dietary supplementation in patients with IBD, and particularly Crohn's disease. Subject numbers are relatively small and statistical significance was not achieved, but no other study on the subject is placebo controlled and double blinded, or has dietary oral calcium intake data for subjects. Although tolerability of the medication was good, results do not provide enough evidence to support the use of oral calcium and vitamin D supplements in all patients with inflammatory bowel disease.

P102 THYROID DISORDERS IN A POPULATION OF ULCE RATIVE COLITIS (UC) PATIENTS

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Introduction: The prevalence of thyroid disorders is 2-4 times more frequent in patients affected by Ulcerative Colitis (UC) than in general population (1). We have screened for these disorders our population of UC patients.

Materials and Methods: We have studied 140 patients (100 females-F and 40 males-M) affected by UC. UC was classified in mild, moderate and severe activity disease according to Truelove classification and the site of disease was specified. Mean age is 43 year (range 18-80). Blood thyroid hormones dosage (FT4, FT3, TSH) was performed in every patient and, only in case of alterations suggestive for thyroid disorders, blood thyroid autoantibodies (anti thyreoglobulin and anti microsomal for hypothyroidism, anti TSH receptor for hyperthyroidism) were studied in association with ultrasound and scintigraphy study.

Results: 30 patients (22 F and 8 M) showed a severe UC, 52 (33 F and 19 M) a moderate UC and 58 (45 F and 13 M) a mild disease activity. 22 patients (15 F and 7 M) had a pancolitis, 60 patients (51 F and 9 M) a left colitis, 30 patients (20 F and 10 M) a proctosigmoiditis and 28 (14 F and 14 M) only a rectal involvement. 4 patients (2 F and 2 M) (2.8%) had thyroid disorders, all patients were affected by severe UC, 3 (1 F and 2 M) with left colitis and 1 F with pancolitis. A clinical picture compatible with hyperthyroidism (blood suppression of TSH, marked blood increase of FT3, FT4 and anti TSH receptor > 15 mU/L n.v.0-1) was present in a female 60 year old and a surgical resection for was needed for histological diagnosis of severe dysplasia; only medical therapy (metimazole to step down from a starting dose of 30 mg/day) for 2 years was needed and, actually, the patient is well. 2 M and 1 F had a diagnosis of autoimmune hypothyroidism (increased blood level of TSH, mean 10 MU/L range 5-15 n.v. 0.6-5), low blood level of FT4 (mean 7 ng/ml range 3-8.5 n.v. 9-18) and presence of anti tiroglobulin and anti microsomal antibodies) and they actually are treated with L Tiroxine therapy (mean dosage 75 mcg/day range 50-200). In all patients ultrasound didn't reveal thyroid nodules, but a marked ultrasound pattern alteration.

Conclusion: Thyroid function should be considered in patients affected by UC and, particularly, in patients with left colitis and pancolitis associated to W. Tillinger1, R.J. Jillc2, U. Köller2, N. Zwerina1, H. Brunner1.

NEUTROPHILS: A NEW DIAGNOSTIC TOOL IN IBD

R. Caprilli2.

P104 THE ROLE OF ANORECTAL MANOMETRY IN ULCE RATIVE COLITIS PATIENTS AFTER RESTORATIVE PROCTOCOE TEOLOGY

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Introduction: Patients after restorative proctocolectomy with pouch formation often present anorectal dysfunction that can be due to motility disorders. AIM OF THE STUDY: The aim of the study was to evaluate the changes in anorectal manometry in patients after restorative proctocolectomy.

Material and Methods: Anorectal manometry was performed in patients suffering from ulcerative colitis after final stage of restorative proctocolectomy with pouch formation. The study group consisted of 12 patients (8 females, 4 men), mean age 44, 21-72. Anorectal manometry was performed with 4-channel water perfused probe with latex balloon. After manometric evaluation the volumetric examination was performed using the balloon.

Results: Anorectal manometry: In 5 patients we found normal manometric features- normal resting and squeeze pressures. In 2 patients we found lower pressures of anal sphincters- in one resting and squeeze in other just squeeze pressure. In 5 (42%) squeeze pressures were far above normal (above 250 mmHg). Volumetric findings: In 2 patients the examination was not performed due to technical reasons. In 7 patients the volumetric finding were within normal: RAIR (recto-an inhibitory reflex) was seen with mean volume of 60ml, first sensation with mean volume of 62ml, urge to defeate with mean volume of 80ml. In 3 patients (25%) first sensation nor RAIR was found to the volume of 100ml. Conclusion: In patients after restorative proctocolectomy the adaptive changes can be seen due to pouch and prevent the involuntairy defection. In 23% changes in volumetric examination was found, probably due to innervation damage after the surgical treatment.
P106
5-AMINOSALICYLIC ACID (5-ASA)-MEDIATED BLOCK OF COLON CANCER CELL GROWTH IS ASSOCIATED WITH DEGRADATION OF CDC25A AND ACCUMULATION OF CELLS IN S-PHASE

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Background and Aim: Epidemiological observations indicate that 5-aminosalicylic acid (5-ASA) reduces the risk of developing CRC in patients with ulcerative colitis. However, the molecular mechanism underlying the antineoplastic effect of 5-ASA remains poorly characterized. In this study we have examined whether 5-ASA modulates CRC cell growth and analyzed its effects on cell cycle checkpoints.

Methods: CRC cell lines (i.e. HCT-116, HT-29 and CT-26) were treated with graded doses of 5-ASA (5-30 mM) for 48 hrs, and then cell cycle and proliferation were evaluated by FACs. Both phosphorylated and total CDC25A, CHK1 and CHK2 were evaluated in total extracts of 5-ASA-treated cells by Western blotting. Moreover, we evaluated the effect of 5-ASA on the development of CT-26-derived xenografts in mice.

Results: 5-ASA dose dependently inhibited CRC cell growth. The 5-ASA-mediated anti-mitogenic effect was reversible and associated with no change in CRC cell survival, and accumulation of cells in S-phase. Consistently, 5-ASA enhanced phosphorylation and degradation of CDC25A, a phosphatase necessary for promoting the G1-S phase transition and S-phase progression. Time-course analysis showed that CDC25A phosphorylation was preceded by activation of the upstream kinase CHK2. Finally we showed that administration of 5-ASA to Balb/c mice markedly reduced the development of CT-26-derived colon cancers.

Conclusions: These data support further the notion that 5-ASA negatively regulates CRC cell growth, thus bringing new insights into the molecular mechanism underlying the antineoplastic action of this drug.

P107
BENIGN INTRACRANIAL HYPERTENSION AND INFLAMMATORY BOWEL DISEASE. A NEW EXTRATESTINAL MANIFESTATION OR AN ADVERSE EFFECT OF THERAPY?

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Benign intracranial hypertension (BIHT) is a rare condition, of unknown cause, in which intracranial pressure is risen without an organic cause, and with a normal cerebrospinal fluid (CSF) composition. The use of some drugs, most notably steroids, can be associated to the production of such condition. We present three cases of BIHT observed in inflammatory bowel disease (IBD) patients, that rise the possibility of BIHT being an extraintestinal manifestation of the disease. Case 1: 28-year-old woman diagnosed of chronic disease Montreal A2 L2 B1 since November 2002. In September 2002 she underwent neurological evaluation for the acute appearance of impaired vision and headaches. Cranial CT and MRI excluded both the presence of a mass in the brain and venous thrombosis. These three cases were observed along three years and represent a 0.04% of 690 patients followed in our outpatient IBD clinic.

Conclusions: 1. Although aminosalicylates are the most frequent cause of headache in IBD patients, one should be aware to exclude other causes, such as BIHT. This is specially true in patients treated with steroids, perhaps more so during weaning. 2. Our findings highlight even more the fact that impaired vision must be evaluated with care in IBD patients, because they can be the manifestation of significant and tratable causes (uveitis, BIHT).

P108
VISILIZUMAB THERAPY IN SUBJECTS WITH MODERATE-TO-SEVERE, REFRACTORY CROHN’S DISEASE

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Purpose: We evaluated the safety and clinical activity of visilizumab, a humanized anti-CD3 monoclonal antibody in an open-label, phase I study in moderate-to-severe inflammatory non-fistulizing Crohn’s Disease (CD).

Methods: Subjects with a CDAI more than 250, a CRP more than 4 mg/L, and endoscopic evidence of active disease were administered i.v. bolus injections of visilizumab 10 µg/kg on 2 consecutive days (Days 0 and 1). Clinical response was defined as a decrease in the CDAI of more than 100 points below the subjects’ baseline value, and remission as a CDAI less than 150 at D59. Biopsies from a subset of 6 subjects were evaluated by immunohistochemistry at pre-therapy and Day 59.

Results: Seventeen of 18 enrolled subjects received both doses (1 subject withdrew after the first dose); 13 treated subjects were followed through to Day 89. The median baseline CDAI was 396 (271–516), and the median baseline CRP was 28 mg/L (2–70). Nine subjects were oral or IV steroid-resistant, 6 were oral or IV steroid-dependent, and 3 were steroid-independent. Seventeen subjects had received prior infliximab (IFX); 5 were primary IFX non-responders, 2 had had intolerable infusion reactions, and 10 had discontinued IFX due to loss of activity. By Day 29, responses were seen in 11/18 subjects, clinical remission in 5/18. More than half (13/18) of the subjects had a clinical response to visilizumab at Day 59, and 5 were responders at 6 months. Remission by Day 59 was achieved in 6/18 subjects. The median D59 CDAI was 276 (46–570). On average, in visilizumab responders, the CRP decreased by more than or equal 50% by or before Day 15. By Day 59, 6 all 14 subjects for whom paired biopsies were available showed evidence of mild to moderate histological improvement. Mild to moderate cytokine release syndrome (CRS) occurred in the majority of subjects. The adverse event (AE) profile, including their incidence, severity, and drug relatedness were similar to that previously seen in IVSR-UC subjects who had received an equivalent dose of visilizumab (10 µg/kg × 2). No lymphoproliferative, malignant or life-threatening AEs were reported.

Conclusion: Two 10 µg/kg visilizumab doses administered as IV bolus injections on consecutive days were tolerated and produced a rapid and sustained improvement in 11/18 subjects with moderate-to-severe, refractory CD.