Calprotectin as a marker of bowel inflammation

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Abstract

In recent years, the need for a non-invasive diagnostic tool that would help to discriminate between organic (e.g.: infections, food allergy-related disorders, inflammatory bowel diseases) and functional gastrointestinal disorders (e.g.: Toddler diarrhea, irritable bowel syndrome, infant colic) directed research towards potential immunological markers. A great number of non-invasive bio-markers have been proposed, including eosinophilic cationic protein, elastase, esterase, myeloperoxidase, lysozyme, lactoferrin, and calprotectin (Limburg PJ, Ahlquist DA, Sandborn WJl, 2000; Roseth AG, 2003; Costa F et al, 2003). Compared to other biomarkers, calprotectin (also called MRP8/14, calgranulin A/B , cystic fibrosis antigen or S100 A8/A9) may offer advantages based on its biological characteristics. Calprotectin is a 36.5-kDa, calcium and zinc binding polypeptide which constitutes about 60% of soluble cytosol proteins in human neutrophils (Poullis A et al, 2003). It is also found in monocytes, keratinocytes, muscle tissue and infiltrating tissue macrophages (Poullis A et al, 2003). When bound to calcium it becomes resistant to proteolysis and colonic bacterial degradation. This make is stable for up to 1 week at room temperature and facilitate its determination in feces (Costa F et al, 2003; Aadland E, Fagerhol MK, 2002). Calprotectin is involved in the regulation of the inflammatory process, participate to the early innate immune response and exert antimicrobial, anti-proliferative and apoptotic properties (Poullis A et al, 2003; Aadland E, Fagerhol MK, 2002; Striz I, Trebichavsky I, 2004). Fecal calprotectin is a direct measure of mucosal inflammation activity and becomes detectable when intestinal inflammation is still at an insufficient level to cause an increase in serum inflammation markers (Roseth AG, 2003). In the last decade fecal calprotectin has been proposed as a marker to rule out acute and chronic intestinal inflammatory diseases in children with typical gastrointestinal symptoms. Many studies demonstrated its diagnostic utility in identifying children and adults with inflammatory bowel disease (Burri E, Beglinger C, 2011; Burri E, Beglinger C, 2012) and correlate with the degree of disease activity (Bunn SK et al , 2001 a; Bunn SK et al , 2001 b). The detection of elevated levels of fecal calprotectin in healthy infants during the first few weeks of age, limits their use as screening test for intestinal inflammatory diseases in early life (Campeotto F et al 2004). Despite this evidence, the measurement of calprotectin in the serum has been proposed to identify neonates with necrotizing enterocolitis (Terrin G et al, 2012). Recent studies have shown higher fecal calprotectin levels in infants with irritable bowel syndrome (IBS) and colics, compared with healthy controls (Shulman RJ et al 2008; Rhoads JM et al, 2009). Additionally a correlation was found between fecal calprotectin concentration and IBS clinical presentation severity (Rhoads JM et al, 2009). However, these studies do not provide data on diagnostic accuracy in distinguish between organic and functional gastrointestinal disorders. Despite significant limitations, these evidences suggest the presence of a subtle inflammatory process underlying functional gastrointestinal disorders and open new perspectives on their pathogenesis. Fecal calprotectin may play a role that could be revealed in further, specifically designed, studies. Changes in microflora, permeability, calprotectin excretion and other inflammatory biomarkers, should be investigated to clarify if a continuum exists between inflammatory conditions and intestinal functional diseases.

References

Aadland E, Fagerhol MK. 2002. Faecal calprotectin a marker of inflammation throughout the intestinal tract. *Eur J Gastroenterol Hepatol*;14:823-5.

Bunn SK, Bisset WM, Main MJ, et al. 2001. Fecal calprotectin: validation as anoninvasive measure of bowel inflammation in childhood inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*; 33:14–22.(a)

Bunn SK, Bisset WM, Main MJ, et al. 2001. *Fecal calprotectin as a measure of disease activity in childhood inflammatory bowel disease. J PediatrGastroenterolNutr*; 32:171–7.(b)

Burri E, Beglinger C. 2011. Faecal calprotectin in the diagnosis of inflammatory bowel disease. *Biochem Med (Zagreb)*;21(3):245-53. Review.

Burri E, Beglinger C. 2012. Faecal calprotectin - a useful tool in the management of inflammatory bowel disease. *Swiss Med Wkly*. Review.

Campeotto F, Butel MJ, Kalach N, Derrieux S, Aubert-Jacquin C, Barbot L, Francoual C, Dupont C, Kapel N. 2004. High faecal calprotectin concentrations in newborn infants. *Arch Dis Child Fetal Neonatal Ed.* 89(4):F353-5.

Costa F, Mumolo MG, Bellini M, Romano MR, Ceccarelli L, Arpe P, et al. 2003.Role of fecal calprotectin as non-invasive marker of intestinal inflammation. *Dig Liver Dis*;35:642-7.

Limburg PJ, Ahlquist DA, Sandborn WJl. 2000. Faecal calprotectin levels predict colorectal inflammation among patients with chronic diarrhoea referred for colonscopy. *Am J Gastroenterol*;95:2831-7.

Poullis A, Foster R, Mendall MA, Fagerhol MK. 2003. Emerging role of calprotectin in gastroenterology. *J Gastroenterol Hepatol*;18:756-62.

Rhoads JM, Fatheree NY, Norori J, Liu Y, Lucke JF, Tyson JE, Ferris MJ. 2009. Altered fecal microflora and increased fecal calprotectin in infants with colic. *J Pediatr*; 155:823-828.e1.

Roseth AG. 2003. Determination of faecal calprotectin, a novel marker of organic gastrointestinal disorders. *Dig Liver Dis*;35:607-9.

Shulman RJ, Eakin MN, Czyzewski DI, Jarrett M, Ou CN. 2008. Increased gastrointestinal permeability and gut inflammation in children with functional abdominal pain and irritable bowel syndrome. *J Pediatr*; 153:646-50.

Striz I, Trebichavsky I. 2004. Calprotectin – a Pleiotropic molecule in acute and chronic inflammation. *Physiol Res*;53:245-53.

Terrin G, Passariello A, De Curtis M, Paludetto R, Berni Canani R. 2012. S100 A8/A9 protein as a marker for early diagnosis of necrotising enterocolitis in neonates. *Arch Dis Child.* 97(12):1102.