

Gastrointestinal Symptoms and Fatigue in Patients with Quiescent Ulcerative Colitis

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien,
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av

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Avhandlingen baseras på följande delarbeten:

- I. Jonefjäll B, Strid H, Öhman L, Svedlund J, Bergstedt A, Simrén M. Characterization of IBS-like symptoms in patients with ulcerative colitis in clinical remission. *Neurogastroenterol Motil* 2013;25(9):756-e578.
- II. Jonefjäll B, Simrén M, Öhman L, Lasson A, Svedlund J, Strid H. The severity of inflammation at onset of ulcerative colitis is not associated with IBS-like symptoms during clinical remission. *J Crohns Colitis*, 2015 Sep;9(9):776-83.
- III. Jonefjäll B, Öhman L, Simrén M, Strid H. IBS-like symptoms in patients with ulcerative colitis in deep remission are associated with increased levels of serum cytokines and poor psychological well-being. *Inflamm Bowel Dis*. 2016 Nov;22(11):2630-2640
- IV. Jonefjäll B, Simrén M, Lasson A, Öhman L, Strid H. Psychological distress, iron deficiency, active disease and female gender are independent risk factors for fatigue in patients with ulcerative colitis. Submitted

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Abstract

Gastrointestinal symptoms compatible with Irritable Bowel Syndrome (IBS) and fatigue are common in patients with quiescent ulcerative colitis (UC). The causes of these symptoms remain to be clarified. The overall aim of this thesis was to characterize patients with quiescent UC to find factors that might contribute to generation of residual gastrointestinal symptoms and fatigue. Two patient cohorts were studied.

In Paper I and II, patients with new onset of UC (n=98) were followed prospectively during three years with yearly follow-up visits. Symptoms compatible with IBS during clinical remission was reported by 29% of the study population. When comparing patients in clinical remission with and without IBS-like symptom, patients with IBS-like symptoms had more severe gastrointestinal symptoms, tendencies toward more severe psychological symptoms and reduced levels of quality of life, but the levels of fecal calprotectin did not differ between the two groups. The patients that would develop IBS-like symptoms while in remission during follow-up experienced more severe gastrointestinal symptoms at disease onset, but the severity and extent of inflammation at disease onset were comparable to the patients who would not report IBS-like symptoms during follow-up. IBS-like symptoms during remission were not explained by pre-existing IBS.

In Paper III and IV, 298 patients with UC were investigated. The criteria for deep remission were met by 132 patients and 18% of these reported IBS-like symptoms. Poor psychological well-being, higher levels of stress and increased systemic cytokine levels, but not colonic low-grade inflammation, were associated with IBS-like symptoms. The prevalence of high fatigue was 40% among the study population. Independent risk factors for high fatigue were: probable psychiatric disorder, iron deficiency, active disease and female gender. No difference was observed comparing levels of calprotectin or systemic cytokines among patients in deep remission with and without high fatigue.

Conclusions: IBS-like symptoms among patients with UC in remission are common, but not as prevalent as previously reported, which emphasizes the importance of using fecal calprotectin and endoscopy to rule out on-going inflammatory disease activity. Psychological factors and increased systemic immune activity are associated with IBS-like symptoms. Psychological distress, iron deficiency and disease activity should be investigated in patients with UC suffering from fatigue.

Keywords: Ulcerative colitis; Irritable bowel syndrome; Fatigue; Calprotectin

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