5 (0.007–0.8)	0.2 (0.1–0.53)

PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR–, negative likelihood ratio.

Table 3 Correlation between the calprotectin and lactoferrin FRT and ELISA test results (n=114 patients).

	Calprotectin FRT vs. lactoferrin FRT	Calprotectin ELISA vs. lactoferrin ELISA	Calprotectin FRT vs. calprotectin ELISA	Lactoferrin FRT vs. lactoferrin ELISA
Cohen's kappa	0.76	0.67	0.69	0.68

Table 4 Diagnostic performance of the combination of calprotectin and lactoferrin FRTs for diagnosing IBD at endoscopy (with calprotectin FRT at cut-off point ≥15 mg/kg).

	IBD+ (n=23)	IBD– (n=91)	Total (n=114)
Calpro FRT+ and lacto FRT+	18 (95%)	1 (5%)	19
Calpro FRT+ and lacto FRT –	4 (44%)	5 (56%)	9
Calpro FRT– and lacto FRT+	0 (0%)	0 (0%)	0
Calpro FRT– and lacto FRT–	0 (0%)	86 (100%)	86
At least one of the two FRTs positive	22 (79%)	6 (21%)	28
At least one of the two FRTs negative	4 (4%)	91 (96%)	95

Calpro FRT, calprotectin fecal rapid test; lacto FRT, lactoferrin fecal rapid test; –, negative result; +, positive result.

one of the two tests was positive, the probability of the presence of IBD was 79% (22/28), and if either one of the two tests was negative, the presence of IBD was 4% (4/95).

Discussion

Recently introduced rapid tests for the detection of calprotectin and lactoferrin in fecal samples have a good diagnostic performance to differentiate patients with IBD from those with IBS, which is at least comparable to that of the ELISA tests. The calprotectin rapid test (at the cut-off value of ≥15 mg/kg) seems to have better diagnostic accuracy than the lactoferrin rapid test, notably to rule out IBD, viewing the higher sensitivity and NPV and the lower LR–. Addition of the lactoferrin rapid test result did not improve the exclusion of IBD; in our study, a negative calprotectin test correctly ruled out IBD already.

The mission of the GP is to select those patients who require specialist attention because of a high risk of serious disease. If the GP performs this gatekeeper function adequately, the referred population will have a high risk for severe gastrointestinal (GI) disease, while the risk in the non-referred group will be below average. Ruling out IBD is the most important diagnostic goal in patients with non-alarming abdominal complaints, especially in the case of diarrhea predominant complaints. A fecal biomarker test can support the GP in this selection process, as in many countries the primary care physician is the first to encounter patients with these symptoms. The calprotectin rapid test could be particularly useful as an initial test to rule out IBD in subjects with chronic lower abdominal complaints, and thus to limit the number of (unnecessary) referrals for endoscopy.

To our knowledge, this is the first study to quantify the accuracy of the rapid fecal tests for discriminating IBD (usually diagnosed with endoscopy) from IBS. We specifically included patients referred for endoscopy for suspicion of presence of IBD, to determine to what extent the tests can discriminate between IBD and IBS. Accordingly, we also included in this initial study patients referred for endoscopy by the gastroenterologist. A substantial number of the patients referred for endoscopy by their GP had rectal blood loss as part of their abdominal complaints. Rectal blood loss can be indicative for colorectal cancer and IBD. This was probably one of the main reasons for the GP to consider referral, even though the predictive value of rectal blood loss for colorectal cancer in primary care is low (21). Of those patients who had IBD at endoscopy, more than half had rectal blood loss as a presenting symptom. Of those who were diagnosed as having IBS after a normal endoscopy, 26.4% had rectal blood loss as a presenting symptom. Hemorrhoids, which are reported to be prevalent in 20% of patients with IBS (22), are the most likely explanation for this blood loss.

We chose a reference diagnostic workup that matches with daily clinical practice. Ileocolonoscopy was considered as reference standard, with biopsies only in the case of clinical suspicion of IBD. Patients were not routinely checked for the rarer causes of upper GI disease, such as gluten intolerance, lactose intolerance or peptic ulcer, unless this was indicated on clinical suspicion.

A strong point of our study – and in line with the STARD (Standards for reporting of diagnostic accuracy) guidelines – is that we included patients on their indication for referral for endoscopy rather than on their true presence or absence of IBD. However, the rapid tests are, as said, particularly useful in a primary care setting to be applied to all patients with non-alarming chronic colonic complaints. Given the promising results of the present study in referred patients with IBS and IBD only, we believe it is timely to quantify the accuracy and cost-effectiveness of the calprotectin test in a primary or family care population. Such research should preferably be larger to allow for a more precise estimation (i.e., with smaller confidence intervals) of the diagnostic accuracy parameters, notably the sensitivity, NPV and LR–. It is very likely that in the primary care setting the prevalence of IBD and organic disorders will be lower than in our referred population. As found for other disorders, this would potentially result in higher NPV and sensitivity, and lower LR– (23).

A number of studies have also reported changes in fecal calprotectin and lactoferrin in patients with colorectal cancer and polyps (24). In a meta-analysis, the pooled sensitivity and specificity of (non-rapid) fecal calprotectin for diagnosing colorectal neoplasia was 36% and 71%, respectively (15). Hence, subsequent studies should not only quantify the ability of these rapid tests to exclude IBD from IBS but rather on their accuracy to discriminate between organic disorders (including diverticulitis and cancer) and functional dis-

orders. Many guidelines recommend an age threshold for a safe non-endoscopic diagnosis of IBS, usually >50 years (25, 26). The patients in our study who were excluded because of colorectal cancer were all older than 50 years. In subsequent studies, the diagnostic contribution of other patient characteristics (age), (blood) test results (such as fecal occult blood test) and lifestyle habits should also be taken into account.

Some studies reported factors that may influence the diagnostic capacity of biomarker tests: marginally elevated fecal calprotectin concentration in patients with physical inactivity, obesity and increasing age, a lower concentration in the case of high fiber intake and vegetable consumption and considerable day-to-day variability in some patients (27). The diagnostic value of calprotectin may be limited in patients with collagenous colitis, as up to 40% of the patients with active collagenous colitis are reported to have a normal calprotectin excretion (28).

Hence, subsequent studies should not only quantify the value of the rapid tests in isolation, but rather in combination with, e.g., the Rome III criteria, family and medical history, physical examination and blood test results (29). Such analysis could result in a multivariable diagnostic model to differentiate between functional and somatic bowel disease without endoscopy (30).

As in all diagnostic tests, the procedure and interpretation of the FRTs need proper instruction and performance improves with experience. This could interfere with the application of the test in primary care, because the tests may be used less frequently than in a hospital setting. We experienced some minor problems with the procedure of the rapid tests. The calprotectin FRT yielded some interpretation problems, as the brightness of the test lines may vary. Although the reading of the lactoferrin FRT is easier than of the calprotectin FRT, the test procedure for calprotectin is easier, because less laboratory devices are required.

In conclusion, in this sample of patients referred for endoscopy, the recently developed fecal calprotectin and lactoferrin rapid tests have good diagnostic performance, comparable to that of the more expensive and time-consuming ELISA tests. The calprotectin test shows better performance to rule out IBD, while the lactoferrin test seems better to detect the presence of IBD. These rapid tests for fecal biomarkers have a potential role to easily and non-invasively determine the absence of IBD in patients with chronic colonic symptoms and signs that seem ideal for use in primary care. The cost-effectiveness of their use in primary care is yet unknown and is a topic for further study.

Acknowledgements

We thank Orange Medical for supplying the calprotectin and lactoferrin tests and the analysts who performed the ELISAs at the laboratory of Hospital Gelderse Vallei Ede.

References

1. Suleiman S, Sonnenberg A. Cost-effectiveness of endoscopy in irritable bowel syndrome. Arch Intern Med 2001;161:369–75.
2. Muris JW, Starmans R, Fijten GH, Knottnerus JA. One-year prognosis of abdominal complaints in general practice: a prospective study of patients in whom no organic cause is found. Br J Gen Pract 1996;46:715–9.
3. Gonvers JJ, Harris JK, Wietlisbach V, Burnand B, Vader JP, Froehlich F. A European view of diagnostic yield and appropriateness of colonoscopy. Hepatogastroenterology 2007;54:729–35.
4. D'Inca R, Dal PE, Di Leo V, Ferronato A, Fries W, Vettorato MG, et al. Calprotectin and lactoferrin in the assessment of intestinal inflammation and organic disease. Int J Colorectal Dis 2007;22:429–37.
5. Kucharzik T, Williams IR. Neutrophil migration across the intestinal epithelial barrier – summary of in vitro data and description of a new transgenic mouse model with doxycycline-inducible interleukin-8 expression in intestinal epithelial cells. Pathobiology 2002;70:143–9.
6. Guerrant RL, Araujo V, Soares E, Kotloff K, Lima AA, Cooper WH, et al. Measurement of fecal lactoferrin as a marker of fecal leukocytes. J Clin Microbiol 1992;30:1238–42.
7. Roseth AG, Fagerhol MK, Aadland E, Schjonsby H. Assessment of the neutrophil dominating protein calprotectin in feces. A methodologic study. Scand J Gastroenterol 1992;27:793–8.
8. Angriman I, Scarpa M, D'Inca R, Basso D, Ruffolo C, Polese L, et al. Enzymes in feces: useful markers of chronic inflammatory bowel disease. Clin Chim Acta 2007;381:63–8.
9. Sugi K, Saitoh O, Hirata I, Katsu K. Fecal lactoferrin as a marker for disease activity in inflammatory bowel disease: comparison with other neutrophil-derived proteins. Am J Gastroenterol 1996;91:927–34.
10. Uchida K, Matsuse R, Tomita S, Sugi K, Saitoh O, Ohshiba S. Immunochemical detection of human lactoferrin in feces as a new marker for inflammatory gastrointestinal disorders and colon cancer. Clin Biochem 1994;27:259–64.
11. Carroccio A, Iacono G, Cottone M, Di Prima L, Cartabellotta F, Cavataio F, 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. Clin Chem 2003;49:861–7.
12. Walker TR, Land ML, Kartashov A, Saslowsky TM, Lyerly DM, Boone JH, et al. Fecal lactoferrin is a sensitive and specific marker of disease activity in children and young adults with inflammatory bowel disease. J Pediatr Gastroenterol Nutr 2007;44:414–22.
13. Costa F, Mumolo MG, Bellini M, Romano MR, Ceccarelli L, Arpe P, et al. Role of faecal calprotectin as non-invasive marker of intestinal inflammation. Dig Liver Dis 2003;35:642–7.
14. Saitoh O, Kojima K, Kayazawa M, Sugi K, Tanaka S, Nakagawa K, et al. Comparison of tests for fecal lactoferrin and fecal occult blood for colorectal diseases: a prospective pilot study. Intern Med 2000;39:778–82.
15. von Roon AC, Karamountzos L, Purkayastha S, Reese GE, Darzi AW, Teare JP, et al. Diagnostic precision of fecal calprotectin for inflammatory bowel disease and colorectal malignancy. Am J Gastroenterol 2007;102:803–13.
16. Kane SV, Sandborn WJ, Rufo PA, Zholudev A, Boone J, Lyerly D, et al. Fecal lactoferrin is a sensitive and specific marker in identifying intestinal inflammation. Am J Gastroenterol 2003;98:1309–14.

17. Tibble JA, Sigthorsson G, Bridger S, Fagerhol MK, Bjarnason I. Surrogate markers of intestinal inflammation are predictive of relapse in patients with inflammatory bowel disease. Gastroenterology 2000;119:15–22.
18. Fine KD, Ogunji F, George J, Niehaus MD, Guerrant RL. Utility of a rapid fecal latex agglutination test detecting the neutrophil protein, lactoferrin, for diagnosing inflammatory causes of chronic diarrhea. Am J Gastroenterol 1998;93:1300–5.
19. Ton H, Brandsnes, Dale S, Holtlund J, Skuibina E, Schjonsby H, et al. Improved assay for fecal calprotectin. Clin Chim Acta 2000;292:41–54.
20. Schoepfer AM, Trummler M, Seeholzer P, Criblez DH, Seibold F. Accuracy of four fecal assays in the diagnosis of colitis. Dis Colon Rectum 2007;50:1697–706.
21. Fijten GH, Muris JW, Starmans R, Knottnerus JA, Blijham GH, Krebber TF. The incidence and outcome of rectal bleeding in general practice. Fam Pract 1993;10: 283–7.
22. Akhtar AJ, Shaheen MA, Zha J. Organic colonic lesions in patients with irritable bowel syndrome (IBS). Med Sci Monit 2006;12:CR363–7.
23. Roberts AP, Childs SM, Rubin G, de Wit NJ. Tests for Helicobacter pylori infection: a critical appraisal from primary care. Fam Pract 2000;17(Suppl 2):S12–20.
24. Hirata I, Hoshimoto M, Saito O, Kayazawa M, Nishikawa T, Murano M, et al. Usefulness of fecal lactoferrin and hemoglobin in diagnosis of colorectal diseases. World J Gastroenterol 2007;13:1569–74.
25. Spiller R, Aziz Q, Creed F, Emmanuel A, Houghton L, Hungin P, et al. Guidelines on the irritable bowel syndrome: mechanisms and practical management. Gut 2007;56:1770–98.
26. Rubin G, De Wit N, Meineche-Schmidt V, Seifert B, Hall N, Hungin P. The diagnosis of IBS in primary care: consensus development using nominal group technique. Fam Pract 2006;23:687–92.
27. Poullis A, Foster R, Shetty A, Fagerhol MK, Mendall MA. Bowel inflammation as measured by fecal calprotectin: a link between lifestyle factors and colorectal cancer risk. Cancer Epidemiol Biomarkers Prev 2004;13:279–84.
28. Wildt S, Nordgaard-Lassen I, Bendtsen F, Rumessen JJ. Metabolic and inflammatory faecal markers in collagenous colitis. Eur J Gastroenterol Hepatol 2007;19: 567–74.
29. Moons KG, Grobbee DE. Diagnostic studies as multivariable, prediction research. J Epidemiol Community Health 2002;56:337–8.
30. Moons KG, van Es GA, Michel BC, Buller HR, Habbema JD, Grobbee DE. Redundancy of single diagnostic test evaluation. Epidemiology 1999;10:276–81.

April 2006 Volume 130 • Number 4 • Suppl 2

Supplement to

Gastroenterology

www.gastrojournal.org

Digestive Disease Week®
and the
107th Annual Meeting of the American Gastroenterological Association Institute

May 20-25, 2006, Los Angeles, CA

- Program of the Annual Meeting of the American Gastroenterological Association Institute, the American Association for the Study of Liver Diseases, the Gastroenterology Research Group, the Society for Surgery of the Alimentary Tract, and the American Society for Gastrointestinal Endoscopy
- Abstracts of Papers Accepted by the American Gastroenterological Association Institute
- Abstracts of Papers Accepted by the American Association for the Study of Liver Diseases
- Abstracts of Papers Accepted by the Society for Surgery of the Alimentary Tract

prospective validation but suggest a role for MDR1/P-gp in the mechanism of action of azathioprine.

Reasons for AZA interruption in IBD	No patients (n=229)	%
Gastrointestinal or general intoleranee	40	17.5
Pancreatic toxicity	24	10.5
Hepatotoxicity	22	9.7
Bone marrow toxicity	16	7.0
Severe infection	14	6.1
Flu-like symptoms	13	5.7
Skin allergy	11	4.8
Cancer/precancerous/lymphoma	4	1.7
Rare causes	2	0.9
Death from other than IBD cause	1	0.4
Long-term disease remission	12	5.2
Ineffectiveness/non-response	56	22.2
Pregnancy	14	6.1

S1314

Comparative Study of New Rapid Bedside Fecal Calprotectin Test with An Established ELISA to Assess Intestinal Inflammation in a Prospective Study

Yogesh Shastri, Nada Povse, Jurgen Stein

Background: Estimation of fecal concentration of the neutrophil granulocyte-derived protein calprotectin has been proposed as a screening non invasive test to assess intestinal inflammation of the gut. However, most assays for detecting calprotectin are Enzyme Linked Immunosorbent Assay (ELISA) based thus require a suitable well equipped laboratory i.e. an ELISA reader, limiting their widespread use because of logistics and higher costs. The biggest advantages of this new bedside IFOBT are its simplicity, rapidity (needs just about 5 min), convenience, no need of cumbersome ELISA readers and the fact that it can be performed at the patient bedside or in physician's office by any health care personnel. Patients and Methods: 301 patients (139 males and 162 females) underwent estimation of fecal calprotectin using a commercial quantitative ELISA (Immunodiagnostik, Bensheim, Germany) and the rapid bedside test (PreventID® CalDetect, Preventis, Bensheim, Germany), which is a semiquantitative immunochromatographic rapid test using monoclonal antibodies. There age ranged from 7 months till 91 years (median being 40 years). The study duration was from January 2005 till November 2005. Both these tests were performed by an experienced technician who was blinded to the patient's clinical profile. As per the manufacturer the cutoff calprotectin level for both the tests was 15 ng/mL. Results: The patient's test characteristics as shown in Table 1. The sensitivity and specificity of the new bedside tests for diagnosing CD and UC were 96.3 % and 94.0% as against quantitative ELISA of 96.0% and 99% (not statistically significant) respectively. Conclusion: This new bedside fecal calprotectin assay has proved to be an accurate, simple, convenient, noncumbersome tool as compared to the routine ELISA based test and can replace the cumbersome ELISA fecal calprotectin estimation.
Table 1. Test characteristics in 301 consecutive patients

Diagnosis (No)	Calprotectin level	ELISA test	Bedside test
CD (109)	<15ng>mL >15ngmL	3 106	4 105
UC (46)	<15ng>mL >15ngmL	1 45	2 44
Cystic fibrosis (41)	<15ng>mL >15ngmL	16 25	19 22
Diarrhea (34)	<15ng>mL >15ngmL	10 24	13 21
Others (21)	<15ng>mL >15ngmL	9 12	11 10
Controls (50)	<15ng>mL >15ngmL	48 2	47 3

S1315

A Panel of Anti-Glycan Antibodies (gASCA, ALCA, ACCA and AMCA) in the Diagnosis and Differential Diagnosis of IBD

Marc Ferrante, Marie Pierik, Liesbet Henckaerts, Nir Dotan, Rom T. Altstock, Iris Dotan, Marie Joossens, Sofie Joossens, Konstantinos Katsanos, Karolien Claes, Nele van Schuerbeek, Gert van Assche, Paul Rutgeerts, Severine Vermeire

BACKGROUND & AIMS: Serological markers have been proposed in IBD for distinction between ulcerative colitis (UC) and Crohn's disease (CD), and also contribute to disease stratification in CD. Given the sub-optimal accuracy of the available markers in daily clinical practice, we tested a new panel of antibodies directed against glycan-epitopes in IBD and controls. METHODS: A total of 1225 IBD patients (913 CD, 272 UC, 40 IC), as well as 200 healthy controls and 113 patients with non-IBD gastrointestinal inflammation (GI-controls) were tested for Anti Saccharomyces cerevisiae Antibodies (gASCA), Anti-Laminaribioside Carbohydrate Antibodies (ALCA), Anti-Chitobioside Carbohydrate Antibodies (ACCA) and Anti-Mannobioside Carbohydrate Antibodies (AMCA) by commercially available ELISA-assays (Glycominds Ltd, Israel) in a blinded way. Using the manufacturers conditions and reconstruction of ROC curves, a cut-off value of 50 (gASCA), 70 (ALCA) or 90 (ACCA and AMCA) units was defined for positivity. Based on the antibody titres of gASCA, ALCA and AMCA a combined serology score (CSS) was computed, ranging from 0 (all 3 markers negative) to 3 (all 3 markers positive), allowing for intermediate titres (which were given a score of 0.5). Accuracy (sensitivity, specificity, positive and negative predictive value) of the individual markers, as well as the combined panel and CSS were calculated using SPSS. RESULTS: The accuracy of the individual markers is depicted in table 1 and for the combined score in table 2. Among the 398 gASCA negative CD patients, 28 were ALCA positive and 50 were AMCA positive. DISCUSSION: Our data show that CD is associated with an adaptive immune response against various glycan-epitopes. Although all antibodies studied in this panel have a high specificity for IBD and CD in particular, gASCA is the preferred antibody given its higher sensitivity. However, the use of a combined serological score, based on gASCA, ALCA and AMCA, further increased the specificity and may have an additional value in differentiating IBD from other causes of abdominal complaints.
Table 1

Disease	gASCA		ALCA		ACCA		AMCA	
	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec
CD vs. UC	56%	90%	18%	93%	21%	85%	28%	82%
IBD vs. control	45%	99%	15%	99%	19%	86%	26%	92%
IBD vs. GI-control	45%	98%	15%	99%	19%	84%	26%	93%

Table 2

Disease	CSS ≧ 1.0		CSS ≧ 1.5		CSS ≧ 2.0		CSS ≧ 2.5	
	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec
CD vs. UC	74%	61%	54%	83%	37%	93%	20%	97%
IBD vs. control	66%	86%	45%	99%	30%	100%	16%	100%
IBD vs. GI-control	66%	82%	45%	98%	30%	100%	16%	100%

S1316

The Positivity of Systemic Cytomegalovirus (CMV) Viral Load Is Highly Predictive of Associated CMV Colitis in Patients Hospitalized for Exacerbation of Ulcerative Colitis Or Crohn's Disease with Colonic Involvement

Sophie Buyse, Joel Gozlan, Corinne Amiel, Nadia Hoyeau, Isabelle Nion-Larmurier, Philippe Seksik, Jacques Cosnes, Jean-Pierre Gendre, Laurent Beaugerie

Latent infection with CMV and Epstein-Barr Virus (EBV) is observed in the majority of healthy adults. In patients with Crohn's disease, transient systemic reactivation of EBV infection may occur in the setting of severe intestinal inflammation and/or treatment by immunosuppressants [1]. **The aims** of this pilot study were to assess whether significant reactivation of systemic CMV infection in patients admitted for active IBD colitis is: i) mostly observed under immunosuppressant therapy; ii) associated with concomitant reactivation of EBV infection; iii) predictive of associated CMV colitis. **Patients and Methods:** Between January 2004 and October 2005, 33 patients (16 males, 17 females), aged from 16 to 68 years (mean: 36)), admitted for moderate to severe attacks of ulcerative colitis (UC, n=19) or Crohn's ileocolitis or colitis (CD, n=14) were studied. All the patients had within the 48 hours following admission a quantification of systemic CMV and EBV viral load by real time PCR and endoscopic evaluation of colonic lesions with biopsies. CMV inclusions were searched for by standard histology and immunohistochemistry. **Results:** The positivity of CMV viral load (above the level of 400 copies/10^6 leukocytes, threshold of reproducible positivity of the technique) was observed in 12 (36%) patients (2(14%) of CD patients vs. 10(53%) of UC patients (p=0.06)). All 12 patients with positive CMV viral load were receiving high doses of steroids (n=7) or immunosuppressants (n=5) at the time of viral load determination. Eleven (92%) of the patients with positive CMV viral load had a concomitant increase (>400 copies/10^6 leukocytes) of EBV viral load. Eight patients had CMV colitis; all of them had a positive CMV viral load. The positive predictive value of CMV colitis in patients with positive CMV viral load was 67%. The negative predictive value of CMV colitis in patients with negative CMV viral load was 100%. **Conclusions:** A significant positivity of systemic CMV viral load (>400 copies/10^6 leucocytes) at admission of patients with active IBD colitis: is mostly observed in UC patients receiving steroids or immunosuppressants; is associated in most cases with a concomitant reactivation of systemic EBV infection, suggesting a status of transient immunodeficiency; is highly correlated with the risk of concomitant CMV colitis. [1] Reijasse D et al. Inflamm Bowel Dis 2004;10: 85.

S1317

Hyperhomocysteinemia, Folate Deficiency, and Carcinogenesis in IBD Patients

Xavier Roblin, Jean Marc Phelip, Veronique Ducros, Jean Luc Faucheron, Bruno Bonaz

In the general population, it is generally admitted that folate deficiency, which induces hyperhomocysteinemia, increases the risk to develop cancerous or precancerous lesions (1). To our knowledge, no data are available in IBD patients. Aim: to evaluate, in a cohort of IBD patients, risk factors of colonic carcinogenesis, in particular folate and homocysteinemia levels. Methods: IBD patients with carcinogenic lesions discovered under colonoscopy (low or high grade adenoma, low or high grade dysplasia, colorectal cancers) were included and compared to the whole population of IBD patients with a normal colonoscopy performed during the same period. Patients with primary sclerosing cholangitis and/or with a family history of colorectal cancers were excluded. The following parameters were collected: age, sex, type-length-activity-extent of the disease, treatment, smoking, vitamin B12-folate-homocysteinemia levels. A univariate analysis and then a multivariate analysis were performed after adjustment according to the main parameters. Results: 110 patients (37 UC, 73 CD; mean age: 44.7 years; sex ratio: 1) were included. Twenty two carcinogenic lesions were isolated: 10 polyps (3 with high grade dysplasia, 7 adenomatous without dysplasia), 6 low grade dysplasia, 2 high grade dysplasia, 4 colorectal cancers. In univariate analysis, risk factors of carcinogenesis were: active smoking (p=0.03), folate level < 145 pmol/l (p = 0.011), hyperhomocysteinemia > 15 µmol/l (p = 0.002), length of the disease > 10 years (p=0.006), UC (p=0.02). In contrast, immunosuppressives, pancolitis, age of onset and

A prospective comparative study for new rapid bedside fecal Calprotectin test with an established ELISA to assess intestinal inflammation

Y. Shastri, [1] N. Povse, [1] W.F. Caspary, [1] J. Stein [1]

[1] Department of Medicine I - ZAFES, Johann Wolfgang Goethe-University Hospital, Frankfurt am Main, Germany

Poster presented at the 107th Annual Meeting of AGA, May 20-25, 2006, Los Angeles

INTRODUCTION

- Estimation of fecal concentration of calprotectin has been proposed as a screening non invasive test to assess intestinal inflammation of the gut.
- However, most assays for detecting calprotectin are Enzyme Linked Immunosorbent Assay (ELISA) based thus require a suitable well equipped laboratory i.e. an ELISA reader, limiting their widespread use because of logistics and higher costs.
- In medicine an objective, simple and convenient test is always welcome.
- Here we compared a routine ELISA with the new bedside semiquantatitative assay in patients with colorectal diseases and healthy controls.

MATERIALS & METHODS

- The study protocol was approved by the Institute's ethics committee.
- Patients underwent estimation of fecal calprotectin using a commercial quantitative ELISA (Immunodiagnostik, Bensheim, Germany) and the rapid bedside test (PreventID® CalDetect, Preventis, Bensheim, Germany), which is a semi quantitative immunochromatographic rapid test using monoclonal antibodies.
- Both these tests were performed by an experienced technician who was blinded to the patient's clinical profile.
- *Statistical Analysis*

For the statistics the Kruskall–Wallis ANOVA test was used (Statistica Vers. 5 USA)

RESULTS

- Included 301 patients (139 males and 162 females).
- Age ranged from 7 months till 91 years (median being 40 years).
- Test results and diagnosis in patients is shown in Table 1.
- The study duration was from January 2005 till November 2005.
- As per the manufacturer the cut-off calprotectin level for both the tests was 15 µg/g.
- The sensitivities of the new bedside tests for diagnosing CD and UC were 96.3 % and 95.6% as against quantitative ELISA of 97.2% and 97.8% (not statistically significant) respectively. Rest of the patient's test characteristics are as shown in Table 2.

Table 1. Test results in 301 consecutive patients

Diagnosis (No)	Calprotectin level	No. of patients with Positive ELISA test	No. of patients with Positive Bedside test
CD (109)	≤15µg/g	3	4
	>15µg/g	106	105
UC (46)	≤15µg/g	1	2
	>15µg/g	45	44
Cystic fibrosis (41)	≤15µg/g	16	19
	>15µg/g	25	22
Diarrhea (34)	≤15µg/g	10	13
	>15µg/g	24	21
Others (21)	≤15µg/g	9	11
	>15µg/g	12	10
Controls (50)	≤15µg/g	48	47
	>15µg/g	2	3

Table 2. Test characteristics of Calprotectin ELISA and Bedside test (cut off value >15µg/g) in different diagnostic groups

Parameters	Calprotectin ELISA	Bedside Calprotectin
Sensitivity (%)		
Crohn's Disease	97.2 (92.1-99.4)	96.3 (90.9-99.0)
Ulcerative colitis	97.8 (88.4-99.9)	95.6 (85.1-99.5)
Cysic Fibrosis	60.9 (44.5-75.8)	53.7 (37.4-69.3)
Diarrhea	30.5 (52.5-84.9)	61.7 (43.6-77.8)
Specificity (%)		
For all diseases	96.0 (86.2-99.5)	94.0 (83.4-98.8)
PPV (%)		
Crohn's Disease	98.1 (93.4-99.7)	97.2 (92.1-99.4)
Ulcerative colitis	95.74 (85.4-99.4)	93.7 (82.4-98.7)
Cysic Fibrosis	92.6 (75.7-99.1)	88.0 (68.8-97.4)
Diarrhea	92.3 (74.9-99.0)	87.5 (67.6-97.3)
NPV (%)		
Crohn's Disease	94.12 (83.76-98.77)	92.2 (81.1-97.9)
Ulcerative colitis	97.9 (89.1-99.9)	95.9 (86.0-99.5)
Cysic Fibrosis	75.0 (62.6-85.0)	71.2 (58.8-81.7)
Diarrhea	82.8 (70.6-91.4)	78.3 (65.8-87.9)

DISCUSSION

- Now since many years fecal concentration of the neutrophil granulocyte-derived a 36 kDa calcium and zinc binding protein, calprotectin has been shown to be a sensitive marker for the presence of infectious, inflammatory or malignant disease in GI tract.
- It represents 60% of the granulocyte cytosolic protein hence its concentration is seen to be directly proportional to neutrophil migration in to the GI tract. Hence is not specific as increased levels indicate GI inflammation irrespective of any specific disease. Thus can be considered akin to ESR of the blood.
- Not only in diagnosing the diseases, recently it has also been shown to be of significant use in non invasive assessment of clinical activity of IBD, thus saving the discomfort, cost, risks and expense of colonoscopy.
- It is very stable marker i.e. remains stable for more than 1 week in stool samples kept at room temperature thus can be send to the clinic/laboratory by post.
- However has a major drawback that it can be found to be raised in subjects using NSAIDs, patients having systemic illness, and also older subjects, these factors may hampers its specificity.
- Performance characteristics of both the tests in the present study almost similar and the difference between the tests are not statistically significant.
- Not only the convenience but costs are also significantly different for both the tests as an ELISA based one costs around 25 € while for bedside test patient has to pay only 4 €.
- This is the first ever report of the use of this newer and quicker immunochromatograhic test.

CONCLUSION

- This new bedside fecal calprotectin test has been shown to be simple, rapid (needs just about 5 min), convenience, no need of cumbersome ELISA readers and the fact that it can be performed at the patient bedside or in physician's office by any health care personnel.
- Its performance characteristics are similar to that of an established ELISA based test, and thus can replace the ELISA tests.
- However further clinical studies are warranted to evaluate this newer bedside calprotectin test.

REFERENCES

1. Vermeire S, Assche G, et al. Gut 2006; 55;426-31
2. Aadland E, Fagerhol M, et al. Eur J Gastroenterol Hepatol 2002:14:823-25.
3. Costa F, Mumolo M, et al. Gut 2005;54;364-68.
4. Gaya D, Lyon T, et al. Q J Med 2005;98:435-41.
5. Carrocio A, Iacono G, etal. Clinical Chemistry 2003:49:6;861-67.

AGA Disclosure
Abstract Number S1314

All the Authors of this poster DO NOT have any financial or other relationship to disclose

Table 1. Test results in 301 consecutive patients

Diagnosis (No)	Calprotectin level	No. of patients with Positive ELISA test	No. of patients with Positive Bedside test
CD (109)	≤15µg/g	3	4
	>15µg/g	106	105
UC (46)	≤15µg/g	1	2
	>15µg/g	45	44
Cystic fibrosis (41)	≤15µg/g	16	19
	>15µg/g	25	22
Diarrhea (34)	≤15µg/g	10	13
	>15µg/g	24	21
Others (21)	≤15µg/g	9	11
	>15µg/g	12	10
Controls (50)	≤15µg/g	48	47
	>15µg/g	2	3

Table 2. Test characteristics of Calprotectin ELISA and Bedside test (cut off value >15µg/g) in different diagnostic groups

Parameters	Calprotectin ELISA	Bedside Calprotectin
Sensitivity (%)		
Crohn's Disease	97.2 (92.1-99.4)	96.3 (90.9-99.0)
Ulcerative colitis	97.8 (88.4-99.9)	95.6 (85.1-99.5)
Cysic Fibrosis	60.9 (44.5-75.8)	53.7 (37.4-69.3)
Diarrhea	70.5 (52.5-84.9)	61.7 (43.6-77.8)
Specificity (%)		
For all diseases	96.0 (86.2-99.5)	94.0 (83.4-98.8)
PPV (%)		
Crohn's Disease	98.1 (93.4-99.7)	97.2 (92.1-99.4)
Ulcerative colitis	95.74 (85.4-99.4)	93.7 (82.4-98.7)
Cysic Fibrosis	92.6 (75.7-99.1)	88.0 (68.8-97.4)
Diarrhea	92.3 (74.9-99.0)	87.5 (67.6-97.3)
NPV (%)		
Crohn's Disease	94.12 (83.76-98.77)	92.2 (81.1-97.9)
Ulcerative colitis	97.9 (89.1-99.9)	95.9 (86.0-99.5)
Cysic Fibrosis	75.0 (62.6-85.0)	71.2 (58.8-81.7)
Diarrhea	82.8 (70.6-91.4)	78.3 (65.8-87.9)

Verdacht auf infektiöse Diarrhoe – Stuhlkultur ja oder nein?
Evaluierung eines Stuhl-Calprotectinschnelltestes als positiver prädiktiver Marker für invasive Erreger

Dominik Bergis, Volker Schäfer*, Nada Povse, Jürgen Stein
Medizinische Klinik I - ZAFES, J. W. Goethe-Universität, Frankfurt am Main
*Institut für medizinische Mikrobiologie, J. W. Goethe-Universität, Frankfurt am Main

Poster
vorgestellt auf der
60. Jahrestagung der DGVS
14. - 17. 9.2005 in Köln

Einleitung

Zum Nachweis pathogener Keime als Ursache einer infektiösen Diarrhoe gibt es heute neben der klassischen Stuhlkultur eine Vielzahl von immunologischen und/oder molekulargenetischen Testsystemen. Die meisten davon, insbesondere die klassische Stuhlkultur, sind jedoch mit einem erheblichen Zeit- und nicht zuletzt Kostenaufwand verbunden. Ein schnell verfügbares, kostengünstiges Testsystem existierte bisher nicht. Es konnte aber gezeigt werden, dass die Bestimmung von fäkalem Calprotectin als Screeningmarker mittels eines monoklonalen Immunoassays diesem Anspruch am ehesten gerecht wird [1]. Eine weitere Verbesserung verspricht ein neuer, schnellerer und leichter durchzuführender Calprotectin-Schnelltest.

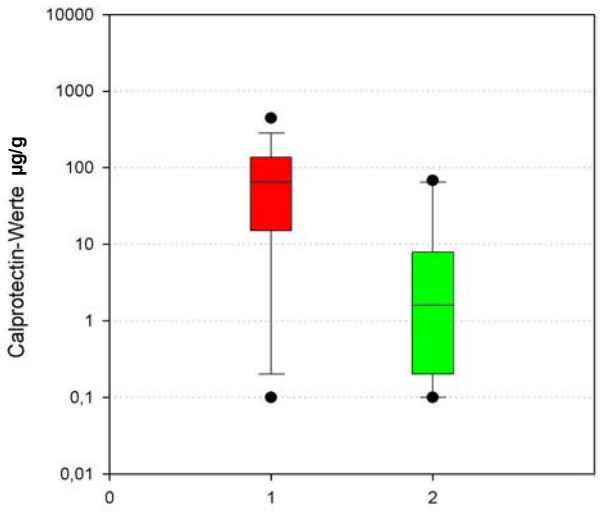
Material & Methoden

Im Rahmen einer prospektiven, monozentrischen Studie wurden die Stuhlproben von 78 Patienten untersucht. Die Proben waren vorher zur Abklärung der Infektiosität einer akuten Diarrhoe mikrobiologisch aufgearbeitet worden. Neben einer klassischen Stuhlkultur wurden Antigennachweise auf Clostridium difficile, Salmonella spp., Campylobacter spp., Shigella spp. und Rotavirus durchgeführt. Anschließend wurde aus den Proben fäkales Calprotectin bestimmt. Zuerst mittels des monoklonalen Immunoassays MRP 8/14, danach unabhängig davon mittels eines neuen semiquantitativen Calprotectin-Schnelltests. Die Ergebnisse aus dem Immunoassay dienten als Referenzwerte.

Ergebnisse

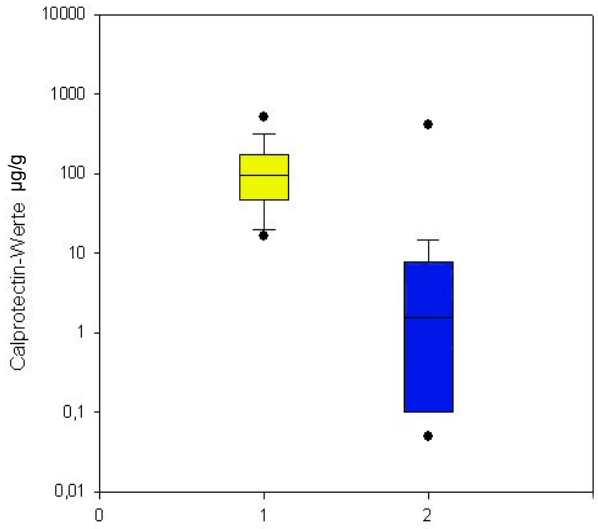
Bei 63 Patienten wurden in der Stuhlkultur pathogene Keime bzw. Antigene nachgewiesen (6 Campylobacter spp,. 45 Clostridium difficile, 2 Rotavirus, 9 Salmonella spp., 1 Shigella flexneri). Bei 15 Patienten war kein Keim als Ursache der Diarrhoe nachzuweisen. Bei Patienten mit positivem Keimnachweis fand sich in 56 Fällen (88,89%) ein positiver Calprotectin-Wert (>15 µg/g Stuhl) im monoklonalen Immunoassay. Bei 7 Patienten (11,11%) war der Calprotectin-Wert trotz Keimnachweis negativ (<15 µg/g Stuhl). Bei den Patienten ohne nachgewiesenen Keim waren die Calprotectin-Werte in 13 Fällen (86,67%) negativ, in 2 Fällen (13,33%) waren sie positiv. Identische Ergebnisse fanden sich auch im Schnelltest. Lediglich bei 4 Proben (5,13%) unterschieden sich die Calprotectin-Werte des Immuoassays von denen des Schnelltests. Der positive prädiktive Wert lag für beide Tests bei 96,55%, der negative prädiktive Wert bei 65%.

Grafik 1: Box Plots der Calprotectin-Werte aus dem ELISA-Test



Legende:
1 = Patienten mit positivem Erregernachweis (n=63)
2 = Patienten mit negativem Errgernachweis (n=15)

Grafik 2: Box Plots der Calprotectin-Werte aus dem semiquantitativen Schnelltest in Bezug zu den Werten aus dem ELISA-Test



Legende:
1 = Proben mit positivem Schnelltest (Calprotectin >15µg/g Stuhl, n=58)
2 = Proben mit negativem Schnelltest (Calprotectin <15µg/g Stuhl, n=20)

Tabelle 1: Ergebnisse aus dem semiquantitativen Calprotectin-Schnelltest

	Patientenzahl mit Schnelltest-Ergebnis >15µg/g („positiv“)	Patientenzahl mit Schnelltest-Ergebnis <15µg/g („negativ“)
Campylobacter species	**6**	0
Clostridium difficile	**45**	4
Rotavirus	**1**	1
Salmonella species	**7**	2
Shigella sonnei	**1**	0
Kein Erreger nachgewiesen	2	**13**

Tabelle 3: Sensitivität, Spezifität, positiver und negativer Vorhersagewert (unter Angabe des 95% - Konfidenzintervalls) des Calprotectin-Schnelltests

	Sensitivität (%)	Spezifität (%)	Positiver prädiktiver Wert (%)	Negativer prädiktiver Wert (%)
Anzahl der Patienten (n=78)	**88,89** (78,44 – 95,41)	**86,67** (59,54 – 98,34)	**96,55** (88,09 – 99,58)	**65,0** (40,78 – 84,61)

Diskussion

Die Ergebnisse bestätigen erneut, dass sich fäkales Calprotectin als Screeningparameter für infektiöse Diarrhoen eignet. Weiterhin zeigen sie, dass der neue Calprotectin-Schnelltest sehr gute Ergebnisse liefert und dem klassischen ELISA-Test somit gleichwertig ist. Er ist jedoch leichter, kostengünstiger und nahezu ortsunabhängig wie ein Bedside-Test durchführbar.

Literatur

[1] Z Gastroenterol 2004; 42: 785

Anmerkungen

Diese Studien wurden von der Else-Kröner-Fresenius-Stiftung gefördert (Bad Homburg, Germany).