

Institutionen för Kvinnors och Barns Hälsa
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FECAL CALPROTECTIN IN CHILDREN WITH SPECIAL REFERENCE TO INFLAMMATORY BOWEL DISEASE

AKADEMISK AVHANDLING

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ABSTRACT

This thesis aims to study the clinical usefulness of fecal calprotectin as a noninvasive marker of colonic inflammation in children with suspected or confirmed chronic inflammatory bowel disease (IBD). Calprotectin, a calcium-binding protein predominantly expressed in neutrophils, is stable in feces for several days, and can be measured by an enzyme-linked immunosorbent assay.

Gastrointestinal symptoms as abdominal pain, diarrhea, bloody stools, and weight loss are common in children presenting with IBD. However, the symptoms can be vague, or even similar to the symptoms of other more common gastrointestinal disorders and functional complaints. Early recognition of IBD is important to prevent adverse effects such as delayed onset of puberty, impaired growth, and unnecessary suffering. The routine investigations include blood tests, fecal cultures, endoscopy, and radiological examinations. Endoscopy with histological examinations of biopsy specimens is the gold standard for diagnosis. It is also used for objective estimation of disease activity and to monitor the efficacy of treatment. However, endoscopy is unsuitable for frequent use as it is an invasive and costly procedure requiring careful bowel preparation and, in children, general anesthesia.

Study I establishes *reference values for fecal calprotectin* by analyzing fecal samples from 117 healthy children and adolescents. The conclusion was that the upper reference value for fecal calprotectin concentration is $<50 \mu\text{g/g}$ in boys and girls aged 4 through 17 years.

Study II evaluates the *feasibility of fecal calprotectin to detect colorectal inflammation in children*. Fecal samples were collected from 36 children with gastrointestinal symptoms suggestive of IBD before undergoing colonoscopy. Elevated fecal calprotectin concentrations strongly predicted the presence of IBD or other colorectal inflammation, and the test had a sensitivity of 95% and specificity of 93%. Thus, fecal calprotectin can be used as a diagnostic tool to facilitate selection of children who should undergo diagnostic colonoscopy.

Study III aimed to *evaluate fecal calprotectin as a quantitative marker of inflammatory activity in pediatric IBD*. Thirty-nine children with IBD delivered fecal samples and underwent colonoscopies. The results demonstrated that fecal calprotectin is a valid surrogate marker for quantitative estimation of colonic inflammation in pediatric IBD. Normalized fecal calprotectin concentration seems to indicate complete, histological mucosal healing.

Study IV compared *plasma calprotectin, high sensitivity C-reactive protein and serum amyloid A with fecal calprotectin and routine blood tests* as markers of histological inflammation in 32 children with IBD. Fecal calprotectin measurement was found to be a more reliable test for estimation of histological inflammatory activity in the colon.

In conclusion, the present thesis demonstrates that fecal calprotectin is a simple and noninvasive method that can be used as a sensitive diagnostic tool to detect colorectal inflammation and IBD in children with gastrointestinal symptoms. Further, the fecal calprotectin method was shown to be useful as a quantitative, surrogate marker of colonic inflammatory activity. The simplicity of obtaining and analyzing fecal calprotectin will facilitate the care of children with gastrointestinal symptoms as well as the monitoring of inflammatory activity in pediatric IBD.

Keywords: biological markers, calcium-binding proteins, Leukocyte L1 Antigen Complex, calprotectin, acute-phase proteins, serum amyloid A, C-reactive protein, ELISA, feces, blood, children, adolescent, colitis, inflammatory bowel disease, colonoscopy, reference values, diagnosis.

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