FIVE THINGS TO KNOW ABOUT ...

Treating *Clostridium difficile* infection

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First-line treatment for mild or moderate *Clostridium difficile* infection is metronidazole; vancomycin is first-line treatment for severe infection

1

A randomized controlled trial (RCT) showed that metronidazole was as effective as vancomycin taken orally for the treatment of mild *Clostridium difficile* infection. However, in cases of severe infection, 97% of patients given vancomycin had clinical resolution compared with only 76% of those given metronidazole.[1] The Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America recommend metronidazole as first-line therapy for mild or moderate *C. difficile* infection and vancomycin for severe infection (Box 1).[2] Although criteria for severe infection differ between guideline and trial, both include a leukocyte count greater than 15×10^9 cells/L.

Box 1: Classification of the severity of *Clostridium difficile* infection[1,2]

Severity	Guidelines[1]	Randomized controlled trial[2]
Mild–moderate	• $< 15 \times 10^9$ leukocytes/L and • Serum creatinine < 1.5 times premorbid level	• Infections that do not satisfy the criteria for severe infection
Severe	• $\geq 15 \times 10^9$ leukocytes /L or • Serum creatinine ≥ 1.5 times premorbid level	Two of: • Age > 60 years • Temperature > 38.3°C • Albumin < 25 g/L • $> 15 \times 10^9$ leukocytes/L or one of: • Colonoscopic evidence of pseudo-membranous colitis • Treatment in intensive care unit

2

Fidaxomicin is as effective as vancomycin for treatment of *C. difficile* infection and results in fewer relapses

In a phase 3 controlled clinical trial, fidaxomicin was noninferior to vancomycin in achieving clinical resolution of *C. difficile* infection.[3] Of note, 13.3% of patients given fidaxomicin had recurrent infection within four weeks, compared with 24.0% of patients given vancomycin.[3]

3

Duodenal infusion of donor feces is more effective than vancomycin for recurrent infection

In an RCT comparing treatment of recurrent *C. difficile* infection with vancomycin or duodenal infusion of donor feces, 81% of patients in the fecal infusion group had resolution of the infection, compared with 31% of patients given vancomycin alone.[4]

4

Probiotics have no role in the treatment of *C. difficile* infection, and their role in prophylaxis is unclear

The latest guidelines do not recommend the use of probiotics for prophylaxis or treatment of *C. difficile* infection.[2] A systematic review and meta-analysis of 20 RCTs found moderate-quality evidence suggesting a 34% risk reduction of *C. difficile* infection with the use of probiotics for prevention, with no increase in adverse events; this finding was limited by the variability of probiotic regimens and missing data in 13 studies.[5] However, a recent high-quality RCT found no evidence that a multistrain probiotic preparation prevented infection.[6]

For references, please see Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.131315/-/DC1

5

Phase 3 clinical trials of *C. difficile* vaccines are underway

The *Cdiffense* study is a phase 3 RCT that will evaluate the efficacy of inactivated *C. difficile* toxoids A and B in preventing *C. difficile* infection. Phase 1 trials showed development of an immune response in humans.[7] Phase 2 results are forthcoming.

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