and finally severe refractory disease needed surgery (patients treated with immunosuppressants, biologic treatment and requiring surgery, score 6).

Results: Of the 2854 patients, representing about 50% of the calculated number of Portuguese patients with CD, 1245 (44%) were male and 1609 (56%) female. The median follow-up years after diagnosis was 6 (IQR 2.0-7.5). 185 patients had five years of disease, 1403 at least five years, 685 at least 10 years, 326 at least 15 years, 178 at least 20 years and 19 at least 25 years of disease. After five years of disease 65% of patients look at least a steroids course and 86% after 10 years, 33% of patients were doing immunosuppressants at five years and this proportion increased to achieved 51% at ten years, remaining constant thereafter. Most of the patients needed at least one intestinal resection. At five years the first surgery rate was 23% and at 20 years was 71%. Twenty percent of patients were taking anti-TNF agents. A minority of patients (5%) persisted without steroids, immunosuppression or surgery and 20% remained during any given year without immunosuppression and surgery. Most of patients needed immunosuppression (40%), and a number significant of patients were submitted to surgery without immunosuppression (20%). Patients with five years of disease the mean severity was 2 (interquartile range 1-4), for those with 15 years was 3 (2-5) and in patients with 25 years was 5 (3-5). In behaviour groups in nonstenosing-nonpenetrating the mean severity was 2 (1-3), in stenosing was 4 (2-5) and in penetrating was 5 (3-5).

Conclusions: Even though Portugal belongs to South European countries CD patients have an aggressive behaviour.

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THREONINE DIPEPTIDE AS POTENTIAL ANTI-INFLAMMATORY AGENT: EFFICACY AT EXPERIMENTAL COLITIS

K. Marakhouski1, T. Vladimirskaia1, I. Shved1, V. Knizhnikov2, Y. Marakhouski3, 1Byelorussian Medical Academy Postgraduate Education, Minsk, Belarus; 2Institute of Physical and Organic Chemistry of the National Academy of Sciences, Minsk, Belarus

Background: Threonine contributing as one of the majority amino acids of the mucins protein and inflammatory bowel disease (IBD) associated with threonine decreased in mucins proteins. Moreover, there is suggest that mucous gel layer enriched threonine has altered integrity and protective function.

Aim: Evaluate threonine derivative, as modified threonin-threonine (di-threonine), efficacy at the dextran sulfate sodium (DSS) model of experimental mouse colitis.

Material and methods: Acute colitis was induced in Swiss-Webster mice by 7 days of oral 2.5% DSS with animals sacrificed daily (DSS group, 8 mouse in each day by 7 days, total 56). In experimental di-threonine groups (DSS+Di-th): di-threonine started to enter oral in dose 0.5 g BID on the third day from the beginning of an DSS induction colitis, with animals sacrificed daily (8 mouse in each day by 7 days, total 56). In each experimental group, the entire colon were examined macroscopically (colon length-Cl) and histologically (histological activity index-HAI) and with clinical symptoms (animals weight-AW, blood in stool, protein content in serum, hematology parameters and colitis activity index -CAI).

Results: In DSS groups was found: 1) acute clinical symptoms (diarrhea and/or grossly bloody stool) were associated with the presence of erosions and inflammation in colon. The earliest histological changes, which predated clinical symptoms, was on day 3; 2) animals loose weight at day 7 on 6.4% (CI95%=3.7-9.0); 3) LC was at day 3 - 8.5 (CI95%=6.4-10.6) and at day 7 - 6.2 (CI95%=5.6-6.7); CAI was at day 7 - 1.9 (CI95%=1.7-2.1), HAI at day 3 - 3.0 (CI95%=2.5-3.5). In DSS+Di-th groups was found: 1) animals had weight increase at day 7 on 2.3% (CI95%=0.9-5.5), p significant vs DSS= 0.02; 2) LC was at day 3 - 7.6 (CI95%=5.1-10.3), and at day 7 - 7.8 (CI95%=7.1-8.4, p significant vs DSS= 0.04); CAI was at day 7 - 0.25 (CI95%=0.06-0.6, p significant vs DSS= 0.01), HAI at day 7 - 2.3 (CI95%=1.6-3.6, not significant vs DSS), Serum protein at 7 days (DSS+Di-th vs DSS= 60.0 (CI95%= 55.6-62.3) vs 53.6 (CI95%= 51.2-56.1) at p=0.008).

Conclusion: This study first time clearly demonstrated that threonine’s dipeptide has positive efficacy at the experimental induced colitis and it may be very promising new medication for IBD.

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DO FREQUENTLY AND CONCOMITANTLY USED DRUGS IN IBD PATIENTS AFFECT THE EXPRESSION OF GR mRNA?

E. Butman, R. Quax, J. Koper, S. Lamberts, E. Kuipers, R. Feelders, J. van der Woude. Erasmus MC, Rotterdam, The Netherlands

Background and aim: Glucocorticoids (GCs) are effective as induction therapy in inflammatory bowel disease (IBD) patients. Known is that there is significant inter individual variation in the response to GCs, partially due to different expression levels of the splice variants of the GC Receptor (GR) mRNA. Few data are available on the interaction of drugs on the expression of splice variants. Three 3’-splice variants of the GR have been described: GR-β is the major, biologically active form; GR-α has been reported to have dominant negative effects after function of GR-β by GR-α action. In IBD frequently drugs are prescribed concomitantly. Therefore we were interested in the interaction of methotrexate (MTX), sulfasalazine (SSZ) and prednisolone (PRED) on the expression of the splice variants of GR mRNA.

Materials and Methods: Mononuclear leukocytes, obtained from buffy coats of healthy blood donors, were incubated with PRED (10^{-7}M, 10^{-6}M, 10^{-5}M), MTX (10^{-7}M, 10^{-6}M, 10^{-5}M) and SSZ (2.5 uM, 15 uM, 30 uM) during 4, 24, 48 and 72h. Concentrations reflect steady state concentrations of these drugs in IBD patients. Levels of GR mRNA were measured using quantitative r-PCR. Statistical analysis was performed by one-way ANOVA with a Newman-Keuls post test. P-values < 0.05 were considered significant.

Results: GR-α mRNA decreased significantly in time for each concentration (MTX p < 0.05, SSZ p = 0.003, PRED p < 0.006). The decrease of GR-α mRNA upon incubation with MTX was equal to the decrease in the controls. For MTX and PRED, there was no difference between concentrations for each period of incubation, however PRED showed a trend to decrease dose dependent (p values PRED: 4h 0.11; 24h 0.12; 48h 0.26; 72h 0.59). For SSZ a reduction was seen at 4 hours of incubation for concentrations 15 uM and 30 uM (p<0.002) and an increase at 24 hours of incubation of 7.5 uM (p=0.007). For GR-β mRNA a trend to decrease in time could be seen, however due to variation, this was not significant. There was no difference among concentrations.

Conclusion: MTX did not influence GR mRNA expression. SSZ however, showed an decrease of GR-α mRNA at 4 hours incubation at high concentration and an increase of GR-α mRNA at 24 hours of incubation at low concentration. PRED shows a trend to dosage- and time-dependent reduction of the level of the GR-α mRNA. These results suggest an interaction of concomitantly used drugs on the GR mRNA isoform expression, however more studies are needed.

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EFFICACY OF INFlixIMAB IN REFRACTORY POUCHITIS AND CD-RELATED COMPLICATIONS OF THE POUCH: A BELGIAN CASE SERIES

M. Ferrante1, G. D’Haens2, G. Devit1, F. Baert1, K. Gebbo3, G. Van Assche1, S. Vermere1, P. Rutgeerts1, 1Department of Gastroenterology, University Hospital Leuven, Leuven, Belgium; 2Department of Gastroenterology, Imelda ziekenhuis, Bonheiden, Belgium; 3Department of Gastroenterology, Université Catholique de Louvain, Brussels, Belgium

Background & Aim: A substantial proportion of patients with ulcerative colitis (UC) undergoing proctocolectomy with ileal pouch-anal anastomosis (IPAA) develop complications of the pouch. Over a median of 6.8 years, 19% of patients develop chronic pouchitis refractory to antibiotics, while 5% develop pouch fistulas (1). Clinical evidence for the use of infliximab (IFX) in these post-operative settings is limited. The aim of this retrospective study was to report efficacy of IFX in these patients.

Methods: Since January 2001, 27 IBD patients (12 female, mean age 46 years) received treatment with IFX (5 mg/kg) at four Belgian IBD referral centers. Indications were chronic refractory pouchitis (n=19), pre-pouch ileitis (n=1) and/or pouch fistula (n=6). For further analysis, patients with chronic refractory pouchitis or pre-pouch ileitis were grouped together (refractory luminal inflammation, n=24). All colectomy specimen were re-assessed by a senior pathologist. Short term IFX efficacy was evaluated at week 10. For refractory luminal inflammation, clinical response was defined as complete in case of cessation of diarrhea, urgency, incontinence, blood loss and abdominal pain and partial in case of marked clinical improvement, but persisting symptoms. The modified pouchitis disease activity index (mPDAI) was calculated and available. Fistula response was defined as complete in case of cessation of fistula drainage and partial in case of reduction of drainage.

Results: All but one patient had undergone IPAA for intractable UC and 26% were active smokers. In two patients the diagnosis of pouchitis was made after revision of the colectomy specimen. Refractory luminal inflammation and pouch fistula developed after a median (IQR) of 8.3 (3.0-15.7) and 3.3 (1.8-5.1) years, respectively. Prior to IFX, all patients had been treated with antibiotics; 41% with 5-ASA, 7% with immunosuppressors, 28% with corticosteroids and 54% with immunosuppressive agents. Forty-eight percent of patients received an induction scheme with IFX at weeks 0, 2 and 6. After 10 weeks, 88% of patients with refractory luminal inflammation showed clinical response (4 partial and 7 complete) and 5/6 patients (83%) showed clinical response at week 24.

Poster Presentations