

TREATMENT

XXVIII. What are important ancillary treatment strategies for CDI?

Recommendations

1. Discontinue therapy with the inciting antibiotic agent(s) as soon as possible, as this may influence the risk of CDI recurrence (*strong recommendation, moderate quality of evidence*).
2. Antibiotic therapy for CDI should be started empirically for situations where a substantial delay in laboratory confirmation is expected, or for fulminant CDI (described in section XXX) (*weak recommendation, low quality of evidence*).

XXIX. What are the best treatments of an initial CDI episode to ensure resolution of symptoms and sustained resolution 1 month after treatment?

Recommendations

1. Either vancomycin or fidaxomicin is recommended over metronidazole for an initial episode of CDI. The dosage is vancomycin 125 mg orally 4 times per day or fidaxomicin

200 mg twice daily for 10 days (*strong recommendation, high quality of evidence*) (Table 1).

2. In settings where access to vancomycin or fidaxomicin is limited, we suggest using metronidazole for an initial episode of nonsevere CDI only (*weak recommendation, high quality of evidence*). The suggested dosage is metronidazole 500 mg orally 3 times per day for 10 days. Avoid repeated or prolonged courses due to risk of cumulative and potentially irreversible neurotoxicity (*strong recommendation, moderate quality of evidence*). (See Treatment section for definition of CDI severity.)

XXX. What are the best treatments of fulminant CDI?

Recommendations

1. For fulminant CDI*, vancomycin administered orally is the regimen of choice (*strong recommendation, moderate quality of evidence*). If ileus is present, vancomycin can also be administered per rectum (*weak recommendation, low quality of evidence*). The vancomycin dosage is 500 mg orally 4 times per day and 500 mg in approximately 100 mL normal saline per rectum every 6 hours as a retention enema. Intravenously administered metronidazole should be administered together

Table 1. Recommendations for the Treatment of *Clostridium difficile* Infection in Adults

Clinical Definition	Supportive Clinical Data	Recommended Treatment ^a	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of ≤ 15000 cells/mL and a serum creatinine level < 1.5 mg/dL	<ul style="list-style-type: none"> • VAN 125 mg given 4 times daily for 10 days, OR • FDX 200 mg given twice daily for 10 days • Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days 	<p>Strong/High</p> <p>Strong/High</p> <p>Weak/High</p>
Initial episode, severe ^b	Leukocytosis with a white blood cell count of ≥ 15000 cells/mL or a serum creatinine level > 1.5 mg/dL	<ul style="list-style-type: none"> • VAN, 125 mg 4 times per day by mouth for 10 days, OR • FDX 200 mg given twice daily for 10 days 	<p>Strong/High</p> <p>Strong/High</p>
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	<ul style="list-style-type: none"> • VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present. 	<p>Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)</p>
First recurrence	...	<ul style="list-style-type: none"> • VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR • Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR • FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode 	<p>Weak/Low</p> <p>Weak/Low</p> <p>Weak/Moderate</p>
Second or subsequent recurrence	...	<ul style="list-style-type: none"> • VAN in a tapered and pulsed regimen, OR • VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR • FDX 200 mg given twice daily for 10 days, OR • Fecal microbiota transplantation^c 	<p>Weak/Low</p> <p>Weak/Low</p> <p>Weak/Low</p> <p>Strong/Moderate</p>

Abbreviations: FDX, fidaxomicin; VAN, vancomycin.

^aAll randomized trials have compared 10-day treatment courses, but some patients (particularly those treated with metronidazole) may have delayed response to treatment and clinicians should consider extending treatment duration to 14 days in those circumstances.

^bThe criteria proposed for defining severe or fulminant *Clostridium difficile* infection (CDI) are based on expert opinion. These may need to be reviewed in the future upon publication of prospectively validated severity scores for patients with CDI.

^cThe opinion of the panel is that appropriate antibiotic treatments for at least 2 recurrences (ie, 3 CDI episodes) should be tried prior to offering fecal microbiota transplantation.