Module 1954

Ulcerative colitis and Crohn's disease: diagnosis and management

From this CPD module you will learn about:

- Inflammatory bowel disease, ulcerative colitis and Crohn's disease
- Typical symptoms and investigations used for diagnosis
- Management of ulcerative colitis and monitoring requirements for pharmacological treatments
- Information that pharmacists and pharmacy technicians can provide to patients

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Inflammatory bowel disease (IBD) is the collective definition for chronic inflammatory gastrointestinal conditions that are classified as ulcerative colitis (UC) and Crohn's disease (CD). Bowel inflammation results in ulceration of the gastrointestinal mucosa in IBD, however there are a number of factors that differentiate the clinical presentation of UC and CD.

Crohn's disease

CD affects the entirety of the gastrointestinal tract from mouth to anus. Often, regions of inflammation along the mucosa are 'patchy', creating areas of both healthy and diseased bowel tissue. CD can also affect the entire thickness of the bowel wall, which can result in changes to the bowel lumen and epithelium.[1,2]

CD can be classified into the following types depending on the affected area: ileocolitis (ileum and colon), ileitis (ileum), gastroduodenal (stomach and duodenum), jejunoileitis (jejunum) and granulomatous (colon).[1]

Ulcerative colitis

Unlike CD, UC refers to inflammation restricted to the large intestine (colon) and rectum.

Classification of UC is also dependent on the location of the area affected extending from the rectum, categorised as one of the following sub-types: proctitis (rectum only), left sided colitis, proctosigmoiditis (rectum and sigmoid colon) and extensive colitis, which includes pancolitis (whole colon involvement). Up to half of people with proctitis or proctosigmoiditis will develop more extensive disease. Of patients initially diagnosed with proctitis, 10% will go on to eventually develop extensive colitis.[1,3,4]

Irritable Bowel Syndrome

Irritable Bowel Syndrome (IBS) is another form of chronic gastrointestinal condition that can present with similar symptoms to IBD. However, IBS does not cause changes in gastrointestinal tissue and therefore should not be confused with or classified under IBD.

What is the prevalence of IBD?

Prevalence of IBD in the Western world is estimated at approximately 0.5% of the general population,[5] with 300,000 people diagnosed with IBD in the UK alone.[1] Rising prevalence of IBD over the last few decades is a major cause for concern. Expenditure related to direct healthcare costs of IBD diagnosis and management within Europe alone is valued between €4.6-5.6 billion annually.[5]

Risk factors and causes in UC

Risk factors for UC include:

- Age – UC commonly presents in early adulthood and adolescence, usually before the age of 30. However, some people may not develop the disease until after the age of 60.
- Race/ethnicity – UC is more common among Western populations, particularly those who are white (Ashkenazi Jewish patients are also at a higher risk of UC development).
- Family history – patients with close relatives diagnosed with UC will more commonly suffer from the condition.

The main cause of IBD is unknown. Evidence suggests a combination of factors including genetic disposition, as demonstrated by increased prevalence with a positive family history, and autoimmunity. It has been suggested that the immune response may be the result of the body attacking an invasive bacterium or virus in the gut, followed by an abnormal response that also causes damage to gastrointestinal tissue.[1,6]

Signs, symptoms and complications

Symptoms of UC are CD are very similar, so further diagnostic tests are required for disease classification. IBD is an incurable chronic condition, hence treatment focuses on symptom management. The term remission is used to identify a period of symptom control.

Alternatively, flare-ups refer to acute or chronic deterioration in disease management. Flare-ups can vary from mild to severe. Common symptoms for recognition of active IBD include:[1,6]

Ulcerative colitis is inflammation that is restricted to the large intestine (colon) and the rectum

- diarrhoea, often with blood or pus – the presence of blood or pus can often be used to differentiate between IBS and IBD
- abdominal pain and cramping (particularly left sided bowel pain in UC)
- rectal pain
- rectal bleeding – passing small amount of blood with stool
- urgency to defecate
- inability to defecate despite urgency (tenesmus)
- weight loss and fatigue – often due to poor absorption of nutrients as well as development of anaemia (anaemia can be caused by blood loss or malabsorption of dietary iron, vitamin B-12 and folate, which are all essential for effective red blood cell function)
- fever
- in children, failure to grow as a result of poor nutrient absorption.

There are several symptoms that would warrant referral for patients with either diagnosed or undiagnosed disease presenting in a community setting. These include:

- severe abdominal pain
- blood in the stool (especially for patients without an IBD diagnosis)
- treatment unresponsive diarrhoea
- nocturnal waking as a result of diarrhoea
- fever that does not resolve within 24-48 hours (this can often indicate an acute flare-up or relapse in IBD patients).

Complications related to UC include strictures (bowel narrowing), perforations (rupture of the bowel wall), fistulae (abnormal channels that develop between internal organs, primarily starting in the intestine) and toxic megacolon (TM). TM causes extensive inflammation due to gas trapped in the colon, which results in severe swelling and abdominal pain. Although it is rare, TM can be fatal and may require surgical intervention.[7]

Extra-intestinal manifestations (EIMs) are problems that can occur outside of the patient's gut, affecting up to 50% of those with an IBD diagnosis. EIMs include:[7]

- **Joint problems** – includes swelling and pain, most commonly affecting the elbows, wrists, knees and ankles, however the spine and pelvis can also be affected.
- **Skin** – erythema nodosum (EN) is a common skin complaint, with one in 10 UC patients being affected. EN causes swellings that are red and painful, mainly manifesting on the legs. Pyoderma gangrenosum is a potential complication, presenting as small blisters that can develop into painful ulcers, often requiring the involvement of a dermatologist.
- **Eyes** – conditions such as episcleritis, uveitis and scleritis can affect UC patients, causing inflammation of various eye tissues, which if not managed can cause loss of vision.
- **Bones** – as a result of malabsorption and inflammation, those with UC are more likely to develop more brittle bones. Patients that smoke are at a greater risk.
- **Mouth** – one in 25 patients with UC will develop mouth ulcers, generally during a flare-up.
- **Hair** – loss of hair is common, with roughly a third of IBD patients experiencing periods of excessive loss. This hair loss as a result of illness or stress is referred to as telogen effluvium, which may in part also be contributed to by malabsorption of minerals such as iron and zinc.
- **Liver** – primary sclerosing cholangitis affects one in 25 UC patients. This condition causes bile duct inflammation resulting in fatigue, jaundice and weight loss. Liver inflammation (hepatitis) is also prevalent amongst UC sufferers.
- **Heart and circulation** – deep vein thrombosis (DVT) is twice as likely to affect patients with UC. This risk is particularly exacerbated during flare-ups where mobility may be limited, eg staying in a hospital bed. Cardiovascular events, such as heart attack and stroke, are slightly more common amongst UC patients. Smoking cessation is a valuable tool to reduce the risk of both DVT and cardiovascular events.
- **Anaemia** – due to malabsorption, iron-deficiency anaemia is common among those diagnosed with UC. Symptoms include malaise, headaches and shortness of breath in more severe cases. Anaemia is often exacerbated in patients with blood loss.
- **Bowel cancer** – prolonged inflammation and the resulting changes to bowel tissue can increase the risk of bowel cancer in UC patients. Those diagnosed with UC are asked to regularly attend check-ups to identify the early signs of bowel cancer.[8]

As many as one third of patients with IBD will experience hair loss, referred to as telogen effluvium

Diagnosis

Diagnosis of IBD is a stepwise process involving a number of sources of information such as a patient's recent history, in addition to haematological and surgical investigations that may be carried out by a gastroenterologist.[8,9]

Clinical history

A GP may be the first point of contact for further investigation of an UC diagnosis.

An appointment should include an in-depth history of the patient's symptoms and general health. A medical history is important to rule out other conditions such as IBS.

Physical examination and blood tests

A physical exam to investigate abdominal tenderness and paleness will be used to identify signs of gastrointestinal inflammation or anaemia.

Furthermore, if the patient's symptoms suggest a potential infection, a stool sample can be taken to rule out gastroenteritis or clostridium difficile. Stool samples are also useful to measure faecal calprotectin (FCP), which is a protein released during an inflammatory process. It is a useful marker to

The aim of UC treatment is to induce disease remission and then to maintain remission

distinguish between IBD and IBS.

Blood samples may be taken to review nutritional deficiencies such as iron, vitamin D or B12.

Other tests, such as platelet count and C-reactive protein, are valuable in determining potential blood loss and non-specific inflammation. Some patients may require investigation using minor surgical procedures.

Endoscopy and biopsy

If further investigation is warranted, patients may undergo an endoscopic procedure. Both a colonoscopy (entire colon) and sigmoidoscopy (rectum and sigmoid colon) use a camera attached to a small flexible tube to examine the bowel.

These procedures may also involve taking a biopsy of bowel tissue to support a clinical diagnosis and/or evaluate the extent of inflammation in the bowel.[8,9]

Imaging

In order to rule out potential complications such as fistulae, strictures, perforations and TM, imaging techniques such as an X-Ray or CT scan can be used to provide a detailed examination of a patient's rectum and colon.

Management

Treatment for UC focuses firstly on inducing remission and then maintenance of remission. There are an array of treatment options available for patients, with further detail provided in the Nice guidance, which can be found at ***tinyurl.com/ulcerativecolitis001***.[10]

This section will provide a brief overview of pharmacological and non-pharmacological management of UC.

Pharmacological Treatment[10]

Acute mild-to-moderate UC

Step 1:

- Induce remission by offering a topical aminosalicylate as first line treatment.
- If poorly tolerated, an oral aminosalicylate can be initiated (it should be noted to the patient that oral treatment is not as effective as topical agents).

Step 2:

- If remission is not achieved within four weeks, an oral aminosalicylate can be added (high-dose in proctosigmoiditis and left-sided UC).

Step 3:

- Addition of a topical or oral corticosteroid for a time-limited course..
- Topical or oral corticosteroid monotherapy for a time-limited course can also be used as an alternative for those intolerant of aminosalicylates.

Step 4:

- For patients not requiring hospital admission for acute severe UC and with moderate to severely active UC but who may be intolerant or unresponsive to conventional therapy, consider immune-modulators (thiopurines eg azathioprine or 6-mercatopurine
- Thereafter, tofacitinib can be given. Tofacitinib is a Janus kinase inhibitor (JAK inhibitor), and is similar to biological therapy, reducing inflammation in active UC.[11,12]

Acute extensive disease

Step 1:

- A topical aminosalicylate and high-dose oral aminosalicylate should be offered as first line therapy.

Step 2:

- If no remission is achieved within four weeks, stop the topical aminosalicylate and offer a high-dose oral aminosalicylate with a time-limited course of oral-corticosteroid.

Step 3:

- For patients not requiring hospital admission for acute severe UC and with moderate to severely active UC, but who may be intolerant or unresponsive to conventional therapy, consider thiopurines. If not tolerated or there is no response within three months, tofacitinib or another biologic therapy can be given. Choice of treatment is dependent on disease severity and patient perference.[11,12]

Acute severe UC

Step 1:

- Intravenous corticosteroids should be started to induce remission, followed by an assessment of the need for surgery.
- Intravenous ciclosporin or surgery should be considered for patients who:
  - cannot tolerate or decline IV corticosteroids
  - have a contraindication to treatment with IV corticosteroids.

Step 2:

- Add IV ciclosporin to IV corticosteroids, or consider surgery for patients who:
  - show little to no improvement within 72 hours of corticosteroid treatments
  - show symptom deterioration despite treatment.
- Infliximab (TNFα inhibitor – blocks inflammatory action of TNFα protein) is an alternative biological treatment for patients in whom ciclosporin is contraindicated or inappropriate, and if surgical intervention is not required.

Maintaining remission

Proctitis and proctosigmoiditis

- A topical aminosalicylate should be initiated as first line monotherapy or,
- An oral aminosalicylate plus a topical aminosalicylate or,
- Monotherapy with an oral aminosalicylate (however, it should be noted to the patient this is less effective than topical treatment).

Left-sided & Extensive UC

- First line therapy should include a low maintenance dose of an oral aminosalicylate.

All UC Extents

- Oral azathioprine or mercaptopurine should be initiated in patients who:
  - have had two or more exacerbations in 12 months requiring IV corticosteroid treatment
  - have not maintained remission using aminosalicylates.

Non-pharmacological treatment

Surgery is an option for high risk patients with acute severe UC. Documentation should be completed on admission, then daily to monitor the patient's ongoing need for surgery. The criteria increased surgery referral can be found via the following link ***tinyurl.com/ulcerativecolitis001.***

Monitoring in the community

With such a complex regimen of treatments available for UC, there are a number of key monitoring points that can be addressed in patient consultations.

Monitoring requirements differ by brand and these can be found in the manufacturer's data sheets. In some areas, aminosalicylates and immunosuppressants are prescribed under shared care agreements between primary and secondary care. In these cases, local guidance for monitoring should be followed.

A brief introduction to the key monitoring parameters for the various therapies are described below:

Aminosalicylates (eg sulfasalazine, mesalazine)[13]

- Patients should be made aware of the potential for blood disorders (dyscrasia). Signs and symptoms include any unexplained bruising, bleeding, sore throat, malaise and fever. These disorders occur primarily within the first 3-6 months of treatment.
- Renal function should be measured at initiation, then at three months, followed by annual monitoring.
- Patients should be advised to report any changes in their condition when switching brands of mesalazine.

Corticosteroids (eg prednisolone, hydrocortisone)[14]

- Corticosteroids should be used as part of a time-limited course. High dose/long courses require tapered dose reductions in order to prevent adrenal insufficiency upon withdrawal.
- There are multiple side-effects with both short-term and long-term use of steroids. Some that may be more evident in the community setting include fluid retention, immunosuppression (eg increased reporting of infections), gastro-intestinal upset and mood changes.
- For high doses or courses lasting over three weeks, patients should receive a steroid card – this can be a useful tool in monitoring steroid courses in the community pharmacy.

Immunosuppressants (eg azathioprine, mercaptopurine)[15]

- Regular blood tests should be used to monitor for neutropenia and thrombocytopenia.

Regular blood tests should be carried out in patients taking immunosuppressant therapy

References

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12. South West London (2019) Inflammatory bowel disease pathway.
13. British National Formulary (2019) Sulfasalazine.
14. British National Formulary (2019) Prednisolone.
15. British National Formulary (2019) Mercaptopurine.

- Patients should be educated on recognising the signs of blood disorders such as bruising, bleeding and infections, as well as signs of hepatoxicity such as abdominal pain, fatigue, jaundice, dark-coloured urine and weight loss/appetite.
- Nausea is common side effect and can be mitigated with divided daily dosing and taking these medicines after food.

Further advice

UC is a complex condition that requires regular monitoring and multi-disciplinary support. Other key areas to consider when supporting patients may include:

- Stoma management – some patients with UC may have a stoma formed either on a temporary or permenant basis. Community pharmacies can help to support patients with complaints relating to their stoma. This may include the integrity of the patient's skin and their stoma output. Often, OTC remedies to prevent skin irritation and reduce high-output, eg loperamide, can be used to support patients.
- Diet and lifestyle – patients should be encouraged to use a food diary to highlight certain foods that may exacerbate their condition. All patients should be advised to seek specialist support from a dietician if they are struggling with this aspect of the disease management.
- Counselling patients when changing between once daily preparations and twice daily preparations.

Patients and their carers can find out more information about the above and about UC management from charities or online sources such as:

- Crohn's and Colitis UK at ***www.crohnsandcolitis.org.uk***
- Guts at ***www.gutscharity.org.uk***
- NHS website for Crohn's disease and ulcerative colitis at ***www.nhs.uk/conditions***.

CPD 5-minute test

1. Ulcerative colitis affects the entirety of the gastrointestinal tract from mouth to anus.
   True or false
2. Inflammatory bowel disease includes the following conditions: Crohn's Disease, ulcerative colitis (UC) and inflammatory bowel disease.
   True or false
3. Ulcerative colitis primarily presents in those under 30 years of age.
   True or false
4. Ulcerative colitis is more common among Western populations.
   True or false
5. Weight gain is a common symptom associated with UC due to dysfunction of nutrient absorption.
   True or false
6. Nocturnal waking as a result of diarrhoea is a serious symptom that requires referral.
   True or false
7. An ulcerative colitis diagnosis can also lead to extra-intestinal manifestations that affects the joints, skin and eyes.
   True or false
8. Diagnosis of UC may include a stool sample to rule out a potential infection such as C.difficile or gastroenteritis.
   True or false
9. IV ciclosporin is first-line for all patients presenting with acute extensive ulcerative colitis.
   True or false
10. Patients switching brands of mesalazine should be advised to not worry about changes to their symptoms.
    True or false

UC and CD CPD planned learning

What are you planning to learn?

I want to learn more about inflammatory bowel disease (IBD), in particular ulcerative colitis (UC), as I often see patients requiring a variety of treatments for their condition in the community pharmacy setting. This learning is relevant to me because these medicines can often be monitored to some extent in a community setting with relation to adverse drug reactions and side effects such as neutropenia.

Furthermore, I often dispense prescriptions for patients using either sulfasalazine or mesalazine, which I understand come in a number of different preparations, hence this learning is relevant to my ability to support patients with their treatment.

This learning will support the pharmacy team to develop their knowledge and raise awareness of IBD and the implications our patients may face, such as being initiated with a stoma bag.

How are you planning to learn it?

- I plan to read the Nice guidance available on ulcerative colitis available at ***www.nice.org.uk/guidance/NG130***
- I will also discuss the main treatments we use within our pharmacy with my colleagues to ensure we can all recognise patients with IBD, particularly UC, to enable shared learning.
- I also plan to complete the five-minute test at ***www.chemistanddruggist.co.uk/update-plus*** to test my knowledge and confirm what I have learned.

Give an example of how this learning has benefited the people using your services.

I recently provided OTC advice to a patient who was complaining of persistent diarrhoea. I recognised that the patient had been in a number of times to purchase loperamide and decided to investigate their medical and drug history further. It quickly became apparent that the patient had been diagnosed with UC two years previously and was currently receiving treatment to maintain remission. The patient had been prescribed both an oral and topical aminosalicylate for management of their condition, which had been effective in maintaining remission.

I confirmed with the patient that they had not had any unexplained bleeding or bruising with an aim to rule out any blood disorders as a result of treatment. The patient did not complain of any such symptoms, however they did describe their ongoing diarrhoea, which was sometimes bloody and accompanied by gastrointestinal pain. I was able to identify that a likely explanation could be a potential relapse of the patient's condition and advised an emergency referral to the GP, or A&E if symptoms became more severe.

The patient revisited the pharmacy a few weeks later to inform me that they had been admitted to hospital for an acute exacerbation, and was grateful for our investigation of their history, which supported their referral.