Treatment of Inflammatory Bowel Disease

Guenter J. Krejs

The etiologies of the two idiopathic inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD), are still poorly understood. There is, however, progress in understanding some of the underlying mechanisms such as changes in barrier function, infection as trigger, genetic predisposition, immunological reactions and inflammatory cascades in the mucosa. Medical therapy entails nutritive measures, and anti-inflammatory and anti-infectious drugs, along with immunosuppressive agents and biologicals.

Sulfasalazine had been the standard of therapy for acute IBD and for maintaining remission following its synthesis by Nana Svartz in the 1940s. It use is limited by its side effects, which are mainly due to the sulfapyridine component. In the context of IBD, it is now mainly used when that disease is associated with arthritis and arthralgias. Thus, the second moiety, 5-amino salicylic acid (mesalazine) was prepared to be given alone, since it is this moiety that appears to have the beneficial effects in IBD due to its anti-inflammatory properties. Mesalazine is available in stomach-coated and slow release form and as an enema. The latest galenic advance is a granulate that is now preferred as a single daily dose. Two 5-ASA molecules have been bonded to osalazine. The bond is split by bacteria in the colon to make 5-ASA available for action on the inflamed mucosa.

Therapy of IBD has also relied heavily on corticosteroids and this is particularly true for CD. Poorly absorbable steroids such as budesonide are now preferred to avoid systemic side effects.

Immunosuppressive agents such as azathioprine and 5-mercaptopurine (in CD) and cyclosporine (in UC) are second- or third-line drugs in the therapy of IBD and their use has markedly increased.

Great advances have been brought about by biologicals such as TNF-alpha antibodies (infliximab and adalimumab). A synopsis of drug treatment for CD and UC is given in the tables.

Table 1

DRUG THERAPY FOR CROHN'S DISEASE		
First line	**Second line**	**Third line**
Active Disease		
Mesalazine (granulate) 3 g/day	Budesonide (9 g/day) or prednisolone (60 mg/day)	Azathioprine or 5-mercaptopurine or metronidazole (perianal disease, fistulas) or TNF-α antibodies (infliximab, adalimuma)
Maintenance of remission		
Azathioprine		

Table 2

DRUG THERAPY FOR ULCERATIVE COLITIS		
First line	**Second line**	**Third line**
Active Disease (Pancolitis)		
Mesalazine (granulate) or sulfasalazine when associated with arthritis	Add or substitute with prednisolone 40 mg/day	Add cyclosporine 5 mg/kg BW/day or tacrolimus or infliximab
Active Disease (left sided)		
Mesalazine enema	Add oral mesalazine (3 g/day) or sulfasalazine (4 g/day) when associated with arthritis	Add prednisolone (40 g/day), if ineffective add cyclosporine (5 mg/kg BW/day) or tacrolimus or infliximab
Maintenance of remission		
Mesalazine 1-2 g/day	or Olsalazine 1-2 g/day	or E. coli Nissle

Guenter J. Krejs, M.D., Professor of Medicine, Medical University of Graz, Austria