Ileal pouch-anal anastomosis (IPAA) is the surgical procedure of choice for patients with ulcerative colitis undergoing elective restorative proctocolectomy (1). It preserves intestinal continuity and sphincter function and removes the entire colorectal mucosa.

The most frequently observed long-term complication of IPAA is acute and/or chronic inflammation of the ileal reservoir, called pouchitis (2). Symptoms of this pathology are dysfunctions associated to endoscopic and histological evidence of acute inflammation (3–4). It is still very difficult to determine the true incidence of pouchitis, and reported incidence rates are between 10% and 59% with ulcerative colitis (UC) (5–6). Patients with preoperative extra-intestinal manifestations and primary sclerosing cholangitis have more risk to develop a pouchitis (7–8). As in UC, smoking may protect against the development of pouchitis (9) whereas the different surgical technique does not influence the frequency of pouchitis (10–11).

The etiology of pouchitis is still unknown and its pathogenesis is still poorly understood (12). The hypotheses could be mucosal ischemia of the pouch, a missed diagnosis of Crohn’s disease (CD), or a novel form of inflammatory bowel disease (13). NSAID use, concurrent Clostridium difficile or CMV infection, celiac disease, cuffitis, irritable pouch syndrome could be other possible causes. It is also generally accepted that bacterial overgrowth plays an important role, and that lesions and symptoms are associated with the over-production of pro-inflammatory cytokines (14–16).

Recently it has been also demonstrated that chronic refractory pouchitis may be associated to an unknown form of inflammatory disease of the ileum (17). Duodenum-jejenum and proximal-middle ileum can present lesions as aphthae, erosions, erythema/edemas, atrophia, scars, polyps, cobblestone pattern and deep-fissural ulcers.

The diagnosis is commonly obtained by means of clinical, endoscopic and histological criteria using the pouchitis disease activity index (PDAI) (18,19). The disease activity of pouchitis can be so defined: remission, mild-moderate (increased stool frequency, urgency, infrequent incontinence) or severe (dehydration, frequent incontinence). On the basis of the duration of disease pouchitis can also be defined as acute (<4 weeks) or chronic (>4 weeks). Another way to classify this syndrome considers the following patterns: infrequent (a single or two acute episodes), relapsing (more than three acute episodes) or chronic (a treatment responsive form requiring a maintenance therapy or a treatment-resistant form).

Until the advent of wireless capsule endoscopy (WCE) there were no endoscopic devices that allowed a complete visualization of the small bowel. WCE could have a role to assess suspected small bowel CD, differentiating to indeterminate colitis, and defining the endoscopic estimation of disease activity and response to therapy in patients with known small bowel CD.
The management of pouchitis is aimed at reducing bacterial overgrowth and inflammation. Many drugs can be used, such as antibiotics, mesalazine, corticosteroids, immunosuppressants and, more recently, probiotics. Approximately 10% to 15% of patients with pouchitis develop a chronic pouchitis. Patients with chronic refractory pouchitis do not respond to conventional available therapies, and continue to suffer symptoms. This condition is a common cause of pouch failure. Medical treatment of patients with chronic refractory pouchitis is particularly difficult and disappointing.

Tumour necrosis factor (TNF-α) has been shown to play a central role in the pathogenesis of chronic inflammatory bowel disorder. Patients with UC have an increased serum TNF levels and high levels of TNFα have been noted in the lamina propria with an increased production of the cytokine by lamina propria mononuclear cells (20,21), and in particular high tumour necrosis factor-alpha expression occurs in the ileal mucosa during pouchitis (14).

Therapy with chimeric monoclonal antibody to TNFα has profoundly changed the management of inflammatory bowel disease and the use of infliximab in refractory pouchitis following IPAA for ulcerative colitis appears to be reasonable.

Thukral, et al (22) evaluated in their study a few open-label and controlled trials about the role of infliximab in the treatment of UC compared with placebo, antibiotics, mesalazine, corticosteroids, and immunosuppressants. On the basis of currently available data, they showed that treatment with infliximab is reasonable and efficacy in patients who have moderate to severe UC and are intolerant or refractory to mesalazine (5-ASA) products and immunomodulators. They also assess that infliximab may be an alternative to cyclosporine in hospitalized patients with UC who do not respond to intravenous corticosteroids.

Moreover, Armuzzi, et al (23,24) compared the efficacy of infliximab for remission induction and maintenance in patients with corticosteroid-dependent moderate to severe UC and concluded that infliximab seems to as effective as corticosteroids. Sands, et al (25) evaluated the efficacy of infliximab in patients with severe corticosteroid-refractory UC in one of the first pilot trials, with the confirmation that infliximab was well tolerated and of clinical benefit in this type of patients.

There is limited experience with infliximab in chronic pouchitis. Viscido, et al (26) showed the efficacy of infliximab in the treatment of chronic refractory pouchitis complicated by fistulae. Their small open study of seven patients resulted in a complete clinical response in six patients and fistulae closure in five patients at the end of 10 weeks.

In our study, we evaluated the efficacy of infliximab in patients with chronic refractory pouchitis and extensive ileal involvement, defined as no response to at least four weeks of standard antibiotic therapies (ciprofloxacin 1 g twice daily or metronidazole 400 mg t.d.s.) and if presented lesions in the jejunum-ileum at WCE study (27). In this small open study, short-term treatment of infliximab, (5 mg/Kg) at 0, two and six weeks, determined a clinical remission in 90% of patients and an endoscopic regression of lesions in 80% of patients. In one patient we revealed a reduction of the lesions in the ileum and in the pouch at WCE and endoscopy, and a significant improvement of clinical symptoms. Also, only one patient was unresponsive to therapy without any clinical and endoscopic improvement, probably related to a long-standing history of disease.

In all patients infliximab was well tolerated and no side effects were recorded, apart of a single case of slight and transient skin rush which appeared at the beginning of the second infusion and disappeared after reduction of the flow.

Clinical and endoscopic remission was maintained in 80% of patients at least six months.

Our preliminary results regarding the treatment of chronic pouchitis with extensive ileal involvement, suggest that short-term therapy with infliximab could be recommended for the treatment of chronic refractory pouchitis complicated by ileitis.

Currently available data suggest that infliximab may be an alternative in patients with UC who have failed to respond to conventional therapies, and in particular, it is safe and efficacious in the treatment of patients with chronic refractory pouchitis complicated either by ileitis and by fistulae. ■

(continued on page 32)
Role of Biologics in Refractory Pouchitis

INFLAMMATORY BOWEL DISEASE: A PRACTICAL APPROACH, SERIES #42

(continued from page 30)

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32 PRACTICAL GASTROENTEROLOGY • JULY 2008