Crohn’s disease (CD) and ulcerative colitis (UC) are chronic inflammatory conditions that affect the GI tract. CD may affect any area of the GI tract from the mouth to the anus whereas UC affects the large intestine. CD is often transmural, affecting many layers of the intestinal wall while UC is a mucosal-based disease. Both diseases are related to immune system dysregulation.

Clinical presentation

The initial presentation of inflammatory bowel disease (IBD) is often insidious and difficult to diagnose. Patients may present with vague abdominal symptoms that can mimic other GI syndromes, such as celiac or irritable bowel disease. The symptoms of CD often include:

• diarrhea,
• abdominal pain,
• bleeding,
• weight loss,
• obstruction,
• fecal urgency,
• tenesmus and
• incontinence.

UC can present with similar symptoms but is classically associated with bloody diarrhea. Extraintestinal symptoms can include:

• arthritis,
• skin involvement,
• aphthous ulcers,
• fever,
• iritis and
• uveitis.

Both conditions tend to have periods of flares and remission.

Treatment strategies

The treatment of IBD consists of using agents to induce medical remission and then maintenance agents that prevent recurrent flare. Corticosteroids have been the mainstay therapy for acute flares of UC and CD. Prednisone is typically used at a dose of 40 mg to 50 mg followed by a taper over 14 to 16 weeks.

Budesonide is a second generation glucocorticoid which is a highly potent topical anti-inflammatory agent. It has lower systemic activity and side-effects since approximately 90% of it is metabolized during its first pass through the liver. It is formulated as a
capsule and released in a pH dependent fashion that allows for the slow release of the drug in the terminal and right colon. Thus it is effective for CD but not UC.

For mild UC, aminosalicylate agents can be considered. These drugs have been used for CD in the past; however, the evidence suggests these drugs are probably not effective. Aminosalicylates are very effective agents for the induction and maintenance of remission in UC.

Suppositories are indicated for patients with disease limited to the rectum, enemas are useful for proctosigmoiditis and may even reach to the level of the splenic flexure. Oral formulations are useful in patients with pancolitis or those who fail enemas.

Immunosuppressants are often indicated for patients who are refractory to steroids, become steroid dependent or who fail aminosalicylates. The agents currently used are methotrexate, azathioprine and 6-mercaptopurine (6-MP). Azathioprine is an effective agent for either CD or UC. It is not effective at inducing remission but is effective at maintaining remission. Thus, it is commonly initiated in patients with moderate to severe disease while they are on corticosteroids. The steroids work to induce remission and azathioprine maintains the remission. Azathioprine is metabolized to 6-MP.

Methotrexate is also a very effective agent for patients with CD. Large randomized controlled trials have been carried out in Canada showing it to be an effective agent for inducing remission in patients with active CD, as well as maintaining a medically-induced remission. Trials for UC have not shown methotrexate to be an effective agent for either induction or maintenance of remission.

### Table 1

<table>
<thead>
<tr>
<th>Medications Available to treat IBD</th>
<th>Ulcerative colitis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminosalicylates</td>
<td>Effective for induction and maintenance</td>
<td>Controversial</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Effective for induction</td>
<td>Effective for induction</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Effective for maintenance</td>
<td>Effective for maintenance</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Not effective</td>
<td>Effective for induction and maintenance</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Effective for induction and maintenance</td>
<td>Effective for induction and maintenance</td>
</tr>
</tbody>
</table>

IBD: Irritable bowel disease
**Take-home message**

1. Aminosalicylates are very effective for the acute treatment of flares and maintenance of remission for patients with ulcerative colitis.
2. Glucocorticoids are effective for acute flares of UC and CD. Patients should be slowly tapered off steroids over a 12 to 14 week course. They are not indicated for long term use.
3. Budesonide is effective for proximal (terminal ileal and right sided colonic) CD.
4. Immunosuppressants (azathioprine and methotrexate) are indicated for moderate to severe disease, steroid-dependent or steroid-refractory disease. Methotrexate is not effective for UC.
5. Infliximab is indicated for steroid dependent or refractory CD or UC.
6. Infliximab is a very effective agent for fistulizing CD.

**Biological agents**

Tumour necrosis factor (TNF) is one of many inflammatory cytokines involved in the pathogenesis of both CD and UC. Antibodies directed at TNF result in relief of symptoms, rapid healing of mucosa, closure of fistulas and improvement of extraintestinal manifestations. Currently, infliximab is approved to treat both UC and CD. It is a monoclonal antibody directed at TNF. The risks associated with infliximab include increased susceptibility to viral, bacterial and opportunistic infections, including TB. Infliximab is also immunogenic meaning there is also the potential to develop antibodies to infliximab which render it ineffective.

Adalimumab is also a monoclonal antibody aimed at TNF. It is administered subcutaneously every two weeks. It has been shown to be effective at induction and maintenance of remission for CD. It has not yet been approved for use in Canada for CD but is currently indicated for the treatment of Rheumatoid Arthritis.

Currently, a step-up approach is used to treat IBD. Mild agents are used to treat mild disease; however, for more active disease, immunosuppressants may be indicated. Immune system dysfunction has been implicated in both CD and UC and new biological agents have been shown to be effective in both these diseases.

**FAQ**

*How fast should prednisone be tapered?*

Prednisone should be tapered slowly over a 12 to 14 week period.

*Should aminosalicylates be continued after an acute flare of UC?*

Yes. Aminosalicylates are effective for both acute flares and as a maintenance therapy.

**References**


For additional references, please contact: cme@sta.ca.