Preface

Biological therapies for Inflammatory Bowel Diseases : Are we finally going to modify the disease course ?

Paul Rutgeerts

It is clear that the introduction of immunomodulation therapy, especially with the chimeric monoclonal anti-TNF antibody, in the past five years is thoroughly changing our approach to the treatment of inflammatory bowel disease (IBD). This novel therapy emerges at a time that immunosuppression with azathioprine finally gained wide acceptance for the treatment of Crohn's disease and ulcerative colitis.

Until recently physicians had to accept that many of their patients had a rather poor quality of life for prolonged periods of time. Standard therapies including 5-ASA drugs and glucocorticosteroids (GCS) offered merely symptomatic control of the disease. Both display broad non-selective anti-inflammatory effects and GCS are associated with troublesome sometimes irreversible side effects when used long-term.

Only azathioprine or 6 MP have disease modifying capacity. Hence, there is a great need for better therapies for IBD. The currently used and tested biologicals all result from new insights, obtained by basic research into immunological mechanisms of IBD. Animal models of gut inflammation have been very useful in that respect. The chimeric monoclonal antibody to TNF, infliximab, has become the standard to which all other biologicals will be compared. The results of this treatment show that antagonizing a single cytokine may result in control of bowel symptoms and healing of mucosal Crohn's lesions. The efficacy of the anti-TNF strategy also confirms that dysbalance of cytokines plays a key role in the pathogenesis of Crohn's disease.

Data on the use of biologicals in ulcerative colitis are scarce. UC is generally considered to be a Thelper 2 mediated inflammation but preliminary data suggest that also in UC therapies targetting TNF may be beneficial.

TNF may not be and is probably not the only cytokine playing a pivotal role in IBD and many cytokines and anti-cytokines are currently under investigation for the treatment of IBD. It is conceivable that different therapies will be used in different phenotypes of disease or that selection of therapies will be based on genotyping of the patients.

The goal of biological therapies will not merely be to control symptoms but we expect these therapies to be disease modifying, i.e. to heal the bowel lesions, to avoid complications and preserve the integrity of the bowel. To achieve this these drugs may have to be used early in the disease course.

The short-term safety of the chimeric monoclonal antibody to TNF (Infliximab) is good but therapeutic successes may not render us blind for potential problems in the long-term. Safety data long-term are scarce and the possibility that the use of such powerful drugs, interfering with the basic cell mechanisms may be associated with yet unrecognized side effects must always be considered.

Current problems are the immunogenicity of the drugs and the autoimmune effects.

The route of administration, parenterally, is also a matter of concern. Much research therefore is directed towards the development of small molecules inhibiting the activity or the production of the target cytokines.

It needs also to be emphasized that the best therapy currently available for long-term control is immunosuppression.

This symposium summarizes the state of the art on biological therapies in IBD early 2001.

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