Clinical utility and outcome analysis of faecal calprotectin in Hawkes Bay District Health Board

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ABSTRACT

AIM: An audit to review the outcome in the use of faecal calprotectin (FCP) to differentiate irritable bowel syndrome (IBS) from active inflammatory bowel disease (IBD) patients, and to detect active flares in known IBD patients in the local Hawkes Bay District Health Board (HBDHB) population from October 2013 to October 2014.

METHOD: Retrospective review of all FCP specimens requested in the HBDHB region from October 2013 to October 2014. Their indication, final diagnosis from clinical records, and endoscopic results are reviewed.

RESULTS: There were 104 FCP registrations during this period. They were ordered by gastroenterologists (67%), followed by medical specialists (31%), GPs (4%) and surgeons (2%). There were 85 FCP samples requested to differentiate IBS from active IBD. Thirty were diagnosed with IBS. The mean FCP level for the 30 patients was 27.23 mcg/g (range 14.1–41.4), which was exclusive of 50 mcg/g. Using the null value of 50 mcg/g from international studies, its p-value was <0.001. There were 19 FCP samples requested to detect a flare in known IBD patients. Seven patients were diagnosed with an active flare endoscopically. The mean FCP for the 7 patients was 378.4 mcg/g (range 275.1–481.8). This was exclusive of 250mcg/g. Using the null value of 250 from international studies, its p-value was 0.007).

CONCLUSION: The use of FCP is effective to both differentiate IBS from active IBD patients, and to detect flares in known IBD patients in the HBDHB population.

Faecal calprotectin (FCP) is a stool-based biochemical test that serves as a marker of intestinal inflammation. This assay measures a zinc and calcium binding heterodimer protein that is abundant in the cytoplasm of neutrophils.[1] Emerging evidence supports the use of FCP in two distinct clinical scenarios: differentiating irritable bowel syndrome (IBS) from inflammatory bowel disease (IBD);[2] and in monitoring disease activity in patients with known IBD.[3] FCP has increasing popularity as an accurate, reliable, economical and non-invasive marker of intestinal inflammation, but it can be elevated in other organic conditions, such as resolving infectious colitis, diverticulitis, non-steroidal anti-inflammatory drug (NSAID)-induced colitis, colonic adenomas or malignancies. Therefore, FCP results should be interpreted with caution.

IBS is a common condition affecting an estimated 10–20% of patients in the Western world,[4] and it is reported to be one of the top 10 reasons for general practitioner (GP) visits.[5] Assessment of patients with IBS, and differentiating this condition from IBD, makes up a significant proportion of the gastroenterology outpatient workload. In the absence of known organic disease, a cut-off value at 50mcg/g has a 93% sensitivity and 91% specificity to differentiate between active IBD and IBS.[6] FCP assessment has been very helpful in this setting, in which it is incorporated into the National Institute for Health and Care Excellence (NICE) guidelines.[7] It has been estimated that its introduction has reduced the demand for colonoscopy to distinguish IBS from IBD by 50%, using a 50 mcg/g cut-off value.[8]

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Box 1: Rome III Criteria for diagnosis of IBS.

Recurrent abdominal pain or discomfort for at least three days/ month in the last three months with symptom onset at least six months before diagnosis associated with two or more of the following:

- Improvement with defaecation
- Onset associated with a change in frequency of stool
- Onset associated with a change in form of stool

The combination of Crohn's Disease Activity Index (CDAI), Simple Clinical Colitis Activity Index (SCCAI), serum markers and colonoscopy are traditionally used to monitor response to IBD treatment and detect relapse. The CDAI and SCCAI are symptom-based, and may not accurately reflect mucosal healing.[9] Serum markers are relatively insensitive and non-specific. Colonoscopy is resource-intensive and it conveys procedural risks to patients. For patients with known IBD, a cut-off value of >250 mcg/g has a 90% sensitivity to detect clinical disease activity when compared to both colonoscopy and histology.[10] It is interesting to review the manner in which FCP is being used at a secondary-level New Zealand hospital, and whether it is effectively helping to differentiate IBS from IBD without the need for colonoscopy. It is also interesting to review the manner of FCP to monitor disease activity in patients with known IBD. Hence, the 1-year local data on FCP use from Hawke's Bay District Health Board (HBDHB) is presented.

Aim

An audit to review the outcome in the use of FCP to differentiate IBS from active IBD patients and to detect active flares in known IBD patients in the local HBDHB population from October 2013 to October 2014.

Method

Patient selection/sample group

Hastings Memorial Hospital, Hawke's Bay, provides gastroenterology service to patients in the HBDHB region with an estimated population of 157,000. All FCP specimens requested in the HBDHB region are registered with the hospital laboratory, and the patients with FCP specimens ordered from October 2013 to October 2014 were recruited into the study.

Clinical and biochemical evaluation

Clinical and endoscopic data were collected from hospital records to assess indication and review end diagnosis. All FCP specimens were sent to the Canterbury DHB laboratory for processing. Only the first FCP measurement within the study period was included in the analysis of this audit. The FCP level recorded in the study must be a specimen produced within 1 week from the clinical assessment date, either in the community or inpatient setting. Any FCP level of more than 500 mcg/g did not proceed to have further dilutional studies to confirm its actual titre, and the results were analysed as "500 mcg/g" for the purpose of this study.

Clinical data obtained include age, date of birth, ethnicity, FCP level, any endoscopy and its histology results.

End diagnosis

A diagnosis of IBS was made on the basis of normal investigations and a compatible history fulfilling the Rome Criteria as per Box 1. A diagnosis of active IBD or IBD flare was made from a combination of endoscopic and histological investigations.

Statistical analysis

The data were analysed using Microsoft® Excel® for Mac 2011 Version 14.1.0. The faecal calprotectin level expressed in the two clinical groups was expressed as a 95% confidence interval (CI).

A two-tailed test with a p-value <0.05 was considered statistically significant.

Ethics Approval

This study was an audit. A Health and Disability Ethics Committees (HDEC) review was not necessary. (HDEC ref: 15/NTA/147)

Results

There were 121 FCP registrations at HBDHB from October 2013 to October 2014. Fourteen were excluded on the basis of having more than one FCP sample collected from the same patient within this time period. Only the first FCP level within this time period was analysed for the purpose of this study. An additional three patients were excluded due to incomplete clinical information. The remaining 104 FCP samples were all collected within 7 days from the assessment date.

In the 104 FCP samples remaining, 67 (64.4%) were ordered by gastroenterology

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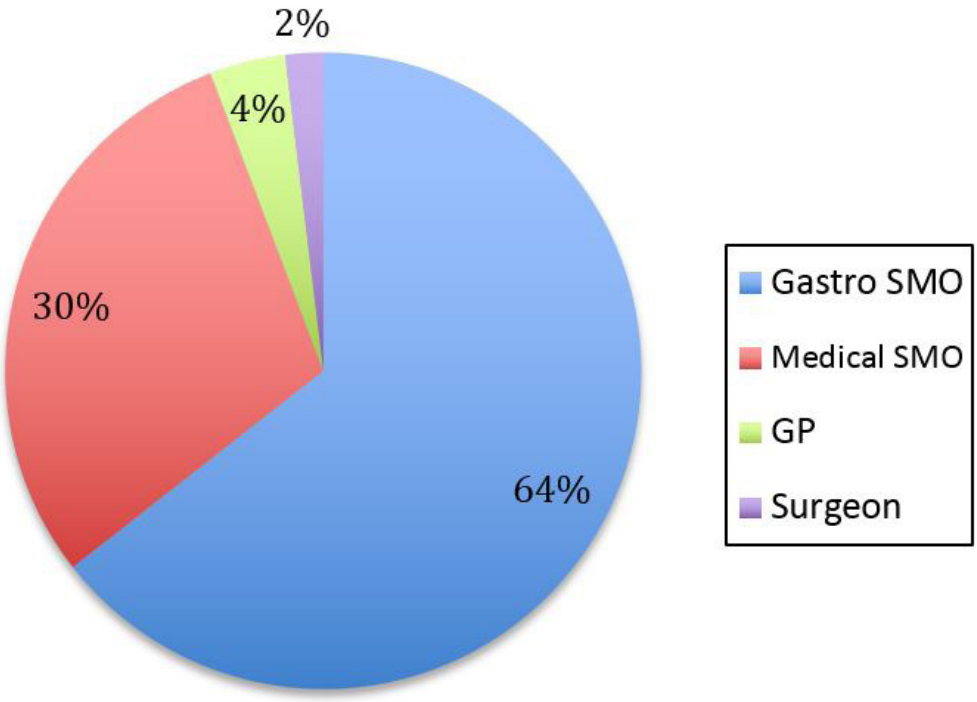
Figure 1: Clinicians who ordered the FCP.



consultants, 31 (29.8%) by general medical consultants, 4 (3.8%) by GPs, and 2 (1.9%) by general surgeons, as shown in Figure 1.

FCP was used for two indications. There were 85 (81.7%) specimens ordered with the indication to differentiate IBS from IBD patients, and 19 (18.3%) specimens ordered with the indication to detect a flare of disease in known IBD patients.

Indication to detect IBS from IBD patients

There were 85 FCP specimens ordered with the indication to differentiate IBS from IBD. Thirty (35.3%) patients were diagnosed with IBS, 4 (4.7%) were diagnosed with active IBD, 2 (2.4%) were diagnosed with microscopic colitis, 3 (3.5%) were diagnosed with bile salt malabsorption and 46 (54.1%) had no diagnosis identified.

Figure 2 presented the FCP values of the 30 patients diagnosed with IBS. The average FCP level in the 30 patients diagnosed with IBS was 27.23 mcg/g (SD 39.46). Given the sample size of 30, its 95% CI was between 14.12 and 41.35 mcg/g, which was exclusive of 50 mcg/g. Using 50 µg/g as the null value, the p-value was <0.001. A null value of 50 µg/g was chosen because internationally published data proved a high sensitivity and specificity to detect a diagnosis of IBS from active IBD patients when FCP level was less than 50 ug/g.[6]

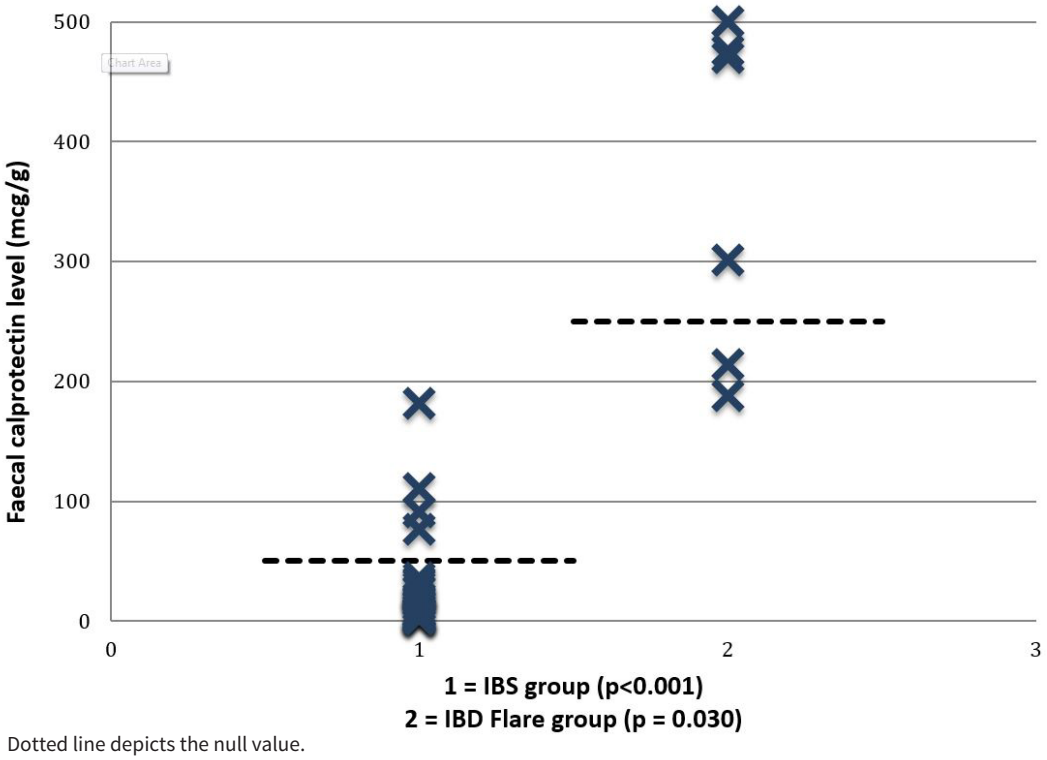
There were four out of the 30 patients diagnosed with IBS with a FCP level higher than 50mcg/g. They all had either endoscopic investigations and were followed up at the gastroenterology clinic to confirm the diagnosis of IBS.

Indication to detect disease flare in known IBD patients

There were 19 FCP specimens ordered with the indication to detect a flare in known IBD patients. Only eight patients proceeded for endoscopic assessment, and seven were diagnosed with an active IBD flare.

Figure 2 presented the FCP levels of the seven patients diagnosed with an active IBD flare. The average FCP level was 378.4mcg/g with a SD of 139.5. Given its sample size of 7, its 95% CI was between 275.1 and 481.8mcg/g. This was excusive of 250 mcg/g. Using 250 ug/g as the null value, the p-value was 0.007 (<0.05). FCP level of 250 mcg/g was chosen as the null value because internationally published data proved a high sensitivity and specificity to detect an IBD flare when the FCP level was more than 250 ug/g.[10]

Figure 2: FCP levels in patients diagnosed with IBS and a flare in patients with known history of IBD.



Dotted line depicts the null value.
(50mcg/g for the IBS group. 250mcg/g for the IBD flare group)

Conclusion

The use of FCP is effective to both differentiate IBS from active IBD patients and to detect flares in known IBD patients in the HBDHB population.

Discussion

FCP is used at HBDHB to predominantly differentiate IBS from IBD patients. The use of FCP level of <50 mcg/g to confirm IBS and >250 µg/gin known IBD patients to detect a flare fit our population well.

FCP is being used in HBDHB primarily to help differentiate IBS from IBD patients. The test performs well in this setting with a cut-off value of <50 mcg/g. Its useful negative predictive value is well established in this setting, and it will be useful to help limit the use of more invasive diagnostic modalities, such as endoscopic investigations. It is, however, important to be aware of the limitations of this test when used in this setting, particularly due to its non-specificity.

A secondary use of FCP in HBDHB is in assessing activity of disease in patients with known IBD. This makes up a smaller proportion of investigations undertaken in the region. Although the six FCP specimens that exceeded 500 mcg/g did not have further dilutional studies to confirm its actual titres, the performance of this test is still in keeping with international published data.

There are several limitations to this study. The sample size is relatively small, and it is not clear from our data what proportion of patients with suspected IBS had a FCP specimen requested. Similarly, the uptake of the test in patients with known IBD to monitor disease activity is likely to represent a small proportion of the local IBD population.

Essentially, FCP is a reliable biomarker of intestinal inflammation to help distinguish patients with IBS from those with active IBD, and to detect flares in known IBD patients in the local HBDHB population. Further research is required to observe its wider role at a national level.

Competing interests:
Nil

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