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Original Article

Comparison of Fecal Calprotectin Level in Inflammatory Bowel Disease and Irritable Bowel Syndrome

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ABSTRACT

Background: Fecal calprotectin (FC) has been suggested as a noninvasive substitute marker to determine the degree of intestinal inflammation in patients with inflammatory bowel disease (IBD). The aim of this study was to compare FC levels in IBD and irritable bowel syndrome (IBS), to show its discriminative value and relationship with clinical disease activity in patients with IBD.

Materials and Methods: During the time period between May 2008 and November 2009, 41 patients with newly diagnosed or relapse of IBD and 40 patients with IBS who referred to Gastroenterology Clinic of Firoozgar Hospital, Tehran, Iran, were selected in a consecutive random manner. A sample of stool was collected from each patient before colonoscopy, and fecal calprotectin levels were measured using an ELISA kit (Buhlmann Co., Switzerland). Differences in FC levels were considered statistically significant where $p<0.05$.

Results: Mean calprotectin level in IBD cases (newly diagnosed and relapse) was 193.57±147.79µg/gr, which was significantly higher than those in IBS cases (28.25±15.13µg/gr) and the difference was statistically significant ($p<0.001$).

Conclusion: FC levels can be used to differentiate patients with IBD from those with non-inflammatory gastrointestinal disorders such as IBS and can be used as a screening tool for selection of patients who need colonoscopy.

Keywords: Calprotectin, Inflammatory bowel disease, Irritable bowel syndrome.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic condition characterized by recurrent episodes of inflammation in the gastrointestinal tract and includes crohn's disease (CD) and ulcerative colitis (UC). Patients with IBD experience diarrhea, abdominal pain and cramps, disrupted digestion, rectal bleeding, weight loss and a substantial personal burden (1-2). The precise etiology of IBD is remained mainly unknown but is thought to be a complex interaction of immunological, genetic and environmental (such as enteric microflora) factors (3-4). Interrelated with IBD is irritable bowel syndrome (IBS), one of the most common gastrointestinal disorders seen in primary health care (5). It is characterized as a functional bowel disorder wherein discomfort or abdominal pain is related with defecation or a change in bowel habit and with features of disordered defecation (6). Several studies

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specified that there is a female predominance and the prevalence is 10-20% in the Western world. (7-8), Calprotectin is a member of the Ca-binding S100 family of proteins, a heterogeneous complex of S100A8/S100A9 proteins (9-10). It is present in neutrophils and monocytes and is released by activation of these cells in plasma, urine, stools and other media as a consequence of disease activity (9). Several studies reported that fecal calprotectin level is associated with invasive markers of gut inflammation such as 99Tc-labeled white cell scans and endoscopic and histological inflammation scores (11-12). Recent studies showed FC is a specific, sensitive, non-invasive, cheap and accessible marker for gut inflammation (13-15). Also, Costa et al., reported in 2005, FC is a strong predictor in IBD diagnosis (16). Furthermore, Von Room et al., showed FC is an accurate diagnostic marker in distinguishing IBD from non-IBD diagnoses (17). The aims of the present study were to define the appropriate role of fecal calprotectin in the investigation of patients with newly diagnosed IBD and those with flare up after treatment and to compare them with those in IBS patients for the first time in this field in Iran.

MATERIALS AND METHODS

In Firoozgar Hospital, Clinic of Gastroenterology, 41 Patients with IBD, (21 newly diagnosed IBD cases and 20 patients with relapse after treatment), and 40 patients with IBS (with normal colonoscopy and biopsy) were recruited in this retrospective case control study, between May 2008 and November 2009. Patients' age ranged 15-51 years (mean 35.4 years) in IBD group and 20-46 (mean 32.3 years) in IBS group. The main primary symptom in all patients was chronic diarrhea of more than 4 weeks with or without abdominal pain. Infectious diarrhea was ruled out for all patients with appropriate cultures. Exclusion criteria were active gastrointestinal bleeding, pregnancy and history of gastrointestinal cancer, familial or non-familial polyposis, colonoscopy and sigmoidoscopy in the past two years and long-term use of NSAIDs, aspirin or anticoagulant. A sample of stool was collected from each patient before colonoscopy and kept in -20°C until the time of analysis. Mean time difference between the time of specimen collection and analysis was 4 months. Analysis was performed using an ELISA kit for calprotectin (Buhlmann Co., Switzerland). riefly, the samples were thawed, and then 50 mg of each sample was added to 2.5 ml extraction buffer, provided in the kit, mixed well and centrifuged at 3500 rpm for 15 minutes. The supernatant was used for ELISA sandwich test. Approval was granted by the local and regional ethics committees, and participants gave informed written consent. We used The Mann-Whitney U test to compare the IBD and non-IBD groups in age and calprotectin levels in feces. The Chi-square test was used to compare sex. Spearman's correlation test was used for all correlations. Differences were considered statistically significant where $p<0.05$.

RESULTS

Eighty-one patients were enrolled in the study, 41 with IBD (20 males, 21 females) and 40 with IBS (19 males and 21 females). There was no significant difference between the two groups in gender (p=0.57) (Table 1).

Table1: comparison of IBD and IBS in age, gender and Mean fecal Calprotectin level

Parameter	IBD(n=42)	IBS(n=40)	p-value
Mean Age	35.4 ± 8.6	32.3 ± 6.8	0.07
Male/ Female(%)	20(48.2) / 21(51.8)	19(42.5) / 21(57.5)	0.57
Calprotectin Mean (µg/g)	193.5 ± 147.7	28.2 ± 15.1	0.00*

* P < 0.001

Mean fecal calprotectin level in newly diagnosed IBD (171.7 ± 124.7 µg/gr) and relapsed cases of

IBD (216.8±170.1 µg/gr) were considerably higher than those in IBS cases (28.2±15.1 µg/gr). There were a significant difference between each group of IBD cases (newly diagnoses and relapsed) with those with IBS in fecal calprotectin level ($p<0.001$).

This difference was still significant ($p<0.001$) when IBD cases were considered as one group, irrespective of primary disease or relapse (193.5±147.7 µg/gr).

DISCUSSION

The course of IBD is characterized by periods of relapse and remission because of increases and decreases in mucosal inflammatory activity, respectively (1-2). An important step in the primary assessment of patients with IBD is measurement of bowel inflammation as it defines the extent and severity of involvement at the beginning of treatment and during monitoring in order to target medical therapies and manage IBD-related complications (1-5). Many methods of assessing bowel inflammation have been proposed, including laboratory indices and clinical scores that generally are considered nonspecific (11,13). An objective assessment of bowel inflammation is provided by invasive tests, but patient's comfort limits their utility. It has been suggested that an inflammatory mediator directly released into the gut lumen from the inflammatory process might be an ideal test to detect bowel inflammation in IBD (13). In recent studies, fecal calprotectin has been claimed to be a specific, sensitive, non-invasive, cheap and accessible marker for gut inflammation. (5,14,15), The fact that calprotectin is stable in room temperature for 5 days makes it more suitable for routine clinical studies (18). In our study, FC levels in IBD cases (both newly diagnosed and relapsed) were considerably higher than those in IBS and the difference between the two groups was statistically significant ($p<0.001$). This finding confirms the results of previous studies; e.g., a study by Tibble et al. on 220 patients with IBD or IBS showed that the sensitivity and specificity of fecal calprotectin for discrimination between organic and functional intestinal disease were 82% and 83%, respectively. These increased to 100% and 97% in distinguishing CD from IBS (19). In another study, fecal calprotectin levels were measured on 602 patients with organic intestinal disease or IBS; 263 (44%) patients were classified as having an organic intestinal disease, and 339 (56%) patients had functional disease. The sensitivity and specificity of fecal calprotectin for diagnosis of an organic intestinal disease were 89% and 79%, respectively (20). It should be reiterated that fecal calprotectin cannot distinguish infectious bowel disease from IBD, so appropriate culture studies should always be performed before diagnosing a patient as IBD when the level of fecal calprotectin is high.

CONCLUSION

In conclusion, based on our findings and previous studies, FC level is a reliable and sensitive test to differentiate patients with IBD from those with other non-inflammatory gastrointestinal disorders such as IBS and it can be used as a screening tool for selection of patients before colonoscopy in adjunct with other clinical and paraclinical examinations.

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