Gastroenterology 110 (no.4) 1996

● Uefulness of infrared video-endoscope for the diagnosis of ulcerative colitis

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Abstract: Only 40 - 50 % of cases of ulcerative colitis can be diagnosed pathologically, and even with macroscopic endoscopy it is often difficult to discriminate between ulcerative colitis and Crohn's disease or tuberculous colitis. It is often the case, therefor, that endoscopists follow up this condition with therapeutic diagnosis. We were interested in submucosal vascular images in inflammatory bowel disease and, in cooperation with Olympus Optical Co., Ltd., developed a video-endoscope that is sensitive to infrared at 805 nm, the maximum wavelength for absorption of indocyanine green (ICG). Using this video-endoscope, we observed infrared rays after intravenous administration of ICG to determine whether submucosal vascular image would be useful in differentiating the diseases.

Patients and Methods: Five cases of Crohn's disease, 3 of tuberculous colitis, 12 of ulcerative colitis, where pathological diagnosis was possible, underwent infrared colonoscopy. Among the ICG concentrations tested, namely, 0.5, 1, and 2 mg/kg, the clearest vascular images were obtained at 1 mg/kg. Further, capillaries were most deeply stained at 30 seconds after ICG intravenous administration. Therefore, infrared images taken 30 seconds after 1 mg/kg of ICG administration were regarded as the original images. These original images were enhanced by subtraction, and the characteristics of such vascular images were compared.

Result: Infrared endoscopy produced images of submucosal terminal capillaries, which cannot usually be observed. In the acute stage of ulcerative colitis, submucosal terminal capillaries showed rigidity as well as dilatation due probably to congestion. These findings were absent in Crohn's disease or tuberculous colitis.

Conclusion: Infrared endoscopy is useful in obseving submucosal vascular images. The images obtained after intravenous administration of ICG are useful in diagnosing ulcerative colitis and in determining the remmision stage.

● METHANOGENESIS AND SULFATE REDUCTION IN PATIENTS WITH AN ILEO-ANAL POUCH.

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Methanogenesis and sulfate reduction are important fermentation processes in the human colon. Most patients with an ileo-anal pouch show a positive lactulose hydrogen breath test, one year after total colectomy, suggesting the establishment of a colon-like flora. Anaerobic bacterial overgrowth in the pouch has been suggested as a possible pathogenic factor in pouchitis. However, the nature of the anaerobic flora in the pouch has not been studied in detail. In this study, we have investigated methanogenesis and sulfate reduction in pouch-patients without pouchitis as compared to healthy controls. Methods: Anaerobic fecal slurries were prepared from 15 patients with an ileo-pouch-anal anastomosis at least one year before the study, 14 due to ulcerative colitis and one due to familial polyposis, and from 20 healthy controls. Patients did not receive antibiotics at least 3 months before the study. Sulfide was measured by gaschromatography (GC) as hydrogen sulfide, after release from the fecal slurries by acid. Methane (in breath and fecal slurries) was also measured by GC. Results: Methane was absent in the breath of all pouch patients (0.0 ppm). This was statistically different from controls, of whom 60% were methane producer (breath methane: 15.3 ± 11.2 ppm) and 40% were non-methane producer (0.1 ± 0.2 ppm). High amounts of methane were found in the fecal headspace of methane producers (mean: 2.5 10^4 ppm), whereas much smaller amounts (1.4 10^2 ppm) were detected in non-methane producers, during fecal incubations from healthy controls for 24 hr at 37°C. Methane was absent in the headspace of the fecal incubations in pouch patients. Total fecal sulfide levels in pouch-patients (0.35 ± 0.50 mmol/kg fecal dry weight) were significantly lower than in controls (1.99 ± 1.64). The hydrogen sulfide levels in the fecal headspace of pouch patients, 24 hr after incubation at 37°C, (mean: 6.5 μmol/kg fecal wet weight) were about 50-fold lower than those in normals (283 μmol/kg). Whereas sulfate reduction was active in all controls, it was absent in about half of the pouch population. Conclusions: The results suggest that in ileo-anal pouch patients a methanogenic and sulfate reducing flora is absent or almost absent. Further studies in ileo-anal pouch patients with pouchitis are warranted.

● SOLUBLE L-SELECTIN AS A NEW SEROLOGICAL INDICATOR FOR ULCERATIVE COLITIS

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Aims: Human L-selectin is a cell surface glycoprotain expressed constitutively on a wide variety of leukocytes. L-selectin plays an essential role in the migration of leukocytes into inflammatory sites. The aim of the present study was to examine whether the determination of the soluble L-selectin (sL-selectin) level in the serum of patients with inflammatory bowel disease (IBD) could be useful for a differential diagnosis between ulcerative colitis (UC) and Crohn's disease (CD). We also evaluated its efficacy as a serological indicator reflecting the severity of inflammation in the affected intestine of UC.
Patients / Methods: Sixty two patients with UC, thirty patients with CD and twenty healthy volunteers were used in this study. Serum sL-selectin level was sequentially determined during the follow-up period with ELISA (Parameter, R&D Systems, Abingdon, UK). Peripheral white blood cell count (WBC) and serum C-reactive protein (CRP) were also measured simultaneously with the sL-selctin determination. Severity of the disease was evaluated by clinical activity index (CAI) by Rachmilewitz et al.
Results: The serum sL-selectin level was significantly ($p<0.0001$) higher in UC patients (mean ± SD: 1458 ± 458 ng/ml) than in CD patients (979 ± 279 ng/ml) and healthy controls (1007 ± 146 ng/ml). Furthermore, the serum sL-selectin level was significantly higher in the active status than in the quiescent status in UC ($p< 0.001$). In patients with UC, circulating sL-selectin concentrations were significantly ($p< 0.0001$) correlated with the CAI scoring ($r= 0.633$).
Conclusions: Serum sL-selectin level is a new serological, non-invasive indicator for the differential diagnosis between UC and CD, and is useful for evaluation of the severity of inflammation in the affected intestines in UC patients.

● THE EFFECTS OF THE ANTI-ICAM-1 MONOCLONAL ANTIBODY ON ACUTE DSS COLITIS

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AIM; Adhesion molecules are known to play key roles in the migration of inflammatory cells to the site of inflammation. In patients with inflammatory bowel disease (IBD), increased expression of several adhesion molecules including ICAM-1 has been reported. Oral administration of dextran sodium sulfate (DSS) induces colitis resembling human ulcerative colitis. We evaluated the effects of prophylactic treatment with an antibody against ICAM-1 in this model of IBD.
METHODS; Colitis was induced by feeding Male Wistar rats (250g) for 4 days with 5% DSS (MW 5000). Hybridoma cells producing anti-ICAM-1 MAb (1A29) was kindly provided by Prof. M. Miyasaka (Osaka univ. Dept. of Bioregulation). Expression of ICAM-1 in the colonic mucosa of DSS rats was evaluated by immunohistochemistry. Anti-ICAM-1 (2mg/Kg) or vehicle alone as controls were injected intraperitoneally on days 0,1,2,3. After blood sampling, the rats were sacrificed on day 4 for assessment of colonic damage.
RESULTS; In the control rats, ulcers with bleeding, erosion, or hyperemia were seen in the cecal and colonic mucosa. At the site of inflammation, ICAM-1 was present on endothelial surfaces.
Effects of MAb

	n	Macroscopic score	WBC(cells/mm^3)
control	6	2.2±0.8	26300±6150
anti-ICAM-1	5	1.0±1.2*	21600±4320#

(*;$p<0.05$, Wilcoxon rank-sum test. #;N.S. student's t test.)
Macroscopic extent of colonic damage was significantly reduced by prophylactic treatment with anti-ICAM-1.
CONCLUSION; ICAM-1 was present in inflamed mucosa of acute DSS colitis. Prophylactic treatment with anti-ICAM-1 monoclonal antibody reduced colonic inflammation induced by DSS. Our results suggest that ICAM-1 plays an important role in this model of IBD.