KY Antimicrobial Stewardship Innovation Consortium

Educational Pearl

High-dose Oral Vancomycin for Non-Fulminant *Clostridioides difficile* Infection: *The More the Better*?

Centers for Disease Control and Prevention (CDC) recognizes *Clostridioides difficile* infection (CDI) as an urgent health threat. Each year, there are roughly 220,000 infections resulting in 12,800 deaths. Currently, the Infectious Diseases Society of America (IDSA)/Society of Healthcare Epidemiology of America (SHEA) guidelines recommend oral vancomycin 125 mg four times daily (500 mg/day) for initial, non-fulminant CDI episode if fidaxomicin is not available.[1] Even though pharmacokinetic study has shown that standard dose vancomycin dose can achieve fecal levels 500-1000 times above of MIC_{90}; practitioners sometimes escalate vancomycin dose to either 250 mg or 500 mg four times daily if patients still have diarrhea after a few days of treatment.[2]

Does high dose oral vancomycin result in better clinical outcome for non-fulminant CDI?

	Fekety et al 1989[3]	Lam et al 2013[4]
Study design	Prospective, randomized, non-blinded	Retrospective cohort study
Patient population	Antibiotic-associated diarrhea with stool specimen (+) for *C. difficile*	18 years or older with diagnosis of severe CDI
Location	University of Michigan Hospitals Ann Arbor Veterans Hospital	Cleveland Clinic
Interventions	Standard dose: 125 mg QID High dose: 500 mg QID	Standard dose: 125 mg QID (500 mg daily) High dose: > 500 mg daily
Results	There was no difference in response at one week between two groups (87.5% vs 95.4%, p >0.05). ~10% patients had diarrhea for > 7 days after therapy.	There was no difference in day 10 cure between two groups (64% vs 60%, p = 0.76). Median time to clinical cure was 7-8 days, p=0.73.
Limitations	Not blinded to physician Small sample sizes Not stratify patients based on severity	Retrospective cohort study Patients in high dose appeared to be more ill with more co-morbidities at baseline
Author's conclusion	Low dose is recommended for patients with non-fulminant CDI due to no difference in efficacy.	No significant clinical cure difference between high dose vs standard dose vancomycin in severe CDI. Note there is a trend toward decreased recurrence in higher vancomycin dose group.

Key takeaway: High dose vancomycin does not result in higher rate of diarrhea resolution or faster time to clinical cure. Roughly 10%-30% of patients continued to have diarrhea after 7 days of treatment regardless of what vancomycin doses were used. Thus, persisting diarrhea by itself does not necessarily indicate failure of treatment. At this time, escalating to high dose vancomycin cannot be routinely recommended for non-fulminant CDI.

References:

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