frontiers in Pediatrics

GENERAL COMMENTARY
published: 06 June 2017
doi: 10.3389/fped.2017.00133

Commentary: Impact of Fecal Calprotectin Measurement on Decision-Making in Children with Inflammatory Bowel Disease

Andrew S. Day[1,2] and Mustafa Adamji[1]*

[1] Department of Paediatrics, Christchurch Hospital, Christchurch, New Zealand, [2]Department of Paediatrics, University of Otago, Christchurch, New Zealand

Keywords: children, inflammatory bowel disease, fecal markers, calprotectin, Crohn disease

A Commentary on

Impact of Fecal Calprotectin Measurement on Decision-Making in Children with Inflammatory Bowel Disease

by El-Matary W, Abej E, Deora V, Singh H, Bernstein CN. Front Pediatr (2017) 5:7. doi: 10.3389/fped.2017.00007

OPEN ACCESS

Edited by:
Séamus Hussey, Our Lady's Children's Hospital, Ireland

Reviewed by:
Juan Cristobal Ossa, Universidad de Chile, Chile
Matthew Wyatt Carroll, University of Alberta, Canada

****Correspondence:***
Andrew S. Day
andrew.day@otago.ac.nz

Specialty section:
This article was submitted to Pediatric Gastroenterology, Hepatology and Nutrition, a section of the journal Frontiers in Pediatrics

Received: *23 March 2017*
Accepted: *22 May 2017*
Published: *06 June 2017*

Citation:
Day AS and Adamji M (2017) Commentary: Impact of Fecal Calprotectin Measurement on Decision-Making in Children with Inflammatory Bowel Disease. Front. Pediatr. 5:133. doi: 10.3389/fped.2017.00133

In their recent publication, El-Matary et al. (1) describe the utility of measurement of fecal calprotectin (FC) in the ongoing management of children with known inflammatory bowel disease (IBD). In this cohort of 77 children, FC was measured upon presentation with key changes in symptoms (most commonly abdominal pain and hematochezia). The child's management was then adjusted according to the level of the FC, with a cutoff of 250 μg/g stool. Almost 90% of those with elevated FC had a change in their management, which resulted in a reduction in clinical activity indices over the subsequent 3–6 months. Repeated FC measurements were not available. Conversely, the majority of those with low FC (below the cutoff) had no change in management in the following months. Reassuringly, 94% of these children were judged to be in remission at their follow-up visit.

Non-invasive markers, especially those measured in stool, have become increasingly important and relevant in recent years in the management of IBD. Numerous markers have now been described. Although calprotectin has been the most utilized to date, other promising markers include S100A12, osteoprotegerin, lactoferrin, and M2 pyruvate kinase (2–4).

Generally, markers such as calprotectin provide greater specificity and sensitivity for the presence of gut inflammation than standard serum-based markers. In one assessment of routine serum markers at the time of diagnosis, erythrocyte sedimentation rate, C-reactive protein, albumin, and platelet counts were each normal in 19 (13%) and all abnormal in just 52 (36%) of 146 children with CD (5). Overall, the platelet count was most often abnormal in this group. Both FC and fecal S100A12 provided much greater utility than any of the same four serum markers in an earlier cohort of 31 children with IBD (6).

Although fecal markers have particular roles in the investigation of an individual with undifferentiated symptoms (to assess the need for further investigations and to reach a diagnosis), they also clearly have important roles in individuals diagnosed with IBD. Such roles include the monitoring of disease control, assessment of response to an intervention, assessment of mucosal healing (MH), and to provide an assessment of the risk of relapse in the coming months.

The current report focused upon children with a change in symptoms, such as the development of rectal bleeding. The key issues in this context are to ascertain whether the change in symptoms is related to an exacerbation of disease, or due to other factors such as an intercurrent infection or due to functional overlap. Both enteric infections and irritable bowel syndrome can result in an elevated FC.

Prompt access to FC measurement clearly provides guidance as to the clinical management required. In practice, however, one would otherwise consider the pattern of symptoms, the routine blood tests, and examination findings and anthropometry as well. It would seem reasonable and appropriate to consider FC measurement in addition to these assessments, rather than instead.

There are some data suggesting that FC levels may vary according to disease location, with it being less reliable in small bowel inflammation (7). Assessment at baseline, at the time of initial diagnostic endoscopy, along with serial measurements over time may be of assistance for the individual patient. Accordingly, a change in FC from a prior measurement may be more helpful than a one-off level.

The other potential roles of fecal markers in monitoring disease progress are also important, especially in children. Several reports indicate that the serial measurement of S100A12 or FC in individuals in clinical remission may predict the risk of a future relapse (8, 9). In addition, fecal markers may enable the early prediction of recurrence after ileo-colonic resection (10). The role of FC in predicting the achievement of MH is less clear: the data are not yet conclusive as to the correlation between FC and MH (11). In addition, FC may have a role in guiding the appropriate indication for repeat endoscopic assessment in children with established disease: optimizing the timing of endoscopy in children will clearly be of benefit to health administrations (given the cost of endoscopy) and also for children and their parents (given the inconvenience of endoscopy for children).

Clearly, the potential roles for FC and other non-invasive markers are likely to expand. Further understanding of the differential information provided by the various markers may lead to the use of more than one marker, or indeed to the use of a panel of markers.

In conclusion, the work of El-Matary and colleagues (1) provides further important information of the utility of FC in children with IBD. Additional prospective assessments are required, ideally with comparisons between available markers and with serial estimations over time.

AUTHOR CONTRIBUTIONS

AD formulated the plan for this commentary along with initial draft manuscript. MA reviewed the draft manuscript and assisted in revisions of the drafts of the manuscript.

REFERENCES

1. El-Matary W, Abej E, Deora V, Singh H, Bernstein CN. Impact of fecal calprotectin measurement on decision-making in children with inflammatory bowel disease. *Front Pediatr* (2017) 5:7. doi:10.3389/fped.2017.00007
2. Turner D, Leach ST, Mack D, Uusoue K, Hyams J, Leleiko N, et al. Fecal calprotectin, lactoferrin, M2-pyruvate kinase, and S100A12 in severe acute ulcerative colitis: a prospective multicentre comparison of predicting outcomes and monitoring response. *Gut* (2010) 59:1207–12. doi:10.1136/gut.2010.211755
3. Lopez RN, Leach ST, Lemberg DA, Duvoisin G, Gearry RB, Day AS. Faecal biomarkers in inflammatory bowel disease. *J Gastroenterol Hepatol* (2017) 32:577–82. doi:10.1111/jgh.13611
4. Sun H, Vesely R, Lee KJ, Klein A, Ikima M, Mulberg AE, et al. Pediatric Crohn disease clinical outcome assessments and biomarkers: current state and path forward for global collaboration. *J Pediatr Gastroenterol Nutr* (2017) 64(3):368–72. doi:10.1097/MPG.0000000000001284
5. Day AS, Hamilton D, Leach ST, Lemberg DA. Inflammatory markers in children with newly diagnosed inflammatory bowel disease. *J Gastroenterol Hepatol Res* (2016) 5:2132–5. doi:10.17554/j.issn.2224-3992.2016.05.647
6. Sidler MA, Leach ST, Day AS. Fecal S100A12 and fecal calprotectin as noninvasive markers for inflammatory bowel disease in children. *Inflamm Bowel Dis* (2008) 14:359–66. doi:10.1002/ibd.20336
7. Gecse KB, Brandse JF, van Wilpe S, Löwenberg M, Ponsioen C, van den Brink G, et al. Impact of disease location on fecal calprotectin levels in Crohn's disease. *Scand J Gastroenterol* (2015) 50:841–7. doi:10.3109/00365521.2015.1008035
8. Däbritz J, Langhorst J, Lügering A, Heidemann J, Mohr M, Wittkowski H, et al. Improving relapse prediction in inflammatory bowel disease by neutrophil-derived S100A12. *Inflamm Bowel Dis* (2013) 19:1130–8. doi:10.1097/MIB.0b013e318280b1cd
9. Zhulina Y, Cao Y, Amcoff K, Carlson M, Tysk C, Halfvarson J. The prognostic significance of faecal calprotectin in patients with inactive inflammatory bowel disease. *Aliment Pharmacol Ther* (2016) 44:495–504. doi:10.1111/apt.13731
10. Wright EK, Kamm MA, De Cruz P, Hamilton AL, Ritchie KJ, Krejany EO, et al. Measurement of fecal calprotectin improves monitoring and detection of recurrence of Crohn's disease after surgery. *Gastroenterology* (2015) 148:938–47. doi:10.1053/j.gastro.2015.01.026
11. Boon GJAM, Day AS, Mulder CJ, Gearry RB. Are faecal markers good indicators of mucosal healing in inflammatory bowel disease? *World J Gastroenterol* (2015) 21:11469–80. doi:10.3748/wjg.v21.i40.11469

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.