

## LENTESYMPIOSIUM VVGE – Mechelen 20 april 2002

### The Outpatient Treatment of Refractory Left-sided Ulcerative Colitis.

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Ulcerative colitis limited to the distal 60 cm of the colon, or distal to the splenic flexure, is referred to as "left-sided" ulcerative colitis. Although affecting only part of the colon, some patients with left-sided ulcerative colitis may prove to be the most difficult to successfully achieve, and maintain, remission of disease.

The sensitivity of the rectum and the sigmoid to distension by stool may be greatly exacerbated by ongoing active colitis. The resulting symptoms of tenesmus, cramping, and frequent rectale discharge of stool, blood, and mucus, may be upsetting for the patient, and troublesome for the treating physician. It is important to realize that a multi-disciplinary approach to these patients may be necessary, due to the sensitive, spastic tendencies of the inflamed distal colon and rectum.

Therapies for patients with refractory left-sided colitis include those targeted at inflammation, as well anti-spasmodics, anti-diarrheals, and even anti-depressants. It is helpful to discuss each of these separately, although often a combination of agents is necessary for successful treatment of these patients. As is always the case in inflammatory bowel disease, it is important to maintain the remission that is achieved with medical therapy, often with the same agent that successfully resulted in inducing that remission. Corticosteroids are unacceptable as maintenance therapies, and efforts to replace them with non-steroid containing agents must be undertaken.

#### **Anti-inflammatory Agents**

Various agents exist for the treatment of patients with left-sided ulcerative colitis, which differ by medication-type and delivery. As the vast majority of symptoms in these patients are due to distal colonic and rectal inflammation, topical therapies are often found to be the quickest acting, most effective, and most reliable upon reintroduction if relapse occurs. Mesalamine enemas, foams, and suppositories have been shown to have superior efficacy to their corticosteroid counterparts, although sometimes are poorly tolerated in the inflamed colon. In such cases, remissions induced with topical steroids can often be maintained with the mesalamine products. Patients allergic or intolerant to mesalamine may benefit from budesonide enemas. Maintenance therapy with topical mesalamine therapy is strongly encouraged, although some patients may be able to decrease the frequency of nightly enemas to every second or third night, or to decrease suppository use from bid to qd. The first signs of relapse should result in resumption of full-dose therapy, and future attempts at tapering (but not discontinuing) therapy attempted with greater caution, if at all.

Oral mesalamine agents, sulfasalazine, and even oral corticosteroids are often ineffective in the treatment of patients with refractory left-sided colitis. The ineffectiveness of oral mesalamine may be due to the fecal stasis that often occurs just proximal to the colitis, preventing the mesalamine from exerting its local anti-inflammatory effect on the inflamed mucosa. The use of olsalazine, which induces a mild diarrhea, has been touted by some as an effective alternative. Balsalazide may also be effective in some individuals. Although the idea of an oral therapy versus a rectally-applied agent may be pleasing for the patient (and physician), the need for high doses of these agents and failure rates must be realized. Dual-therapy with oral and topical therapies may be a logical choice for patients refractory to single-agents. Steroid-refractory or steroid-dependant cases of left-sided ulcerative colitis often require institution of the same therapies used in patients with pan-colitis, namely 6-mercaptopurine or azathioprine. Other agents, such as methotrexate, mycophenolate mofetil, thioguanine, infliximab, and various probiotic therapies have either not been well studied or have had their effectiveness questioned. Oral tacrolimus may be effective in some cases, but is not appropriate for long-term therapy due to renal toxicity.

### **Antispasmodics**

The irritability of the distal colon and rectum has resulted in the use of antispasmodics (typically anticholinergics), as are used in patients with irritable bowel syndrome. Agents such as dicyclomine, hyoscyamine, propantheline, or combination therapies with atropine, scopolamine, etc. may be effective. Unlike the anti-inflammatory drugs, it may be possible to taper these agents, or use on a prn basis, once the inflammation has subsided. Low-dose tricyclic antidepressants, such as nortriptyline and amitriptyline, are effective in some patients, and should be dosed at bedtime due to their sedating side effects.

### **Anti-depressants and Anti-anxiety Agents**

In addition to the tricyclic antidepressants, some patients benefit from any of a variety of antidepressant or anxiolytics. As is the case in patients with irritable bowel syndrome, the mechanism of action upon the bowel is unknown, but may be related to alteration in neurotransmitter levels, resulting in better control of the enteric nervous system, and/or the brain-gut interactions.

### **Antidiarrheals**

The dosing of antidiarrheal agents, such as loperamide, diphenoxylate, or diphenoxin (often in combination with atropine) may be effective in patients with diarrhea, especially if doses prior to meals or to the installation of a nightly medicated enema. Bile-acid sequestrants such as cholestyramine or colestipol may be used with success in certain individuals. Antidiarrheals should be avoided in patients with distal colitis or proctitis who suffer mainly from constipation and tenesmus ; in those individuals, fiber-based therapies may be helpful.

### **Diet**

Ulcerative colitis patients who suffer from diarrhea are often encouraged to avoid high-fiber food items, or other products that may exacerbate diarrhea in certain individuals (such as dairy, alcohol, caffeine, and spicy or fatty foods). On the other hand, those patients with left-sided colitis or proctitis who have constipation may benefit from the introduction of these same items back into their diet. Decreasing intake of carbohydrate-rich foods, or the use of dietary supplements containing agents such as pancrelipase, simethicone, or cellulase may alleviate symptoms of gas and bloating in some patients.

### **Smoking !**

Patients who experience new onset or flares of their ulcerative colitis following smoking cessation may benefit from the temporary reinstatement of smoking, or the use of nicotine-containing agents. Although generally discouraged (particularly in America !), it may be reasonable to take such steps in treatment-refractory patients if induction of remission is successful, and then try to wean off the nicotine-products once adequate maintenance medications have been established. Careful discussions between physician and patient are needed, and include issues such as prior smoking history, difficulty in previous successful smoking cessation, duration and severity of colitis, etc.

### **Summary**

Although they may have the shortest segment of diseased bowel, patients with left-sided ulcerative colitis and proctitis may prove to be the most difficult to treat in some instances. An initial endoscopic assessment of the extent and severity of inflammation, followed by a combination of effective anti-inflammatory agents, anti-spasmodics, and diet is successful in many cases. Maintenance of remission is critical, and should not be forsaken in the interest of stopping "embarrassing" but effective therapies, as outlined above. The recent emergences of novel therapies for the treatment of ulcerative colitis will hopefully provide further future choices for physicians and patients alike.