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GUT PH AND TRANSIT TIME IN ULCERATIVE COLITIS APPEAR SUFFICIENT FOR COMPLETE DISSOLUTION OF PH-DEPENDENT 5-ASA-CONTAINING CAPSULES.

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Background: A pH-dependent formulation of 5-aminosalicylic acid (5-ASA) requires exposure to pH > 7.0 for at least 30 minutes for complete dissolution to occur in vitro (Riley SA, Br J Clin Pharmacol 1988;26:173-7). It has been suggested that low colonic luminal pH in patients with ulcerative colitis (UC) may impair the release of 5-ASA from these capsules. Aim: To compare gut luminal pH and transit time in normal controls and in patients with UC taking a 5-ASA preparation. Methods: Using a standardised ambulatory and dietary protocol, 4 normal controls and 8 patients with active UC had gut pH and segmental transit recorded by a freefall pH-sensitive radiotelemetry capsule(RTC). Results: See Table (mean and (SD) are shown). In all subjects small bowel pH rose as the RTC passed distally and exceeded pH 7.0 for at least 4 hours. There was no difference in mean colonic pH between healthy controls and UC patients. However, low pH (<5.5)in the left colon was found in 2 patients, both with active distal UC. Transit time of the RTC through the small bowel was similar for controls and UC patients. RTC transit in UC through the left colon was slower than through right ($p< 0.03$). Conclusion: We have confirmed that colonic pH is sometimes low and shown that left colonic transit is prolonged in patients with active UC. Using the RTC as a marker of transit, small bowel pH appears to be sufficiently high for a long enough time to ensure complete dissolution of a pH-dependent capsule containing 5-ASA.

GUT pH AND TRANSIT TIME IN NORMAL CONTROLS and MILD-MODERATELY ACTIVE ULCERATIVE COLITIS PATIENTS.

		SMALL BOWEL				COLON		
	N	Transit (hours)	Proximal pH	Distal pH	Right transit (hours)	Left transit (hours)	Right pH	Left pH
Controls	4	6(2.6)	7.9(0.6)	8.4(0.3)	8(9.2)	7(1.4)	6.5(0.6)	6.7(0.1)
Active UC	8	7(2.3)	7.3(0.5)	8.3(0.5)	7(5.5)	12(6.9)	6.7(0.5)	6.7(0.9)

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BUDESONIDE IN THE TREATMENT OF CROHN'S DISEASE. A META-ANALYSIS.

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Purpose. To assess the effectiveness and safety of budesonide in inducing remission in active Crohn's disease and in preventing relapse in Crohn's disease with medically or surgically-induced remission. Data sources. Pertinent studies were selected from the Medline Database, references from published articles and reviews, and abstracts from major Gastrointestinal meetings. Study selection. Twelve randomized controlled trials of budesonide therapy were identified: 6 addressed active disease (1 budesonide vs placebo, 1 budesonide vs mesalazine and 4 budesonide vs conventional corticosteroids) and 6 addressed quiescent disease (4 medically- induced remission and 2 surgically-induced remission). Data extraction. Data were extracted by two independent observers on the basis of intention-to-treat principle. Data synthesis. Conventional meta-analysis according to DerSimonian and Laird method was used for the pooling of the results. Compared to conventional corticosteroids budesonide had a pooled rate difference (RD) of -8.5% (95%CI -16.4% to -0.7%; $p=0.02$) for inducing remission in active Crohn's disease. The Number Needed to Treat(NNT) was 12. Corticosteroid-related adverse events were reduced with budesonide therapy compared to conventional corticosteroids (RD -22.4%; 95%CI -32.0% to -12.8%; $p<0.001$; NNT=5). In quiescent Crohn's disease budesonide compared to placebo had a pooled RD of -0.8% (95%CI -9.9% to 8.3% $p=0.42$) for preventing relapse in medically-induced remission and of -3.5%(95%CI -16.9% to 9.8%; $p=0.30$) for preventing endoscopic recurrence in Crohn's disease after surgery. Considering the occurence rate of corticosteroid-related adverse events in the long term treatment (12 months), budesonide compared to placebo had a pooled RD of 5.3% (95%CI -3.9% to 14.5%; $p=0.30$). Conclusions. Budesonide is significantly less effective than conventional corticosteroids for inducing remission in active Crohn's disease but the risk of corticosteroid-related adverse events is significantly reduced. Budesonide is not effective in preventing relapse in Crohn's disease with medically or surgically-induced remission.

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COMBINATION OF ANTIBIOTIC AND PROBIOTIC TREATMENT IS EFFICACIOUS IN PROPHYLAXIS OF POST-OPERATIVE RECURRENCE OF CROHN'S DISEASE: A RANDOMIZED CONTROLLED STUDY VS MESALAMINE.

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Background: Previous studies have suggested the efficacy of nitromidazole antibiotics and mesalamine in prophylaxis of post operative recurrence of Crohn s disease. Aim: The aim of our study was to evaluate the efficacy and safety of the combination of a high dose non-absorbable antibiotic and a highly bacterial concentrated probiotic preparation vs mesalamine in prevention of post-operative recurrence of Crohn s disease. Patients and methods: Forty patients were randomized to receive either rifaximin 1.8g/d for 3 months followed by VSL#3 (300 billions of viable lyophilized bacteria of 8 different strains) 6 g/d for 9 months (n=20) or mesalamine 4 g/d for 12 months (n=20). Endoscopic examination was performed after 3 and 12 months by an independent physician and a previously described score of severity of endoscopic recurrence was used (Gastroenterology 1990;99:956). Results: After one year 4 patients in the antibiotic/probiotic group had a severe endoscopic recurrence (20%; 2 after 3 months, 2 after 12 months) compared to 8 patients (40% all after 3 months) in the mesalamine group. No side effects were reported in the antibiotic/probiotic group. Conclusions: These results suggest the efficacy of the combination of a non-absorbable antibiotic with a highly concentrated probiotic preparation in the prevention of severe endoscopic recurrence of Crohn s disease after surgical resection. Evaluation of the clinical outcome will be performed.

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ORAL ADMINISTRATION OF *LACTOBACILLUS GG* (*L.GG*) INDUCES AN ANTIINFLAMMATORY, TH-2 MEDIATED SYSTEMIC IMMUNE RESPONSE TOWARDS INTESTINAL ORGANISMS.

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Background: In patients with inflammatory bowel disease (IBD) there is evidence for an overly aggressive immune response towards their own intestinal flora. Peripheral $CD4^+$ T-Lymphocytes ($PBTL^{CD4}$) from healthy volunteers proliferate extensively upon stimulation with foreign intestinal flora. The aim of this pilot study was to determine if *L.GG* is able to immunomodulate this aggressive immune response and wether there is evidence for a change in cytokine profile. Methods: Healthy volunteers (n=8) were treated with a daily dose of $2x10^9$CFU *L.GG* for 5 weeks. Prior and after the treatment period, magnetically separated $PBTL^{CD4}$ were stimulated for 24hrs with heat-killed own and foreign intestinal flora, *Bacteroides fragilis sp.*, *E.coli*, *L.GG*, PHA, and LPS. The proliferative response following stimulation was determined by measuring the amount of ATP released by lysed $PBTL^{CD4}$ using a Luciferase assay and given in relative light units (rlu). Levels of IL-10, IFN-γ, and TNF-α were measured by ELISA. Results: Treatment with *L.GG* significantly increased the proliferative response of $PBTL^{CD4}$ following stimulation with *L.GG* (3,250±682rlu vs. 70,310±16,894rlu; $p\leq0.008$). The response towards foreign intestinal flora significantly decreased (204,637±67,969rlu vs. 65,306±17,927rlu; $p\leq0.04$). Even the response towards the own intestinal flora decreased (63,794±27,544rlu vs. 33,644±9,356rlu; $p\leq0.16$). Orally administered *L.GG* induced increased secretion of IL-10 (234±81pg/ml vs. 44±15pg/ml; $p\leq0.02$) but decreased secretion of IFN-γ (63±23pg/ml vs. 340±79pg/ml; $p\leq0.001$) and TNF-α (274±83pg/ml vs. 411±45pg/ml; $p\leq0.08$) by $PBTL^{CD4}$ upon stimulation with own intestinal flora. The same significant pattern was observed upon stimulation with foreign gut flora, own and foreign *Bacteroides fragilis sp.* and *E.coli*. Discussion: Oral treatment with *L.GG* led to a decrease of the intitially strong proliferative response towards foreign intestinal flora and their bacterial components. The secretion of IL-10 (Th-2) by $PBTL^{CD4}$ was increased, whereas levels of IFN-γ and TNF-α (Th-1) were decreased. Further studies are needed to evaluate the effects of an adjuvant administration of *L.GG* within the therapy regimens if IBD.