Cryptosporidial Infection Presenting as Relapse in Children With Inflammatory Bowel Disease
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Introduction: Cryptosporidiosis is an enteric parasitic infection that is associated with a self-limiting illness in healthy patients. However, it can cause prolonged and severe life-threatening complications, especially in immunocompromised patients. The most common symptoms associated with Cryptosporidial infection include abdominal pain and diarrhea. In the absence of appropriate stool studies, Cryptosporidiosis in patients with inflammatory bowel disease (IBD) can be misdiagnosed as disease relapse and can lead to inappropriate therapy. Cryptosporidial infection has been well described among transplant recipients however, there is only a limited data available among children with IBD. Aim: The aim of this study is to describe the clinical characteristics and outcomes of Cryptosporidial infection among children with IBD. Methods: All the stool studies from children with a known diagnosis of IBD presenting with presumed relapse during the period 2009-2011 were reviewed after obtaining institutional review board approval. A positive Cryptosporidial infection is confirmation by identification of Cryptosporidial cysts on microscopic examination of stool sample. Results: Medical records of 170 patients treated for IBD were reviewed. Cryptosporidial infection was found in seven patients (four with Crohn's disease and three with ulcerative colitis) presenting with symptoms of disease relapse. Five patients were female and the median age was 13 years (range: 3-17). Four patients were on immunosuppressive medications (one on 6-mercaptopurine and three on infliximab) as their maintenance therapy and all required hospitalization due to worsening of symptoms. Immunomodulatory agents (CRF and ESR) were elevated in all but one patient. Three of the five patients treated with nitazoxamide had a shorter duration (mean = 6 days) of illness. All patients had complete resolution of symptoms without steroids over three weeks and no infection related complications were noted. No significant association between disease location and severity of infection was identified. However, all the patients had one or more of the following risk factors for Cryptosporidial infection: malnutrition, history of asymptomatic viremia and recent travel history. Conclusion: Cryptosporidiosis can cause significant illness and lead to increased need for hospitalization in patients receiving immunosuppressive therapy. It is important that all children presenting with IBD flare should have their stools examined for Cryptosporidium along with other pathogens. Nitazoxamide appears to be effective in addition to supportive therapy.

Mucosal Healing With the Specific Carbohydrate Diet in Pediatric Crohn’s Disease: Preliminary Results of a Prospective Pilot Study
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Due to both perceived and real risks of current medical therapies for Crohn’s disease (CD), along with other pathogens. Nitazoxanide appears to be effective in addition to supportive therapy. The control of the disease may necessitate the use of immunosuppressive therapy. The most common symptoms associated with this therapy are yet to be fully defined. The adhesion molecule CEACAM6 is upregulated in active CD, is implicated in the attachment of AEC and has roles in innate immune defence. We hypothesised that nutritional stimuli as provided by enteral formula, modulate the activity and expression of CEACAM6 by human intestinal epithelial cells. Methods: The human adenocarcinoma cell line Caco-2, is an established In vitro model of epithelial cells and commonly used in studies of intestinal inflammation. This model was utilised to explore the effects of enteral formula (EF) upon CEACAM6. Caco-2 cells were treated with EF (Osmolite™, Abbott) or the proinflammatory cytokine, interferon-gamma (IFN) in two types of treatment conditions: I) and II) assessing Caco-2 viability and in vivo blue exclusion assay. mRNA expression was defined by quantitative real-time polymerase chain reaction assay, while the expression of CEACAM6 protein within the cells was determined by dot blotting. In addition, the levels of secreted CEACAM6 protein were quantified by enzyme-linked immunosorbent assay (ELISA). Results: Up to 50% v/v EF exposure for 24 hours had no effect on the viability of Caco-2 cells compared to unexposed controls (p>0.05). EF stimulation lead to a dose dependent increase (up to 48%) in the production of CEACAM6 protein after 24 hours, while 20% v/v EF significantly upregulated CEACAM6 mRNA expression 3-fold. Furthermore, IFN doubled the shedding of CEACAM6 protein from the cells in vivo. Conclusions: CEACAM6 expression is modified by nutritional exposure, suggesting that innate defence activities may be mediated by FF in the setting of CD.

Efficacy of Infliximab for Japanese Paediatric Crohn’s Disease Patients
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Background: In recent years, the therapeutic application of the anti-tumour necrosis factor (TNF) antibody, infliximab (IFX) has expanded for both inducing and maintaining remission in young Crohn's disease (CD) patients. However, there are very few outcome reports from Japan in this clinical setting. With this in mind, we became interested to evaluate the clinical efficacy and safety of IFX in paediatric CD patients. Patients and Methods: In a single centre setting, we enrolled 15 paediatric CD patients, age 11-17 yr, with mild to severe disease, CD activity index (CDAI) 236-388, and CD duration 4.1-24 yr. All patients had received 5-aminosalicylic acid based medications, but none had received an immunomodulator (IM) like azathioprine or 6-mercaptopurine. The primary and secondary end points were week 10 and 52 following the first IFX infusion. Clinical response was defined as a decrease in CDAI by at least 70 points, while clinical remission was defined as CDAI <150. Further, loss of response was defined as the need for escalating IFX dose to maintain remission. Results: At the primary end point, 12 of 15 patients (80%) responded, of those, 10 achieved clinical remission (66.7%) achieved clinical remission (Remission group). The age at CD diagnosis was younger in the non-remission group vs remission group, 15.2±1 vs 12.8±1.5 (P<0.05). At the secondary end point, 6 of 15 patients (40%) had maintained clinical remission (IFX effective group). Nine of 15 patients (60%) had lost response to IFX (IFX failure group). Patients’ weight at first IFX infusion was smaller in the IFX failure group vs IFX effective group. 42±11.7 vs 53±4.7 (P<0.05). Additionally, the L2 type (disease location, colon) and high serum C-reactive protein (CRP) before the first IFX infusion were associated with IFX failure. Only one patient developed mild dyspnoea at the 15th IFX infusion. No other serious adverse events or opportunistic infection during our observation time. Discussion: The short-term response and remission rate in the present paediatric cohort are similar to the levels in the Reach 1 study (1) and also the study in France (2), while the long-term outcome is less impressive. Likewise, IFX failure rate was higher in our study as compared with the aforementioned studies. However, the above two studies believe that IFX monotherapy is the one factor for weaker long-term efficacy in our cohort vs earlier studies. Accordingly, IFX therapy in paediatric CD patients may be influenced by concomitant IM, CD refractoriness, poor nutrition, and disease location. (1) Hyams J, et al. Gastroenterol. 2007, (2) Crombe V et al. Inflamm Bowel Dis. 2011.