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RAPID COMMUNICATION

Usefulness of fecal lactoferrin and hemoglobin in diagnosis of colorectal diseases

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Abstract

AIM: To evaluate prospectively usefulness of fecal lactoferrin (Lf) and fecal hemoglobin (Hb) in the diagnosis of colorectal diseases.

METHODS: Fecal Lf and Hb were measured using ELISA in 872 patients before they underwent colorectal endoscopy.

RESULTS: Lf was positive in 18 (50%) of 36 patients with colorectal cancer, 25 (15.9%) of 157 with colorectal polyps, 29 (46.8%) of 62 with ulcerative colitis, and 25 (62.5%) of 40 (62.5%) with Crohn's disease. The Hb-positive rates were 50%, 12.1%, 41.9% and 32.5%, respectively. Of the 318 patients free of abnormalities by colorectal endoscopy, Lf was positive in 29 (9.1%) and Hb was positive in 15 (4.7%). Among patients with Crohn's disease, the Lf-positive rate was significantly higher than the Hb-positive rate. If either high Lf or Hb levels were considered positive, the positive rates rose to 61.1%, 51.6%, and 67.5% in the colorectal cancer group, ulcerative colitis group, and Crohn's disease group, respectively. If both high Lf and Hb levels were rated positive, the positive predictive values (PPV) were 21% for colorectal cancer, 33% for ulcerative colitis, and 17% for Crohn's disease, and PPV of high Hb level alone was 18%, 25% and 13%, respectively.

CONCLUSION: Fecal Lf and Hb were found useful in the detection of colorectal diseases, and the combination of the two measurements appears to increase the sensitivity and efficacy of diagnosis.

Key words: Feces; Lactoferrin; Hemoglobin; Diagnosis; Colorectal disease

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INTRODUCTION

In the United States, colorectal cancer is the second leading cause of death[1]. In Japan, the prevalence of colorectal cancer and the percentage of this cancer among all cancer deaths have recently been rising as well. Because the prognosis of patients with colorectal cancer depends on the stage of cancer at the time of detection, screening for early diagnosis of colorectal cancer is considered essential[2,3]. In the United States, fecal occult blood testing by the guaiac method has been used as a screening method for colorectal cancer. A randomized study found that this method reduced the mortality rate of colorectal cancer[4,5]. In Japan, immunological fecal occult blood testing with a target of hemoglobin (Hb) has often been used in screening for colorectal cancer[6]. Fecal occult blood testing is also useful in the diagnosis and evaluation of various colorectal diseases other than colorectal cancer[7-9]. However, Hb in feces is unstable, which can be a cause of false-negative cases. Furthermore, Hb is not useful in the detection of lesions not accompanied by bleeding. For these reasons, a fecal marker with a high sensitivity and specificity has to be developed. Lactoferrin (Lf), which is released from neutrophil-specific granules, is stable in feces and is an excellent marker of activity of inflammatory bowel diseases such as ulcerative colitis and Crohn's disease[10]. It has also been reported that fecal Lf level is higher in the patients with not only inflammatory bowel diseases but also colorectal tumors than in healthy individuals[11]. In a pilot study comparing fecal Lf level with fecal occult blood testing (immunological qualitative method) in 351 patients, Lf was found as useful as fecal occult blood testing in the diagnosis of colorectal diseases[12].

This prospective study involved a larger number of subjects than in previous studies to compare the usefulness of fecal Lf with that of fecal Hb as a quantitative parameter for the diagnosis of colorectal diseases and to evaluate the combination of fecal Lf and Hb using fecal samples collected from patients on the day before colorectal endoscopy.

MATERIALS AND METHODS

Subjects and fecal sampling method

The subjects of this study were 872 patients scheduled to undergo colorectal endoscopy at the Second Department of Internal Medicine, Osaka Medical College University Hospital, who provided written informed consent to participate in the study. Their ages ranged from 12 to 90 years (14 > 20 years; 34, 20-29 years; 51, 30-39 years; 116, 40-49 years; 244, 50-59 years; 274, 60-69 years; 130, 70-79 years; and 9 over 80 years). Examination for colorectal cancers and polyps was also performed in 657 subjects over 50 years of age. Patients with severe diseases of liver, gallbladder or pancreas were excluded from this study. Feces were collected from each patient on the day before colorectal endoscopy. The container used for fecal sampling had a stick type, designed to allow collection of about 10 mg feces into 1 mL buffer solution by thrusting the stick into feces at several points. On the day of the test, each subject was pretreated with intestinal lavage in the morning and underwent colorectal endoscopy in the afternoon. During endoscopy, the entire large intestine was examined, with biopsy performed as needed.

Measurement of Lf and Hb

Lf and Hb levels in feces were measured by sandwich ELISA, using 96-well microplates. For measurement of Lf, rabbit anti-human Lf antibody (Dakopatts, Glostrup, Denmark) and peroxidase-labeled anti-human Lf antibody were used, with tetramethylbendizine as a color developer[13]. For Hb, anti-human Hb antibody and alkaline phosphatase-labeled anti-human Hb antibody were used by the Kind-King method for color development[7]. Concentrations were calculated, referring to the standard curves prepared from Lf originating from human colostrum (Cappel Co. Durham, NC) and Hb derived from the blood of healthy adults. All samples were subjected to measurement in blind fashion.

Statistical analysis

McNemar's test was used for statistical analysis. $P < 0.05$ was considered significant. For a given disease, sensitivity was defined as the positive rate, while specificity was defined as (number of true-negative cases)/(number of true-negative cases + number of false-positive cases). To compare the usefulness of fecal Hb and Lf, a operating characteristic analysis (ROC) was conducted. The ROC analysis involved preparing a sensitivity-false-positive rate curve and comparing areas under the curve (AUC), with an AUC of 0.5 uninformative and an AUC of 1 perfect[13].

Table 1 Comparison of fecal Lf and Hb between normal and abnormal groups

Group		Fecal Lf			Specificity	% (No.)
		+	-	Sum		
Normal group						
Fecal Hb	+	7	8	15	Lf	90.9 (289/318)
	-	22	281	303	Hb	95.3 (303/318)
	Total	29	289	318	$P = 0.0176$	
Abnormal group						
Fecal Hb	+	59	27	86	Lf	29.6 (164/554)
	-	105	363	468	Hb	15.5 (86/554)
	Total	164	390	554	$P < 0.0001$	

Table 2 Sensitivity of fecal Lf and Hb in various diseases

Diseases	*n*	Sensitivity	
		Hb > 100 % (No.)	Lf > 65 % (No.)
Colorectal cancer	36	50.0 (18/36)	50 (18/36)
Colorectal polyp	157	12.1 (19/157)	15.9 (25/157)
Ulcerative colitis	62	40.3 (25/62)	46.8 (29/62)
Crohn's desease	40	32.5 (13/40)	62.5[b] (25/40)
Colorectal diverticulum	73	1.4 (1/73)	19.2[b] (14/73)
Internal hemorrhoids	142	4.2 (6/142)	27.5[b] (39/142)
Nonspecific colitis	20	15.0 (3/20)	20 (4/20)
Other diseases1	24	4.2 (1/24)	41.7[b] (10/24)

[b]$P < 0.01$ *vs* Hb. 1Including 4 cases of previous intestinal tuberculosis, 4 of submucosal tumor, 2 of ischemic colitis, 2 of rectal carcinoid, 2 of Behcet disease, 2 of rectal mucosal prolapse syndrome, 2 of Cronkhite-Canada syndrome, 2 of Cowden disease, 1 of mucosa-associated lymphoma, and 1 of periappendiceal abscess.

RESULTS

Diagnosis

Of the 872 subjects, 554 were found to have abnormalities on colorectal endoscopy, while 318 were rated as free of abnormalities (Tables 1 and 2). Polyps were defined as adenomas over 5 mm in size. Individuals with colorectal polyps were classified as having colorectal polyps even accompanied with internal hemorrhoids and/or colorectal diverticula. Individuals with both internal hemorrhoids and colorectal diverticula were classified as cases of internal hemorrhoids.

Establishment of cut-off levels for fecal Lf and Hb

For the 25 healthy individuals, the mean + 2SD (the upper limit of the normal range) was 5.96 μg/g for fecal Lf and 9.18 μg/g for fecal Hb[10]. In this study, feces were diluted 1:100 with the buffer solution in the container, the mean + 2SD for healthy individuals was equivalent to 59.6 ng/mL for Lf and 91.8 ng/mL for Hb. We therefore set the cut-off levels for this study at 65 ng/mL (Lf) and 100 ng/mL (Hb).

The AUC of the ROC curve was greater for Lf (0.600) than for Hb (0.556), although this difference was not statistically significant.

Analysis of groups with and without abnormalities

In the abnormality-free group ($n = 318$), fecal Lf was

Table 3 Diagnosis value using combination of fecal Lf and Hb

Diseases	*n*	Sensitivity	
		Hb > 100 or Lf > 65 % (No.)	Hb > 100 and Lf > 65 % (No.)
Colorectal cancer	36	61.1 (22/36)	38.9 (14/36)
Colorectal polyp	157	25.5 (40/157)	2.5 (4/157)
Ulcerative colitis	62	51.6 (32/62)	35.5 (22/62)
Crohn's desease	40	67.5 (27/40)	27.5 (11/40)
Colorectal diverticulum	73	19.2 (14/73)	1.4 (1/73)
Internal hemorrhoids	142	28.9 (41/142)	2.8 (4/142)
Nonspecific colitis	20	20.0 (4/20)	15.0 (3/20)
Other diseases	24	45.8 (11/24)	0.0 (0/24)

Table 4 Positive predictive value (PPV) of fecal Lf and Hb in colorectal diseases

Diseases	*n*	PPV	
		Hb > 100 % (No.)	Hb > 100 and Lf > 65 % (No.)
Colorectal cancer	36	17.8 (18/101)	21.2 (14/66)
Colorectal polyp	157	18.8 (19/101)	6.1 (4/66)
Ulcerative colitis	62	24.8 (25/101)	33.3 (22/66)
Crohn's desease	40	12.9 (13/101)	16.7 (11/66)
Colorectal diverticulum	73	1.0 (1/101)	1.5 (1/66)
Internal hemorrhoids	142	5.9 (6/101)	6.1 (4/66)
Nonspecific colitis	20	3.0 (3/101)	4.5 (3/66)
Other diseases	24	1.0 (1/101)	0.0 (0/66)

Table 5 Comparison of fecal Lf and Hb in subjects aged over 50 yr

		Fecal Lf			Specificity	% (No.)
		+	-	Sum		
Normal group						
Fecal Hb	+	7	8	15	Lf	89.7 (217/242)
	-	18	209	227	Hb	93.8 (227/242)
	Total	25	217	242	$P = 0.0776$	
Abnormal group						
Fecal Hb	+	32	20	52	Lf	26.0 (108/415)
	-	76	287	363	Hb	12.5 (52/415)
	Total	108	307	415	$P < 0.0001$	

Table 6 Sensitivity of fecal Lf and Hb in colorectal cancer

Colorectal cancer	*n*	Sensitivity	
		Hb % (No.)	Lf % (No.)
Total	36	50.00 (18/36)	50.00 (18/36)
Early stage	17	11.80 (2/17)	29.40 (5/17)
Right side	5	20 (1/5)	40.00 (2/5)
Left side	12	8.30 (1/12)	25.00 (3/12)
Advanced stage	19	84.20 (16/19)	68.40 (13/19)
Right side	6	66.70 (4/6)	83.30 (5/6)
Left side	13	92.30 (12/13)	61.50 (8/13)

Note: *n*. number of cases.

positive in 29 cases (specificity: 90.9%) and fecal Hb was positive in 15 cases (specificity: 95.3%). Specificity was thus significantly higher for Hb than for Lf. In the group with abnormalities ($n = 554$), fecal Lf was positive in 164 cases (sensitivity: 29.6%) and fecal Hb was positive in 86 cases (sensitivity: 15.5%). Sensitivity was thus significantly higher for Lf than for Hb.

Analysis in each disease group

Sensitivities were compared between fecal Lf and Hb in each disease group (Table 2). The sensitivity of fecal Lf was significantly higher than that of fecal Hb in the Crohn's disease, internal hemorrhoid, and colorectal diverticulum. There was no significant difference in sensitivity between Lf and Hb in the colorectal cancer, colorectal polyp, and ulcerative colitis.

Diagnosis using a combination of fecal Lf and Hb

When either high Hb or high Lf (Hb > 100 or Lf > 65) was rated positive, sensitivity in disease detection rose to 61.1% for colorectal cancer, 25.5% for colorectal polyps, 51.6% for ulcerative colitis, 67.5% for Crohn's disease, 19.2% for colorectal diverticulum, 28.9% for internal hemorrhoids, 20.0% for nonspecific colitis, and 45.8% for other diseases (Table 3). When both high Hb and high Lf (Hb > 100 and Lf > 65) were rated positive, the number of individuals rated positive among the 318 abnormality-free individuals decreased to 7 (Table 1). The positive rate by each disease group also decreased (Table 3), though the magnitude of the decrease was relatively mild in the colorectal cancer, Crohn's disease, and ulcerative colitis. Positive predictive value (PPV) (number of positive cases positive cases) rose to 21.2% (14/66) for colorectal cancer, 33.3% (22/66) for ulcerative colitis, and 16.7% (11/66) for Crohn's disease (Table 4).

Analysis of subjects over 50 years of age

Because examinations for colorectal cancer are usually performed in individuals aged 50 years or older, we performed an analysis confined to the 657 individuals aged over 50 years[14]. Among the 242 subjects free of abnormalities, Lf was positive in 25 (specificity, 89.7%) and Hb was positive in 15 (specificity, 93.8%), as shown in Table 5. Among the 415 patients with abnormalities, Lf was positive in 108 (sensitivity, 26.0%) and Hb was positive in 52 (sensitivity, 12.5%) (Table 5). We then examined the sensitivity in detection of colorectal cancer and polyps. In the 33 patients with colorectal cancer aged over 50 years, Hb was positive in 16 (sensitivity, 48.5%) and Lf was positive in 17 patients (sensitivity, 51.5%). When either high Lf or high Hb was rated positive, sensitivity rose to 60.6% for colorectal cancer and 25.2% for colorectal polyps. When both high Lf and high Hb were rated positive, PPV rose to 33.3% in the colorectal cancer group.

Analysis of patients with colorectal cancer

Of 36 patients aged 36-81 years with colorectal caner, 14 had both Lf and Hb levels below the cut-off levels. Twelve of the 14 patients had colorectal cancer at an early stage confined to the submucosal layer. When analyzed by location (left or right side of the colon) and stage of cancer (early and advanced), the Hb-positive rate (12/13) was higher than Lf-positive rate (8/13) in patients with advanced left side colon cancer (Table 6). Among patients with right side colon cancer, however, the Lf-positive

early and advanced patients(2/5 *vs* 1/5 and 5/6 *vs* 4/6, respectively). Macroscopically, bloody stool was noted in 10 of the 36 patients with colorectal cancer. Therefore, excluding these 10 cases, routine fecal test was enough for screening of colorectal cancer. Among the 26 cases, the Lf-positive rate (46.2%) was higher than the Hb-positive rate (38.5%).

Analysis of patients with ulcerative colitis or Crohn's disease

Ulcerative colitis was considered in active stage if active lesions were revealed by colorectal endoscopy. Among the 38 cases of active ulcerative colitis, Lf and Hb were positive in 26 and 22 cases, respectively. Among the 24 cases of inactive ulcerative colitis, Lf and Hb were positive in 3 and 3 cases, respectively.

Crohn's disease was considered active if the Crohn's disease activity index (CDAI) was over 150 or if active lesions were detected by colorectal endoscopy[15]. Among the 26 cases of active Crohn's disease, Lf and Hb were positive in 18 and 12 cases while in the 12 cases of inactive Crohn's disease, Lf and Hb were positive in 8 cases and 1 case, respectively. In patients with Crohn's disease, minor active lesions of the small intestine often persist, but the CDAI is likely to be lower than 150 during treatment, often leading to the judgment that the patient has inactive disease clinically.

DISCUSSION

Lf is an ironbound protein with a molecular weight of about 80000. It is found not only in neutrophil-specific granules but also in milk, tears, saliva, etc.[16,17]. The presence of Lf in the cytoplasm of colorectal cancer and adenoma cells has also been reported[18,19]. The high Lf level in the feces of patients with intestinal inflammation is believed to originate from the neutrophils which have infiltrated the intestinal mucosa[20-22]. The reason for elevation of fecal Lf level in patients with colorectal cancer has not yet been fully determined. It has been reported that some colorectal cancers are accompanied by local inflammatory reaction, and that leukocyte scintigraphy is sometimes positive in patients with colorectal cancer[23-25]. Neutrophil elastase and calprotectin, which are neutrophilic granular proteins, are absent in tumor cells, though their levels in feces of patients with colorectal cancer are high[26, 27]. Neutrophils thus appear to be a more important source of fecal Lf than exfoliated tumor cells in patients with colorectal cancer. In this study, the usefulness of fecal Lf in the diagnosis of various colorectal diseases was prospectively evaluated.

Among the subjects free of abnormalities, the LF-positive rate was 9.1% (29/318) and the Hb-positive rate was 4.7% (15/318), both of which were higher than those in the general screening. In patients with symptoms such as diarrhea and abdominal pain, fecal Lf may be rated positive due to transient or minor inflammation not detectable with colorectal endoscopy, even when they are considered free of abnormalities by colorectal endoscopy. In patients who have been found positive for fecal occult of the patients who are fecal Hb-positive without any abnormality is high.

Many of our patients were positive in fecal occult blood prior to visiting the hospital or visited the hospital complaining of macroscopically bloody stool. This suggests that patients with colorectal lesions of hemorrhagic subtype accounted for a high percentage of the subjects of this study. For example, colorectal cancers which likely cause bleeding or positive findings for fecal occult blood were found in a high percentage of patients with colorectal cancer in this study. Thus, based on the fact that Hb is expected to be more useful than Lf, the sensitivity of Lf was significantly higher than that of Hb in patients with abnormalities. Because this study involved quantitative measurement of both Lf and Hb, we compared the usefulness of Lf and Hb in the diagnosis of colorectal diseases by means of ROC analysis. A greater AUC was found in Lf than in Hb, although this difference was not significant. These findings suggest that Lf is comparable to or more useful than Hb in detecting colorectal diseases.

By type of disease, the sensitivity of testing for Lf was comparable to that for Hb for colorectal cancer, colorectal polyps, ulcerative colitis, and nonspecific colitis. For Crohn's disease, internal hemorrhoids, colorectal diverticulum, and other colorectal diseases, the sensitivity of Lf testing was significantly higher than that of Hb testing.

In patients with Crohn's disease, the Lf-positive rate was high even the disease was rated as inactive. It seems more rational to interpret this result as that inflammation of the intestine persists in patients with Crohn's disease with high fecal Lf levels, rather than as a false-positive result for the following reasons: (1) in Crohn's disease, the intestine often remains inflamed even after the CDAI decreases to below 150 after treatment; and (2) complete evaluation of residual inflammation of the intestine is difficult even with colorectal endoscopy. The "other diseases" mentioned above include important diseases such as old intestinal tuberculosis, submucosal tumor, rectal carcinoid, Behcet disease, Cronkhite-Canada syndrome, Cowden disease, and mucosa-associated lymphoid tissue lymphoma (MALT). Significantly higher sensitivity of testing for Lf than that for Hb in the "other diseases" group is clinically important.

The results of this study suggest that it is possible to increase the accuracy of screening based on the conventional fecal occult blood test with a target set at Hb by combining Hb with Lf. For example, when immunological fecal occult blood testing is used for screening of colorectal cancer, feces are often sampled repeatedly to increase the sensitivity of detection. However, if a combination of Hb and Lf is used and results are considered positive in cases with high Lf or Hb, it is possible to perform a highly sensitive screening that requires only one fecal sampling. In addition, if results were considered positive in cases with both high Lf and Hb, PPV rose in the colorectal cancer, ulcerative colitis, and Crohn's disease. If PPV is high, it will be easier to convince patients to take further examinations such as colorectal endoscopy etc. because of the likelihood of the

Hb is likely to be degraded by bacteria or enzymes contained in feces, resulting in loss of antigenicity. In buffer fluid, both fecal Lf and fecal Hb remained stable for 3 days, retaining 75% or greater activity compared to that recorded immediately after sampling[12]. In this study, feces were collected into a buffer fluid. For this reason, we believe that stability after sampling was not different between Lf and Hb in this study. In the intestine, however, Lf is believed to be more stable than Hb. We therefore, analyzed Lf- and Hb-positive rates by location of colorectal cancer, and found that Hb was highly sensitive in detecting advanced cancer of the left side of the colon, i.e., the sensitivity of Hb was lower in detection of colorectal cancer than in advanced cancer of the left side of the colon. This finding appears to be related to the following factors: (1) relatively low stability of Hb within the intestine, as noted above; and (2) the feces in the right portion of the colon are still too soft to cause bleeding. Although the sensitivity of Lf in detecting cancer of the left side of the colon was lower than that of Hb, it was higher in detecting cancers affecting other portions of the colon compared to Hb. The low sensitivity of fecal occult blood testing in the detection of early colorectal cancer has been noted in previous reports. In this study, only 2 of the 17 cases of early colorectal cancer were positive by this method. However, of these 17 patients with early colorectal cancer, 14 had been found in other clinics to be positive for fecal occult blood and visited our hospital for this reason. This suggests that in cases of early colorectal cancer, bleeding is often intermittent rather than continuous. On the other hand, Lf was positive in 5 of the 17 cases of early colorectal cancer, and its sensitivity in detecting early colorectal cancer was higher than that of Hb. Thus, the findings of the analyses by location and stage of colorectal cancer also suggest that a combination of Lf and Hb can compensate the shortcomings of these two parameters used individually for detection of colorectal cancer.

Examinations for colorectal cancer are usually performed in individuals over 50 years of age. When analysis was confined to this age group, specificity of Lf was slightly lower (89.7%) than that of Hb (93.8%), while sensitivity of Lf was slightly higher (51.5%) than that of Hb (48.5%). When results were considered positive if both Lf and Hb were high, PPV rose to 33.3%. The combination of Lf and Hb is thus useful in judging whether an individual aged over 50 years has a high risk for colorectal cancer.

Numerous studies have been published concerning noninvasive screening methods, which may replace the fecal occult blood test used for screening of colorectal caner[28,29]. A multi-target assay, designed to detect abnormal DNA in feces, exhibited a high sensitivity in detecting colorectal cancer, although no comparison of this assay had been made with fecal Hb measurement. Furthermore, this assay is too expensive for general use in clinics or health checkups[30]. Measurement of calprotectin, one of the neutrophil-specific granules, is highly sensitive in detecting colorectal cancer, though its specificity is low. Furthermore, no comparison of calprotectin with fecal Hb

In conclusion, our results suggest that the usefulness of fecal Lf measurement appears comparable to that of fecal Hb measurement in detection of colorectal diseases. Furthermore, the combination of Lf and Hb measurement appears to increase the sensitivity and efficacy of diagnosis.

COMMENTS

Background

The high Lactoferrin (Lf) level in the feces of patients with intestinal inflammation is believed to originate from the neutrophils which have infiltrated the intestinal mucosa. The presence of Lf in the cytoplasm of colorectal cancer and adenoma cells has also been reported. The reason for elevation of fecal Lf level in patients with colorectal cancer has not yet been fully determined. It has been found that some colorectal cancers are accompanied by local inflammatory reaction, and that leukocyte scintigraphy is sometimes positive in patients with colorectal cancer. Neutrophil elastase and calprotectin, which are neutrophilic granular proteins, are absent in tumor cells, although their levels are high in feces from patients with colorectal cancer. Neutrophils thus appear to be a more important source of fecal Lf than exfoliated tumor cells in patients with colorectal cancer. Therefore, the usefulness of fecal Lf in the diagnosis of various colorectal diseases was prospectively evaluated in this study.

Research frontiers

In the United States, fecal occult blood testing (FOBT) by the guaiac method has been used as a screening for colorectal cancer. A randomized study found that this method lowered the mortality rate of colorectal cancer. In Japan, immunological FOBT with a target of hemoglobin (Hb) has often been used in screening for colorectal cancer. FOBT is also useful in the diagnosis and evaluation of various colorectal diseases other than colorectal cancer. However, since Hb in feces is unstable, it may result in false-negative cases. Furthermore, Hb is not useful in the detection of lesions not accompanied by bleeding. For these reasons, development of a fecal marker with high sensitivity and specificity is needed. Lf, which is released from neutrophil-specific granules, is stable in feces and is an excellent marker of activity of IBD. Fecal Lf level has been reported to be higher in the patients with not only IBD but also colorectal tumors than in healthy individuals. In a pilot study comparing fecal Lf level with fecal occult blood testing in 351 individuals, Lf was found to be as useful as fecal occult blood testing in the diagnosis of colorectal diseases.

Innovations and breakthroughs

The measurement of fecal Lf and Hb was found to be useful in the detection of colorectal diseases, and the combination of the two measurements appears to increase the sensitivity and efficacy of diagnosis.

Applications

The combined measurement of fecal Lf and Hb should be useful for screening of colorectal diseases including colorectal cancer.

Terminology

Lf is an ironbound protein with a molecular weight of about 80 000. It is found not only in neutrophil-specific granules but also in milk, tears, saliva, etc. The high Lf level in the feces of patients with intestinal inflammation is believed to originate from the neutrophils which have infiltrated the intestinal mucosa.

Peer review

Hirata *et al* demonstrated the usefulness of fecal Lf and Hb levels for screening of colorectal cancer and IBD. This study might be clinically relevant. The reliability of their data is dependent on the presentation of determination method. More precise methods of their ELISA for lactoferrin and hemoglobin should be described.

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