INTENSIFICATION OF INFLIXIMAB (IFX) THERAPY IN CROHN’S DISEASE: EFFICACY AND SAFETY

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Introduction: The response of Crohn’s disease to IFX therapy is initially high. However, a loss of efficacy is observed in some cases over time. In such patients with loss of response, an IFX therapy “intensification” has been recommended. Nevertheless, it is still unknown whether the beneficial effect of this intensification is prolonged or just transient.

Aims: 1) To study the short- and long-term response of Crohn’s disease patients treated with IFX intensification (e.g., higher doses or shortened intervals). 2) To evaluate the adverse effects associated to therapy intensification.

Methods: Retrospective multicenter study. We included Crohn’s disease patients who had been treated with at least the three induction doses of the standard IFX therapy (5 mg/kg 0-2-w), and who later on needed treatment intensification (10 mg/kg/bw or 5 mg/kg/4w), because of loss of response. Short-term (after the first intensification dose) and long-term (at the end of follow-up) efficacy of the intensified therapy was analyzed. Harvey-Bradshaw’s index was used in luminal Crohn’s disease. In fistulizing Crohn’s disease, complete response was defined as closure of all fistulas, and partial response as a 50% or more reduction in the number or the debit of fistulas. Safety was evaluated by collection of adverse events.

Results: We included 33 patients (mean age, 39 years; 50% male; 33 smokers; 60% with ileocolic LS disease; 50% with fistulizing BS phenotype; 70% with perianal disease). The majority (70%) of the patients was treated with immunomodulators. The mean follow-up for intensified treatment was 40 weeks (range: 16-72 w). Mean time of IFX exposure before intensification was 12 months (range: 3-29 m). On the short-term, after the first intensification dose, 83% responded (31% complete response, 52% partial response). On the long-term, after the last intensification dose, only 65% were still responding (17% complete response, 48% partial response). One patient suffered an infusion reaction after 36 doses of intensified treatment, which subsided with slower infusion. One patient suffered an episode of herpes zoster, that did not interrupt the treatment.

Conclusions: The intensification of IFX therapy is sometimes necessary after a mean drug exposure of one year. A high proportion will initially respond, but 20% of all cases lose effect again a mean of 10 months after intensification. Safety of the intensified IFX therapy intensification is good, having no severe adverse effects.

P180 INCREASED THROMBOSIS GENERATION IN INFLAMMATORY BOWEL DISEASES

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Inflammatory Bowel Diseases (IBD) are characterized by an increased thrombotic risk. Endogenous Thrombin Potential (ETP), a parameter of the thrombin generation curve, represents a new tool in the evaluation of thrombotic and bleeding disorders.

Aim: to study ETP in IBD patients and to correlate the results with clinical and biochemical features.

Materials and Methods: 74 IBD patients (37 ulcerative colitis and 37 Crohn’s disease) and 57 healthy controls enrolled. ETP values, measured with or without thrombomodulin, are expressed as nM thrombin times minutes.

Results: In the presence of thrombomodulin, IBD patients with increased C-reactive protein (CRP) had significantly higher mean (± SD) ETP values (1,721.3 ± 458.0 nM/min) than either patients with normal CRP (1,356.6 ± 394.5 nM/min) and controls (1,277.1 ± 402.7 nM/min) (p<0.001). A significant correlation was observed between ETP and CRP (r=0.25, 95% CI, 0.06-0.48, p=0.015) and erythrocyte sedimentation rate (ESR) (r=0.26, 95% CI, 0.04-0.47, p=0.022). ETP values higher than the 95th percentile of control values were significantly more frequent in IBD patients than in controls (RR 1.71, 95% CI, 1.33-2.20; p<0.002).

Conclusions: ETP is increased in IBD patients, markedly in those with increased acute-phase reactants. ETP may help to identify IBD patients at increased thrombotic risk, regardless the underlying causes.

P179 INTENSIFICATION OF INFlixIMAB (IFX) THERAPY IN CROHN’S DISEASE: INTEnsification of INFliximab (IFX) THERAPY IN CROHN’S DISEASE
abnormality. Fifty consecutive patients (29 F; age range 20-69 yrs), with normal serum biochemistry, CBC, thyroid function, EMA, and normal ileum-colonoscopy were evaluated. Patients matched the symptom-based diagnosis of IBS (n=27), of functional diarrhea (FD n=7), and unspecified functional bowel disorders (UBD n=16). The terminal ileum (n=2) cecum (n=1), ascending (n=1), transverse (n=1), descending (n=1), sigmoid (n=1) colon, and rectum (n=1) were stained with H-E for microscopic assessment by a pathologist unaware of the clinical diagnosis.

Results: Histological abnormalities were found in 14 (28%) patients: 4 IBS-D, 4 functional diarrhea and 6 UBD. Increased lymphoplasmacytic infiltrate and granulocyte clusters were present at the level of a) the ileum only in 1 IBD patient, and in 2 UBD patients; b) the cecum only in 1 IBD patient. Altered crypt architecture was present in the rectum only in 1 UBD. Microscopic colitis was present in 1 IBS-D, 3 functional diarrhea, and 1 UBD patients.

Conclusions: Mucosal biopsies at multiple sites of colon, rectum, as well as terminal ileum are required to detect non-specific microscopic inflammatory abnormalities and specific microscopic collagenous colitis that may be equally present in patients with different clinical presentation of endoscopy negative symptom-based diagnosis of functional bowel disorders.

P183 TREATMENT WITH ANTI-TUMOR NECROSIS FACTOR ALPHA ANTIBODIES AND SUB-OBSTRICTIVE SYMPTOMS IN CROHN’S DISEASE: PROSPECTIVE LONGITUDINAL STUDY

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Background: The development of strictures has been reported using anti-TNFα monoclonal antibodies (MoAbs) in Crohn’s Disease (CD). The possible correlation between anti-TNFα therapy and development of symptomatic stenosis is unknown.

Aim: The main purpose was to assess, in a prospective longitudinal study (and in a retrospective analysis), the frequency of sub-obstructions in CD pts treated with different anti-TNFα therapies. Secondary end point was to evaluate possible changes of sonographic findings after anti-TNFα therapy.

Methods: Prospective longitudinal study. From Jan 2004 to Oct 2007, 20 CD pts (11 M, median age 41.5 yrs, range 17-69 yrs) were treated with anti-TNFα MoAbs including Infliximab (n=11), Certolizumab (n=4), Adalimumab (n=5) according to standard protocols. At baseline, the pattern of the lesions was fibrostringuring in 8, fistulizing in 4 and inflammatory in 8 pts. The median follow up was 47 weeks (range 22-47) in the Infliximab, 134 wks (range 32-134) in the Certolizumab and 21 weeks (range 19-23) in the Adalimumab group. Clinical assessment (CDAI), including the development of sub-obstructive symptoms after biological therapy was recorded at each drug administration. Small Intestine Contrast Ultrasonography (SICUS) was performed before and after anti-TNFα MoAb therapy in 11 pts (Infliximab n=8, Certolizumab n=3). Sonographic parameters were considered bowel wall thickness (≥3 mm), submucosal stricture (diameter <1 cm) with or without prestenotic dilation (≥25 mm), fistulae, abscesses, lesion extent (cm). Retro- spectral analysis. Clinical records of CD pts in follow up from Jan 1999 to 2007 showed that additional 60 consecutive CD pts (24 M, median age 45 yrs, range 21-71) were treated with Infliximab. Sub-obstructive symptoms after treatment were considered.

Results: Prospective longitudinal study: 4/20 pts (20%) treated with anti-TNFα MoAb developed sub-obstructive symptoms (2 with Infliximab, 2 with Certolizumab). All these pts were treated with steroids and 2 pts (Infliximab group) required surgery (after 8 and 4 mths). Subobstructive symptoms were observed after therapy in 4/8 pts with fibrosestrictrure disease before treatment. The median time from the first anti-TNFα therapy and subobstructive symptoms was 21 mths (range 6-23). Sonographic findings did not significantly change after treatments. Retrospective analysis. Development of sub-obstructive symptoms was observed in 10/60 pts (16.6%) treated with Infliximab. 9/10 received steroids and 5/10 pts required surgery.

Conclusion: Prospective and retrospective analyses suggest the possible role of anti-TNFα therapies in inducing sub-obstructive symptoms in CD.

P184 OUTCOME OF POUCH SURGERY FOR ULCERATIVE COLITIS: SINGLE CENTER EXPERIENCE

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Aim: The purpose of the present study is to present the experience and evaluate the outcome of pouch surgery for patients with ulcerative colitis (UC).

Materials and Methods: Fifty eight patients underwent surgery for UC between 1996 and 2007 at Mansoura Gastroenterology Center. A retrospective analysis has been done of all patients with UC undergoing surgery which includes details of the patient’s history, indication of surgery, type of operation, postoperative morbidity, and functional outcome.

Results: The main indication for operation was failed medical treatment (n=42, 72%). Pouch surgery was performed in 25/58 patients (43.1%). The majority of patients, 23/25 (92%) had J-shaped pouch and most patients, 19 (76%) underwent a stapled anastomosis. Twenty patients (80%) had a defunctioning ileostomy. There was one postoperative mortality and one pouch leak. Long term follow-up data were available for 14 patients. The most common long-term complication was anastomotic stricture (n=9, 64%). Six patients (43%) presented with pouchitis. Median daytime stool frequency was 5.1. Three patients (21%) presented with fecal incontinence.

Conclusion: Pouch surgery is a major one that attains many complications. However, the long term results and patient’s satisfaction are reasonable.

P185 MEDIUM-TERM EFFICACY OF INFlixIMAB INDUCTION THERAPY WITHOUT RETREATMENT IN PATIENTS WITH CROHN’S DISEASE

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The high cost of infliximab inhibits the regular retreatment of all patients in Hungary with Crohn’s disease (CD) after beneficial induction therapy. This study set out to evaluate the medium-term efficacy of induction therapy with infliximab without retreatment in CD patients with chronic activity and/or fistularefractory to conventional therapy.

Methods: A retrospective 1-year review was undertaken of all CD patients with successfully induced remission or fistula closure with 3 infusions of infliximab. Infliximab was administered in a dose of 5 mg/kg 3 times, in weeks 0, 2 and 6 after the last infusion, and the needs for hospitalization and surgical intervention during this period.

Results: The data on the 50 patients (19 luminal, 31 fistulizing disease; average age 29.3 [13-59], disease localization: 23 colon, 1 ileum, 13 ileocecal, 1 duodenum) were suitable for analysis. Infliximab induction therapy without retreatment resulted in a beneficial effect lasting for at least 1 year in 22 of the 50 patients (44%). 11 of the 19 patients (57.9%) with luminal disease remained in steroid-free complete remission, while the fistula persisted closed in only 11 of the 35 patients (31.5%) (p<0.05).

Conclusion: Infliximab induction therapy alone may result sustained remis- sion mainly in patients with luminal disease. These results suggest the need for regular retreatment after induction therapy in patients with fistulae, while luminal CD patients could possibly participate in regular treatment only if needed. If these data are confirmed, this modification of the therapeutic procedure could well increase the cost-effectiveness of infliximab.

P186 MAY THE GASTROESOPHAGEAL REFLUX DISEASE INFLUENCE ON INTENSITY OF SYMPTOMS IN PATIENTS WITH CROHN’S DISEASE?

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Background: One of the most important and predominating ailment in pa- tients with Crohn disease (CD) is a severe abdominal pain. However, some- times in that patients during upper gastrointestinal tract endoscopy, changes in oesophageal mucosa are found and it is probably result of gastroe- sophageal reflux disease (GERD).

Aim of the study: Aim of our study was to confirm GERD in patients with Crohn Disease and its estimation on intensity of symptoms in patients with CD.

Material and method: We examined 30 patients with CD, 11 male and 19 female in age 19 - 69 (mean age 4). Each patient underwent gastroe- sophageal manometry, pH-metry and anamnesis regarding reflux disease symptoms was collected.

Results: Only 8 patients (26,6%) had a typical GERD symptoms, 22 pa- tients (73,4%) had no complaints during upper gastrointestinal tract. In en- doscopy we diagnose oesophagitis a LA 2 patients (6,6%), 1 person (3,3%) had a oesophageal ulcer and 27 (90,1) patients had no changes in oeso- phageal mucosa. All of the examined patients had chronic gastritis. Ac- cording to pH-metry GERD was diagnosed in 25 patients (83,3%) with CD.