



**Karolinska  
Institutet**

**Institutionen för Medicin, Solna**

# Inflammatory markers for evaluation of inflammatory bowel disease therapy

**AKADEMISK AVHANDLING**

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentlig försvaras i L8:00, Centrum för Molekylär Medicin (CMM), Karolinska Universitetssjukhuset, Solna

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## ABSTRACT

The lack of reliable biomarkers for predicting the clinical course or monitoring therapeutic outcome in inflammatory bowel disease is an indisputable problem. The aim of this study was to evaluate markers of inflammation during inflammatory bowel disease therapy.

Blood chemistry markers were evaluated along with clinical activity and quality of life assessment during infliximab therapy in Crohn's disease patients, both the immediate response (one week) and long-term effect (up to five years). A majority of the patients showed improvement in clinical activity and quality of life as well as in hemoglobin, albumin and C-reactive protein levels. Using Harvey-Bradshaw index and Short Health Scale, infliximab demonstrated a prompt effect on clinical activity and quality of life and patients showed a maintained responsiveness over years.

Systemic inflammatory markers were followed along with clinical activity in Crohn's disease patients undergoing the first year of infliximab therapy. Healthy subjects were used as controls. Clinical activity improved with each infusion. High-sensitive C-reactive protein, calprotectin and nitrite improved after at least one infusion. However, calprotectin, nitrite and soluble urokinase plasminogen activator receptor were elevated compared with healthy controls throughout the study, indicating a continuous subclinical inflammation.

Fecal calprotectin and C-reactive protein were compared with clinical activity index in patients with Crohn's disease and ulcerative colitis during infliximab induction therapy. Calprotectin decreased significantly in responders following induction therapy. Moreover, fecal calprotectin exceeding a cut-off of 221  $\mu\text{g/g}$  was associated with a flare-up during the following 24 weeks.

Assessment of luminal NO concentrations in acute colitis patients prior to and after three days of corticosteroid therapy onset showed that NO levels were higher both at baseline and day 3 in patients responding to therapy than in non-responders. Furthermore, NO could be used as a predictor of colectomy as study endpoint. Baseline NO level below 2239 ppb was significantly associated with colectomy within one month from onset of corticosteroid therapy.

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