Fidaxomicin Failures in Recurrent Clostridium difficile Infection: A Problem of Timing

TO THE EDITOR—Recurrent Clostridium difficile infection (CDI) is an increasing-ly vexing problem for patients and clinicians. Despite successful initial therapy, up to 35% of patients have recurrent diarrhea shortly after completing treatment, with a subset developing a chronic relapsing form of disease that becomes disabling and costly [1]. Recent studies have shown fidaxomicin to be potent against C. difficile. Also, with limited activity against the normal fecal microflora, fidaxomicin was found to be an effective treatment for first or second episodes of CDI, with a lower relapse rate than oral vancomycin [2, 3]. The relapsing C. difficile is presumed to occur due to persistent disruption of the intestinal microflora and inadequate local immune responses [4]. Fidaxomicin would be expected to have less impact in those with multiple relapses, yet we have seen several patients prescribed fidaxomicin for recurrent CDI who have failed this therapy. 

A 62-year-old woman experienced 3 weeks of diarrhea in April 2011. She received ciprofloxacin then metronidazole without improvement. She developed severe hypokalemia and tested positive for C. difficile on 12 May 2011. She received 14 days of metronidazole; this was followed by Saccharomyces boulardii therapy. She then relapsed, and this treatment was repeated twice. A colonoscopy showed moderate colitis, and the C. difficile toxin was positive. Weight loss, fatigue, and diarrhea persisted after C. difficile therapy was stopped. She received multiple courses of oral vancomycin and several 6-week tapered vancomycin courses, each complicated by recurrent symptoms at completion. In November 2011, she received 10 days of fidaxomicin with improvement followed by relapse within 2 weeks. Fidaxomicin was repeated for another 10 days with a similar result and then followed by oral vancomycin with control of diarrhea while awaiting fecal transplant.

A 44-year-old woman developed CDI in 2010 following several antibiotic courses. She took 2 courses of oral metronidazole for 14 days, each followed by recurrence within 2 weeks. After a third course she became asymptomatic for 6 months until antibiotics were given again for a dental infection. In 2011, she developed recurrent CDI, was treated with metronidazole followed by two 10-day courses of oral vancomycin, a rifaximin “chaser” regimen, and then 30 days of fidaxomicin with improvement. Within 2 weeks of completion, her symptoms recurred and she was referred for fecal transplant.

Fidaxomicin does not appear to be effective for patients with multiple relapses and should be used, as approved, early in the course of CDI, rather than in late recurrent disease.
Notes

**Financial support.** No funding was provided related to this paper.

**Potential conflicts of interest.** Author certifies no potential conflicts of interest.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases 2012;55(4):613–4
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