Ulcerative colitis: management in adults, children and young people – concise guidance

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ABSTRACT

Ulcerative colitis is a chronic, relapsing and remitting inflammatory disease of the colon and rectum. Effective management requires prompt recognition and treatment of those with acute relapses as well as appropriate choice and monitoring of drugs for maintenance of remission. This therefore involves specialist gastroenterology teams as well as acute and general physicians and primary care clinicians. Treatment options need to be discussed with those with ulcerative colitis and their families and appropriate information provided. This concise guideline focuses (with the generalist particularly in mind) on recommendations from the National Institute for Health and Care Excellence clinical guideline 166 considered of key importance for implementation.

KEYWORDS: Diagnosis, inflammatory bowel disease, management, ulcerative colitis

Introduction

Ulcerative colitis (UC) is a chronic inflammatory condition of the colon and rectum with an estimated incidence of 10 per 100,000 and a prevalence of 240 per 100,000.[1–3] It runs a relapsing and remitting course.[4] Long-term care is often shared between specialist gastroenterology teams and primary care, during both remission and relapse. A multidisciplinary approach has become central to service delivery. Early recognition and treatment of acute severe UC is essential and may therefore require initial management by emergency, acute and general physicians. Monitoring of treatments for UC involves both primary and secondary care clinicians.

The aim of treatment is to reduce symptoms, improve or restore quality of life and achieve healing of inflamed mucosa.

Scope and purpose

This concise guideline highlights key recommendations of the National Institute for Health and Care Excellence (NICE) clinical guideline 166 *Ulcerative colitis: management in adults, children and young people*,[5] focusing (with the generalist particularly in mind) on recommendations identified by the guideline development group as of key importance for implementation.

Related NICE technology appraisals cover biological treatments approved for use in UC (TA163, TA329 and TA342),[6–8] but are not included in this concise guideline.

Recommendations

Patient information and support

Because of the chronic and potentially debilitating course, with the need for long-term medication and surgery, 'discuss the disease and associated symptoms, treatment options and monitoring:

- with the person with UC, and their family members or carers as appropriate
- within the multidisciplinary team (the composition of which should be appropriate for the age of the person) at every opportunity.'[5]

Induction of remission

Treatment for active UC is helpfully informed by assessment of disease severity and current or previous assessments of disease extent.

Severity of an acute exacerbation of UC can be assessed using the criteria of Truelove and Witts (Table 1). Acute severe colitis is defined as at least six bowel motions per day with blood, associated with at least one of the following: pyrexia, tachycardia, anaemia or a raised erythrocyte sedimentation rate.[9]

In children and young people these categories are based on the Paediatric Ulcerative Colitis Activity Index.[10] The term 'subacute' – defined as moderately to severely active UC that would normally be managed in an outpatient setting, and does not require hospitalisation or the consideration of urgent surgical intervention – is also used in this guideline.[7]

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The National Institute of Health and Care Excellence (NICE) has accredited the process used by the Royal College of Physicians to produce the concise clinical guidelines published in *Clinical Medicine* with effect February 2010 to March 2018 (abstracted guidance) and July 2013 to July 2018 (*de novo* guidance). More information on accreditation can be viewed at: www.nice.org.uk/about/what-we-do/accreditation.

Table 1. Truelove and Witts classification of disease severity in ulcerative colitis

Disease activity	Mild	Moderate	Severe
Bowel movements (no per day)	≤4	4–6	≥6 plus at least one of the features of systemic upset (marked with * below)
Blood in stools	No more than small amounts of blood	Between mild and severe	Visible blood
Pyrexia (temperature >37.8°C)*	No	No	Yes
Pulse rate ≥90 bpm*	No	No	Yes
Anaemia*	No	No	Yes
Erythrocyte sedimentation rate (mm/h)*	≤30	≤30	>30

Treating acute severe ulcerative colitis: all extents of disease

Acute severe UC requires hospital admission for intravenous corticosteroids and prophylaxis against venous thromboembolism. The likelihood of the person requiring surgery or escalation of medical therapy should be assessed on admission and on a daily basis. Careful monitoring is required to ensure that an adequate response occurs or that there is timely, further escalation of treatment – to ciclosporin, anti-tumour necrosis factor (TNF) agents or emergency surgery.

The recommendations are summarised as an algorithm in Fig 1.

The use of infliximab in acute severe ulcerative colitis

The use of infliximab for acute severe UC is addressed in NICE TA163.[6] Subsequently, two trials have demonstrated comparable efficacy and safety for ciclosporin and infliximab in those who do not respond to intravenous steroids.[11,12]

Multidisciplinary management

Organised multidisciplinary collaboration is central to all effective management of UC, and this is emphasised in the recommendations for acute severe episodes.

'For people admitted to hospital with acute severe ulcerative colitis:

- ensure that a gastroenterologist and a colorectal surgeon collaborate to provide treatment and management
- ensure that the composition of the multidisciplinary team is appropriate for the age of the patient
- seek advice from a paediatrician with expertise in gastroenterology when treating a child or young person
- ensure that the obstetrics and gynaecology team is included when treating a pregnant woman.'[5]

Inducing remission in mild to moderate ulcerative colitis

Step 1 therapy

Proctitis/Proctosigmoiditis: Disease affecting the rectum or rectum and sigmoid colon

Topical aminosalicylates

To induce remission in people with a mild to moderate first presentation or inflammatory exacerbation of proctitis or proctosigmoiditis, topical aminosalicylates are more effective than topical corticosteroids. Therefore:

- 'offer a topical aminosalicylate alone (suppository or enema) or
- consider adding an oral aminosalicylate to a topical aminosalicylate or
- consider an oral aminosalicylate alone, taking into account the person's preferences and explaining that this is not as effective as a topical aminosalicylate alone or combined treatment.'[5]

In patients who cannot tolerate, decline or have contraindications to aminosalicylates, topical corticosteroids or oral prednisolone should be offered.

Left-sided/extensive UC: more extensive disease with inflammation extending proximal to sigmoid colon

'To induce remission in adults with a mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive UC

- offer a high induction dose of an oral aminosalicylate.'[5]

The delivery characteristics of oral aminosalicylate preparations may vary. The direct evidence is limited and does not demonstrate that any one aminosalicylate preparation is clinically more effective than another. Therefore, it is not currently possible to recommend one preparation over another. In children and young people, paediatric doses should be calculated by body weight.[13]

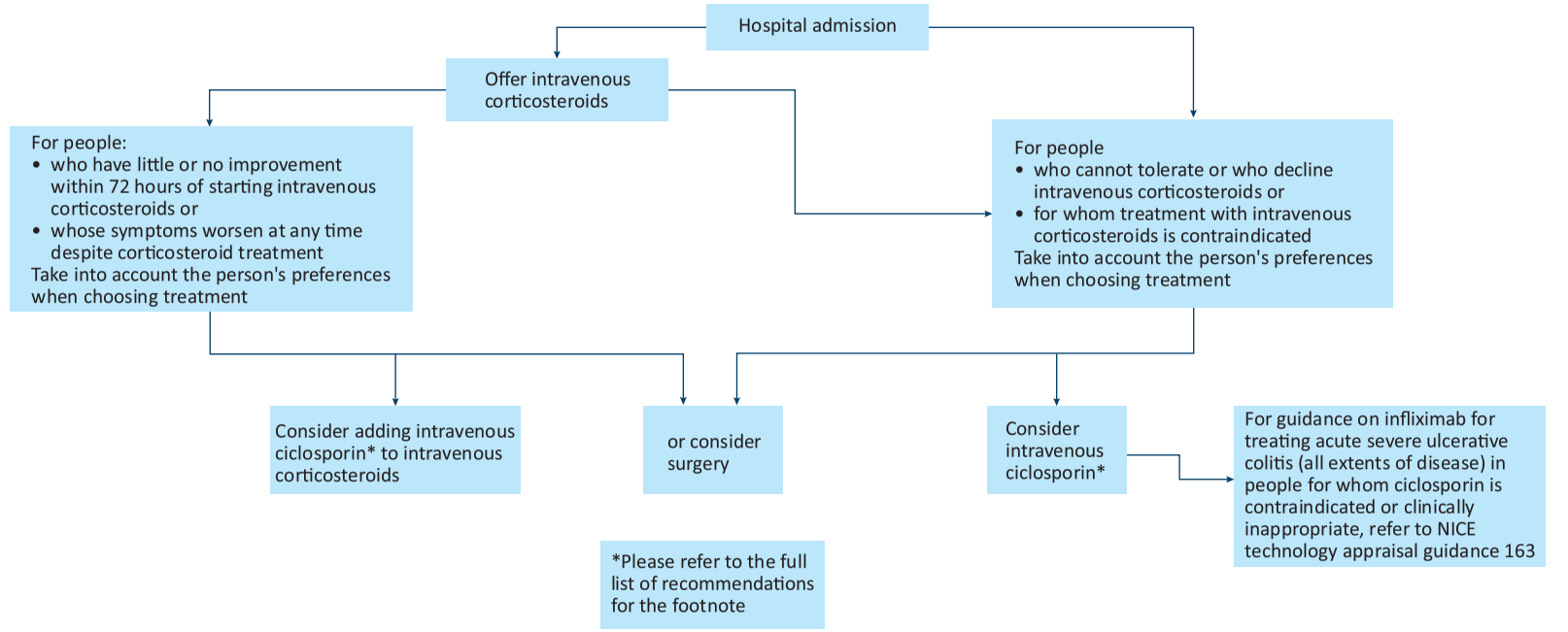
- 'Consider adding a topical aminosalicylate or oral beclometasone dipropionate taking into account the person's preferences.
- In people who cannot tolerate or who decline aminosalicylates, in whom aminosalicylates are contraindicated or who have subacute UC, offer oral prednisolone.'[5]

Systemic corticosteroids are clearly effective in active UC, but their use should be limited to reduce the occurrence of steroid side-effects. Although beclometasone dipropionate is suggested as an option for this group, there is limited data on longer-term use and, therefore, no definitive recommendation on duration of treatment.

Step 2 therapy

Prednisolone and tacrolimus

- 'Consider adding oral prednisolone to aminosalicylate therapy to induce remission if there is no improvement within 4 weeks



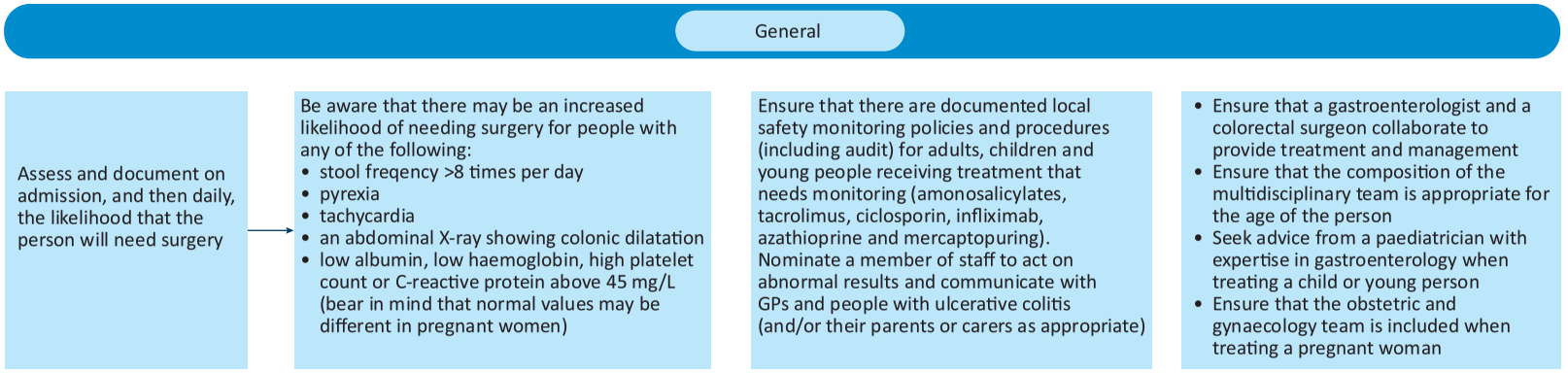


Fig 1. Inducing remission in people with acute severe ulcerative colitis: all extents of disease.[5]

of starting aminosalicylate therapy or if symptoms worsen despite treatment. (Beclometasone dipropionate is stopped if adding oral prednisolone).
- Consider adding oral tacrolimus to oral prednisolone to induce remission in people with mild to moderate UC if there is an inadequate response to oral prednisolone after 2–4 weeks.'[5]

Studies showing benefit of tacrolimus have been of just 12 weeks' duration.[14,15] Again, therefore, no recommendation is currently possible on treatment duration. Nephrotoxicity and opportunistic infections may be an issue with longer-term use, reinforcing the need for careful monitoring.

Biological agents

The role of anti- TNF-α agents (infliximab, adalimumab and golimumab) or vedolizumab, a human monoclonal antibody to α4β7 integrin, to treat moderate to severely active UC in those who cannot tolerate, have contraindications to, or have not responded adequately to conventional therapy is outlined in NICE TA329[7] and TA342,[8] but is also incorporated into the pathway for induction of remission.[16] In practice, patients failing treatment with prednisolone will be considered for treatment with biologic agents – including anti-TNF agents or vedolizumab – before considering tacrolimus.

Maintenance of remission

Proctitis and proctosigmoiditis

'To maintain remission after a mild to moderate inflammatory exacerbation of proctitis or proctosigmoiditis, consider the following options, taking into account the person's preferences:

- a topical aminosalicylate alone (daily or intermittent) or
- an oral aminosalicylate plus a topical aminosalicylate (daily or intermittent) or
- an oral aminosalicylate alone, explaining that this may not be as effective as combined treatment or an intermittent topical aminosalicylate alone.'[5]

Left-sided and extensive ulcerative colitis

'To maintain remission in adults after a mild to moderate inflammatory exacerbation of left-sided or extensive UC:

- offer a low maintenance dose of an oral aminosalicylate.'[5]

Choice of dosing regimens should take into account the opportunity to enhance adherence to treatment. Consider a once-daily dosing regimen for oral aminosalicylates when used for maintaining remission. Take into account the person's preferences and explain that once-daily dosing can be more effective, but may result in more side effects.

All extents of disease

'Consider oral azathioprine or oral mercaptopurine to maintain remission:

- after two or more inflammatory exacerbations in 12 months that require treatment with systemic corticosteroids or
- if remission is not maintained by aminosalicylates or
- after a single episode of acute severe UC.'[5]

It is important to ensure screening prior to immunosuppression use is undertaken. This should include testing for red cell thiopurine methyltransferase activity and viral serology.[17]

Monitoring

'Ensure that there are documented local safety monitoring policies and procedures (including audit) for adults, children and young people receiving treatment that needs monitoring.'[5]

Limitations of the guideline

Studies included in the network meta-analyses that informed the recommendations for induction of remission in people with left-sided or extensive UC compared with placebo were mostly of very low to low quality with the majority of the networks comprising just one study per arm.[18,19]

Recommendations for 'step 2' therapy are based on indirect evidence and consensus and this is reflected in the strength of the recommendations. None of the evidence for the induction of remission was in people clearly identified as failing first step therapy and therefore the treatment effect in this situation, as a second step therapy, may be overestimated.

The use of biological agents is evaluated in NICE technology appraisals;[7,8] therefore, they are not considered within the clinical guideline (CG166).[5] As a result, the evidence for treatment options for the same clinical scenario – for example acute severe or moderately severe UC unresponsive to corticosteroids – may not have been considered together.

There is increasing awareness of the importance of mucosal healing as an endpoint for treatment, but this outcome was not uniformly available in the studies included in the guideline.

Surveillance review 2017

A surveillance review of CG166 was undertaken by NICE in June 2017,[20] suggesting an update to focus on medicines used to induce remission in mild-moderate UC and acute severe UC, including the use of infliximab and ciclosporin. Systematic reviews identified in the 4-year surveillance review reported that both beclomethasone dipropionate and budesonide multimatrix were superior to placebo or aminosalicylates for induction of remission. Currently, NICE guideline CG166 does not make recommendations on budesonide.

Studies were identified that assessed new, more cost-effective aminosalicylate preparations, which may have implications for the wider healthcare economy.

Implications for implementation

The recommendations from CG166 informed the development of NICE quality standard QS81 (covering both UC and Crohn's disease),[21] which includes four quality statements (Table 2) particularly emphasising the multidisciplinary approach to care. ■

Conflicts of interest

Alan Lobo (Chair) and Adam Harris are both members of the CG166 guideline development group (GDG).

Table 2. Quality statements in inflammatory bowel disease[21]

Statement 1	People with suspected inflammatory bowel disease have a specialist assessment within 4 weeks of referral
Statement 2	Services provide age-appropriate support from a multidisciplinary team for people with inflammatory bowel disease and their family members or carers
Statement 3	People having surgery for inflammatory bowel disease have it undertaken by a colorectal surgeon who is a core member of the inflammatory bowel disease multidisciplinary team
Statement 4	People receiving drug treatment for inflammatory bowel disease are monitored for adverse effects

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