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Local barrier dysfunction identified by confocal laser endomicroscopy predicts relapse in inflammatory bowel disease

R Kiesslich, C A Duckworth, D Moussata, A Gloeckner, L G Lim, M Goetz, D M Pritchard, P R Galle, M F Neurath, A J M Watson.

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Introduction

Increased intestinal permeability has been reported in inflammatory bowel disease (IBD) patients and is associated with occurrence of relapses [1]. An intestinal barrier function defect is thought to be one of the mechanisms leading to the pathogenesis of IBD development and subsequent flare. Measurement of small-molecular-weight saccharides, chromium-EDTA or in vitro techniques (trans-epithelial electrical resistance and 3H-mannitol flux) are the methods currently used to evaluate it, but no in vivo evidence of these defects has so far been available. Whether this suggested tight junction dysfunction has a clinical impact also needs to be demonstrated [2].

What is this paper about?

This interesting work used confocal laser endomicroscopy (CLE) with fluorescein as an intramucosal marker of epithelial defect in order to study the in vivo integrity of the intestinal barrier and its impact on disease outcome in a prospective study of 55 IBD patients (47 ulcerative colitis and 11 Crohn's disease) in clinical and mucosal remission.

First, as a proof of principle, CLE enabled the direct visualization of the plume-like efflux of fluorescein after shedding of epithelial cells in IBD patients which was not present in healthy controls and which could be interpreted as a local barrier defect.

Second, a grade, based on the appearance during CLE (Watson grading system), was given to each patient by two blinded investigators and correlated with disease outcome to predict relapse. Increased cell shedding with fluorescein leakage (= indicator of barrier function loss; Watson grade II) and microerosion, defined as the loss of more than one adjacent cell from a single site, but not visible under white-light endoscopy (= sign of structural defect; Watson grade III) was associated with a significant 1-year risk of relapse compared to "endomicroscopical healing" (=normal; Watson grade I). Moreover, the grading system was able to predict a flare with a sensitivity of 63% (95%CI: 41-80%) and a specificity of 91% (95%CI: 75-98%).

Conclusion

This innovative technique is highly useful for confirming the concept of a link between the pathogenesis of IBD flares and an intestinal barrier defect. According to the authors, prospective evaluation of the intestinal barrier integrity of IBD patients in remission should help in anticipating relapses. The remaining questions are whether this quite cumbersome and expensive endoscopic technique is really usable in a routine clinical setting. In particular, will this examination be accepted by patients in remission in order to predict relapse? Based on these results, should less invasive intestinal permeability measurement techniques be reevaluated as alternative methods or will "endomicroscopical healing" be the future quest for the Holy Grail?

References

1. Wyatt J, Vogelsang H, Hubl W, et al. Intestinal permeability and the prediction of relapse in Crohn's disease. *Lancet* 1993;341:1437-9.
2. Zeissig S, Burgel N, Gunzel D, et al. Changes in expression and distribution of claudin 2, 5 and 8 lead to discontinuous tight junctions and barrier dysfunction in active Crohn's disease. *Gut* 2007;56:61-72