INTRODUCTION

Ulcerative colitis (UC), characterized by periods of active disease and remission, is challenging to manage. Recent studies have identified mucosal healing as an optimal patient outcome.

AIMS

In this study, we investigated whether blood and fecal biomarkers of inflammation are able to distinguish between mucosal healing defined by endoscopy from intestinal inflammation, to differentiate between clinical remission and sustained clinical remission and to show predictive value for a flare if levels at baseline are elevated.

METHODS

Endoscopy (index EI - Rachmilewitz <1 indicating mucosal healing) (baseline, 12 month), clinical activity index (CAI - Rachmilewitz), fecal Lactoferrin (FLA, cut-off =>7.36µg/g), Calprotectin (CAL, >50µg/g) and PMN-elastase (PMN-e; >0.065µg/g) (IBD-SCAN from Techlab, Blacksburg, USA for lactoferrin, ELISA-Kits from Immunodiagnostics, Bensheim, Germany for calprotectin and PMN-elastase), serum CRP (≥0.5mg/dl) and white blood count (WBC: ≥8.5 x 10³/µl) (baseline, 1, 3, 6, 9, 12 month) were determined repeatedly and in events of acute flares.

Inflammatory status was defined by the CAI as follows: Patients in an acute clinical flare (CAI > 4), in clinical remission (CAI2 and 54 and in sustained clinical remission (CAI < 2, normal bowel frequency and no blood in stool).

Clinical status was defined by the CAI and endoscopy as follows: Patients in an acute clinical flare (CAI > 4), in clinical remission (CAI≤2 and ≤4) and in sustained clinical remission (CAI < 2, normal bowel frequency and no blood in stool).

RESULTS

In 91 patients (45 female, mean age 52±13.4 years), 620 CAI and 179 endoscopies were performed. A total of 42 (46%) patients developed a clinical flare. Results for Clinical status as defined by the CAI are shown in table 1 and 3. Results for Inflammatory status as defined by the CAI and endoscopy are shown in table 2 and table 4.

Using pre-defined cut-offs, only increased levels for FLA at baseline were associated with a significant higher risk of flaring (RR 1.69, p<0.018).

Using optimized cut-offs (for FLA were 11.99µg/g, CAL 13.99µg/g, PME-e 0.035µg/g and CRP 0.25mg/dl), patients with elevated FLA at baseline had a relative risk (RR) of 1.99 (95% CI 1.47-2.71, p<0.000) to develop a flare, CAL RR=1.58, (1.20–2.09, p=0.000) PMN-e RR=1.67 (1.21–2.29, p=0.000), CRP: RR=1.52 (1.15–2.0, p=0.001) (WBC: n.s.) as shown in table 5.

CONCLUSIONS

Fecal biomarkers have the potential to distinguish between mucosal healing and intestinal inflammation and to differentiate between active clinical flare and sustained clinical remission. Using pre-defined cut-offs, only fecal lactoferrin had predictive potential. Using optimized cut-offs, FLA, CAL, PMN-e and CRP were predictive of a flare.

SUMMARY OF RESULTS

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Using pre-defined cut-offs, only increased levels for FLA at baseline were associated with a significant higher risk of flaring (RR 1.69, p<0.018). Using optimized cut-offs (for FLA were 11.99µg/g, CAL 13.99µg/g, PME-e 0.035µg/g and CRP 0.25mg/dl), patients with elevated FLA at baseline had a relative risk (RR) of 1.99 (95% CI 1.47-2.71, p<0.000) to develop a flare, CAL RR=1.58, (1.20–2.09, p=0.000) PMN-e RR=1.67 (1.21–2.29, p=0.000), CRP: RR=1.52 (1.15–2.0, p=0.001) (WBC: n.s.) as shown in table 5.