Crohn's disease, CRP, smoking, previous use of infliximab (IFX) and previous response to IFX. To assess which factors are predictive for a dose escalation, the group with a dose-escalation was compared to the group without a dose-escalation. RESULTS: In total 108 Crohn's disease pts (M/F 48/60, median age 35 yrs, range 18-66 yrs) were treated with ADA for at least 3 months. Median disease duration was 9 yrs (range 0-48). In total 32% of pts (34/108) required a dose-escalation. The median time to dose escalation was 4 months of ADA treatment (range 0-22). There was no difference between both groups with respect to sex, age, disease duration, Montreal-classification, concomitant immunosuppressants, fistulizing disease, previous resection, CRP, smoking and previous use of infliximab (IFX). However, IFX response rate was lower in pts requiring a dose-escalation (4%, 1/32) compared to pts not requiring a dose-escalation (32%, 13/41, p=0.01). CONCLUSION: One third of pts treated with ADA required a dose-escalation within 4 months of treatment. Previous non-response to IFX treatment is predictive for the need of a dose-escalation during ADA treatment.

W1336

Concomitant Immunomodulator and Infliximab Therapy for Crohn's Disease: A Survey of Physician Practice

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BACKGROUND: The use of concomitant immunomodulators with infliximab for Crohn's disease remains an area of controversy. Concomitant immunomodulators may decrease the formation of antibodies to infliximab and improve efficacy, but may also increase the risk of infectious or neoplastic complications. METHODS: Four case vignettes of hypothetical Crohn's disease patients requiring infliximab treatment were developed along with accompanying multiple choice questions. Questions and answers were developed based on careful review of the literature. The case vignettes were distributed four times as an electronic survey to 1000 randomly selected members of the American College of Gastroenterology and 56 experts in Crohn's disease, selected by the investigators. The response to each question was analyzed to identify differences in practice between experts and general gastroenterologists (GI's). Homogeneity of response between the expert group and the general GI group was assessed using a Chi-Squared test. RESULTS: Thirty-four experts (61%) and 87 GI's (8.7%) completed the survey. No significant difference in the number of years in practice was found between experts and GI's. Ninety-seven percent of experts and 36% of GI's reported prescribing infliximab at least a few times per month. In patients treated with concomitant immunomodulators and infliximab, experts were more likely to discontinue the immunomodulator after achieving remission than were GI's, but this difference was not statistically significant. Of the twelve questions in the survey, a significant difference between the two groups was found on only one question regarding the choice of a second-line biologic treatment after infliximab failure. Experts disagreed amongst themselves most on the decision to administer concomitant therapy to patients naïve to both immunomodulators and infliximab. GI's disagreed amongst themselves most on the decision to discontinue concomitant immunomodulator therapy after remission. Although 40% of GI's and 44% of experts answered more than 70% of the questions correctly (p = 0.562), there remained a large variation in clinical practice within each group, as evidenced by a 19% standard deviation of percent correct answers for both groups. Using linear regression, no demographic predictors of answering the survey questions correctly could be identified. CONCLUSION: This survey indicates that among both experts and GI's there remains a large variation in the treatment of Crohn's disease patients receiving concomitant infliximab and immunomodulator therapy. These data suggest a need for consensus guidelines and standards of practice to ensure optimal patient care.

W1337

Therapy With Gastric Pentadecapeptide BPC 157 (PL14736) and L-NAME in Short Bowel Syndrome and Entero-Enteral Anastomosis Healing in Rats

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Aim: Gastric pentadecapeptide BPC 157 safe in trials for inflammatory bowel disease (IBD) (PL14736) (Gastroenterology, 2005), could also be useful in IBD complications. It successfully heals the intestinal anastomosis in rats (Surg Today, 2007) and has a therapeutic effect on the short-bowel syndrome that compromises nutritional status and healing process (Dig Dis Sci, 2008). Also, it interacts with the NO-system and counteracts the effects of NOS-inhibition, induced by application of NOS-inhibitor, N-G-nitro-L-arginine-methyl ester (L-NAME) (Eur J Pharmacol, 1997, J Pharm Sci, 2008). Thereby, this study investigates whether the therapeutic effect of the pentadecapeptide BPC 157 on the short-bowel syndrome could be abolished by L-NAME application. Materials and methods: Extensive small bowel resection (from the 4th ileal artery cranially of the ileocecal valve to 5 cm underneath the pylorus) and entero-enteral anastomosis were carried out in male rats as described before (Surg Today, 2007, Gastroenterology, 2007). Medication (BPC 157 (10 µg, 10 ng, 10 pg), L-NAME (5 mg) or an equivolume of saline (5 ml) was given once daily, i.p. (/kg), first application 30 min following surgery, last 24 h before sacrifice (at the post-operative day 1, 3, 5, 6, 7, 14). The assessment includes macroscopic presentation (body weight, mass of small intestine (3 cm cranially to 3 cm caudally from anastomosis), diameter measurements (jejunal, ileal and anastomosis diameter), biomechanical presentation (the volume (ml) instilled through a syringe-perfusion pump system (1ml/10 sec)) to the induction of leakage), microscopic presentation (Surg Today, 2007, Dig Dis Sci, 2008). Results: A severe bowel syndrome was observed (severe body weight loss, jejunal diameter increase, a small volume (2-3 ml) before leakage, particularly decreased height of the villi distal to anastomosis). This was completely counteracted by both pentadecapeptide BPC 157 regimens. Weight gain to healthy values along with markedly higher volume values (4-6 ml) was obtained without leakage. Anastomosis healing is improved (edema markedly attenuated, granulocyte number decreased, necrosis attenuated, granulation tissue, reticulin and collagen formation markedly increased, and finally epithelization increased). All measured diameters were similar to diameter of healthy animals, the height of the villi distal to the anastomosis were higher than in controls. BPC 157 therapeutic effect could be not abolished by L-NAME application. Alone, L-NAME application aggravated short bowel syndrome. Conclusion: Short bowel syndrome and entero-enteral anastomosis healing may be a particular target for therapy with BPC 157.

W1338

The Pentadecapeptide BPC 157 Effective in Healing the Colon-Colon Anastomosis Complicated With Cysteamine Induced Colitis

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Introduction. The efficient healing of bowel anastomosis belongs to one of the crucial factors that bring to the structural and functional recovery of the operated segment of bowel. The inflammation affects the quality of healing. The pentadecapeptide BPC 157, a small, stable, peptide, has already been proved effective in healing of the ileoileal anastomosis (Surg Today. 2007;37(9):768-77. Epub 2007 Aug 27.) , colon-colon anastomosis (Cell injury and protection in the GI tract, 1997; 249-258.), colocutaneous fistulas (J Pharmacol Sci. 2008 Sep;108(1):7-17.) and the cysteamine induced colitis (J Physiol Paris. 2001 Jan-Dec;95(1-6):261-70.). Therefore we assessed its activity onto the healing of the colon-colon termino-terminal anastomosis complicated by the cysteamine induced colitis. Materials and methods. We used male Wistar Albino rats in our experiments. All the experiments and procedures on the animals were approved by the Local Ethical Committee. Onto the animals in deep anesthesia the cysteamine was applied directly at the colonic mucosa through the catheter at 8 cm of distance proximal from the anus. After the application of cysteamine the median laparatomy was performed, the colon was cut transversally 5 cm proximal to anus and the termino—terminal anastomosis was created. The animals were randomly assigned into control group treated with saline (4mL/kg)and groups treated with pentadecapeptide BPC 157 (10 µg/kg; 10 ng/kg). The animals were treated once daily and assessed at the end of each experimental period (3, 7, 14 days) macroscopically, microscopically, biomechanically (the bursting pressure of anastomosis and the one at part of the proximal segment of colon affected with colitis). We performed the functional analysis that included the assessment of the passage of the faecal stream and the presence of the retention and obstruction. The consistence of the stool was noted, the same as the body mass changes. Results. The animals treated with the BPC 157 have shown the milder body weight loss, the better survival rate, formed feces already at the earliest time period of 3 days and the absence of passage impairment. The anastomosis in controls healed poorly, leaked at the lower bursting pressure, the same as the bowel wall proximal to the anastomosis. The pentadecapeptide was found effective in both oral and intraperitoneal application. Conclusion. The pentadecapeptide BPC 157 brought to the efficient healing of both the anastomosis and the inflammatory damaged bowel wall that reached the resistance comparable to those of normal bowel in healthy animals, which was not achieved at the controls even at the longest time intervals.

W1339

Safe Anti-Ulcer Peptide, in Trial for Inflammatory Bowel Desease, Stable Gastric Pentadecapeptide BPC 157 (PL14736) Can Cure Rats With Short Bowel Syndrome Complicated With Ulcerative Colitis

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Aim: Stable gastric pentadecapeptide BPC 157 recovered short bowel sydrome in rats after massive small bowel resection, improved intestinal adaptation, villus height, crypt depth, and muscle thickness (and inner (circular) and/or outer (longitudinal) muscular layer)), induced weight gain in weight of normal healthy rats (Dig Dis Sci, 2008 in press). BPC 157 is a safe anti-ulcer peptide (PL-14736, Pliva) in trial for IBD, and wound therapy, no toxicology reported (Gastroenterology, 2005) that healed intestinal anastomosis and fistulas (Dig Dis Sci, 2008, J Pharm Sci, 2008). BPC 157 also prevented and reversed ulcerative colitis induced by cysteamine enema (J Physiol, 1999). However, BPC 157 was not tested after small bowel massive resection in rats with ulcerative colitis. Materials and methods: Small bowel resection. Throughtout a 4 week period we tested rats with escalating bowel syndrome and progressive weight loss that had only 20% of small bowel (Dig Dis Sci, 2008, in press). Ulcerative colitis. Cysteamine enema 400 mg/kg i.r., 1ml/rat. Ulcerative colitis+small bowel resection. Enema was applied at 10 min before surgery. BPC 157 medication. BPC 157 (10 µg, 10ng/kg i.p. or in drinking water) first application 30 min following surgery, last 24 h before sacrifice (7, 14, 21, 28 days). Results: Small bowel resection. The rats had an escalating bowel syndrome and progressive weight loss despite the fourfold muscle thickness increase and twofold villus height and crypt depth increase during the first week. BPC 157 groups recovery showed improved intestinal adaptation, villus height, crypt depth, and muscle thickness (and inner (circular) and/or outer (longitudinal) muscular layer)) additionally increased. The rats immediately gained weight, ultimately to the weight of normal healthy rats. Ulcerative colitis. Controls exhibited pertinent ulceration, initial weight loss, and then decreased weight gain. BPC 157 rats immediately gained weight, ultimately to the weight of normal healthy rats, and had consistently less ulcerations. Ulcerative colitis+small bowel resection. Ulcerative colitis significantly aggravated all these parameters. BPC 157 retained the same beneficial effects, decreased ulcerative colitis, improved intestinal adaptation, villus height, crypt depth, and muscle thickness (and inner (circular) and/or outer (longitudinal) muscular layer)) additionally increased, early weight gain, ultimately to the weight of normal healthy rats. Conclusion: In addition to the recovery of the rats with short bowel syndrome or ulcerative colitis, BPC 157 can cure rats with short bowel syndrome complicated with ulcerative colitis.