Management of *Clostridium difficile* infection requires a multidisciplinary team approach, prompt isolation of patients, enhanced cleaning arrangements and a targeted management plan

**Clostridium difficile**

**managing infections**

By Mark Gilchrist, MSc, MRPharmS, Nick Cooley, DipClinPharm, and Luke S P Moore, MSc, FRCPath

Patients with *Clostridium difficile* infection (CDI) are best managed by a multidisciplinary team; evidence suggests that this should include doctors, nurses and pharmacists, all specialising in the management of infections. The team should also be able to draw on the resources of dietitians, gastroenterologists and gastrointestinal surgeons.

**Assessing disease severity**

To manage a CDI appropriately the severity of a patient’s condition must be established; several scoring systems exist for this purpose. A recent prospective observational study, which looked at accuracy of eight common severity scores, showed that the “Hines VA index” was best able to predict the more severe forms of CDI (see Box 1). Further information around severity of a patient’s infection can be obtained through flexible sigmoidoscopy or imaging (eg, X-ray or computed tomography).

**A stepped approach**

For all patients, management should start with a review of the causative systemic antibiotic. The fluid status of all patients should also be assessed and rehydration provided, using oral or intravenous fluids depending on severity of their diarrhoea. Addressing these two issues has historically been found to be effective in 15–23% of mild cases of CDI. Nevertheless, most patients will require antibiotics to treat their infection (see below). Clinicians should also stop any antimotility medicines and review the need for any laxatives or proton pump inhibitors that are prescribed.

If severe or complicated CDI is suspected targeted *C difficile* treatment should be started promptly, even if confirmation of the diagnosis is pending. Patients who deteriorate despite optimal medical therapy — including antibiotics and other treatments such as intravenous immunoglobulin (see below) — can be considered for subtotal colectomy (with preservation of the rectal stump). There is no consensus around criteria for colectomy in patients with fulminant CDI, but Infectious Diseases Society of America practice guidelines cite toxic megacolon, colonic perforation, acute abdomen and septic shock as indicators for possible surgery. Laboratory parameters can inform the timing of surgery — if surgery is delayed until serum lactate climbs to over 5mmol/L, or the white blood cell count rises above 50,000 cells/ml, perioperative mortality can be as high as 75%.

**Monitoring patients**

Daily monitoring of patients with CDI should include:

- Review and recording of stool frequency and consistency (using the Bristol stool chart)
- Assessment of response to current CDI therapy; if no response, or deterioration of the patient, the infection team should be informed

**SUMMARY**

Management of a patient with *Clostridium difficile* infection (CDI) will depend on the severity of the infection. However, most patients will require antibiotic treatment — usually with oral metronidazole or oral vancomycin — and fluid replacement. If possible, any causative antibiotics should be stopped.

Healthcare organisations should have strategies in place to manage patients with CDI. Organisations should ensure that infected patients are isolated promptly, strict policies around hand hygiene and personal protection are set out and affected areas are cleaned appropriately.

**Box 1: Severity of C difficile infection**

The Hines index is commonly used to assess the severity of *Clostridium difficile* infection. A patient’s score is calculated based on the following clinical parameters:

- Fever (38C or higher) — 1 point
- Ileus — 1 point
- Systolic blood pressure <100mmHg — 1 point
- White blood cell count: <15,000/mm³ — 0 points; >15,000/mm³ but <30,000/mm³ — 1 point; >30,000/mm³ — 2 points
- Findings on computed tomography (thickened colonic wall, colonic dilation, ascites): none — 0 points; one — 1 point; two or more — 2 points

Hines VA index scores of 3 or higher have shown the strongest correlation for predicting more severe forms of *C difficile* infection.

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Antibiotic therapy

There are four antibiotics licensed in the UK for the treatment of CDI — metronidazole, vancomycin (oral), teicoplanin (oral) and fidaxomicin. However, others can be used off-licence (see Box 2). Generally, treatment focuses on the use of oral metronidazole (400mg three times a day) or oral vancomycin (125mg four times a day) for 10 to 14 days. Many studies have shown that these medicines are equally effective for the treatment of non-severe CDI. However, metronidazole tends to be used more often than vancomycin because it is cheaper and less likely to induce resistance (eg, vancomycin-resistant enterococci).

For severe disease, oral vancomycin (125–500mg four times a day) is the treatment of choice. For patients who develop fulminant disease the combination of oral high-dose vancomycin (500mg four times a day) and intravenous metronidazole (see Box 3, p259) is considered the treatment of choice.

In 2011 a Cochrane review examined 15 studies, including over 1,100 patients, investigating nine different antibiotics — bacitracin, fidaxomicin, fusidic acid, metronidazole, nitazoxanide, rifampicin, rifaximin, teicoplanin and vancomycin. The review concluded that no single antibiotic was better than vancomycin, with the exception of oral teicoplanin (200mg twice a day) in severe disease. Teicoplanin is licensed in the UK for the management of CDI but is not used often because of its cost.

Recurrent infection

Some 15–35% of patients relapse within two months after a first episode of CDI. Ideally, clinicians should ascertain whether these patients are infected with the same strain or a new strain, but this can be difficult to do in practice. Current advice around the management of first relapse is to re-treat with the antibiotic used for the initial infection. Treatment of patients who relapse again should be in consultation with an infection team. Metronidazole should be considered carefully if it is going to be used long term due to the potential for neurotoxicity. Other treatment options are outlined below.

Alternative vancomycin regimens

For patients who relapse despite successful initial treatment of CDI, a reducing course of oral vancomycin can be used to prevent another relapse. However, attention needs to be given to the potential for growth of vancomycin-resistant organisms. An example of a dose-reducing regimen for vancomycin is:

- Week 1 — 125mg four times a day
- Week 2 — 125mg three times a day
- Week 3 — 125mg twice a day
- Week 4 — 125mg daily
- Week 5 — 125mg on alternate days
- Week 6 — 125mg every third day, then stop

Fidaxomicin

In December 2011 fidaxomicin was approved in Europe for the treatment of CDI (200mg, orally, twice a day for 10 days). Fidaxomicin is a macrocyclic antibiotic, which acts through inhibiting RNA synthesis via bacterial RNA polymerase. It inhibits C difficile sporulation and has been shown to be effective for the treatment of recurrent disease. Data demonstrate that it is non-inferior to oral vancomycin for the treatment of CDI (except against the BI/NAP1/027 strain).

Faecal transplant

Research suggests that faecal transplant (from a healthy donor) can be used for the treatment of CDI (donor faeces, usually obtained from a patient’s relative, is administered via enema or nasogastric tube). A recent systematic review by Guo and colleagues looked at evidence from seven case series, including 124 patients with refractory CDI, and found that faecal transplant was safe and effective — 83% of patients experienced immediate symptomatic improvement after the first procedure. Benefits of the procedure also appear to be lasting, with one study showing a cure rate of up to 98%.

Intravenous immunoglobulin

In the UK, use of intravenous immunoglobulin (IVIG) is reserved for severe or recurrent cases of colitis where other licensed therapies have failed. There is some evidence to suggest that the addition of oral rifampicin (300mg twice a day) to treatment with IVIG may be of benefit. If IVIG is indicated, a single dose of 0.4g/kg should be prescribed. Repeating the dose can be considered if clinically warranted.
Probiotics

Generally, the use of probiotics, either for prevention of CDI or as part of treatment regimens, remains controversial. To date, studies have been small and the results inconclusive. Nevertheless, there is some evidence suggesting that the use of Saccharomyces boulardii in combination with high-dose vancomycin can reduce the rate of relapse.

It should be noted that there have been case reports of systemic infections (fungaemias and bacteraemias) following use of probiotics in immunocompromised patients, so use for this patient population should be considered with caution. Further studies are required to determine which probiotics are the most effective and which patients are most likely to benefit.

Organisational considerations

Over recent years, in the UK and internationally, there have been several instances where outbreaks of C. difficile have garnered intense political and public interest. Following investigation of these cases, and examining the lessons learnt, some clinical and non-clinical strategies for managing this infection have been set out. For example, healthcare organisations should ensure that:

- Affected patients are isolated promptly
- Appropriate specimens are sent to microbiology
- Patient symptoms, fluid balance and stools are documented
- Strict policies around hand hygiene and personal protection are in place
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sporicidal and may in fact encourage sporulation).24

remain viable for prolonged periods and are resistant to

required for these newer methods must be cleaned before

vapour, chlorine dioxide or ozone, as well as ultraviolet

contamination in patient rooms and in reducing rates of

hospitals, and can be found on the hands and in the stool

commodes, toilets, bedding, mops, scales and furniture in

CDI in hospital units where rates are high.25

Use of soap and water As part of a strict hand hygiene

policy, all staff and visitors should be made aware that

alcohol gel does not eradicate C difficile spores. Therefore,

staff and visitors should wash their hands with soap and

water after being in contact with a patient who is infected

with C difficile or has diarrhoea of unknown cause.23,24

Personal protective equipment Gloves,22 aprons and

other personal protective equipment should be considered

when reviewing patients with CDI.

Cleaning C difficile spores commonly colonise floors,

commodes, toilets, bedding, mops, scales and furniture in

hospitals, and can be found on the hands and in the stool

of asymptomatic hospital personnel.21 These spores can

remain viable for prolonged periods and are resistant to

standard cleaning and disinfection practices, such as use of

quaternary ammonium-based detergents (which are not

sporicidal and may in fact encourage sporulation).29

Cleaning with sodium hypochlorite disinfectant has

been shown to be effective in reducing environmental

contamination in patient rooms and in reducing rates of

CDI in hospital units where rates are high.27

Alternatives include the use of hydrogen peroxide

vapour, chlorine dioxide or ozone, as well as ultraviolet

light-based technologies. However, because the equipment

required for these newer methods must be cleaned before

use, and because there are limited data supporting their

use, their role is debatable.28

Multidisciplinary approach In the first instance, the

infection prevention and control (IPC) team should be

told about all patients with diarrhoea. Where CDI is

suspected or confirmed a multidisciplinary infection

management team, consisting of a doctor, nurse and

pharmacist, should review the patient (in addition to the

patient’s designated clinical team). Gastroenterologists,

gastrointestinal surgeons and dietitians should be involved

in the care of CDI patients as appropriate.

Within healthcare organisations it is important that the

occupational health department informs the IPC team of

any staff with diarrhoea. Generally, staff should not return

to work until they have been free of diarrhoea for 48

hours.

Also important are the members of the non-clinical

team, including the domestic and facilities staff. Such staff

are responsible for ensuring that the environment and

toilet areas are cleaned regularly and fresh linen is

available.

Hospital managers should be kept informed about

cases of CDI because these can impact on bed strategy

and patient pathways.

Surveillance Following a documented case of CDI, it is

recommended that a case review and cause analysis are

undertaken. As well as reacting to cases of C difficile,

healthcare organisations should have mechanisms in place

to prevent such infections occurring.

For example, trusts should have:

- An effective antimicrobial stewardship programme

- Strategies to ensure that good antimicrobial

  prescribing becomes embedded at ward and patient

  level

- A system of routinely auditing hand hygiene and

  cleaning

- Engagement at board and managerial level

  regarding the reduction and control of C difficile

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Clostridium difficile

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To complete the module, you will need to log in to the site. If you are a new visitor, it is simple to register as a user (free to all Royal Pharmaceutical Society members).

Questions

This month’s Lifelong Learning questions are based on the CLINICAL FOCUS articles on Clostridium difficile, which were commissioned from independent authors. The information in the Box (below) is there to help you identify knowledge gaps and undertake continuing professional development. This online module will close on 29 November 2012.

Answers from the July/August module

Systemic lupus erythematosus

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Questions

1. (a) T, (b) F, (c) T, (d) T, (e) F
2. (a) T, (b) F, (c) T, (d) F, (e) T
3. (a) T, (b) F, (c) T, (d) T, (e) T
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Answers

1. (a) T, (b) F, (c) T, (d) T, (e) F
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Questions:

Answers:

How to undertake continuing professional development

Our CLINICAL FOCUS articles and the online Lifelong Learning modules can help you plan your CPD and record the benefits of the activity at www.uptodate.org.uk.

Reflect on your gaps in knowledge

- What are the signs of Clostridium difficile infection (CDI)?
- What are the main risk factors for CDI and how is it diagnosed?
- What strategies are used to treat patients with CDI?
- What organisational factors need to be considered to limit the spread of CDI?

Act to enhance your practice

- Read the CLINICAL FOCUS articles in this issue (pp250–61)
- Test your knowledge by completing the questions at www.clinicalpharmacist.com
- Evaluate the activity

What have you learnt?

- How has it added value to your practice?
- What will you do now and how will this be achieved?

Consider making this activity one of your nine CPD entries this year.