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Lay Version of Canadian UC Clinical Practice Guidelines

Canadian Clinical Practice Guidelines for the Medical Management of Non-hospitalized Ulcerative Colitis

December 2015

Introduction

Clinical practice guidelines are important for healthcare professionals as they provide an overview of a clinical problem (in this case non-hospitalized ulcerative colitis) and recommendations on the best way to medically manage a condition.

Consensus guidelines are developed by health care experts who review all of the currently available scientific information, come to an agreement and make recommendations about the optimal treatment strategy. The statements and recommendations contained within the guidelines are intended to guide doctors in their decisions to use certain medications or treatments. They do not necessarily take into account that there may be unique patient circumstances that require a different approach to be taken – each patient requires individualized care.

The relationship between a physician and patient is critical. Together they make important decisions on treatment plans. Access to accurate information about treatment options will help patients have informed discussions with their physician and choose the best path forward. When patients are truly involved in making decisions about their treatments they feel empowered, which in turn means they are more likely to stick to the plan.

This lay version of the *Canadian Clinical Practice Guidelines for the Medical Management of Non-hospitalized Ulcerative Colitis* is intended to empower patients to take charge of their health and become equal partners with their care providers.

Definitions

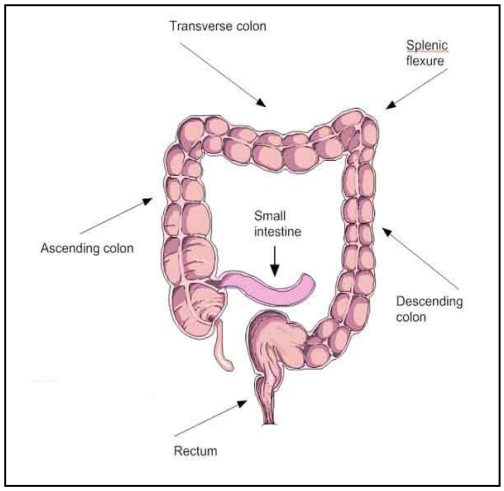
Clinical practice guidelines are written in highly scientific language and typically only understood by medical specialists. The following helps to define the important points within the guidelines so that patients can better understand them.

Definition of Ulcerative Colitis (UC)

The guideline recommendations are subdivided depending on the category of disease extent of ulcerative colitis. It is important to first understand these categories before looking at the medications recommended for each category.

'Ulcerative colitis' is subdivided into three categories based on which part of the bowel is affected:

1. **Ulcerative Proctitis**: The inflammation found in the bowel is limited to the rectum and is generally considered to be a milder form of the disease.
2. **Left-sided UC**: There is continuous inflammation that begins at the rectum and extends as far as the bend in the colon near the spleen (called the splenic flexure).
3. **Extensive colitis**: The inflammation extends beyond the splenic flexure.



Definition of Severity of Ulcerative Colitis

Throughout the guidelines the severity of ulcerative colitis is also mentioned and is categorized as **mild, moderate or severe.** Doctors use a scoring chart to determine the severity based on four categories. The first two are the responsibility of the patient to fill in:

1. **Stool frequency:**
    a. Normal number of bowel movements (based on when in remission)
    b. 1-2 more bowel movements than normal
    c. 3-4 more bowel movements than normal
    d. 5 or more bowel movements than normal

2. **Rectal bleeding:**
    a. No blood seen
    b. Streaks of blood with bowel movements less than half the time
    c. Obvious blood with bowel moments most of the time
    d. Passing blood alone

In addition, the physician also includes two other findings to the overall assessment of disease severity:

3. **Endoscopic findings** (defined below)
    a. Normal/inactive disease
    b. Mild
    c. Moderate
    d. Severe

4. **Physician's global assessment**
    a. In this section, the physician gives a score that takes into account the patient's general sense of wellbeing.

The overall numeric score (based on stool frequency, rectal bleeding, endoscopic findings, and physician's global assessment) determines whether the severity of ulcerative colitis is classified as mild, moderate or severe.

Definition of Remission

Achieving total disease remission is the optimal or best outcome for the treatment of ulcerative colitis. There are two different forms of remission, defined here:

1. **Symptomatic remission**: This means that there has been meaningful improvement of symptoms as judged by both the patient and physician. These usually include normal stool frequency (less than 3/day) and no blood in the stool.
2. **Complete remission**: This is the preferred outcome and includes both symptomatic as well as endoscopic remission. Endoscopic remission is determined using a procedure called endoscopy (defined below).

Evaluating Effectiveness of Treatment

1. **Endoscopy** – is a procedure where the physician can see if the inner lining of the colon has 'healed' – this is called mucosal healing. Colonoscopy and sigmoidoscopy are specific types of endoscopic procedures that are used to evaluate mucosal healing. Physicians often perform an endoscopy when important decisions need to be made regarding possible changes in medications.
2. **Therapeutic drug monitoring (TDM)** – is a test that measures the amount of drug in a patient's blood to ensure the right dose is being used.

Medications

These clinical practice guidelines focus on five main medication classes, defined here:

1. **5-aminosalicylate (5-ASA)**: These drugs are typically referred to as 'anti-inflammatories' and work by limiting the production of certain chemicals that trigger inflammation. Medication names within this category include mesalamines (Asacol®, Mezavant®, Pentasa®, Salofalk® and Sulfasalazine®).
2. **Corticosteroids**: These drugs are used to reduce inflammation. Medication names within this category include prednisone and hydrocortisone.
3. **Immunosuppressants**: These drugs reduce inflammation in the bowel by suppression of the immune system. Methotrexate, azathioprine (Imuran®) and 6-mercaptopurine (Purinethol®) are examples of immunosuppressants. Azathioprine and 6-mercaptopurine are closely related and are in a class of immunosuppressants called thiopurines.
4. **Anti-tumor necrosis factor (TNF) therapies**: These drugs target and block molecules involved in inflammation. Anti-TNF therapies are biologic medications. Examples include adalimumab (Humira®), infliximab (Remicade®) and golimumab (Simponi®).
5. **Other therapies**: Another type of biologic treatment is the integrin blocker vedolizumab (Entyvio®).

Ulcerative Colitis Treatment Guidelines

In most situations, the management of UC follows a 'step up' approach. This means that when an initial treatment stops working (or doesn't work from the start) patients will be moved on to the next group of medications to try. These will hopefully be more effective in treating the patient, but are also more costly and/or may increase the potential for side effects.

Typically, a patient starts at the lowest step along the treatment path. For patients with more severe disease, it may be required to start treatment higher up the 'step up' approach.

The treatment guidelines are organized by therapy type. The guidelines also provide recommendations for dosing, when to evaluate for effectiveness, and what to do if the disease progresses or remission is achieved.

Recommendations Regarding 5-Aminosalicylates (5-ASA)

5-ASA treatment is typically the first-line treatment for patients with mild to moderate active UC to bring about complete remission.

Treatment steps	**5-Aminosalicylates (5-ASA) guidelines**
Mild to moderate ulcerative proctitis	A rectal suppository of 5-ASA (1 gram per day) is recommended as an initial treatment to bring about symptomatic remission
Mild to moderate left-sided UC	A rectal enema of 5-ASA (minimum 1 gram per day) is recommended as an initial treatment to bring about complete remission
Mild to moderate UC of any disease extent beyond proctitis	Oral 5-ASA preparation (dosage between 2.0 and 4.8 grams/day) is recommended as an initial treatment option to bring about complete remission
Mild to moderate UC of any disease extent beyond proctitis	Alternatively, the combination of oral and rectal 5-ASA is preferred over using an oral 5-ASA alone to bring about complete remission
Evaluation	
Recommendation	Patients should be evaluated 4 to 8 weeks after starting oral and/or rectal 5-ASA to see if they are responding to the treatment or if the treatment needs to change
Remission Achieved	
Mild to moderate left-sided UC or proctitis	Patients who are brought into remission with either oral and/or rectal 5-ASA should continue the same treatment on a daily basis to maintain complete remission
Mild to moderate left-sided UC or proctitis	Patients who are brought into remission with oral 5-ASA alone should continue oral 5-ASA preparation (dosage of at least 2.0 grams/day) to maintain complete remission
Mild to moderate left-sided UC or proctitis	Patients who are not experiencing symptoms while on oral corticosteroids and who have not previously taken 5-ASA, an oral 5-ASA (dosage of at least 2.0 grams/day) is suggested to see if complete remission can be maintained without the need for further corticosteroids
Disease Progression	It is not recommended to switch to another oral 5-ASA preparation to bring about remission in UC patients who did not respond to another oral 5-ASA
Dosing	Once-a-day oral 5-ASA is suggested over more frequent dosing to bring about or maintain complete remission in UC. Once-a-day dosing is more convenient and may lead to better adherence with the treatment plan, including fewer missed doses

Recommendations Regarding Corticosteroids

Corticosteroids are used in several different ways and as part of several different steps along the stepped up approach to managing UC. Corticosteroids are not intended for long-term use but can be very beneficial at certain times.

Treatment steps	**Corticosteroids guidelines**
Moderate to severe UC	Oral corticosteroid is recommended as the initial treatment to bring about complete remission
Mild to moderate UC	Oral budesonide MMX is suggested as an alternative initial treatment to bring about complete remission
Disease Progression	
Mild to moderate UC	Patients who did not respond to 5-ASA therapy should switch to an oral corticosteroid to bring about complete remission
Mild to moderate left-sided UC or proctitis	Patients who did not respond to rectal 5-ASA should switch to a rectal corticosteroid to bring about complete remission
Remission Achieved	
All UC patients	It is not recommended that oral corticosteroids be used to maintain complete remission because over the long term they are ineffective and linked to other serious side effects
Evaluation	
Recommendation	Patients should be evaluated 2 weeks after starting corticosteroids to see if they are responding to treatment or if the treatment needs to change

Recommendations Regarding Immunosuppressants

Immunosuppressant medications are typically used for the management of moderate to severe active UC. As with the other medication categories, immunosuppressants are also used primarily with the goal of bringing a patient into remission. They are also used to reduce or eliminate the need for corticosteroid therapy.

Treatment steps	**Immunosuppressant guidelines**
All UC patients	Thiopurine therapy alone is not recommended to bring about complete remission
UC patients who achieve symptomatic remission with corticosteroids	In some patients who have achieved symptomatic remission using oral corticosteroids, thiopurine may be an option to maintain complete corticosteroid-free remission
All UC patients	Methotrexate therapy alone is not recommended to bring about or maintain complete remission

Recommendations Regarding Anti-TNF Therapy

There are different types of anti-TNF biologics, discuss with your physician about which option is most appropriate for you.

Treatment steps	**Anti-TNF therapy guidelines**
UC patients who do not respond to thiopurines or corticosteroids	Anti-TNF therapy is recommended to bring about complete remission in patients who do not respond to thiopurines or corticosteroids
UC patients starting anti-TNF for first time	When anti-TNF therapy is started for the first time, it is recommended that it be combined with a thiopurine or methotrexate rather than used alone to bring about complete remission
UC patients who are corticosteroid dependent	Anti-TNF therapy is recommended to bring about and maintain complete and corticosteroid-free remission
Evaluation	
Recommendation	Patients should be evaluated 8 to 12 weeks after starting anti-TNF therapy to see if they are responding or if the treatment needs to change
Remission Achieved	
All UC patients	Patients who are brought into remission with anti-TNF therapy should continue the same treatment to maintain complete remission
Disease Progression	
All UC patients	Patients who have not fully responded to anti-TNF therapy should have their dose adjusted (increased) to bring about complete remission
All UC patients	Patients who stop responding to anti-TNF treatment should have the dose and/or frequency of anti-TNF increased to bring about complete remission
Dosing	
All UC patients	The optimal dose of anti-TNF therapy should be guided by therapeutic drug monitoring (TDM) when available.

Recommendations - Other Agents

Vedolizumab is another biologic therapy that works differently than anti-TNFs and finds itself on the top of the stepped up approach to treatment.

Treatment steps	**Other agents guidelines**
UC patients who do not respond to anti-TNF therapy	In patients who do not respond to an anti-TNF therapy, vedolizumab is recommended, rather than switching to another anti-TNF therapy, to bring about complete remission
UC patients who stop responding to anti-TNF therapy	In patients who stop responding to anti-TNF therapy based on the results of the therapeutic drug monitoring, it is recommended that patients switch to another anti-TNF therapy or vedolizumab to bring about complete remission
Moderate to severe UC	Vedolizumab is recommended to bring about complete remission in patients who did not respond to corticosteroids, thiopurines, or anti-TNF therapies
Evaluation	
Recommendation	Patients should be evaluated 8 to 14 weeks after starting vedolizumab to see if they are responding or if the treatment needs to change
Remission Achieved	
All UC patients	Patients who are brought into remission with vedolizumab should continue the same treatment to maintain complete remission

The following two treatments – fecal transplantation and probiotics – are still scientifically unproven and are only recommended for use within a clinical trial setting.

Other therapies	
All UC patients	Fecal transplantation (or fecal therapy) is not recommended to bring about or maintain complete remission, outside of a clinical trial
All UC patients	Probiotics are not recommended to bring about or maintain complete remission, outside of a clinical trial

Conclusion

Medical professionals have several goals in treating ulcerative colitis patients, including bringing their patients' disease into a state of complete remission, minimizing exposure to corticosteroids, avoiding surgery and ensuring that remission is maintained. Research has been conducted that demonstrates that the more empowered patients are in their health, the more likely they will become equal partners with their care providers, and take their medication as prescribed.

Crohn's and Colitis Canada is pleased to have developed this lay version of the *Canadian Clinical Practice Guidelines for the Medical Management of Non-hospitalized Ulcerative Colitis.* It is intended to empower patients to take charge of their health and become equal partners with their care providers.

It is important to remember, however, that these specific guidelines do not address potential surgeries that patients may undergo, or focus on patients hospitalized as a result of their UC. The guidelines also do not include issues that are related to 'quality of life', specifically environmental factors, stress management strategies and dietary methods of symptom management.

Disclaimer

Clinical practice guidelines are not intended to replace medical advice. Consult with your medical professional before making any changes, including stopping, your therapy.

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[i] Bressler, B., Marshall, JK., et al. Clinical Practice Guidelines for the Medical Management of Nonhospitalized Ulcerative Colitis: The Toronto Consensus. *Gastroenterology.*2015 Volume 148, Issue 5, 1035-1058.